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**Determinants of malaria transmission in the highlands of**  
**Ethiopia: The impact of global warming on morbidity and**  
**mortality ascribed to malaria**

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## Abstract

A study was undertaken in Debre Zeit sector, central Ethiopia to identify the most important determinants of malaria transmission with a specific purpose of assessing whether global warming was the main cause of increased morbidity and mortality ascribed to malaria in the highlands of Ethiopia. Both retrospective and prospective methods were employed to conduct the study in 430 localities with a total population of 406,891. Some nine data sets were collected including altitude, malaria incidence and prevalence, hospital morbidity and mortality, outbreaks of malaria, vector control, climate patterns and *in-vivo* drug resistance mostly on a monthly basis with varying time periods ranging from 1951 to 1993.

Morbidity analysis revealed a 67-fold increase in monthly incidence of malaria in about two decades. Mortality patterns showed a 13-fold increase in deaths ascribed to malaria in the last decade alone. Furthermore, highland communities living in localities lying between 2,000 and 2,200 metres were affected by *P. falciparum* transmission for the first time since 1986. Time series analysis of climate patterns revealed a trend of increased climatic warming in both day-time and night-time temperature especially since 1988, at which time a coincident peak in the incidence rate of malaria was also observed despite a decrease in total rainfall. Each °C rise in monthly mean night-time temperature was associated with up to 64% and 58% estimated rise in monthly incidence of falciparum malaria two and three months later respectively. The historic epidemic of malaria in which 150,000 people were

estimated to have died among 3 million cases of malaria in Ethiopia in 1958 was associated with abnormally high ambient temperature and rainfall. This year also saw a very strong El Niño event. A simultaneous peak was seen in incidence of malaria, hospital admissions and hospital deaths ascribed to malaria together with an abnormal rise in mean night-time temperature in 1988.

Based on current data it is concluded that epidemics of malaria in the highlands of Ethiopia that were observed during the past decade were mainly due to an increase in night-time temperature. The coincident peak in both malaria and ambient temperature together with statistical evidence suggested that global warming was the main cause of the rise in incidence of highland malaria. This appeared to be the cause of new foci of transmission at high altitude localities while also increasing both the rate and duration of transmission in previously known epidemic-prone areas from highly seasonal to perennial transmission. Furthermore, non-climatic biological and human conditions such as chloroquine resistant falciparum malaria, decreased vector control efforts and large scale population migration were also identified as important factors amplifying the impact of global warming on morbidity and mortality ascribed to highland malaria by affecting more distal parts of the causal pathway.

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## **Introduction**

The current thesis is based on work carried out in Ethiopia to study the determinants of malaria transmission in the highlands and especially to know whether global warming was the main cause of increased morbidity and mortality ascribed to malaria. It consists of three main parts. The first part sets the scene for the study by describing the background for the research emphasising the special characteristics of malaria in Ethiopia and reviewing the literature on global warming and highland malaria in the first chapter. It then proceeds to a second chapter in which the objectives of the research are defined and the design of the study methods along with the data sets collected are described.

The second part includes the results of the study and discussion. It consists of six chapters including the level and trend of malaria over the past two decades, altitude effects on malaria transmission, climate pattern in the study area over the past four decades, effectiveness of current treatment regimens, the pattern of vector control and the relationship between malaria and climate in which a model for both is defined and discussed.

The third part includes synopsis of findings, summary and conclusion. Here, the main findings in each of the previous eight chapters are summarised in the context of the overall study and the implication of the findings is discussed. The final sections include a summary of the whole study and the conclusions reached based on the available data.

**Part one:**

**Research Background , Objectives and Data sets**

**Chapter 1 :**      Research Background

**Chapter 2 :**      Objectives and Data sets

# **Chapter 1**

## **Research Background**

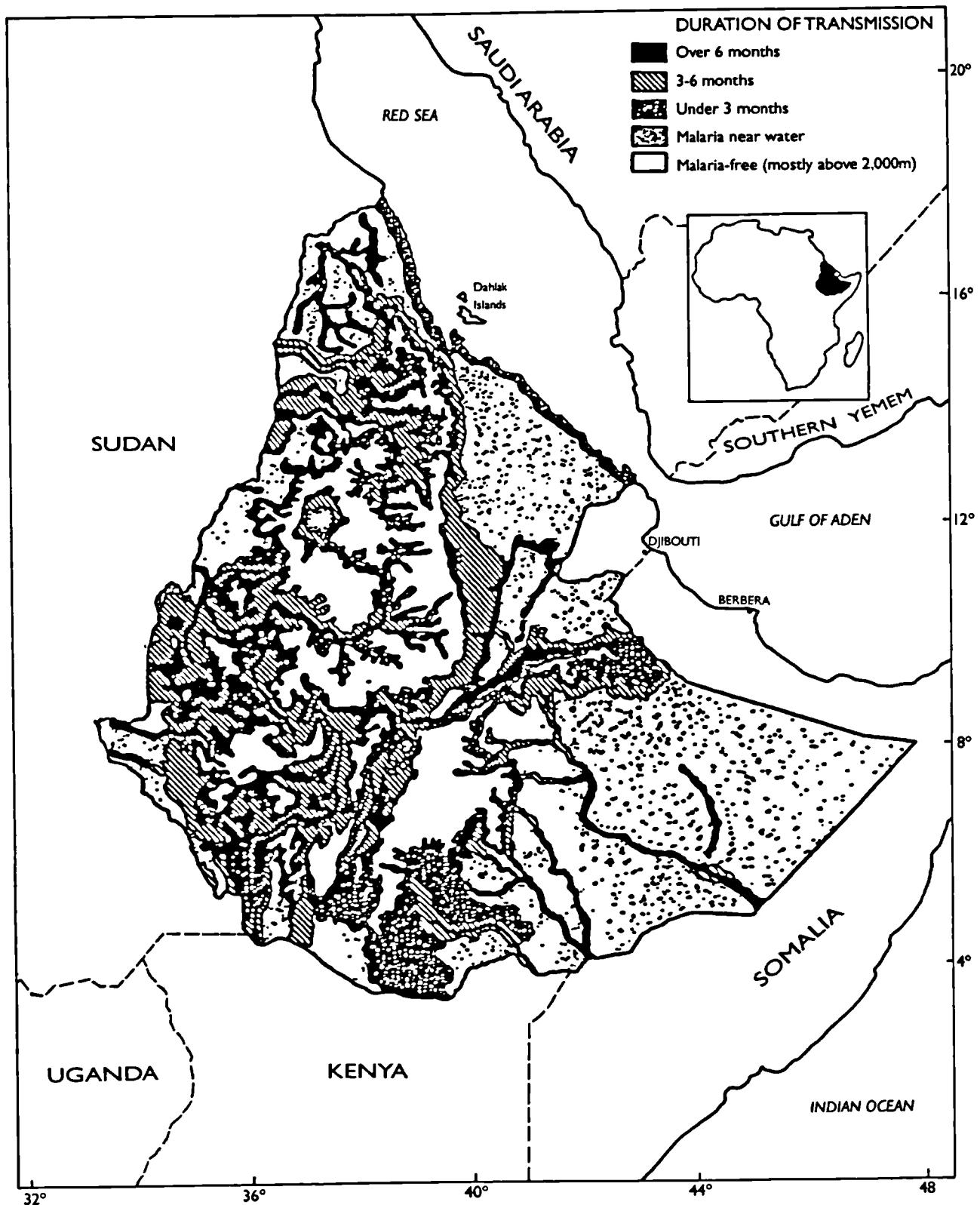
### ***1.1 Characteristics of malaria in Ethiopia***

There are three major topographical features of Ethiopia; extensive high plateaux in the central and northern parts of the country, lowlands along the borders with Sudan, Kenya, and Somalia, and the great Rift Valley that bisects the high plateaux into eastern and western sections. About 80% of the estimated 56 million people in the country reside in the highlands mainly earning their living as subsistence farmers. Pastoral nomads and shifting cultivators inhabit the lowlands (Kloos, 1993).

Some three-quarters of the total geographical area of the country is malarious and two-thirds of its inhabitants, 37 million people, are at risk of malaria. Due to the varied physical and climatic features of the country, all levels of malaria transmission exist. In the lowlands, malaria is largely stable. The intensity and duration of transmission appears to vary with the length of the wet season, proximity to permanent breeding sites, and altitude as depicted in Figure 1.1.

All levels of endemicity of malaria exist in the country depending on altitude and the prevailing climate. In the lowlands, malaria is generally endemic with moderate to high intensities of transmission. Here, epidemics of malaria are rare except in the event of

**Figure 1.1 The Spatial Distribution and Annual Occurrence of Malaria.**  
 Based on unpublished data of the National Organization for the Control  
 of Malaria and Other Vector-Borne Diseases, MOH.



massive influx of non-immune populations such as those seen during resettlement programmes and mobilisation of troops. In contrast, the characteristic feature in the highlands is highly seasonal and unstable malaria with frequent waves of epidemics. These result in high morbidity and mortality during the planting season when the rains start and during the harvesting season when the rains cease. A notable and disastrous epidemic struck in 1958, resulting in 3,000,000 cases and 150,000 deaths (Fontaine et al., 1961).

### **1.1.1      *Vectors of malaria in Ethiopia***

The existence of ancient local names such as “weba” and “nidad” from Amharic indicating its association with high fever and “busa” from Oromo showing its debilitating nature testify to the fact that malaria has been known as an important public health problem in traditional Ethiopian communities over the centuries. However, studies of malaria in Ethiopia were initiated during the period of Italian occupation in the Second World War, from 1936 to 1941. Corradetti (1938-39) carried out entomological studies that described the anopheline fauna in Wollo, Jijjiga, and the Danakil regions. Brambilla (1940) described the malaria situation in Dire Dawa, eastern Ethiopia. Giaquinto Mira (1945-48) also published papers related to the distribution and biology of mosquitoes of Ethiopia. Observations on the anopheline fauna around the Addis Ababa region were recorded by Ovazza and Neri in 1955.

Subsequently, observations on the malaria situation were made by the British, most notably by Sir Gordon Covell. He made the first extensive attempt to describe epidemiology of malaria in Ethiopia during surveys carried out in 1952 and 1955 (Covell, 1957). Surveys in villages around Lake Tana revealed the presence of 17 mosquito species from three genera; *Anopheles*, *Culex* and *Aedes*. Potential malaria vectors identified at the Natural History Museum in Britain were *Anopheles gambiae s.l.*, *An. funestus* and *An. pharoensis*.

Later, studies carried out by the Malaria Control personnel in Ethiopia showed the presence of some 42 anopheline species among which *An. gambiae s.l.* was the most widely distributed and frequent. It is the primary malaria vector in Ethiopia. Entomological surveys were carried out during the 1984-88 period at observation posts representing areas of low, moderate and high intensities of transmission. They showed that *An. gambiae s.l.* comprised 75.5% of 19,352 specimens collected . The relative density of the primary and secondary vectors of malaria in Ethiopia in terms of their feeding and resting habits during this period is depicted in Table 1.1 from data by the National Organization for the Control of Malaria and Other Vector-borne Diseases.

As shown in Table 1.1, *An gambiae s.l* is the most frequent vector mostly feeding outdoors but resting indoors. Cytotaxonomic studies conducted in the Gibe (Omo) Valley revealed that *An. arabiensis* was the most important vector responsible for malaria transmission while *An. quadriannulatus* was essentially a zoophilic species among

the six sibling species of the *An. gambiae* s.l. complex ( White, 1980). This was also confirmed by more recent cytotaxonomic studies in central, eastern and southern parts of Ethiopia suggesting that *An. arabiensis* is the main malaria vector. A sporozoite rate ranging from nil in the dry season to 5% in the rainy season was observed in Gambella ( Krafur, 1971). Recent field studies suggested that small, temporary, sunlit water collections with emergent vegetation, such as those created during the rainy season were breeding sites preferred by *An. arabiensis* (Tulu, 1993). Other breeding sites include discarded tyres, construction holes, depressions left by hoof prints of animals, tractors and other vehicles, small water collections in river beds during the dry season and poorly maintained irrigation canals in agricultural development schemes in the lowlands.

**Table 1.1. Relative densities and behaviours of malaria vectors based on day-time indoor resting collection and night-time man-landing catches of local vectors at 14 sentinel posts in Ethiopia (1984-88)**

<i>Anopheles</i> <i>species</i>	No. collected	% total	% feeding indoor	% feeding outdoor	% resting indoor	% resting outdoor
<i>An. gambiae</i> s.l.	14,602	75.5	27.6	72.4	80.3	19.7
<i>An. pharoensis</i>	3,666	18.9	34.9	65.1	88.5	11.5
<i>An. funestus</i>	613	3.2	23.8	76.2	36.5	63.5
<i>An. nili</i>	471	2.2	54.4	45.6	0.2	99.8

Secondary vectors of malaria in Ethiopia include *An. pharoensis*, *An. funestus* and *An. nili* in that order of decreasing frequency. *An. culicifacies adenensis* appeared restricted to the Red Sea coast primarily in the Assab area. *An. pharoensis* breeds in

large, shaded permanent water bodies. It prefers irrigation canals, rice fields and lake shores. It is widespread in its distribution and has been found in the Baro and Awash rivers, Lake Tana, and the Lake regions of Shewa and Sidamo (Covell, 1957, Jolivett, 1959, O'Connor, 1967).

*An. funestus* also breeds in shaded, large permanent water bodies such as those which are found along the shores of lakes and large rivers such as Lake Tana, Baro, the lake regions of Shewa and Sidamo (Covell, 1952, O'Connor, 1967, Gebremariam et al., 1988). *An. funestus* has been found in all Administrative Regions of Ethiopia. Mosquito dissections revealed sporozoite rates ranging from 0% in March and April to 2.62% in September and November in the Gambella area (Krafsur, 1971). *An. nili* is a more localised species than the previous three. Some known foci of this vector are the Bilate River Valley in Sidamo, the Sagan Valley in Gamo Gofa (Mira, 1950), and the Baro River Valley in Gambella (Krafsur, 1971). Sporozoite rates ranging from 0% during the dry season to 4.17% in November after the rains were reported by the latter author.

### **1.1.2           *Malaria parasites in Ethiopia***

All four human malaria parasites exist in Ethiopia. However, the two epidemiologically important species are *P. falciparum* and *P. vivax*. They account for 60% and 39% of reported cases of malaria in the country respectively. *P. malariae* comprises about 1% of reported cases and *P. ovale* is rarely seen (Tulu, 1989).

*P. falciparum* causes the most frequent and fatal malaria in Ethiopia often resulting in severe and complicated malaria. The case fatality rate is about 10% in hospitalised adults and up to 33% in children less than 12 years old (Tulu, 1993). It was also reported that *P. falciparum* malaria was the second leading cause of acute renal failure among 136 adults admitted to a central referral teaching hospital from January 1989 to December 1992 (Zewdu, 1994). *P. falciparum* has been diagnosed in all the Administrative Regions of Ethiopia and was responsible for most epidemics of malaria. Chloroquine resistant *P. falciparum* is increasingly becoming an important medical and public health problem in Ethiopia and will be dealt with in a separate chapter.

*P. vivax* is also a widely distributed malaria species. This parasite is not a major cause of mortality but it is an important cause of morbidity due to its relapsing characteristic. A study conducted in the Gambella area demonstrated that residents of Nilotc origin were more resistant to *P. vivax* infections than those of Hamito-Semitic origin (Armstrong, 1978). This was later found to be due to the absence of Duffy antigen in persons of Nilotc origin (Mathews and Armstrong, 1981).

A study conducted on 1,261 subjects revealed that glucose-6-phosphate dehydrogenase deficiency was present only in the Anuak and Nuer tribes of the South-western lowlands as well as in the Afars in the Danakil depression with a prevalence of 1.4%, 6.7%, and

6.3% respectively. Only one case of sickle cell trait (Hb AS) was found (Perine et al., 1974).

## ***1.2 Evolution of the Malaria Control Programme in Ethiopia***

The first attempt to control malaria in Ethiopia was made through pilot control projects at four sites with the support of USAID & WHO/UNICEF. These pilot project areas were the Upper Awash Valley, Kobo-Chercher plain, the Dembia plain, and Gambella in the years 1955, 1956, and 1957. The main objective of these projects was to test the effectiveness of spraying of houses with DDT in representative malarious areas and to provide training for national staff. A significant decrease in prevalence was demonstrated but the anticipated interruption of transmission was not achieved. Failure of interruption of transmission was attributed to incomplete coverage of spraying operations, new construction of houses, extradomiciliary transmission, replastering of houses, and reintroduction of cases from outside the project area (Fontaine and Najjar, 1959, Gebremariam et al. , 1988).

The nation-wide epidemic of malaria which struck Ethiopia in 1958 that led to a loss of about 150,000 lives then brought malaria to the top of the public health agenda. This epidemic, the success stories with DDT in other parts of the world and the decrease in prevalence demonstrated in the pilot projects, and the presence of bilateral and international donor agencies (USAID, UNICEF/WHO), appeared to have persuaded the

then Imperial Government of Ethiopia to establish a National Malaria Eradication Service in 1959. Emperor Haile Selassie himself is said to have sprayed the first house in the Upper Awash Valley with DDT to demonstrate that he lent his full support to the programme.

The country was divided into four operational areas, i.e. areas A, B, C, and D. Area A included Eritrea, Tigre (currently Tigray), Begemider & Simen (currently Gondar), Eastern Wollo, Northern Harar, Eastern Shewa and Northern Arsi. Area B consisted of Gojjam, Western Wollo, Western Shewa, North-eastern Wellega, Northern Kaffa, and Eastern Illubabor. Area C comprised South-western Wellega, Western Illubabor, Southern Kaffa, Gamo Gofa, and Western Sidamo. Area D was composed of Southern Harar, Southern Arsi, Bale and Sidamo.

The antimalarial campaign was planned to progress through preparatory, attack, consolidation, and maintenance phases. Area A was given priority and the preparatory phases consisting of collection of baseline malariormetric data and geographical reconnaissance were initiated. The first residual insecticide spraying programme was initiated in 1966. Active case detection was emphasised between the years 1967 to 1969 but was later found to be futile and was gradually tapered down to a total cessation in 1971.

The status of the whole programme was reviewed by three multidisciplinary teams in May 1970, June 1972, and April 1977 following the recommendations of the 22<sup>nd</sup> World Health Assembly Resolution of 1969. The major recommendations of these teams were the following;

- (a) retention of malaria eradication as a long term goal,
- (b) maintenance of the gains already achieved and extension of control activities into high priority sections of areas B, C, and D as the necessary and valid steps towards the long term goal of eradication,
- (c) application of selective control methods, primarily selective spraying of residual insecticides based on the epidemiology of malaria; and
- (d) integration with basic health services.

As a result of this, the strategy was converted to a control programme instead of eradication, and selective spraying in contrast to blanket coverage was introduced in 1971. The short term objectives of the control programme included reduction of mortality, reduction of infection rate and level of transmission, reduction of the period of incapacity and work disability, and conducting feasibility studies of introducing other methods of control. In the medium term it was hoped to reduce malaria to a level where it no longer became a major public health problem. The long term objective was to eradicate malaria with effectively planned and selected control measures through the primary health care system.

The malaria control methods in the past three decades emphasised vector control that included use of DDT as an adulticide at a dose of 2 gram per square metre (75% WDP) and the larvicides temephos (abate) and used motor oil in selected areas. Detection and treatment of cases was carried out through 110 sentinel diagnostic centres supported by over 1,400 peripheral detection and treatment posts. The first line antimalarial drug was the blood schizontocidal drug chloroquine at a dose of 25 mg/kg body weight over three consecutive days. Primaquine was also used as gametocytocidal agent for *P. falciparum* malaria and against the tissue forms of *P. vivax* malaria.

### ***1.3 The trend of malaria in Ethiopia in the past decade***

Some four specific ecologies of transmission of malaria in Ethiopia have been described. These are resettlement areas, agricultural development schemes, urban areas and disaster stricken areas (Tulu, 1989, Tulu, 1993). A fivefold increase in the number of reported cases of malaria occurred in Ethiopia during the last half of the 1980's. The mean number of reported cases rose from 43,545 in 1980-84 to 235,992 per annum in 1985-89 as shown Table 1.2.

The slide-positive rate increased fourfold from 8.9% per annum to 33.1% per annum during the same period. Malaria also became the second leading cause of outpatient attendance, hospitalisation, and the leading cause of hospital deaths in 1988-89. Three main reasons were forwarded to explain the increase in the number of reported cases;

firstly, the massive resettlement of about 600,000 non-immune highland people into lowland malarious areas, secondly, the emergence and rapid spread of chloroquine resistant *P. falciparum* malaria , thirdly, the failure of control efforts to curb the increased incidence of malaria (Tulu, 1989). The malaria situation in all the resettlement schemes is shown in Figure 1.2 . As shown in Figure 1.2, the predominant parasite was *P. falciparum* and malaria transmission appeared to be particularly high during the years 1987, 1988 and 1989 in that order.

**Table 1.2 Annual number of malaria cases in Ethiopia**

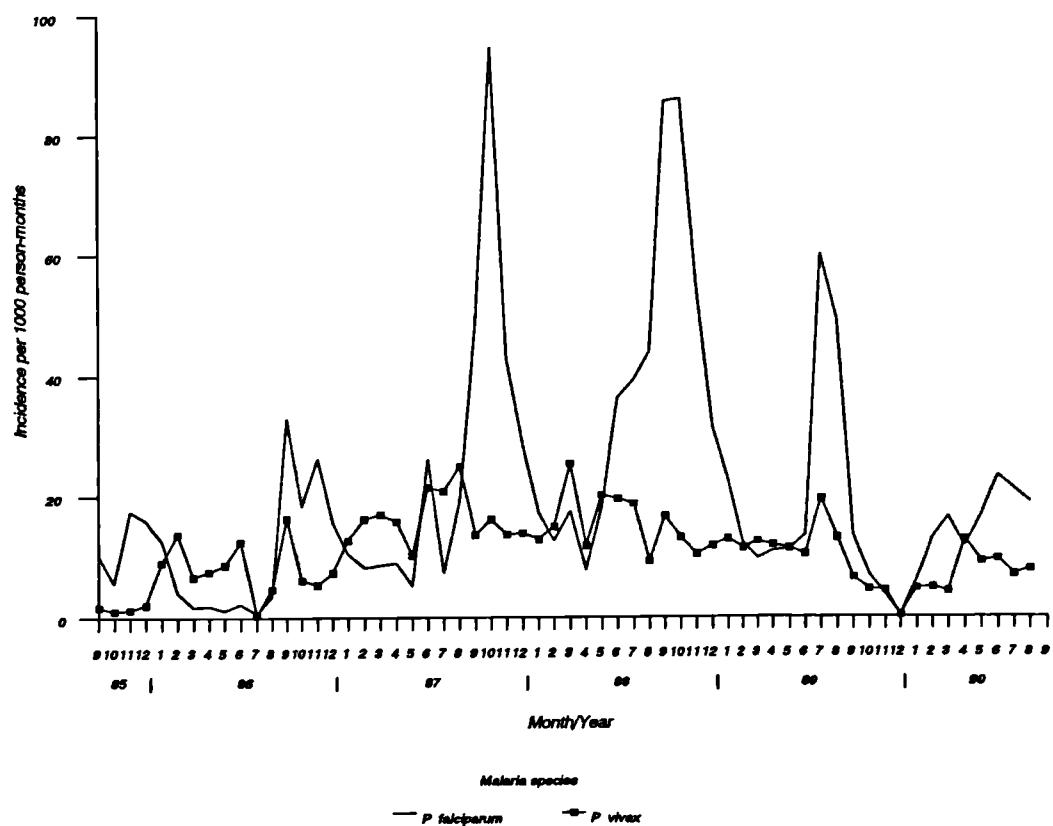
<b>Year</b>	<b>Examined</b>	<b>PF</b>	<b>PV</b>	<b>PM</b>	<b>PF+PV</b>
1980-81	555,876	38,489	33,802	234	540
1981-82	457,209	12,443	19,304	194	153
1982-83	430,164	13,490	12,872	173	116
1983-84	512,657	19,352	24,748	161	272
1984-85	494,250	40,459	34,658	327	457
1985-86	575,187	64,157	75,201	656	619
1986-87	697,544	118,011	114,970	156	375
1987-88	967,544	271,089	136,985	117	569
1988-89	826,604	233,939	91,504	53	300

Note: PF = *P. falciparum*, PV = *P. vivax*, and PM = *P. malariae*

The level and trend of malaria in Ethiopia in the 1980's is shown in Figure 1.3. The frequency of *P. vivax* and *P. falciparum* malaria was about the same up to 1987 but a rapid increase of *P. falciparum* in that year suggested the occurrence of an epidemic.

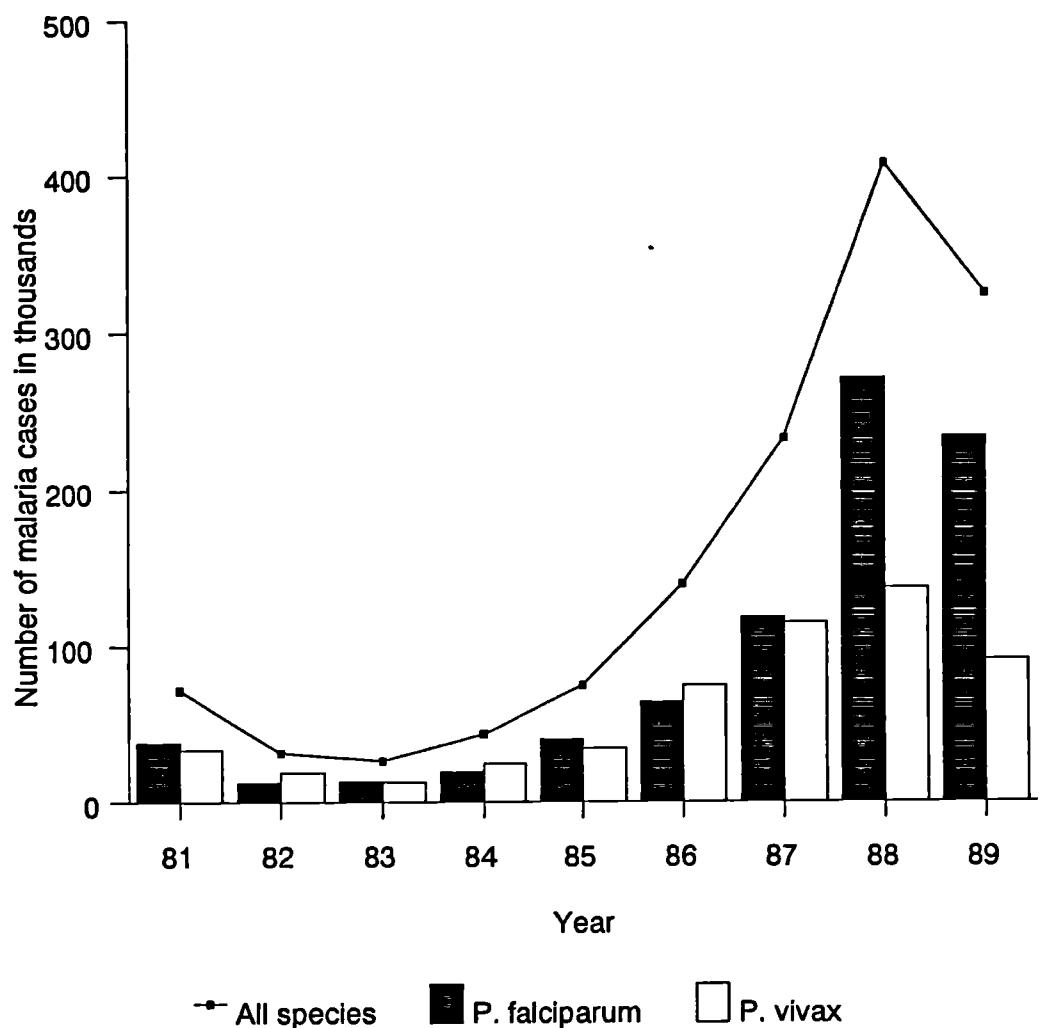
The above observation led to a further review of the malaria situation in a highland area where the population has been stable. The number of reported malaria cases during the 1980-89 period was examined in Debre Zeit sector. It revealed that the reported incidence of malaria has increased from 1.1 per 1000 person-years in 1980 to 65.9 per 1000 person-years in 1989, that is about a 60-fold increase in a decade. This seemed unlikely to be due to population migration alone. An increase in the ambient temperature over time (global warming) was put forward as a working hypothesis. A project protocol was prepared which ultimately received support from the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

**Figure 1.2      Monthly incidence rate of malaria in the resettlements in Ethiopia (1985-90)**



**Figure 1.3**

*Annual frequency of reported malaria cases in Ethiopia*



## **1.4 The malaria problem in the highlands of Ethiopia**

About 50% of the land above 2,000 metres in Africa is in Ethiopia. A highland is defined as a geographical area above an altitude of 1,500 metres. Covell studied the spleen rates of children aged 2-10 years old at 18 sites in Ethiopia in 1952 and 1955 and concluded that malaria was non-existent above 1980 metres, epidemic between 1670 and 1980 metres and endemic below 1670 metres (Covell, 1957).

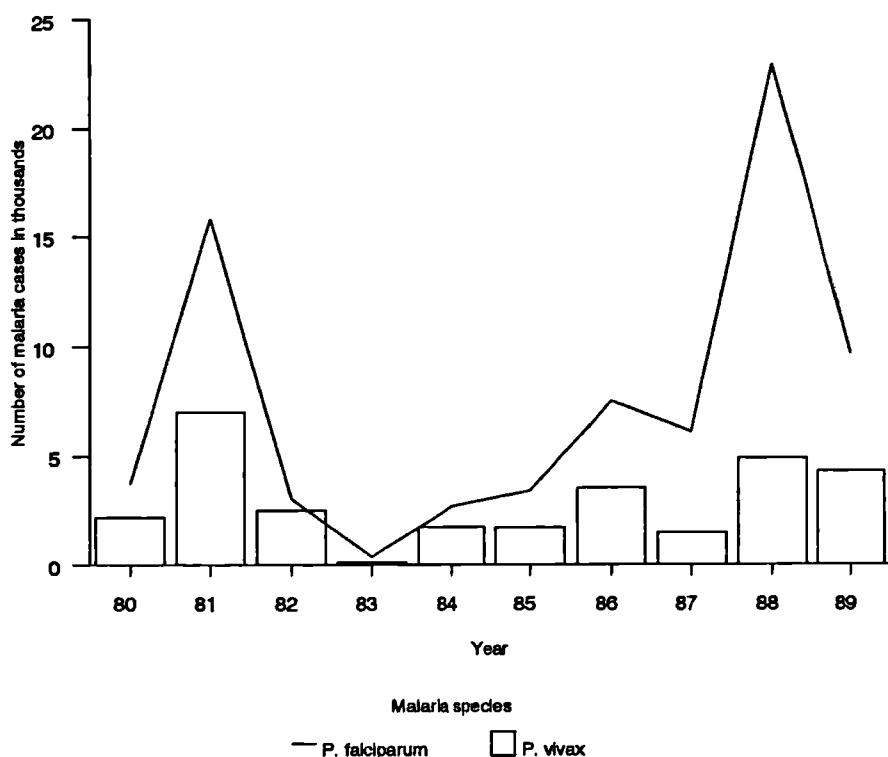
Some 7,000 malaria related deaths occurred in the Dembia plain (altitude 1,830 to 1,980 metres) in 1953. The epidemic of malaria which struck Ethiopia in the last half of 1958 affected four central highland provinces. These were Shewa, Gojjam, Begemeder, and Wollo. The morbidity exceeded 75% of the total population in many rural settlements. In contrast, the lowland provinces bordering on the Sudan, Kenya, and Somalia did not show any evidence of the epidemic (Fontaine et al., 1961).

The most complete information on the progress of the epidemic was obtained from the Ziquala Plain (mean altitude 1,850 metres) and the Lake Akaki district (mean altitude 2000 metres), two of the four districts included in the present study. The epidemic began in July 1958 and continued into December 1958. *P. falciparum* malaria was diagnosed and *An. gambiae s.l.* was the vector. About 150,000 inhabitants of the two districts were affected. A total of 4,094 malaria cases were admitted to Debre Zeit hospital in 1958, but, 3,018 cases (73.7%) occurred in the months of September, October and November

1958. The number of admissions related to malaria in Debre Zeit hospital was four times greater than the average for the previous 4 years (948 cases per year).

Case fatality rates reached as high as 20% in undernourished populations. Three to three and a-half million people may have contracted malaria. Using a minimum case fatality rate of 5% and three million as the total malaria cases, the number of deaths was estimated to be 150,000 (Fontaine et al., 1961). The altitudinal limits of the epidemic ranged from 1,600 to 2,150 metres. *P. falciparum* malaria was the predominant parasite and constituted 71% of the infections. It was responsible for severe morbidity and a high case fatality rate. *An. gambiae s.l.* was the only vector observed. Excessive rainfall, abnormally high temperatures and relative humidity were the three important weather factors associated with the epidemic. Subsequent to this epidemic in 1958, the frequency of malaria cases appeared to be particularly high during certain years in the highlands where outbreaks are commonly reported as shown in Figure 1.4.

**Figure 1.4 Occurrence of reported outbreaks of malaria in Ethiopia**



## 1.5 Climatic effects on malaria in the highlands

While the resurgence of malaria appears a global event across many endemic areas in the tropics and subtropics, epidemics of malaria are confined to the highlands, most notably in East and Northeast Africa as well as parts of Southeast Asia. It is well known that climate has a major effect on the distribution of malaria. First, the female *Anopheles* vector that propagates the malaria parasite needs the presence of a suitable water body, and small rain pools commonly provide this. Second, the malaria parasite needs a suitable temperature to complete its life cycle in the *Anopheles* vector. The minimum temperature

for sporogonic development of *P. falciparum* is about 18 °C, and the extrinsic development of *P. vivax* ceases at temperatures below 14 °C. Extreme weather conditions, like heavy rains and flooding on the other hand may flush away eggs, larvae and pupae, reducing the density of vectors. Excessive temperatures in arid and semi-arid areas result in rapid evaporation and drying up of breeding habitats with consequent desiccation of eggs, larvae, and pupae. Thus, climatic change especially an increase in the ambient temperature in countries with a highland profile due to global warming is expected to provide a suitable condition that facilitates the transmission of malaria. An increase in ambient temperature may allow the completion of the sporogonic cycle of the *Plasmodium* parasite in the *Anopheles* vector and can reduce the period between successive ovipositions thereby increasing the frequency of blood meals on humans.

Certain factors support the hypothesis of global warming ; (a) an increase of 0.30 to 0.6 °C over the past 100 years, (b) a recession of alpine glaciers, (c) increasing depth of the active layer of permafrost in the Canadian Arctic and, (d) the occurrence of the six warmest years on meteorological record since the 1980's (Haines and Fuchs, 1991). An increase in temperature favours malaria transmission . This could be due to a combination of many factors such as an increase in water temperature favourable for breeding of vectors, a decrease in the extrinsic incubation period, an increase in the frequency of blood meals, and the presence of a suitable temperature to complete sporogonic development inside the vector particularly in high altitude areas. All these are factors involved in the basic case reproduction rate, which is simply a measure of the

number of cases of malaria that may arise out of a single infection in the absence of immunity.

“Greenhouse” gases ( $H_2O$ ,  $CO_2$ ,  $CH_4$ ,  $N_2O$ , CFCs, HCFCs, etc.) have increased over the past 100 to 150 years and global temperature records also show an increase of 0.3-0.6 °C over the past 100 years (Maskell et al., 1993). But, debate about the exact cause of the rise in temperature does not yet appear settled. The Intergovernmental Panel on Climate Change (IPCC) predicts a rise of 1 °C by 2025 and 2.5-3 °C by the end of the next century, based on computer models (IPCC, 1990).

A WHO task group has assessed the potential impact of climate change on human health. The potential effects of an increase in temperature on human health range from psychiatric disorders to infectious diseases and cancers. Vector-borne and water-borne diseases were emphasised among the infectious diseases as likely to have an increased incidence. Among the vector-borne diseases, an increased incidence of malaria appeared highly likely. Second in rank were schistosomiasis and dengue based on the possible effect of favourable climatic conditions on the expansion of risk areas due to the spread of the snail intermediate host and the mosquito respectively (WHO, 1990). It was also stressed that climate change may first have its impact on vector-borne diseases at the margins of their current distribution. Disease free highlands such as parts of Ethiopia, Indonesia, and Kenya may have a rise in transmission of malaria above the existing threshold because of an increase in temperature.

Furthermore, an increased transmission of malaria in the highlands has been reported since the latter half of the 1980's in many countries. These include Madagascar (Lepers et al., 1988; Fontenille et al., 1990), Tanzania (Matola et al., 1987; Lines et al., 1991), Indonesia (Anthony et al., 1992), Kenya (Rees, 1994; Some, 1994), and Rwanda (Loevinsohn, 1994). Although factors such as drug resistance and population migration may have played some role in increased transmission of malaria in all these countries, it is unlikely that such a very marked increase of malaria transmission occurred in these highlands at about the same time due to these factors alone. The increased incidence of malaria in Rwanda was attributed to a rise in the mean minimum ambient temperature in 1987 (Loevinsohn, 1994). Periodic epidemics of malaria in India and Pakistan were associated with the occurrence of the warm ocean currents related to the phases of El Niño-Southern Oscillation. Resurgence of malaria with outbreaks of malaria were associated with excessive monsoon rains. The outbreaks of malaria occurred one to three years following the El Niño events (Bouma and van der Kaay, 1994).

The 1958 epidemic of malaria in Ethiopia was associated with abnormally high rainfall during the wet season and there was an appreciable amount of rain during the normally dry months before and after the regular wet season. In all the four central and northern highland provinces affected by the epidemic, rainfall exceeded that of all previous years on record. Maximum day-time temperature and night-time minimum temperature were higher than any previous year on record. Relative humidity also approached 60%

whereas it is normally 50% or less in the cool highlands. The climatic conditions that led to this epidemic will be dealt with in greater detail in Chapter 5.

Anomalies in climate have already caused substantial damage to many communities in the highlands of Ethiopia which came to the attention of international relief agencies. The irregularity of the rains and increasingly frequent droughts have caused serious food shortages particularly in the northern and central highlands of Ethiopia. This has resulted in the loss of many millions of lives due to hunger in 1972-73 and 1984-85. If this is also associated with an increased incidence of malaria, as suggested by available data, the country would suffer a great disaster. The following chapter will deal with the methods used to conduct an exploratory study of climatic and non-climatic factors that were associated with an increased incidence of malaria in a typical highland area in Ethiopia.

## **Chapter 2**

### **Research objectives and & data sets**

#### ***Objectives***

The following general and specific objectives were set to conduct a study of factors associated with an increased incidence of malaria in the highlands of Ethiopia. The specific hypothesis was to see whether an increased incidence of malaria in the highlands is linked to an increase in the ambient temperature, i.e., is global warming the cause of increased incidence of malaria in the highlands of Ethiopia?

#### ***2.1 General objectives***

- (a) Determine the association between transmission of malaria and climate change in the highlands
- (b) Identify non-climatic factors related to malaria transmission in the highlands

## ***2.2 Specific objectives***

- (a) Determine whether malaria transmission has exceeded previous altitudinal limits in the highlands
- (b) Assess the level of change in temperature in the highlands
- (c) Estimate the degree of association between change in temperature and malaria transmission in the highlands
- (d) Determine whether other climatic factors such as rainfall and relative humidity have had an effect on malaria transmission
- (e) Estimate the change in the level of morbidity and mortality due to malaria in the highlands
- (f) Assess the rate of treatment failure and drug resistant malaria in the highlands
- (g) Determine the pattern of drug and insecticide distribution in the highlands

## ***2.3 Study area***

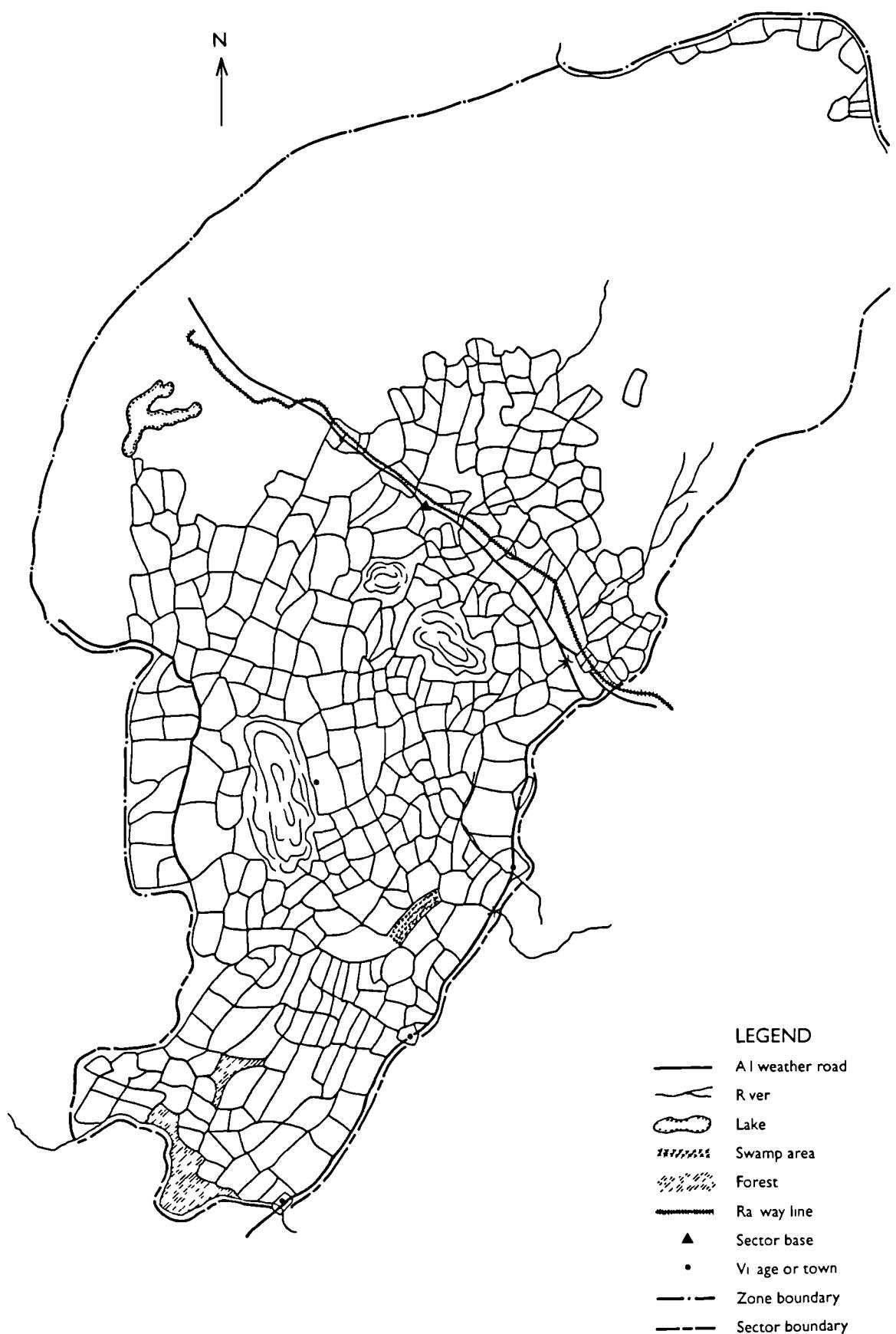
The choice of the study area was based on four main criteria. First, the area should be highland, where malaria is unstable and the likelihood of epidemics is high. Second, the study area has to be a place where there are reliable data sets on malaria over the past two decades. Third, the place has to be an area where there are sufficient weather stations where data on climatic conditions could be obtained for the past two decades.

Fourth, the area has to be politically stable and accessible throughout the wet and dry season in order for an *in-vivo* drug sensitivity study to be conducted.

Based on the above criteria, the study was conducted in Debre Zeit sector, Nazareth zone, Shewa Administrative Region. The sector consists of four districts (Weredas), namely, Akaki, Adeia, Liben Ziquala, and Lume. It is bounded in the east by Nazareth sector, in the south by Ziway sector. Weliso sector borders the study area in the west, and in the north Efeson sector and the capital city, Addis Ababa. There are two man-made lakes, Koka dam and Aba Samuel in the sector. Furthermore, there are some six crater lakes, three of them surrounding the town of Debre Zeit. The main rivers are River Awash and its tributary, Mojo.

Figure 2.1 shows a sketch map of the study area. The study area is roughly about 100 square kilometres and it includes a total of 430 localities. The mean locality population is 946 persons. The total population of the study area based on data from the 1984 census and spraying activity reports is 406,891. The following demographic indices were from the 1984 census report on Shewa Region to provide some idea about the structure of the population in the study area. Urban residents constitute 31.5% while rural dwellers comprise 68.5% of the total population. Some 49% of the total population is below 15 years of age. The median age is 16 years old. Ethnic composition of the population constitutes Oromo 42.7%, Amhara 20.7%, Gurage 18.6% and other minorities 18%. About 75% of the population are Christian while 23% are Moslem. The remaining 2%

Figure 2.1 DEBRE ZEIT SECTOR



are not specified. Average household size is 4.5 persons per house. Crude birth rate is 38.2 per thousand. Crude death rate is 9.2 per thousand. Life expectancy at birth is about 51 years for males and 53 years for females. Infant mortality rate is 111 per 1000 live-births. Total fertility rate is 6.3 per woman and average parity is 5.3 per woman.

The economy of the rural population is based on subsistence farming and cattle rearing. The majority of urban dwellers are small scale merchants. There are also some factory workers in textile, food processing, tannery, and electricity in the towns of Akaki, Debre Zeit, Mojo, and Koka. Major crops grown in the area include the staple diet teff (*Ergrostis abyssinica*), wheat, barley, maize, bean and pea. Some fruits including orange & banana are also grown.

Main health facilities in the study area include a hospital and four health centres. They are located in towns on the major highway that links the Red Sea port of Assab to Addis Ababa. The health institutions are concentrated in the towns of Debre Zeit, Akaki, Dukem, Mojo, and Koka. The population in the rural areas has only a limited access to these health facilities, particularly during the rainy season.

The climate of the study area is characterised by a long dry season and a short rainy season. The rainy season lasts three months. These are June, July and August. However, very small short-lived showers also occur in the months of March and April. There are variations of rainfall, relative humidity and temperature from place to place and from

year to year. The rainy season is the planting season during which every rural adult spends the day on the farms. After the cessation of the rains, the crops mature and then comes the harvesting season from September to December. Unfortunately, as discussed in the following chapters, this is also the time during which peak transmission of malaria occurs in many highlands of Ethiopia.

## ***2.4 Study design and data sets***

Figure 2.2 shows a summary of the theoretical flow of logic behind the study design that was preferred to conduct the study. It was thought that increase in temperature may be a gradual process that has occurred over the past several years and the analysis of such historical data sets on malaria over many years in several villages lying at different elevations could be the best method to tackle the problem. Furthermore, the selection of a study area in the highlands where fluctuations in incidence of malaria were more likely, the existence of reliable data on malaria based on systematic cross-sectional blood surveys and surveillance activities supported by an efficient laboratory service, as well the existence of a good weather centre and the previous acquaintance of the investigator with the malaria problem in the area and staff of the sector provided a good opportunity to examine the research question.

A retrospective descriptive study of annual seasonal blood surveys conducted from 1974 to 1987, monthly surveillance of malaria carried out between 1968 and 1993, outbreaks

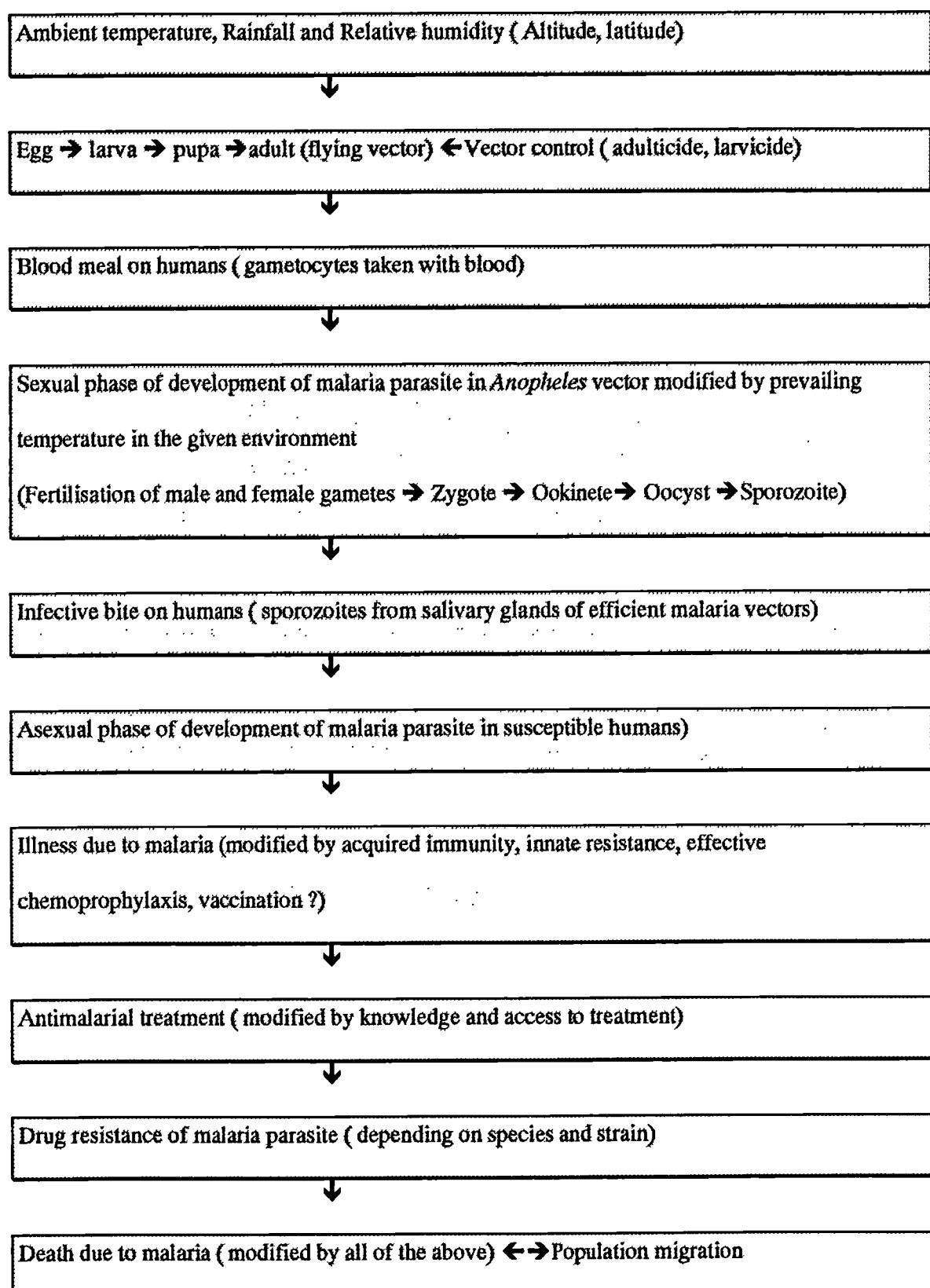
of malaria between 1975 and 1994, morbidity and mortality due to malaria from 1975 to 1993, and monthly climate data from 1951 to 1993 was carried out. Furthermore, the relative importance of non-climatic factors for the increased incidence of malaria was also explored. Data on vector control by DDT spraying was collected for 430 localities during the period 1965 to 1993. This data set was also the source from which data on altitude and population were obtained.

A further prospective study was conducted to assess the rate of treatment failure and the level of chloroquine resistant *P. falciparum* malaria. A total of eight data sets was collected. This was done by preparing separate data bases in EPIINFO according to a previous protocol which was agreed upon by the investigator and a panel of assessors. The type of data set, frequency of collection and the time period covered by each of them is tabulated in Table 2.1. Details about the methods employed and content of each data set are dealt with separately in relevant chapters.

**Table 2.1 Data sets, frequency of collection and period covered in years**

<i>Data set</i>	<i>Frequency of collection</i>	<i>Period covered in years</i>
Climate	monthly	1951-1993
Altitude	biannual	1968-1993
Blood surveys	annual	1974-1987
Passive surveillance	monthly	1968-1993
Outbreaks	annual	1975-1992
Hospital admissions and deaths	monthly	1975-1993
Vector control	biannual	1965-1993
Drug resistance	daily	1993-1994

**Figure 2.2 Flow chart of the natural course of development of malaria infection**



## **2.5 Summary**

Malaria in the highlands of Ethiopia appears to be characterised by unstable transmission with frequent epidemics. These epidemics claim many lives. Among the six sibling species of *An. gambiae s.l.*, *An. arabiensis* is the main vector of malaria in Ethiopia. *P. falciparum* and *P. vivax* are the two main malaria species. *P. falciparum* is responsible for severe malaria and deaths due to malaria during the epidemics. A very marked increased incidence of malaria was seen since 1987 even in areas where the population has been stable with no massive migration.

A study was planned to find factors associated with the increased incidence of malaria in the highlands of Ethiopia. A study protocol was prepared with a hypothesis that the increased incidence of malaria transmission in the highlands may be linked to global warming. A field study was then conducted in a highland area in central Ethiopia. Some eight data sets were gathered during the study. These included data on malaria, climate, vector control and drug resistance. Data on malaria were obtained from cross-sectional blood surveys , passive surveillance of malaria cases, and outbreak investigation results. Furthermore, data on the magnitude and severity of malaria related morbidity and mortality was collected from hospital records.

A prospective *in-vivo* drug sensitivity study was carried out to assess the level of chloroquine resistance in the study area. Data on DDT spraying activity were also gathered to see the relative contribution of vector control efforts to an increase in the level of malaria. Details of the methods employed in the field and during analysis and results of the study will be dealt with in subsequent chapters.

## **Part two:**

### **Results and Discussion**

**Chapter 3 :**      The level and trend of malaria in Debre Zeit

Sector

**Chapter 4 :**      Altitude effects on transmission of malaria

**Chapter 5 :**      Climate patterns in Debre Zeit

**Chapter 6 :**      Effectiveness of treatment in *P. falciparum* and  
*P. vivax* malaria

**Chapter 7 :**      The use of D.D.T. for the control of malaria in  
Debre Zeit sector

**Chapter 8 :**      Climatic effects on the transmission of malaria  
in Debre Zeit sector

## **Chapter 3**

### **The level and trend of malaria in Debre Zeit Sector**

#### ***3.1 Introduction***

While publications on the epidemiology of malaria in the lowlands of Ethiopia are available by different authors (Armstrong, 1969; Krafsur, 1971; Krafsur and Armstrong, 1982; Teklehaimanot, 1986; Tulu, 1993), reports on the level and trend of malaria in the highlands were rarely published. The only published information on the level and trend of malaria among the population in the present study area, Debre Zeit sector, comes from observations made by Italian investigators during the Second World War (Melville et al., 1945) and during the 1958 epidemic of malaria in Ethiopia (Fontaine et al., 1961).

At the height of the malaria season in 1941, a spleen rate of 72% was recorded among school-age children by Melville (1945) in the town of Mojo, situated some 75 kilometres south-east of Addis Ababa on the tributary of the Awash river, located at an altitude of 1,780 metres. It was then thought that this place was the nearest permanently endemic centre of malaria to Addis Ababa (Covell, 1957). But later, during the epidemic in 1958, many cases of malaria were seen among residents living in the Ziquala plain (mean altitude, 1,850 metres) and the Lake Akaki district (mean altitude, 2,000 metres). About 150,000 inhabitants were estimated to have been at risk of the epidemic which began in

July 1958 and extended to December 1958. *An. gambiae s.l.* was the vector and *P. falciparum malaria* was the cause of the epidemic. The number of malaria related admissions to Debre Zeit hospital in 1958 was 4,094 and this was about four times greater than the average for the previous four years (948 cases per year). About 73% of these admissions occurred in the months of September, October and November.

In spite of malaria control efforts over the past three decades, outbreaks of malaria are known to have occurred since 1958, but no published information is available about the periodicity of these epidemics. There was no detailed evaluation of the magnitude of the malaria problem in terms of the burden of morbidity and mortality attributable to malaria among the communities residing in the study area.

### **3.2      *Objectives***

Analysis of the malaria situation in the present study area was carried out with the following specific objectives;

- a) to assess the current level of malaria transmission in the study area ,
- b) to determine the magnitude of increase in the level of transmission during the period from 1968 to 1993, and
- c) to estimate the change in the level of morbidity and mortality attributable to malaria in the highlands from 1975 to 1993.

### **3.3 Data sets and analytic methods**

Four data sets related to the epidemiology of malaria in Debre Zeit sector were examined. These included blood survey data from 1974 to 1987, passive surveillance data from 1968 to 1993, data on outbreaks of malaria from 1975 to 1992, and data on hospital admissions and deaths.

#### **3.3.1 Seasonal blood surveys**

Seasonal blood surveys were conducted during the peak transmission months of September, October and November of each year. About 95% of these surveys were conducted in the latter two months. Some 80 localities and 11,399 persons in 2,533 households were examined over the 1974 to 1987 period annually. A systematic random sample of finger-prick blood specimens was collected from all residents in every seventh household in each locality. A total of 148,357 slides were examined. Retrospective analysis of this data set was carried out to describe the age and sex-specific prevalence of malaria and to assess the pattern of malaria during the 13 year period. The limitation of this data set was that the surveys were carried out only during the peak transmission period and the level of malaria during the remaining nine months of each year was not represented. Furthermore, there were no data on the level of malaria since 1987.

### **3.3.2 *Passive surveillance***

Data on passive surveillance of symptomatic cases of malaria who visited the malaria diagnosis and treatment centre at Debre Zeit sector office from September 1968 to August 1993 were examined. A total of 131,664 records were seen. The records included data on patient characteristics such as age, sex, place of residence, history of travel during the past one month, microscopic diagnosis of blood sample, date of diagnosis and specific treatment given. Age and sex-specific slide positive rates were calculated to describe the pattern and identify risk groups. Monthly incidence was calculated based on the population count made during the DDT spraying campaigns of each year where available and otherwise by extrapolation from the 1984 census report, assuming a population growth rate of 2.9% per annum. This data set was essential to provide a picture of the monthly fluctuation of malaria over a 25 year period and to identify particular months and years during which the population of the study area was exposed to an excess risk of malaria.

### **3.3.3 *Outbreaks of malaria***

Records of reports of outbreaks were also examined. These dated from January 1975 to November 1992. The reports were based on results of microscopic examination of blood



samples obtained from the affected population. The number of cases diagnosed during these outbreaks was plotted by month and year to see the periodicity of these outbreaks. Furthermore, age and sex-specific slide positive rates were calculated to determine the group most at risk. The limitations of this data set were that, (a) there was no information about the number of persons who died during these outbreaks of malaria, (b) reports of outbreaks were made either by the residents or health workers which may mean that there could be under-reporting, (c) although a parasite prevalence rate of greater than 5% was the national definition of an outbreak, it is possible that a strict classification was not made, particularly after the cessation of the annual blood surveys in 1987.

### ***3.3.4 Hospital admissions and deaths***

Summary records of patients admitted to Debre Zeit Hospital from 1975 to 1993 were examined. The proportion of hospital admissions attributable to malaria were calculated to see whether a change occurred over time and to estimate the burden of disease in relation to other health problems prevailing in the area. Furthermore, hospital deaths were also examined and the proportion of malaria related deaths was calculated. This data set was particularly useful to complement the parasitological data in providing evidence for the relative increase in the magnitude and severity of malaria as a public health problem in the study area.

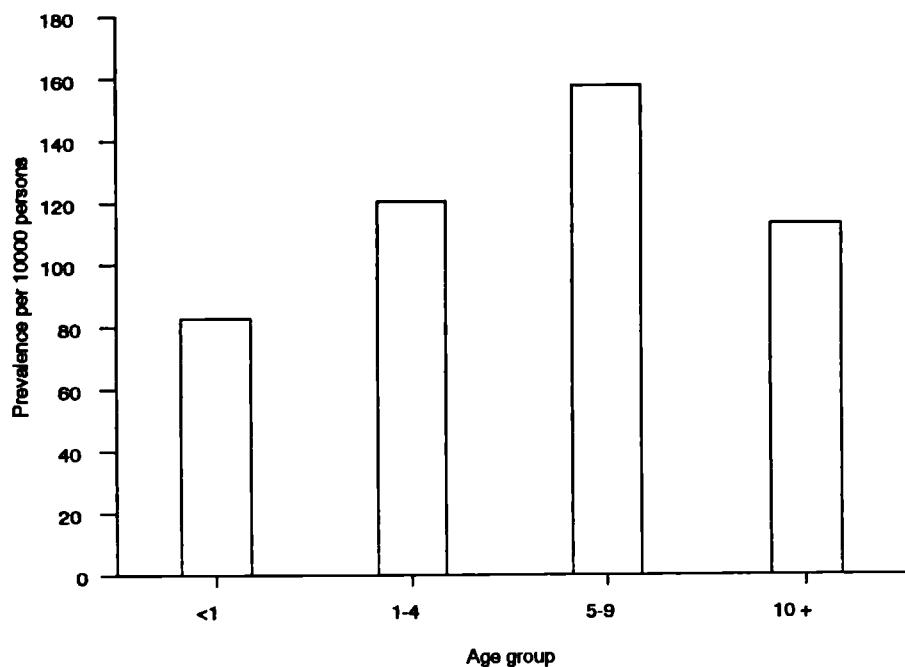
### **3.4 Results**

#### **3.4.1 Prevalence of malaria**

A total of 148,357 slides were examined during surveys carried out between October 1973 and November 1987. Among these, 3,068 slides were positive for malaria. The overall prevalence of malaria was 2%. The relative frequency of malaria parasites was as follows; 52.6% were due to *P. falciparum*, 46.6% were *P. vivax* and the remaining 0.8% were mixed infections of *P. falciparum* and *P. vivax*.

Data on gender was available for 148,063 (99.8%) of blood samples examined. The prevalence of malaria parasites in males was 130.5 per 10,000 persons and in females it was 115.6 per 10,000 persons. The higher prevalence of malaria observed in males than in females seemed unlikely to have occurred due to chance,  $\chi^2 = 6.67$ ,  $P < 0.01$  (d.f. =1). Prevalence of malaria seemed to increase progressively during early childhood until it reached its peak in children aged 5 to 9 years, after which it declined as depicted in Figure 3.1. A similar pattern was also observed in the data from outbreak investigations in which a significantly greater proportion of males were affected and children aged 5 to 9 years had the greatest burden of malaria.

**Figure 3.1 Age-specific prevalence of malaria during peak transmission in Debre Zeit sector**



### **3.4.2 Slide positive rates among outpatients**

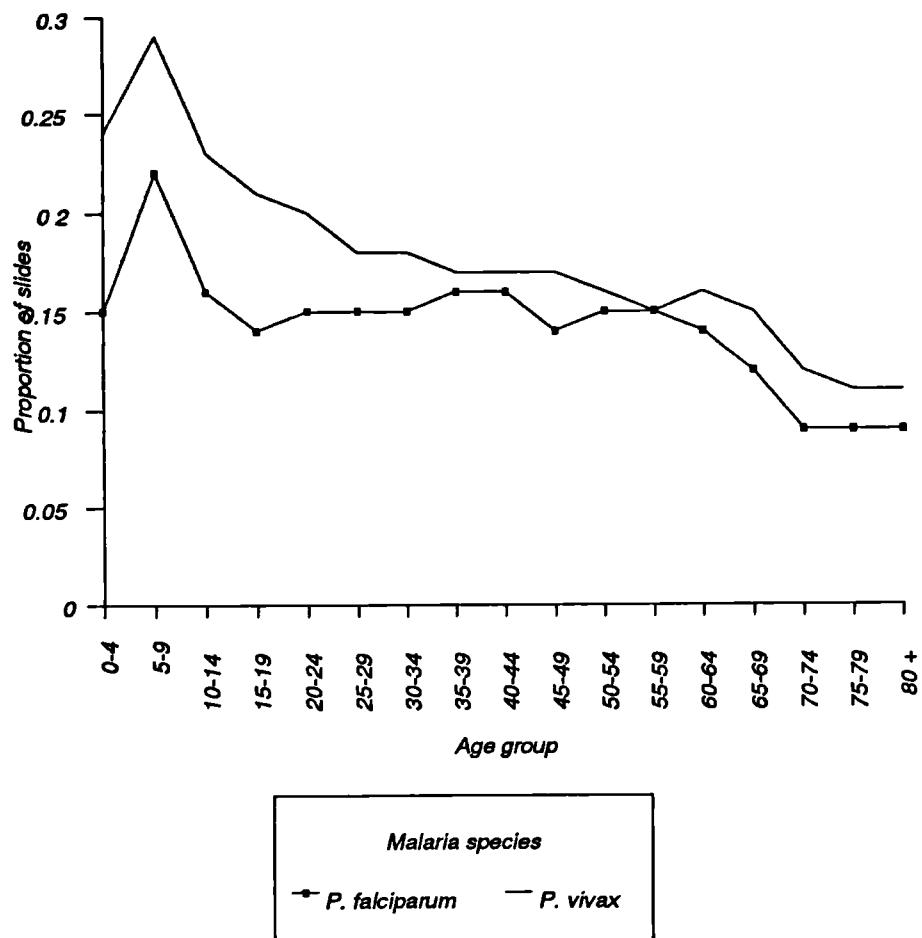
Records of outpatients who visited Debre Zeit malaria clinic from January 1968 to September 1993 were examined. A total of 131,664 blood samples were taken and microscopic diagnosis of Giemsa stained blood films was done. Among these, 46,269 (35.1%) slides were positive for malaria. The relative frequency of *P. vivax* was 57% while *P. falciparum* contributed 43%. Data on *P. falciparum* gametocytes was available for 109,528 records. Among these, 5,139 (4.7%) had gametocytes.

The age-specific distribution of the slide positive rate was plotted for the two malaria parasites as depicted in Figure 3.2. A greater proportion of *P. vivax* malaria was seen throughout all age groups except at 55-59 years where the proportion of the two malaria parasites was about equal. Furthermore, in both *P. falciparum* and *P. vivax*, the greatest proportion of positive slides was seen among patients aged 5 to 9 years old. Thereafter, the slide positive rate declined with increasing age.

Overall, the proportion of positive slides for *P. falciparum* malaria was greater in males than in females, i.e. 0.16 (N= 49,591) Vs 0.14 (N=81,687). This observed difference in the proportion of positive slides among males and females also seemed unlikely to have been due to chance,  $\chi^2 = 106.7$ , P < 0.01.

Further analysis of the slide positive rate by age and sex showed a consistently higher proportion of males with *P. falciparum* malaria among patients aged 10 years and above. But, in patients below 10 years, the proportion of *P. falciparum* malaria was equal for males and females as depicted in Figure 3.3. A similar pattern of slide positive rates was observed among patients diagnosed with *P. vivax* malaria. More males were affected than females and the proportion of positive slides declined with increasing age among male and female patients.

**Figure 3.2 Proportion of slides which were positive among clinical patients by age and sex in Debre Zeit sector**



**Figure 3.3 Proportion of slides which were *P. falciparum* positive by age and sex**



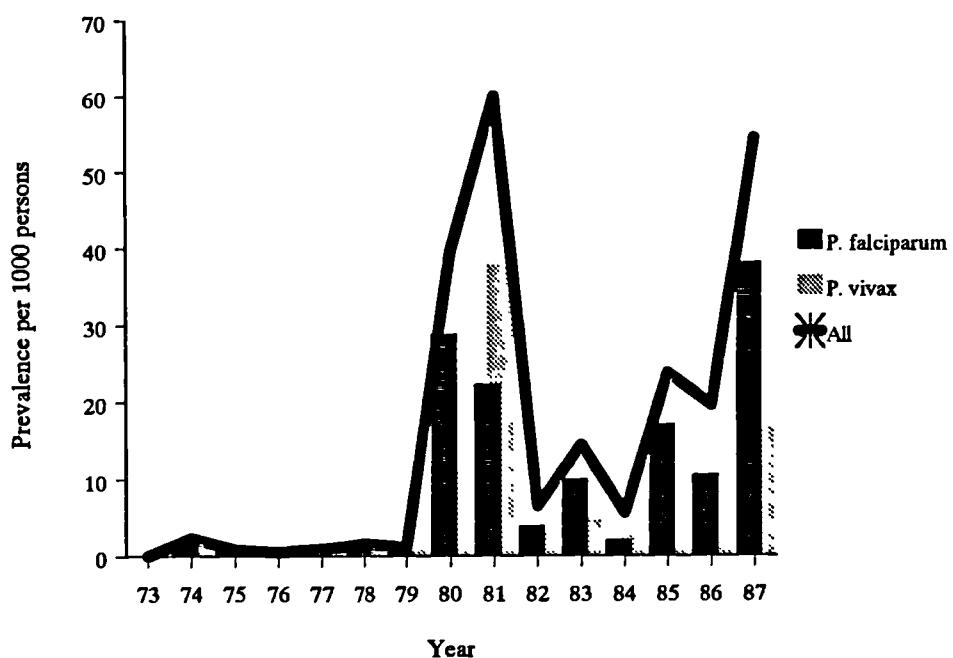
### **3.4.3 Seasonality of malaria**

#### **3.4.3.1 Point prevalence of malaria**

Data on the point prevalence of malaria were obtained from seasonal blood surveys carried out during the peak transmission season from 1973 to 1987. Prevalence was

estimated for *P. falciparum* and *P. vivax* per 1000 persons examined and plotted against time (month/year) as shown in Figure 3.4. Here, it is shown that peak prevalence of malaria relative to the 1973-1987 period was seen during four years only, i.e., 1980, 1981, 1985 and 1987. It is also clearly depicted that the prevalence of *P. falciparum* malaria was consistently higher than *P. vivax* except in 1981.

**Figure 3.4** Point prevalence of malaria during peak transmission in Debre Zeit sector



### **3.4.3.2 Monthly incidence of malaria**

Incidence of malaria was computed from passive surveillance data collected during the January 1968 to August 1993 period. The monthly incidence of *P. falciparum* malaria during this period is depicted in Figure 3.5.1 and 3.5.2 on arithmetic and log scales respectively. Here, it is clearly seen that an increasingly higher monthly incidence of malaria was noted since 1980 though with fluctuations over the years. Furthermore, peak incidence rates were most conspicuous in the years 1985, 1988, 1991 and 1992.

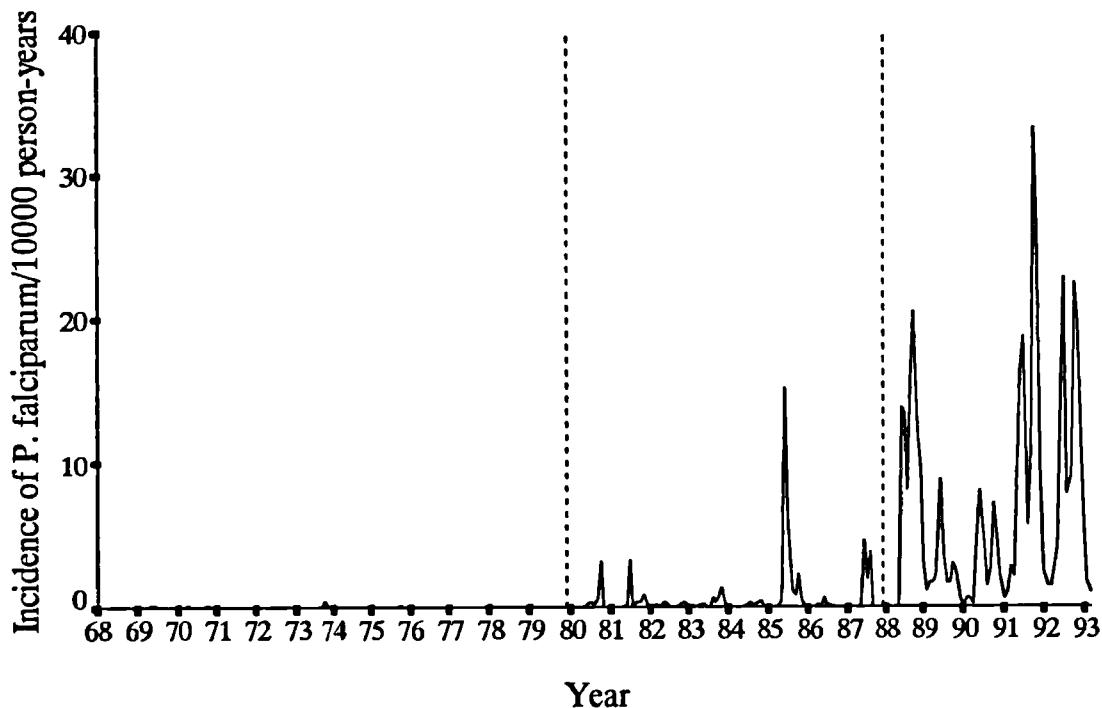
The scale of the problem of increasingly higher incidence of *P. falciparum* malaria may best be appreciated in the following peak monthly incidence data, 0.5 per 10,000 person-years in October 1973, 3.3 per 10,000 person-years in July 1981, 15.3 per 10,000 person years in June 1985, 20.5 per 10,000 person-years in October 1988 and 33.4 per 10,000 person-years in October 1991. This showed an increase of 66.8-fold in *P. falciparum* incidence over an eighteen year period between October 1973 and October 1991.

Furthermore, as shown in Figure 3.5, it is notable that not only has monthly incidence increased but what was a highly seasonal transmission seemed to have been transformed into perennial transmission particularly during the years 1988, 1991 and 1992. The overall trend in *P. falciparum* incidence relative to *P. vivax* monthly incidence is seen in Figure

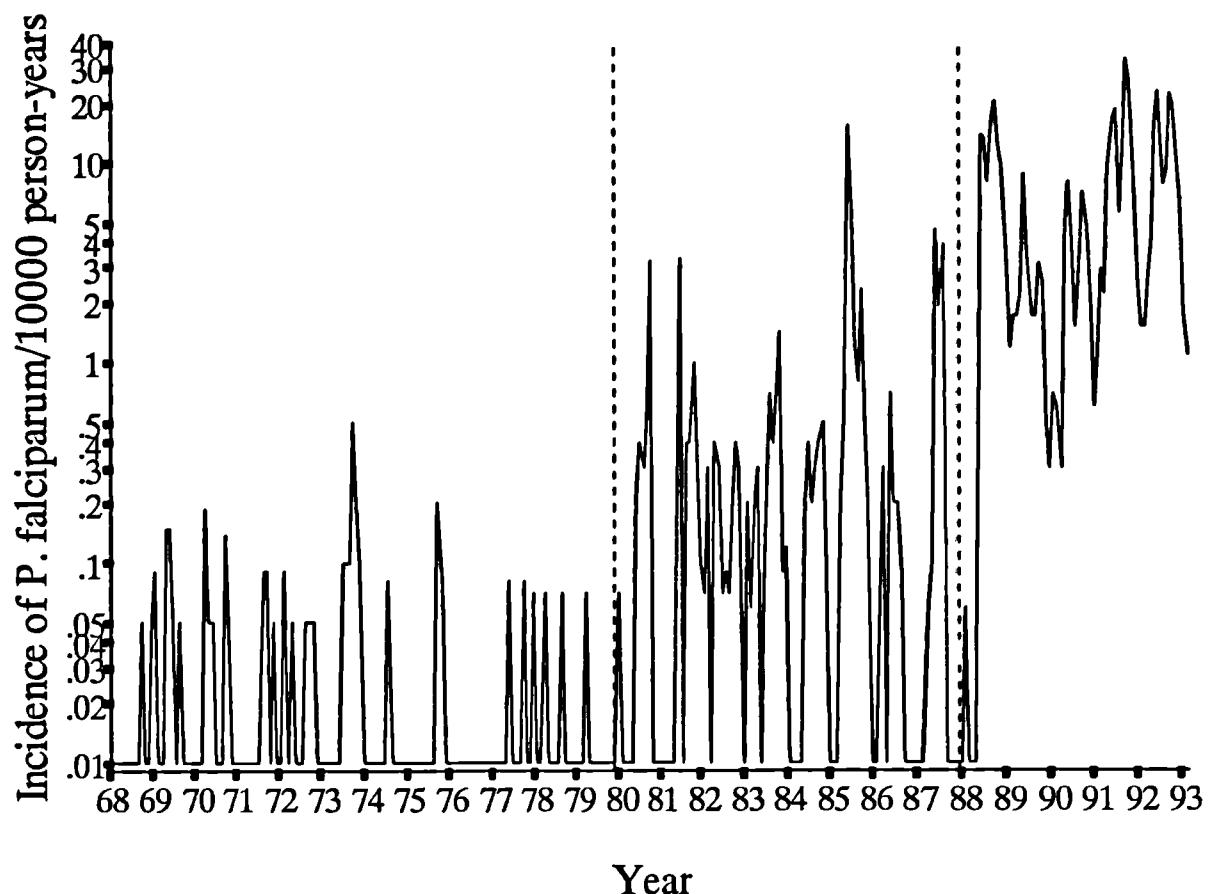
3.6 which depicts an increasingly higher rate of the former species in 1985, 1990 and 1991.

The monthly incidence of *P. vivax* malaria is depicted in Figure 3.7. Here also, a trend of increasingly higher incidence of malaria is noted particularly during the years 1983, 1988, and 1992. Less conspicuous but relatively important increases in monthly incidence seem to have occurred also in 1980, 1981, 1985, 1987 and 1991. Thus, it seems that the reported high monthly incidence of *P. vivax* malaria preceded that of *P. falciparum* malaria by about five years.

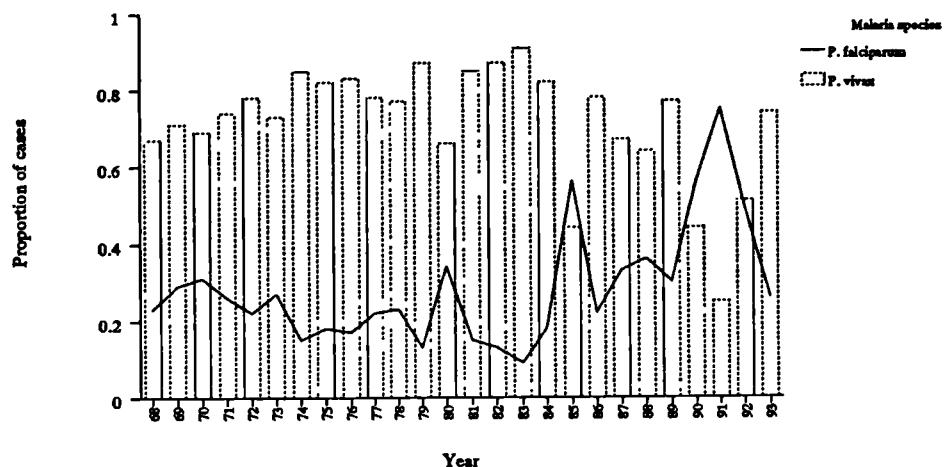
**Figure 3.5.1** Monthly incidence of *P. falciparum* in Debre Zeit sector (arithmetic scale)



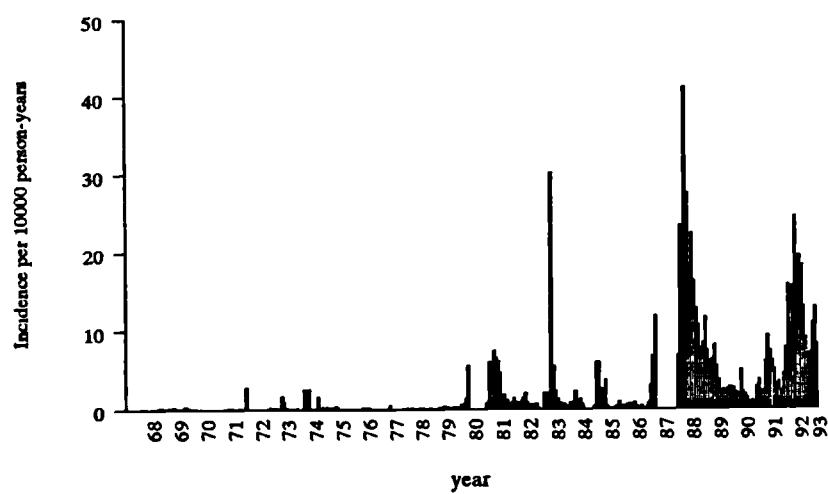
**Figure 3.5.2** Monthly incidence of falciparum malaria in Debre Zeit sector (log scale)



**Figure 3.6** Trend in the relative frequency of *P. falciparum* and *P. vivax* in Debre Zeit sector



**Figure 3.7** Monthly incidence of *P. vivax* in Debre Zeit sector



### **3.4.4 Periodicity of outbreaks of malaria**

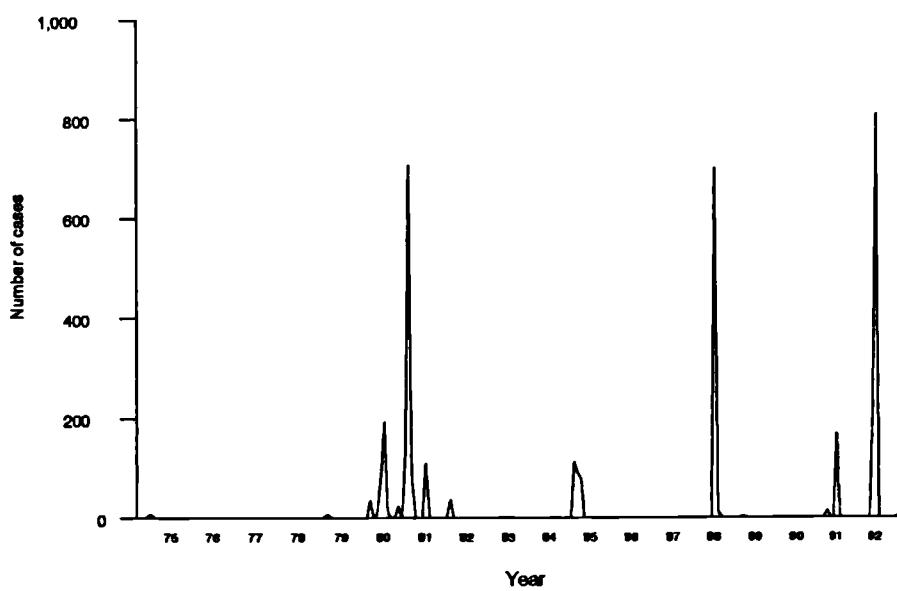
Records on reported outbreaks of malaria for the period January 1975 to June 1993 were examined. The dates during which the epidemics were reported and investigations were carried out were noted and the number of cases of malaria diagnosed were plotted against time. The occurrence of *P. falciparum* outbreaks is seen in Figure 3.8. As shown in the figure, some pattern of periodicity of these outbreaks is apparent. During the observation period between January 1975 to June 1993, only three years appear to have been posing enormous risk of *P. falciparum* malaria to residents of the population in Debre Zeit sector, i.e. 1981, 1988, and 1992. However, the month during which a peak number of cases occurred in these outbreaks and the level of incidence varied during these years. In 1981, 706 cases of *P. falciparum* malaria were diagnosed among 5,823 persons (121.2 per 1000 person-years) examined in the month of June alone. In 1988, 700 cases of *P. falciparum* malaria were diagnosed among 1,843 persons (379.8 per 1000 person-years) in the month of November. In 1992, 809 cases of *P. falciparum* malaria were diagnosed among 1,889 persons (428.3 per 1000 person-years) in the month of November alone.

Thus, it seemed that the incidence of *P. falciparum* outbreaks has increased by 3.5-fold between 1981 and 1992. While the interval between the outbreaks in 1981 and 1988 is seven years, that between the outbreaks in 1988 and 1992 is only four years. Furthermore,

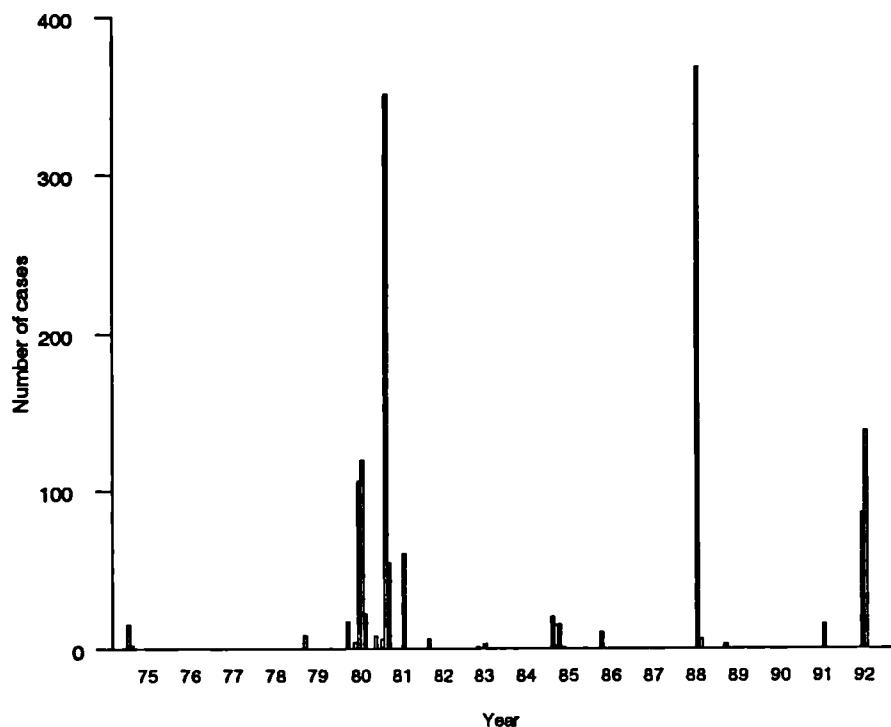
there were two small but probably significant outbreaks in 1985 mid-way between 1981 and 1988, and in 1991 only three years after the outbreak in 1988.

The periodicity of *P. vivax* outbreaks is depicted in Figure 3.9. As illustrated in the figure also, a similar pattern of periodicity of outbreaks is apparent. Peak number of cases seem to have occurred in 1981, 1988 and 1992. But, a less obvious but early herald peak was seen in 1980. A progressive increase in the incidence of *P. vivax* malaria was seen during the peaks in 1980 and 1988. In November 1980, 119 cases were diagnosed among 1,959 persons (6%) and in November 1988, 368 cases were diagnosed among 1,843 persons (20%).

**Figure 3.8      Occurrence of *P. falciparum* outbreaks in Debre Zeit sector**



**Figure 3.9    Occurrence of *P. vivax* outbreaks in Debre Zeit sector**



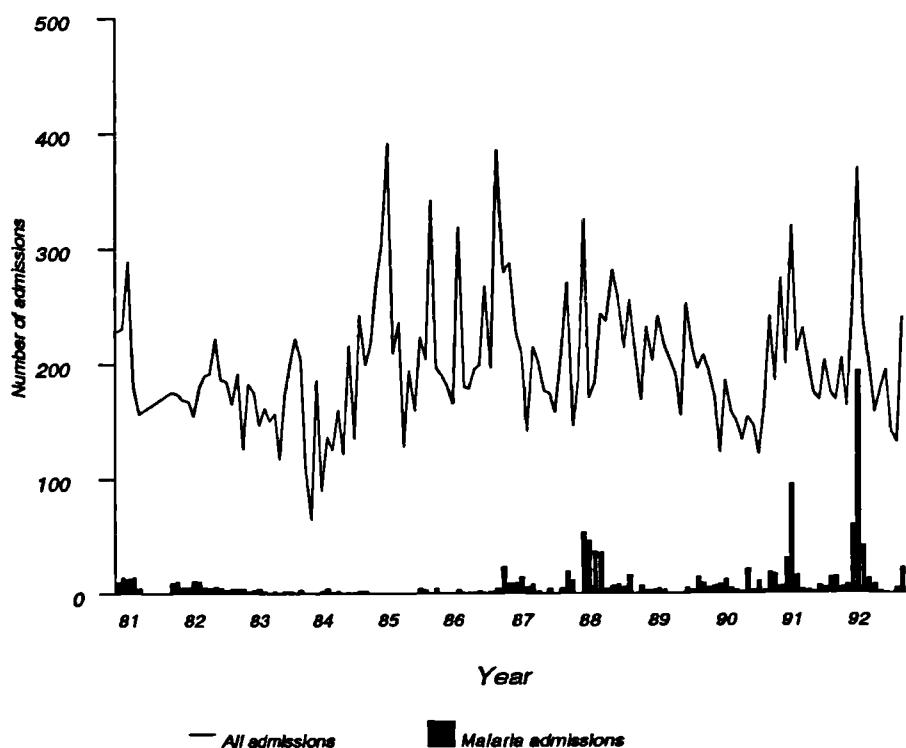
### **3.4.5 Severe morbidity and mortality attributable to malaria**

An attempt was made to see the relative contribution of malaria related illness to severe morbidity and mortality in the population in Debre Zeit by making a closer examination of hospital records of patients admitted to Debre Zeit hospital during the period September 1981 and December 1992.

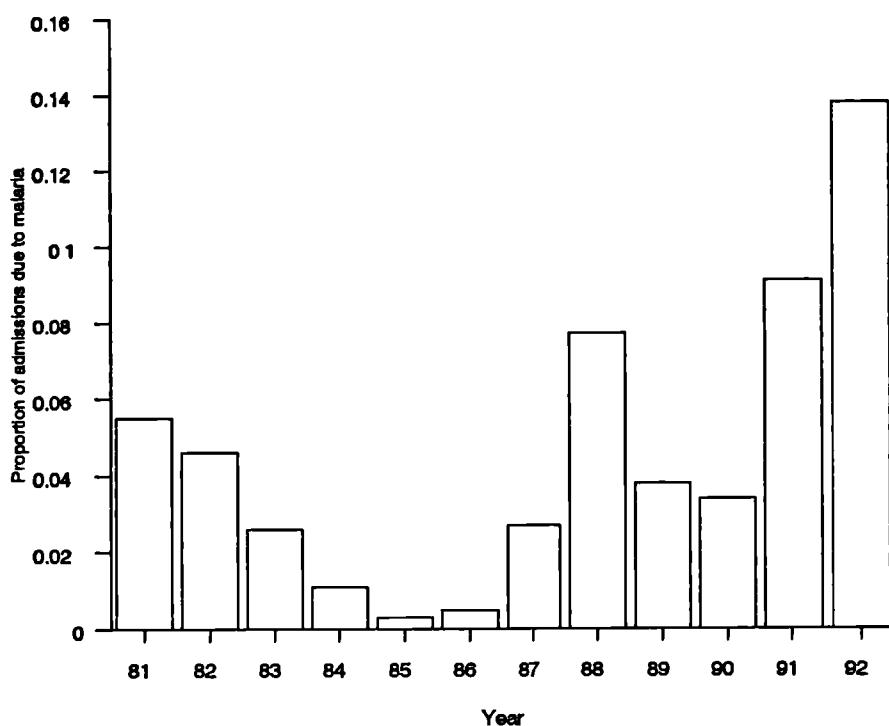
A total of 27,090 patients were admitted to the hospital during the period mentioned above. Among these, the number of admissions related to malaria of all types was 1,247 (

4.6%). Data on date of admission was available for 25,844 patients (95.4%). As with data on prevalence and incidence, the number of admissions due to malaria also showed marked seasonality as shown in Figure 3.10. Here, it is notable that admissions due to malaria were relatively rare before 1987 after which a very marked increase was observed. Furthermore, when the proportion of malaria related admissions relative to admissions due to all causes was plotted by year, particularly high proportions of admissions attributable to malaria were seen in 1988, 1991 and 1992 as depicted in Figure 3.11.

**Figure 3.10 Monthly admissions in relation to malaria in Debre Zeit Hospital**

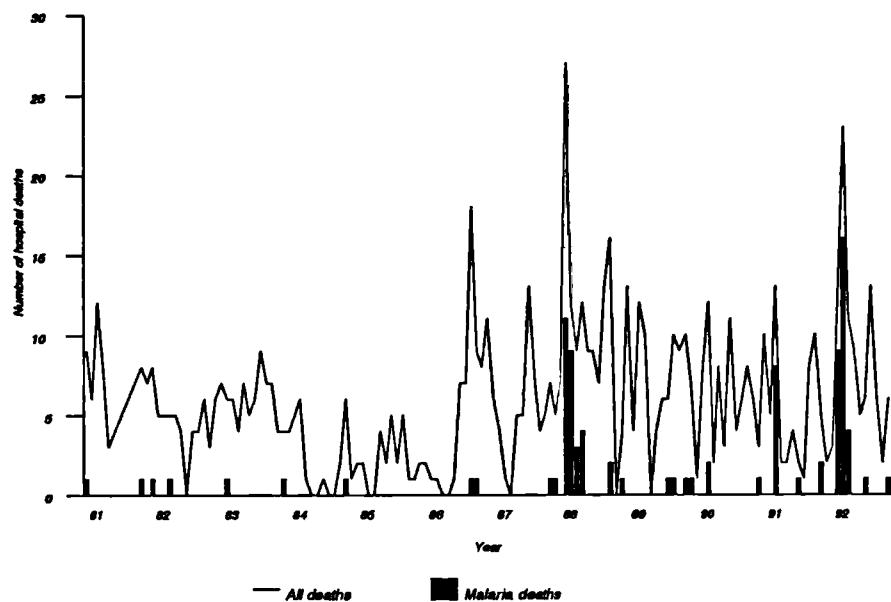


**Figure 3.11 Proportion of admissions related to malaria at Debre Zeit Hospital**



The pattern of deaths due to all causes and deaths attributable to malaria were also plotted by month as depicted in Figure 3.12. A similar pattern of seasonality of deaths as admissions was also observed. Deaths attributable to malaria appeared to be relatively rare before 1988 after which the relative contribution of malaria to overall mortality appears to have increased almost in epidemic proportions as depicted in Figure 3.13. In 1981, deaths attributable to malaria contributed only 2.9% of overall mortality in Debre Zeit Hospital, while in 1992, 38.6% of all deaths were attributed to malaria which is an increase of 13.3-fold over a decade.

**Figure 3.12** Distribution of monthly deaths in relation to malaria at Debre Zeit Hospital



**Figure 3.13** proportion of deaths ascribed to malaria at Debre Zeit Hospital

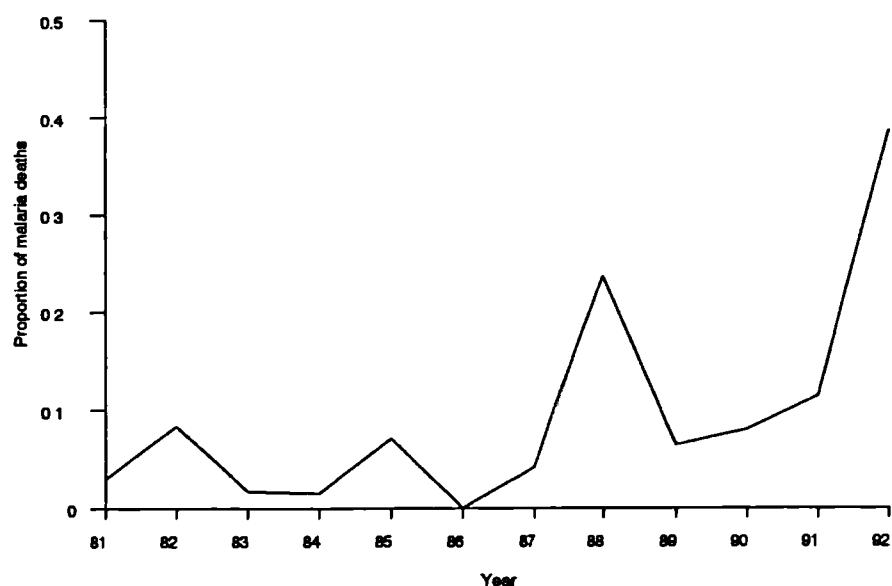
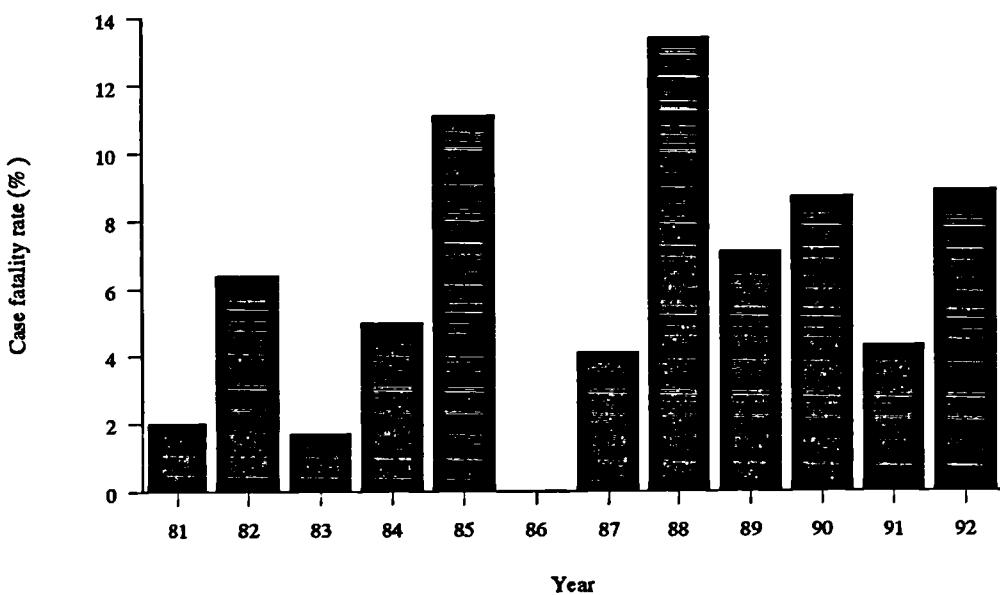


Figure 3.14 shows the cases fatality rate among malaria patients admitted to Debre Zeit Hospital from 1981 to 1992. Peak case fatality rate was in 1985 and 1988. There was no death ascribed to malaria in 1986. It is notable in the figure that although a peak occurred in 1988 there is no great rise that showed a persistent upward trend despite a huge rise in the number of admissions, and deaths attributable to malaria. However, when analysis was carried out by classifying patients according to species of malaria parasite, peak case fatality rate of 21.5% ( $N = 149$ ) occurred in 1992 among those with *P. falciparum* malaria.

**Figure 3.13 Malaria case fatality rate among patients admitted to Debre Zeit Hospital (1981-92)**



### **3.5 Discussion**

The overall prevalence of malaria parasitaemia in Debre Zeit sector as shown in surveys conducted during the peak transmission season was 206.8 per 10,000 persons (2.1%). This suggested that the level of malaria transmission was low. The greater prevalence and slide positive rate of *P. falciparum* malaria seen among males than females particularly after ten years may be attributable to a greater degree of exposure to outdoor infective bites among males. This could be plausible when one considers the greater degree of outdoor activity by males during the planting and harvesting seasons including evenings during which peak transmission of malaria is known to occur. The similarity of the slide positive rate before the age of ten years between males and females on the other hand may be due to the equal distribution of risk of exposure to infective bites in both groups during childhood.

Data from blood surveys, outbreak investigations and surveillance in the population of these highlands showed that children aged 5 to 9 years had the greatest prevalence and slide positive rate of malaria. This may be explained by the lower rate of transmission that postponed the chance of first infection to a later age. This is in contrast to what may be seen among residents living in the lowlands of Ethiopia where malaria transmission is much higher and children less than five show the greatest prevalence, illness and death due to malaria (Tulu, 1993). This could be due to the lesser number of infective bites before 5

years to the population in the highlands, conferring immunity to infection and disease at a later age.

Data on prevalence during peak transmission months showed a greater preponderance of *P. falciparum* while year round surveillance data showed a greater frequency of *P. vivax*. This discrepancy may be explained by the greater rate of transmission of *P. falciparum* during the peak transmission months of October and November while *P. vivax* transmission was more frequent during the remaining ten months of the year. Furthermore, the overall slide positive rate among patients was 35.1% while the prevalence of malaria during surveys was 2.1%. This could be explained by the difference of the population in the denominator. The denominator in the surveillance data set with a slide positive rate of 35.1% were self presenting patients who suspected that they were suffering from malaria and thus a higher rate of positive slides. However, the denominator in the blood surveys were residents living in randomly selected houses irrespective of whether they were ill or not and hence a very low prevalence of malaria.

Point prevalence data from surveys during peak transmission and monthly incidence from surveillance show a marked fluctuation of malaria that suggested that the transmission of malaria in the study area is highly seasonal and unstable. Furthermore, the relatively high monthly incidence in malaria particularly during the years 1988 and 1991 may be due to the presence of favourable conditions for transmission. This could be due to one or more of the following factors; (a) an increased density of vectors due to the abundance of breeding sites, (b) increase in the

longevity of vectors with increased probability of survival of the mosquito through one day, (c) a decrease in the extrinsic incubation period of the malaria parasite in the *Anopheles* vector, (d) an increase in the human-biting habit of the *Anopheles* vector, (e) a greater number of infected individuals, and /or (f) a decrease in the rate of recovery of infected individuals. All these factors may affect the level of transmission of malaria in an area. But, the effect that each of the factors mentioned has on the incidence and prevalence of malaria varies.

Among the factors mentioned, an increase in the longevity and human-biting habit of the vectors of malaria may have the greatest impact on the level of transmission of malaria ( Macdonald, 1953). An increase in the density of vectors due to more breeding sites could be due to numerous small rain pools due to heavy rains or alternatively due to relaxation of vector control efforts particularly due to interruption of indoor spraying of DDT. Favourable climatic conditions such as rains during normally dry months or unusually heavy rains during the rainy season with abundant rain pools may increase the density of vectors. Increases in the ambient temperature may shorten the extrinsic incubation period thereby shortening the time it takes for the generation of a case of malaria, i.e. the time from gametocyte uptake by the female *Anopheles* vector to the time of appearance of gametocytes in an infected individual. An increase in relative humidity may increase the longevity of the *Anopheles* vector offering a greater chance for the completion of the sexual phase of development of the malaria parasite. An increase in ambient temperature may also shorten the period between successive ovipositions and mean ambient temperatures below 16.1 °C (61 °F) do not allow the completion of the mosquito cycle, i.e. from egg to larva, pupa and adult (Garnham, 1948).

Furthermore, an increase in the number of infected individuals could also lead to an increase in the parasite pool. A decrease in the recovery rate of infected individuals may increase morbidity and mortality while also enhancing transmission of malaria particularly when the number of gametocyte carriers in the community increases. The degree to which each of the above factors contributed to the increased incidence of malaria either singly or in combination will be examined in greater detail in subsequent chapters on climate, vector control and drug resistance.

The periodicity of reported outbreaks of malaria also followed a pattern similar to point prevalence and monthly incidence data. There were only three years during which an abnormally excessive number of cases were reported; i.e, 1981, 1988 and 1992. While the earlier frequency of reported outbreaks in 1981 and 1988 appears to have occurred at an interval of 7 years the epidemic in 1992 occurred with an interepidemic interval of only 4 years. Furthermore, the outbreak in 1981 was reported during the months of May and June while that in 1988 and 1992 was in October and November. The months of May and June are the period during which the rainy season begins and the density of malaria vectors is expected to increase due to the presence of small rain pools suitable for breeding. The months of October and November are normally dry months as the rains often cease in September. Although entomological data are lacking, the explanation for the occurrence of outbreaks in October and November in 1988 and 1992 may lie in the presence of conditions that increased the longevity of vectors and thus the probability of survival of vectors through one day.

As with data on prevalence, incidence and outbreaks, data from hospital admissions and deaths related to malaria showed a very marked periodicity. Furthermore, the relative importance of malaria as a cause of hospital admissions and deaths has increased very much in recent years, particularly in the years 1988, 1991 and 1992. More than one-third of all hospital deaths in 1992 were attributable to malaria.

A trend of increased incidence of malaria in highlands in other parts of Africa was reported particularly in the latter half of the 1980's. An increased transmission of malaria in the highlands of Madagascar (Lepers et al., 1988; Fontenille et al., 1990; Raharimalala et al., 1993) was attributed to heavy rains and lack of vector control measures. An increased incidence of malaria in the highlands of Tanzania (Matola et al., 1987; Lines et al., 1991) was attributed to chloroquine resistant *P. falciparum* malaria. Epidemics of malaria with increased morbidity and mortality were also reported from Kenya (Some, 1994) although the cause of the epidemic was not known. The increased incidence of malaria in the highlands of Rwanda was attributed to an increase in the ambient temperature. The problem with these data was that all seem to have used different criteria to describe the cause of the epidemics, which seems to have led to varying conclusions.

Thus, there is a need for a more exploratory analysis of the cause of increased incidence of malaria in the highlands taking into account climatic and non-climatic factors. A more

systematic analysis of the effects of altitude and climate on the transmission of malaria in the present study area will be carried out in Chapters 4 and 5 respectively.

### **3.6 Summary**

The most notable event in the analysis of the malaria situation in Debre Zeit sector over the past 25 years was the enormous increase in the level of transmission, hospital admissions and deaths attributable to malaria, particularly since 1988. Prevalence data from blood surveys suggested that the transmission of malaria in the study area was relatively low, children aged 5 to 9 years were most affected, and significantly more males than females were infected with malaria.

Monthly incidence data from surveillance showed that malaria was highly seasonal and unstable but with an increasingly higher incidence that increased 66.8-fold in the period from October 1973 to October 1991. The greatest incidence of *P. falciparum* occurred in 1985, 1988, 1991 and 1992. Peak incidence of *P. vivax* occurred in 1981, 1983, 1988, and 1992. Reported outbreaks of both *P. vivax* and *P. falciparum* occurred in 1980-81, 1988, and 1992. Furthermore, the proportions of admissions and deaths attributable to malaria showed a great increase particularly since 1988. The proportion of deaths attributable to malaria increased from 2.9% in 1981 to 38.6% in 1992 which is a 13.3-fold increase. Factors that were associated with this pattern of increased incidence of malaria in the area will be dealt with in subsequent chapters.

## **Chapter 4**

### **Altitude effects on transmission of malaria**

#### ***4.1 Introduction***

Previous studies suggested that the distribution of malaria and its intensity of transmission in Ethiopia were related to altitude (Tulu, 1993). This may be due to ambient temperature, rainfall or other factors associated with different altitudes, which could have an effect on the distribution and density of vectors of malaria at a given time and in a particular area.

Generally, three climatic zones are known to exist in the country; namely, the cold zone, the temperate zone and the warm zone. The cold zone comprises areas that lie above 2,500 metres, mean monthly temperature is about 15 °C, total rainfall is about 1,600 mm per annum on average, and consists of some 8% of the total land mass of the country. There are no published reports of local transmission in this zone. This was thought to be in line with the known epidemiology of malaria transmission in that the extrinsic development of *P. vivax* ceases at a temperature of 14-15 °C while that of *P. falciparum* stops at 18 °C (Macdonald, 1952, Detinova, 1962).

The temperate zone extends from 1,500 to 2,500 metres above sea level, average temperature is 20 °C and rainfall varies from 400 to 2,400 mm. It covers about 48% of the land mass of the country which constitutes the greater portion of the Ethiopian highlands. Malaria transmission in this zone is characterised by epidemics affecting all age groups that occur every seven to eight years. The most disastrous of these epidemics struck the nation in 1958, with an estimated 3 million cases and 150,000 deaths (Fontaine et al., 1961), but have become more frequent in recent years such as the ones which occurred in 1988-89 and 1991-92. This is the most suitable zone for agriculture and about 80 % of the total population of the country are estimated to live in the highlands of Ethiopia above an altitude of 1,500 metres.

The warm zone covers areas less than 1,500 metres and extends over the lowlands of the Danakil depression, the deep valleys of the big rivers such as Abbay (Blue Nile), Tekeze, Anger, Diddessa, Baro, Akobo, Omo, Genale, Wabi Shebelle, and Awash. Rainfall is unpredictable and varies from 100 to 900 mm per annum and mean temperature ranges from 20 to 30 °C. Malaria is endemic in this zone. Morbidity and mortality is limited to under-five children and non-immune migrants (Tulu et al., 1993). Only 16 % of the total population are known to inhabit this zone.

The high prevalence of malaria, trypanosomiasis, leishmaniasis and onchocerciasis in the warm lowlands was probably a major factor in limiting the settlement of

populations in these lowlands. On the other hand, the low prevalence or absence of these diseases in the highlands may have been one of the factors in overpopulation, deforestation and land degradation along with primitive subsistence agricultural practices.

#### **4.2     *Objectives***

The present section aims to achieve the following specific objectives in the context of the overall study;

- a) to determine whether the transmission of malaria parasites in the community has exceeded the previously accepted altitudinal limit of 2,000 metres over the past two decades,
- b) to assess whether a change in the relative frequency of the two main malaria parasites in the study area has occurred at higher altitudes over the past two decades, and
- c) to see whether *P. falciparum* and *P. vivax* malaria transmission has occurred in localities lying at higher altitudes where it was previously absent over the past two decades

## **4.3 Methods of analysis**

### **4.3.1 Data sets and methods of collection**

The study was conducted in Debre Zeit (Bishoftu) sector, Nazareth zone, Ethiopia during the period January 1993 to August 1994. However, data on both altitude and malaria were gathered for the period from 1966 to 1993. A total of 406,891 people in 430 localities, lying at average altitudes between 1,490 to 2,200 metres above mean sea level, were included in the study.

Formats that were suitable for data entry were prepared in EPIINFO. Routine surveillance data, annual blood survey results, epidemic investigation results, and spraying operation data were then entered by two field assistants and the author. Validation was done in EPIINFO/VALIDATE for the first 40,000 consecutive records on which double data entry was possible. All data were saved regularly in duplicates with a copy kept with the author while the other remained with field assistants.

On completion of data entry, data collected by different assistants were merged, compressed, zipped in XtreeGold and copied to high density diskettes after which they were transported to London. Data cleaning was then done by carrying out range and consistency checks for each data base. Retrospective descriptive analysis of historical data sets related to malaria and altitude was undertaken. These consisted of passive

surveillance from January 1966 to September 1993, systematic annual blood surveys from 1974 to 1987, results of investigation of reports of outbreaks of malaria from 1975 to 1992, and data on altitude for each locality.

Passive surveillance data contained a total of 131,664 individual records that contained details on age, sex, place of residence and place of travel one month prior to onset of illness, result of slide examination, date of diagnosis, as well as type and number of antimalarial tablets administered.

#### ***4.3.2 Methods of estimation of altitude effects on malaria transmission***

Average altitude of the maximum and minimum elevation of each locality was calculated after which localities were sorted by altitude. A cumulative frequency of 5% was used to stratify localities into 20 strata with each stratum containing about 21 localities lying at mean altitudes ranging from 1,490 metres to 2,200 metres . This was done to standardise the size of the denominator (population) at each range of altitude.

The population of each locality was obtained from the vector control data base for each year and when missing, from backward and / or forward projection, assuming a population growth rate of 2.95% per annum, based on the 1984 census (CSO,1984). The place and time at which patients were seen and the total number detected for each

species was categorised into each stratum. Incidence was calculated for each stratum with the number of malaria patients diagnosed by passive surveillance in the numerator and the total population estimated to inhabit the study localities at the same time in the denominator. Results were then summarised by calculating mean annual incidence at five year intervals and plotted in Harvard Graphics.

Prevalence was calculated based on annual blood survey results that were conducted during the period 1974 to 1987 in the months of April, September, October and November. About 95% of these surveys were done during the latter two months of each year. Relative frequency was calculated by taking the species identified in the numerator and the number of positive slides in the denominator from the surveillance data set. Prevalence was also calculated to estimate the magnitude of malaria outbreaks from results of blood samples obtained from the affected population at each range of altitude.

## **4.4 Results**

Both *P. falciparum* and *P.vivax* malaria were diagnosed among clinical patients during the 1966-93 period. These two species were also present in annual cross-sectional surveys from 1974 to 1987 that were carried out during the peak transmission season. There was no evidence of *P. malariae* or *P. ovale*. Results of analysis relating to the incidence and prevalence of both species with respect to altitude and year during which the diagnosis was made are presented below.

### ***4.4.1 Changes in incidence of falciparum malaria in relation to altitude from 1966- 1993***

Data from the passive case detection and treatment post at Debre Zeit sector were used to calculate incidence. The incidence of *P. falciparum* malaria was derived from the number of patients with slide-confirmed diagnosis of malaria in the numerator and the number of people estimated to be at risk during a year allowing for the natural rate of increase ( population growth) per annum in the denominator and then multiplying it by 1000, i.e. per 1000 person-years in each stratum of localities by altitude. The most conspicuous observation is the very marked increase in incidence of *P. falciparum* malaria since 1986 at all elevations . However, the magnitude of this increase was not uniform in all elevations over the past decades as shown in Figure 4.1.

Cases of malaria due to *P. falciparum* appeared to be absent in clusters of localities lying above an altitude of 1,960 metres before the year 1976. Then, there was an early occurrence of *P. falciparum* malaria cases in clusters of localities lying at higher altitudes up to a mean altitude of 1,995 metres from 1976 to 1980. This was an early indication of the establishment of transmission of this species among communities residing in localities where the transmission of malaria was previously unknown.

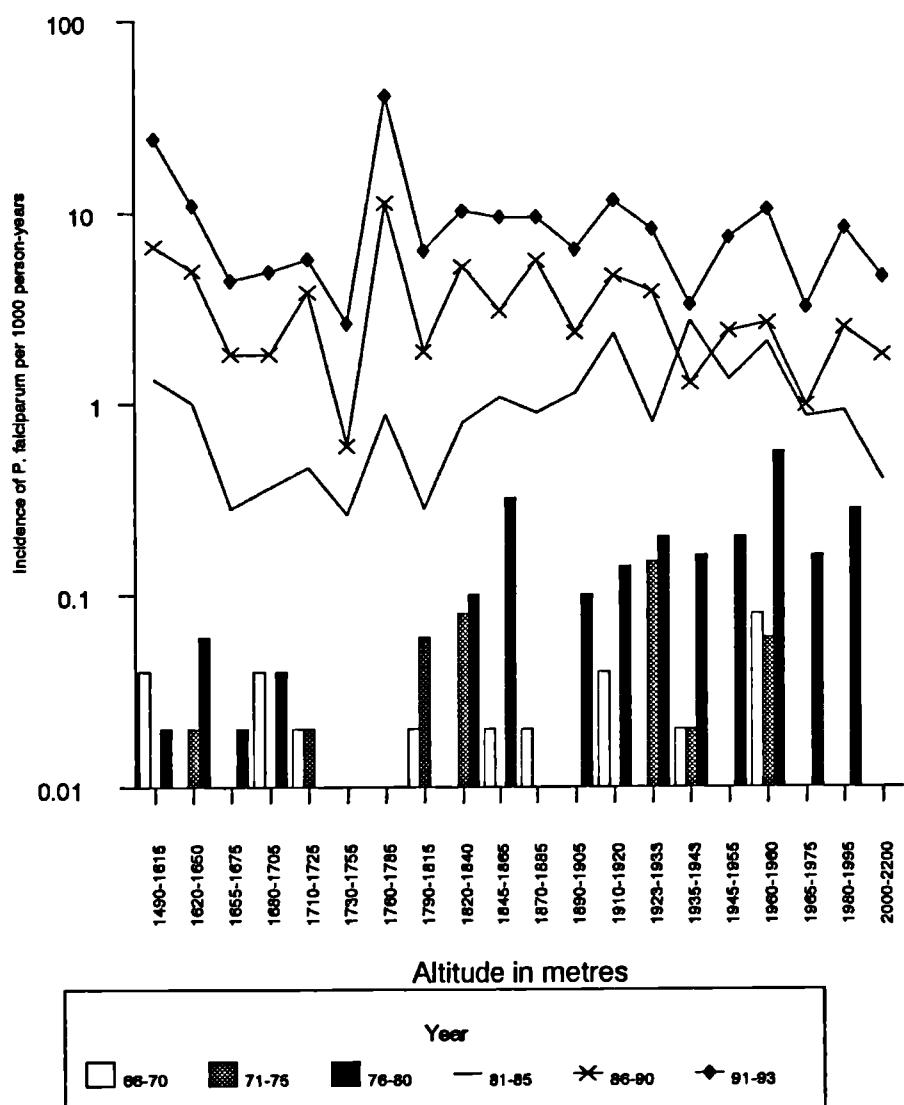
Thereafter, a progressive establishment of *P. falciparum* malaria cases was seen in localities lying up to an altitude of 2,200 metres above sea level during the 1986 to 1993 period. These were localities in which the highest proportional increase in incidence occurred. The incidence of *P. falciparum* malaria increased markedly in clusters of localities lying at altitudes between 1,790 metres and 1,995 metres during the 1976 to 1980 period. Peak incidence of *P. falciparum* malaria occurred from 1991 to 1993 in all localities lying at various altitudes throughout the sector.

Localities lying at altitudes between 1,760 and 1,785 metres showed the greatest incidence of *P. falciparum* malaria since 1986. This is difficult to explain by the effect of altitude alone. These localities are neither on the lower nor on the upper altitudinal range among the 430 localities included in this study. Some local factor other than altitude such as the proximity of localities to permanent breeding sites may be responsible for this observation which seemed an outlier. This is probably a more

plausible explanation considering the close proximity of these localities with high incidence of falciparum malaria to the Awash river and to its tributary, the Mojo river.

**Figure 4.1 Incidence of *P. falciparum* at 5 yearly intervals from 1966 to 1993**

*in Debre Zeit sector plotted against altitude*



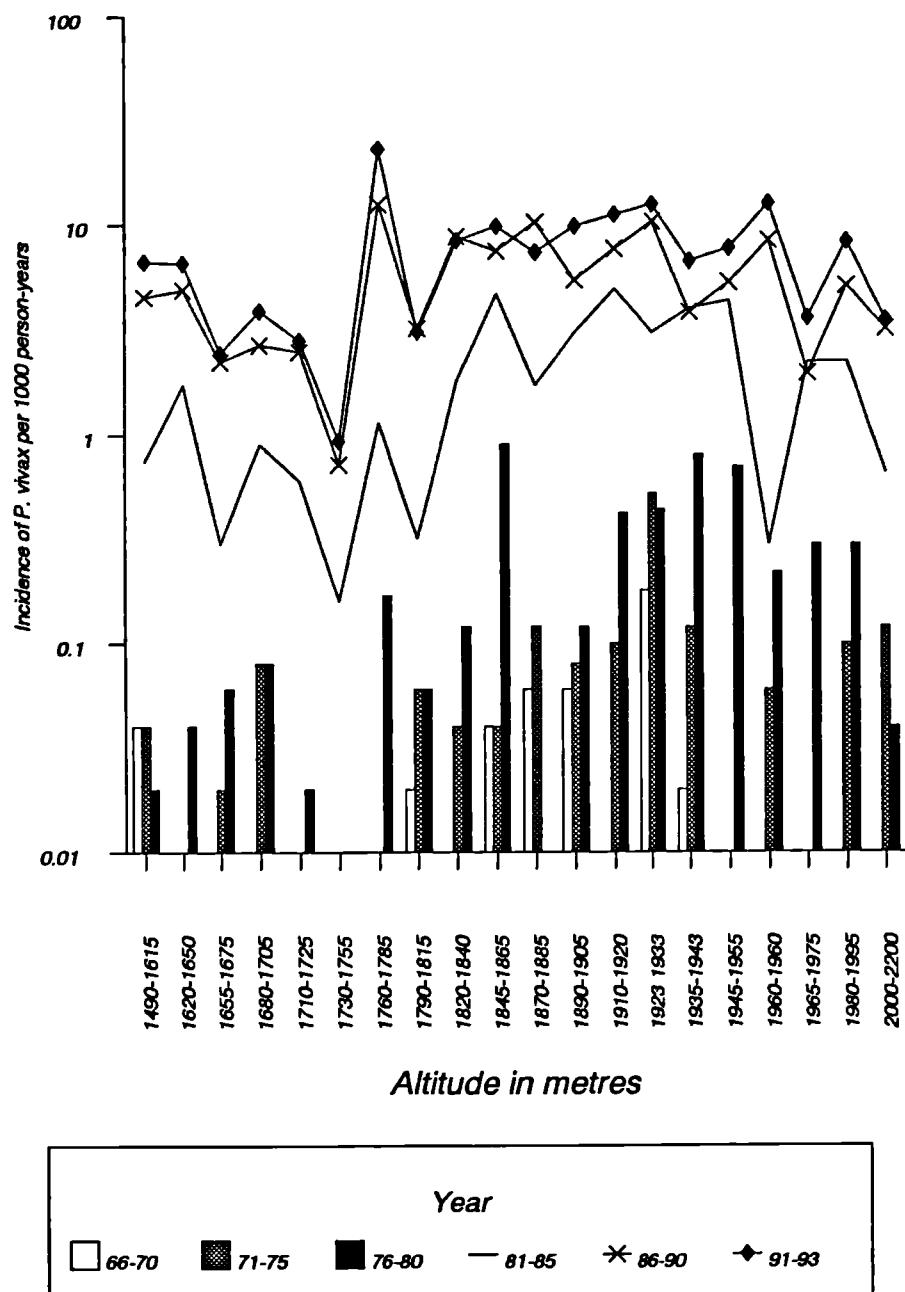
#### **4.4.2 Changes in incidence of vivax malaria in relation to altitude from 1966-1993**

The incidence of vivax malaria also seems to have increased markedly over the past decade in Debre Zeit sector. But, the increase in incidence of *P. vivax* seems to have occurred at least five years earlier than the increase in *P. falciparum* incidence in the sector. While a marked increase in incidence of *P. falciparum* malaria was seen since 1986 as depicted in Figure 4.1, a very marked increase in the incidence of *P. vivax* was seen since 1981 as shown in Figure 4.2.

The incidence of *P. vivax* malaria appeared to be limited to localities lying below an altitude of 1,945 metres before 1970 as shown in Figure 4.2. But, this upper limit was extended to localities lying up to an altitude of 2,200 metres above sea level by 1975. Thereafter, there was a progressive rise in incidence of vivax malaria that reached a peak during the 1991-1993 period.

The rise in incidence was more marked in localities lying above 1,755 metres. Here also, localities lying at altitudes between 1,760 and 1,785 metres showed the greatest incidence of *P. vivax* malaria during the 1986-93 period. This could not be explained by the effect of altitude alone.

**Figure 4.2** Incidence of *P. vivax* at 5 yearly intervals from 1966 to 1993 in  
*Debre Zeit sector plotted against altitude*



#### **4.4.3 Altitude effects on prevalence of falciparum malaria**

Data based on systematic cross-sectional annual blood survey results from 1974 to 1987 were used to calculate prevalence. A total of 148,184 slides were examined. An average of 80 localities and 11,399 persons were screened annually in Debre Zeit sector. A general trend of decreased prevalence was seen with increasing altitude as shown in Figure 4.3a. Note in the figure that mean altitude of a cluster of 20 localities is represented on the Y axis while the X axis shows the actual prevalence of falciparum malaria in each cluster.

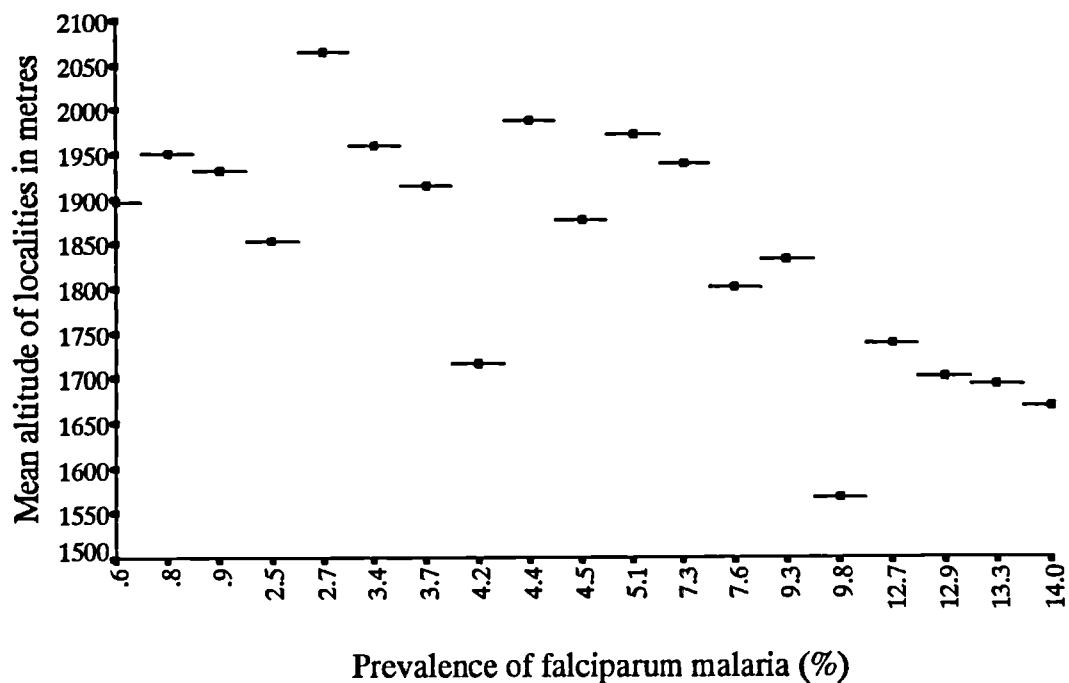
Peak prevalence of *P. falciparum* malaria was seen in localities lying at altitude range of 1,650 and 1,700 metres. A second peak was seen in localities lying at an altitude range of 1,700 and 1,800 metres. Localities lying at altitude between 1,900 and 2,000 metres showed a very low prevalence of *P. falciparum* malaria.

Figure 4.3b depicts the impact of an increase in altitude on the prevalence of falciparum malaria. Note that there is a strong negative correlation between altitude and prevalence. As altitude increased by about 100 metres there was a steep fall in prevalence of falciparum malaria that appeared strongly unlikely to have been due to chance ( $r = -0.75$ ,  $t = 4.81$ ,  $P < 0.001$ , d.f. = 18).

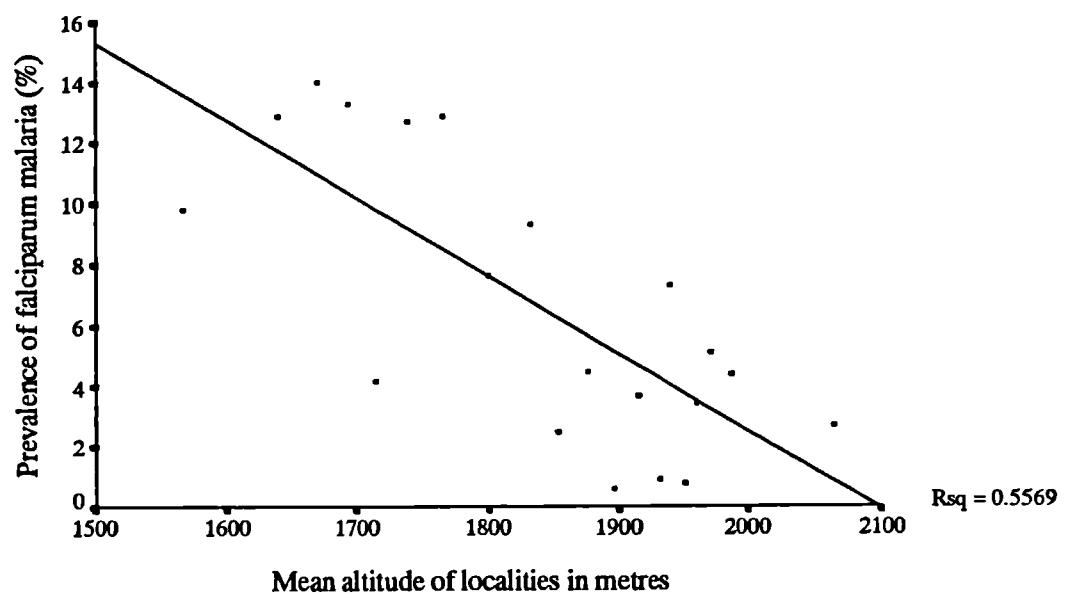
Figure 4.4 shows a dot map of the overall prevalence of falciparum malaria by locality during the cross-sectional blood surveys. Each dot represents the prevalence of falciparum malaria in a locality lying at a certain altitude. Here, it is notable that the number of localities surveyed was very variable at each range of altitude with few localities represented from 1,500 to 1,600 metres and from 2,000 to 2,200 metres. The prevalence of falciparum malaria by locality appeared to vary a lot even in localities lying at a similar range of altitude. However, the lack of a clear correlation of prevalence by locality and altitude as seen in the dot map in Figure 4.4., in contrast to the one seen above for a cluster of 20 localities in a range of altitude in Figures 4.3a & 4.3b, may be due to the small size of the population sampled in each locality during the blood surveys thereby inflating the prevalence. In the case of the latter, prevalence was standardised by population size and altitude that helped to demonstrate a strong negative correlation between altitude and prevalence of falciparum malaria.

Furthermore, the prevalence of *P. falciparum* malaria was shown to vary a lot with time. Peak prevalence was observed in 1980-81 and 1987. A persistent increase in the prevalence of falciparum malaria was seen since 1983 which appeared to have reached epidemic proportions in 1987 as discussed in Chapter 3. Thus, it seemed clear that the risk of increased malaria transmission was particularly high during certain years. This suggested that factors other than altitude may be responsible for the abnormal peaks in the observed prevalence of malaria during certain years.

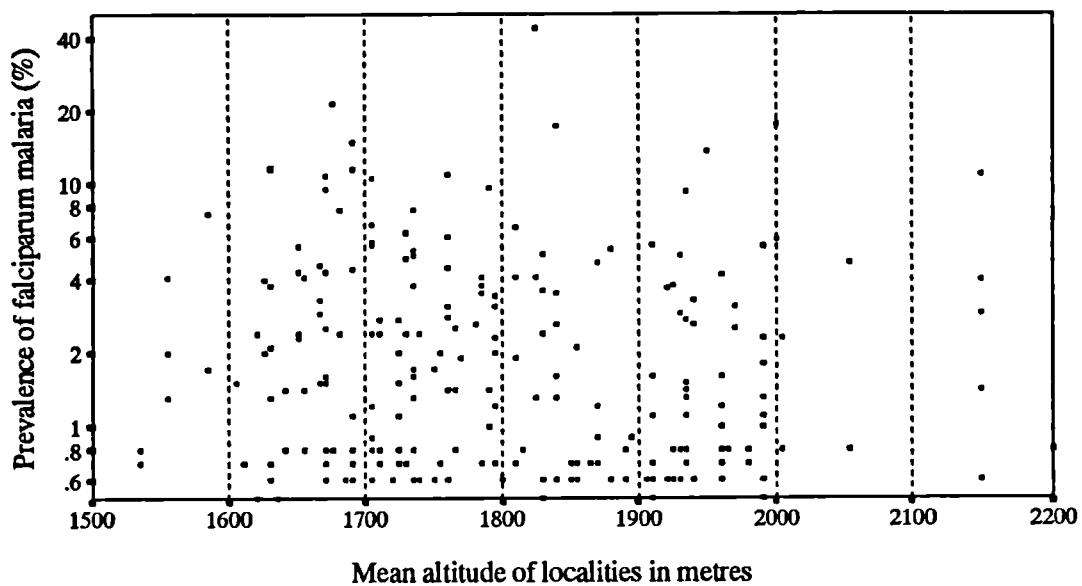
**Figure 4.3a** Altitude effects on prevalence of *P. falciparum* in Debre Zeit sector



**Figure 4.3b** Altitude effects on prevalence of falciparum malaria



**Figure 4.4** Dot map of prevalence of falciparum malaria by locality and altitude

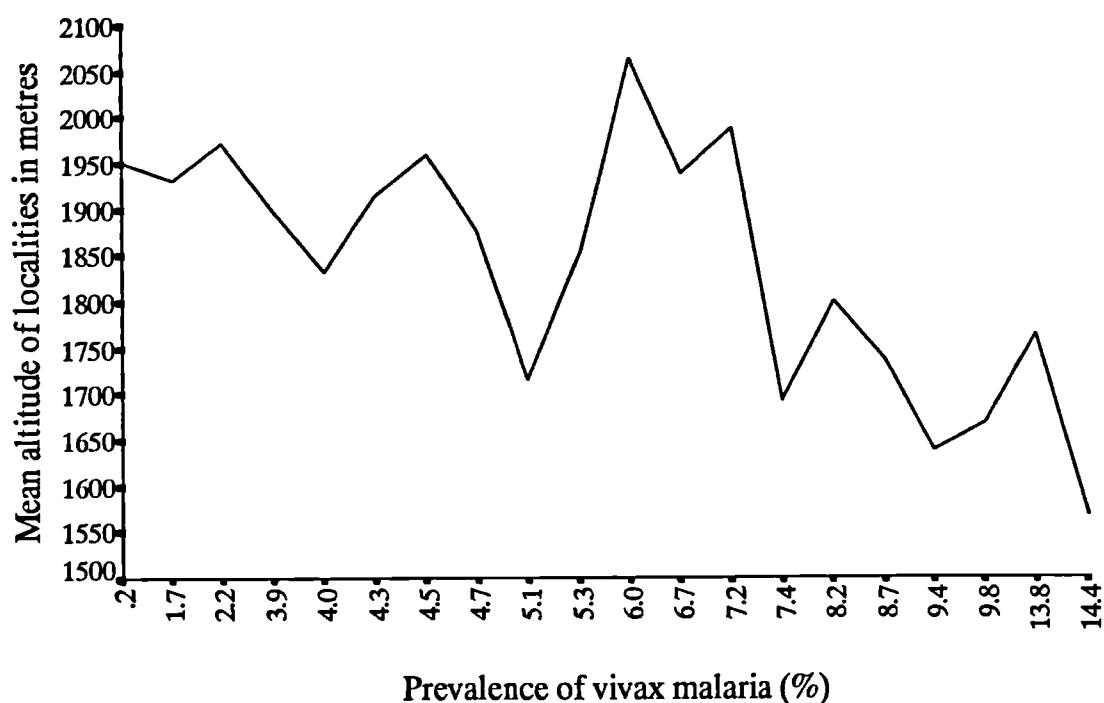


#### 4.4.4 Altitude effects on prevalence of vivax malaria

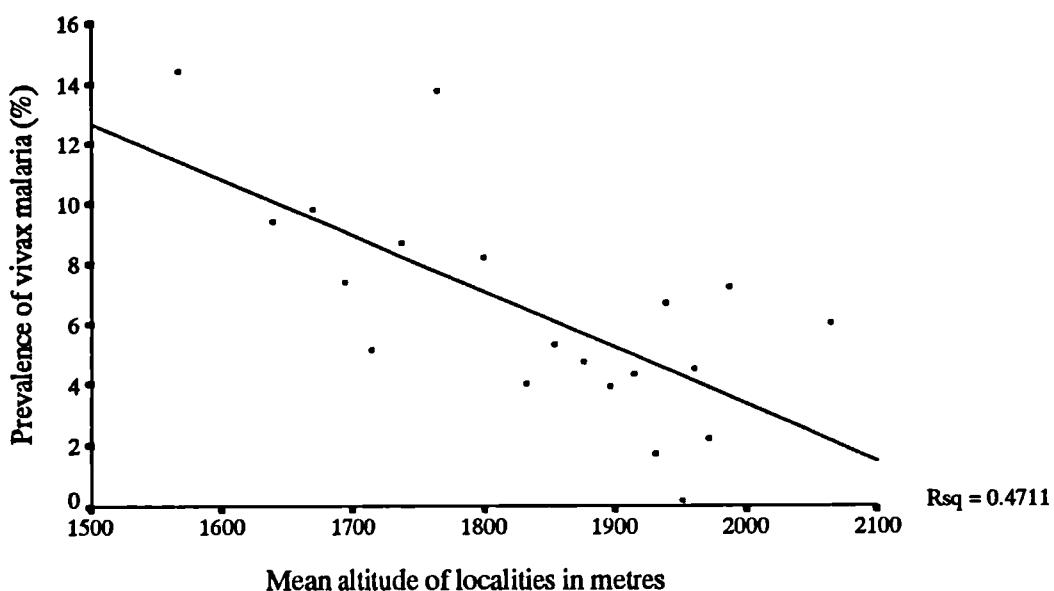
The prevalence of vivax malaria also decreased with increasing altitude as shown in Figure 4.5a. Two peak prevalence rates occurred with *P. vivax*. These peaks were seen in localities lying at altitude range of 1,500 and 1,600 as well as in localities lying between 1,750 and 1,800 metres. The lowest prevalence was seen in localities that lie at about 1,950 metres. Figure 4.5b depicts the effect of altitude on the prevalence of vivax malaria. As in the case of falciparum malaria, prevalence seemed to vary inversely with altitude, i.e., as altitude increased the prevalence of vivax malaria fell sharply which seemed highly unlikely to have been due to chance ( $r = -0.69$ ,  $t = 4.04$ ,  $P < 0.001$ , d.f. = 18).

The prevalence of *P. vivax* malaria also varied markedly with time as discussed in Chapter 3. Peak prevalence of vivax malaria was seen in 1981. This year appeared to be the time during which a major epidemic of *P. vivax* malaria occurred in relation to the prevalence noted between 1974 and 1987. Furthermore, a gradual rise in prevalence of *P. vivax* seemed to occur since 1984. Thus, it was also likely that factors other than altitude may have affected the fluctuation in the prevalence of vivax malaria in Debre Zeit sector.

**Figure 4.5a Altitude effects on prevalence of *P. vivax* in Debre Zeit sector**



**Figure 4.5b Altitude effects on the prevalence of vivax malaria**



#### **4.4.5 Altitude effects on the relative frequency of malaria parasites**

The relative frequency of species was obtained by calculating the proportion of slide-confirmed malaria cases. The proportion of the two species observed in each stratum during the period January 1966 to September 1993 was calculated. Results are depicted in Figure 4.6 as seen below.

The greatest proportion of *P. falciparum* malaria was seen in localities lying between 1,700 and 1,750 metres. The least proportion of *P. falciparum* was seen in localities between 1,900 and 1,950 metres. A general trend of decreased proportion of *P. falciparum* malaria with increasing altitude was seen. However, there was an increase in the proportion of *P. falciparum* in localities found between 1,950 and 2,100 metres.

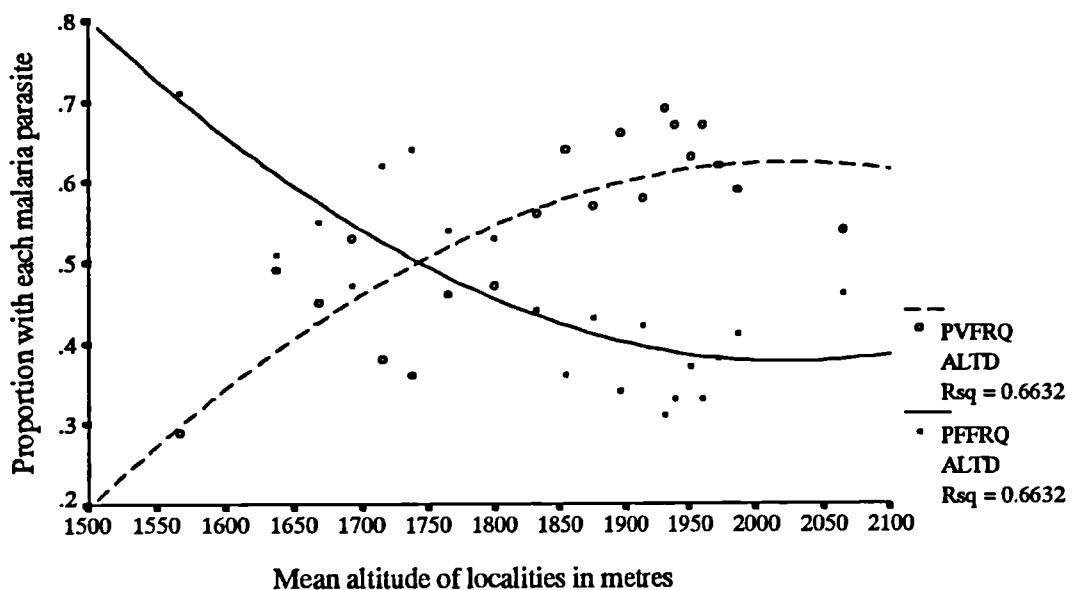
Thus, it may be that some factor other than altitude influenced the occurrence of an increased proportion of *P. falciparum* in these localities found at the upper limit of malaria transmission in the highlands.

A peak proportion of *P. vivax* malaria was seen in localities lying between 1,900 and 1,950 as depicted in Figure 4.6. The least proportion of *P. vivax* was seen in localities lying between 1,500 and 1,650 metres. These localities were places in which an opposite observation was made with regard to the proportion of *P. falciparum*.

A general trend of increased proportion of *P. vivax* malaria was seen with increasing altitude. However, the proportion of *P. vivax* seemed to be decreasing with increasing altitude in localities lying between 1,950 and 2,100 metres. This was the altitude range at which a recent establishment of *P. falciparum* took place. It seemed that there was a factor other than altitude that was more favourable for the occurrence of *P. falciparum* in such high altitude areas during recent years.

Overall, the likelihood of observing *P. falciparum* increased in localities lying below 1,750 metres. On the other hand, *P. vivax* appeared in a greater proportion in localities above 1,800 metres. In localities found between this altitudinal range, the proportion of both species may be about equal.

**Figure 4.6 Altitude effects on the relative frequency of *P. falciparum* and *P. vivax* in Debre Zeit sector**



#### 4.4.6 Altitude effects on reported outbreaks of malaria

An attempt was made to see the effect of altitude on the occurrence of outbreaks of malaria. These were based on the reports of local residents or health personnel. A team of investigators was sent to identify the cause of the outbreaks and manage it according to the results.

Examination of records of outbreak reports during the 1975-1993 period showed that malaria outbreaks occurred only in 1980-81, 1988-89, and 1991-92. The localities in which these outbreaks occurred were sorted by altitude and the result was plotted to

see whether a trend of an increased frequency of outbreaks at high altitude localities emerged as shown in Figures 4.7 and 4.8.

As shown in Table 4.1 and Figure 4.7, the outbreak of falciparum malaria was limited to localities lying below 1,960 metres in the year 1980. Peak prevalence in 1980 was seen in communities residing in localities lying at altitudes between 1,490 to 1,615 metres. In 1981 reported outbreaks of falciparum malaria were limited to localities lying below 1,995 metres. Peak prevalence of *P. falciparum* malaria occurred in localities lying between 1,815 and 1,840 metres of altitude in 1981. But, a less marked peak also occurred in localities lying between 1,845 and 1,865 metres of elevation.

In 1988, the outbreak was more widespread and it affected communities residing in localities lying up to 2,200 metres. But, peak prevalence of *P. falciparum* malaria occurred among communities residing in localities lying between 1,910 and 1,920 metres, i.e. about 55 to 65 metres higher than what was seen during the previous peak in 1981.

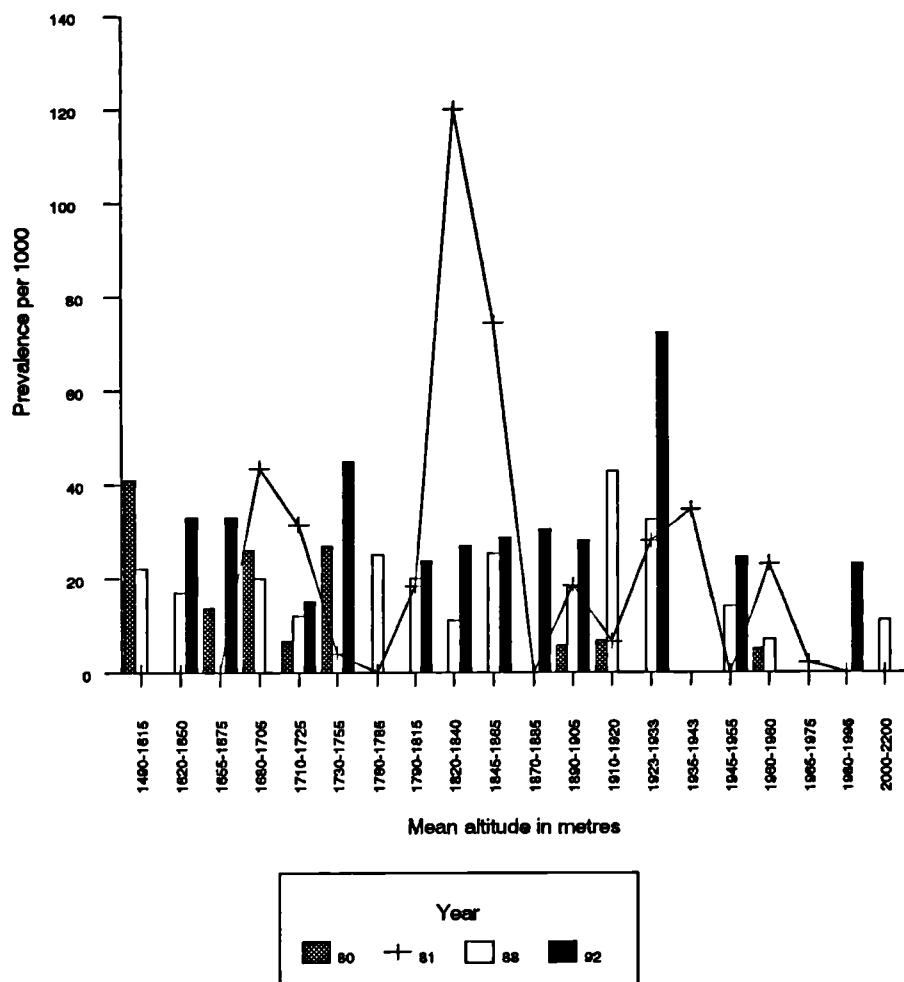
The outbreak in 1992 was also extensive but peak prevalence occurred among communities residing in localities lying between 1,923 and 1,933 metres; i.e. some 13 metres higher than what was seen during the outbreak in 1988. It therefore seemed that more and more people residing in localities lying at increasingly higher altitudes were affected during successive outbreaks in recent years.

The pattern of outbreaks of *P. vivax* malaria was also sorted by altitude and plotted as shown in Figure 4.8. As shown here, it seemed that the outbreak in 1980 was limited to localities lying below 1,960 metres. In 1981, the outbreak of *P. vivax* malaria extended to localities lying up to 1,965 metres. The outbreak of *P.vivax* malaria in 1988 appeared the most widespread and affected communities residing in localities lying up to 2,200 metres of altitude. In 1992, the outbreak of *P. vivax* malaria affected people living in localities lying up to 1,965 metres.

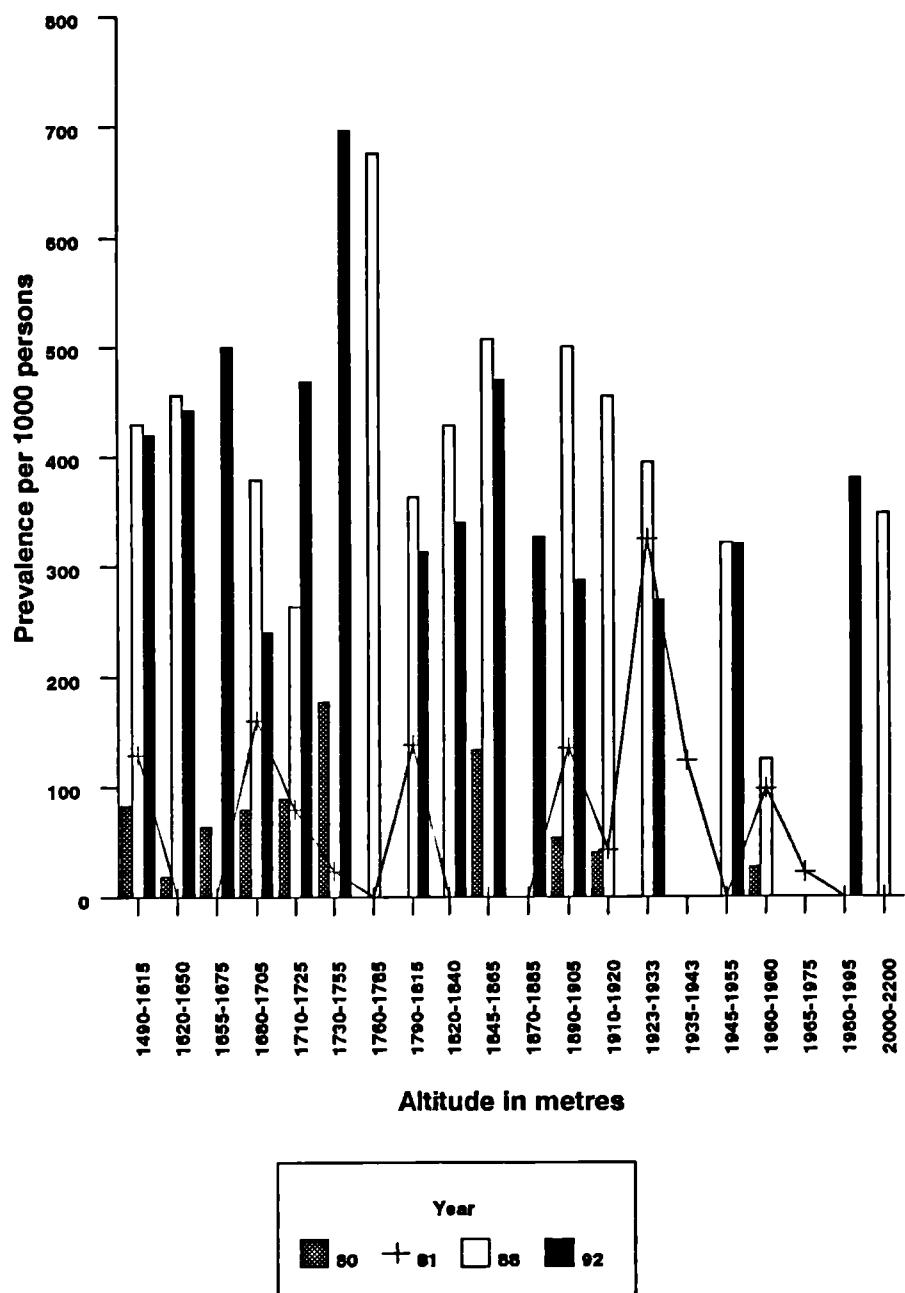
**Table 4.1 Altitude effects on peak prevalence of *P. falciparum* in reported outbreaks**

<i>Year</i>	<i>Altitude range</i>
1980	1,490 to 1,615 metres
1981	1,820 to 1,840 metres
1988	1,910 to 1,920 metres
1992	1,923 to 1,933 metres

**Figure 4.7 Altitude effects on occurrence of *P. falciparum* in Debre Zeit sector**



**Figure 4.8 Altitude effects on occurrence of *P. vivax* outbreaks in Debre Zeit sector**



#### **4.5 Discussion**

Early observations by epidemiologists and entomologists in the Malaria Eradication Service in Ethiopia concluded that the critical altitude up to which malaria transmission in Ethiopia occurred was 2,000 metres above sea level (Chand, 1965). Nevertheless, results of the present study suggest that this may have been exceeded as evidenced by the existence of both *P.falciparum* and *P. vivax* malaria in localities lying up to an altitude of 2,200 metres above sea level.

The mean annual reported incidence of *P.falciparum* malaria was 35 per 10,000 person-years while that of *P.vivax* malaria was 40.2 per 10,000 person-years during the period 1988-93 in a cluster of 20 localities lying between 2,000 and 2,200 metres. At present, this may be the upper edge of transmission of malaria due to both species in Debre Zeit sector. However, it may be possible that the actual incidence of falciparum malaria in the community was higher than is seen in this analysis because of a possibility of under-reporting for reasons related to limited access to health facilities by patients suffering from the disease.

Peak prevalence of reported outbreaks of falciparum malaria was noted among communities living in localities lying at a maximum altitude of 1,615 metres in 1980. This was extended to 1,840 metres after one year in 1981. There was a more extensive and further spread of reported outbreaks of falciparum malaria in which peak

prevalence was observed in localities lying up to 1,920 metres in 1988. This peak prevalence during reported outbreaks of falciparum malaria was then extended to localities lying up to a mean altitude of 1,933 metres in 1992.

The demonstration of an increased incidence of both falciparum and vivax malaria since 1981 with an abrupt and persistent increase since 1987 in all localities lying at different altitudes may suggest the existence of a common agent/agents somewhere in the causal path-way which aggravated the transmission of malaria in the community. These factors will be examined in subsequent chapters.

The introduction of infection due to malaria by a massive influx of semi-immune reservoirs of infection from localities in low-lying endemic areas and hence an increased transmission of malaria in these highlands (Tulu, 1989), appeared unlikely. This was based on data on usual place of residence of patients which showed that 93.2% of the patients were from Adea and Lume districts which were two of the nearest districts to the diagnostic centre in Debre Zeit sector.

The observation that a greater proportion of falciparum malaria was noted below 1,750 metres and vivax malaria above 1,800 metres may be due to the inhibition (through decreased ambient temperature) of sporogony of *P.falciparum* up to a certain critical threshold altitude. Above this altitude, the sporogony of *P. vivax* has an advantage in the *Anopheles* vector.

An increased incidence of malaria in the highlands of Madagascar in 1987 was attributed to an increase in the distribution and density of local vectors, *An. funestus* and *An. arabiensis*. This was ascribed to the heavy rains and lack of vector control measures (Raharimalala et al., 1993). The pattern of malaria was described as endemo-epidemic. In Kenya, an increased mortality due to malaria by 8.6 times and morbidity by 3.7 times was reported in a highland district that borders the Lake Victoria basin (Some, 1994). The increase in morbidity and mortality rate was relative to the average seen during months of previous years (1985-1989) that preceded the epidemic. But, no attempt appears to have been made to measure the altitude up to which transmission occurred. The exact cause of the epidemic of malaria in the highlands of Kenya was not identified.

The 1987 malaria epidemic in Rwanda affected villages lying up to 1,700 metres (Loevinsohn, 1994). The increase in incidence of malaria and the resulting high mortality was seen mostly in children less than two years of age. These children lived in the high zone. The altitude range between the high and low zone was 110 metres. It was reported that the case fatality rate was greatest in children because of their lack of immunity related to malaria. But, recent establishment of malaria in an area would be expected to affect all age groups, including adults, due to the absence of malaria-specific immunity.

Malaria transmission in Ethiopia was thought to be absent above 1980 metres when Sir Gordon Covell conducted his surveys in 1955 (Covell, 1957). This was refuted during the 1958 epidemic when many localities lying up to an altitude of 2,150 metres were affected. Both the vector, *An. gambiae s.l.* and the malaria parasites, *P.falciparum* and *P. vivax* were seen during investigation of the epidemic in these localities (Fontaine et al., 1961). *An. gambiae s.l.* was abundant from June to September, 1958.

Thus, it seems the altitudinal limit of malaria transmission in the epidemic zone varies from year to year depending on whether other conditions favourable for transmission occurred. The great majority of the population in Ziquala and Akaki which were then estimated at 150,000 were affected by this epidemic. These were two of the four districts included in the present study area. The altitudinal limit of this epidemic was reported to be between 2,000 and 2,150 metres.

The climatic conditions during the 1958 epidemic were reported as extreme. Average relative humidity which was usually 50% in the cool highlands rose to 60% in 1958. Average day-time temperatures also were higher than those reported during any of the previous 35 years. Both maximum day-time temperatures and minimum night-time temperatures were also reported higher than those observed in any previous year. Abnormally high rainfall was also recorded during the 1958 epidemic. Rainfall was not only high during the wet season but it was also recorded in appreciable amounts during the normally dry season (Fontaine et al., 1961).

However, there was no detailed analysis of the relation between this epidemic and the climate conditions in the country. The exact level of temperature and rainfall which favoured the epidemic was not analysed in relation to the incidence of malaria. Thus, no strategy for the early recognition and containment of such an epidemic of malaria was developed. A focused analysis of the climatic conditions during this epidemic will be undertaken in the chapter that deals with climate in Debre Zeit sector.

The absence of *falciparum* malaria before 1976 in localities lying above 1,975 metres was noted in the present study. Furthermore, a progressive appearance of this species was also seen in localities lying at higher altitudes particularly since 1986. This may be due to some factor other than altitude that affected the distribution of malaria in high altitude localities.

In his analysis of the cause of the epidemic in villages lying at high altitudes in Rwanda, Loevinsohn (1994), concluded that climatic warming and particularly the increase in minimum ambient temperature in 1987 was responsible for the increased incidence of malaria. Although the occurrence of the epidemic was favoured by a suitable climate, it is possible that non-climatic factors such as the level of development of preventive health services in the early recognition and containment of this epidemic, availability of an alternative antimalarial for chloroquine resistant *P. falciparum* cases may have affected the magnitude and severity of the epidemic.

The finding that a greater increase of vivax malaria was noted in villages lying at higher altitudes in the current study may be attributable to a higher threshold of the critical temperature required for the extrinsic development of *P.vivax*. A progressive rise in incidence of falciparum malaria at increasingly higher altitudes suggests the creation of a more conducive environment for vector breeding, sporogonic development of the parasite in the *Anopheles* vector and the presence of susceptible hosts to maintain transmission.

The absence of a clear altitude gradient in relation to the incidence of both vivax and falciparum malaria in Figures 4.1 and 4.2 may be related to the fact that patients living near the diagnostic and treatment centre in Debre Zeit had a greater opportunity for case detection and treatment facilities than those living in more remote areas with no diagnostic services. This is supported by the observation that 93% of all the patients seen were from Adea and Lume districts while the remainder were from two other districts in Debre Zeit sector, Liben-Ziquala and Akaki. The latter two districts generally lie at a much higher altitude than the former. This could also explain why there was a strong negative correlation between altitude and prevalence of both falciparum and vivax malaria in the data from active blood surveys as seen in Figures 4.3b and 4.5b in contrast to the data from passive surveillance. The blood surveys were conducted in all representative localities in each of the four districts found in the sector during the peak transmission season irrespective of the distance of localities from the diagnosis and treatment centre.

#### **4.6 Summary**

The transmission of malaria in Ethiopia seems to be determined by altitude and climate. Localities lying between 1,500 and 2,200 metres appeared prone to epidemics. These epidemics were reported to be associated with abnormal weather conditions such as high rainfall, high day-time maximum temperature, high night-time minimum temperature, and high relative humidity during certain years. A negative correlation was demonstrated between altitude and prevalence of both *falciparum* and *vivax* malaria that appeared highly unlikely to have been due to chance. Furthermore, the relative frequency of *P. falciparum* malaria decreased with increasing altitude while that of *P. vivax* increased with increasing altitude. There was a progressive rise in the incidence of *P. vivax* since 1981. A very dramatic rise in the incidence of *P. falciparum* was seen since 1986. Some localities lying at higher altitudes, particularly those between 2,000 and 2,200 metres, appeared at risk of transmission of malaria for the first time during the past decade only. Outbreaks of malaria were increasingly being reported in localities lying at high altitudes. The factors that contributed to this marked rise in incidence of malaria in the highlands will be the subject of further analysis and discussion in subsequent chapters.

## **Chapter 5**

### **Climate patterns in Debre Zeit**

#### ***5.1 Introduction***

The detrimental effects of climate extremes, particularly the shortage of rainfall, in rural highland communities in Ethiopia with subsequent drought and famine, appeared to have a link with political upheavals, mass migrations and major health crises (Nurhussein and Leonidas, 1985). Amongst other socio-economic factors, the downfall of Emperor Haile Selassie was attributed to the famine in 1973 which is estimated to have claimed 300,000 lives. The Emperor was accused of negligence that resulted in mass up-rising which ended in a bloody coup d'etat by the military.

The Military Government which overthrew the Emperor, was forced to resettle about 600,000 non-immune highland people in highly endemic malarious areas as a result of the 1984 drought and famine (Tulu, 1989). Some 7.9 million people starved and 1 million people are estimated to have died during the 1984 famine (Department of State, U.S.A., 1988). This, and other factors particularly overpopulation, land degradation and famine in the northern highlands were the subject of subsequent

heated national debate among politicians which resulted in the demise of the military government.

Leaving aside the political consequences of climate extremes, particularly drought and famine in Ethiopia, the present chapter tries to examine the pattern of rainfall, relative humidity and temperature in the central highlands of Ethiopia. As discussed in Chapters 1 and 4, both climate and altitude seemed to determine the distribution of human populations and disease vectors in Ethiopia. The highlands are generally characterised by greater density of the population and the incidence of malaria is relatively low. In contrast, the lowlands are sparsely populated and the incidence of malaria and other tropical diseases is high. However, this traditional pattern has changed most dramatically since the late 1980's with a high incidence of malaria of epidemic proportions in most highland communities in Ethiopia.

A recent supplementary report to the Intergovernmental Panel on Climate Change (IPCC) Scientific Assessment revealed that a decadal mean anomaly of +0.22 °C occurred during the 1981-90 period relative to the 1951 to 1980 mean when world wide anomaly patterns of climate were analysed (IPCC, 1992). However, this increase in the mean temperature varied between regions and months. The 1980's were up to 1 °C warmer than the 1951-1980 climatology in northern China. During the months of December, January and February from 1980 to 1990, very large positive anomalies, exceeding 1 °C were recorded over the high latitude Northern Hemisphere continents,

with centres of over 2 °C. Furthermore, it was reported that the observed warming over the past several decades was primarily due to an increase of the daily minimum (night-time) temperature with little contribution from the daily maximum (day-time) temperature.

In spite of the critical importance of climate pattern to both agriculture and public health in Ethiopia, little effort appears to have been exerted to analyse the situation and publish the results. In relation to malaria, the effect of climatic variables such as temperature, rainfall and relative humidity seem obvious. The *Anopheles* vector needs water to lay its eggs and the subsequent developmental stages of larvae and pupae are all water dependent. This aquatic environment is commonly provided by small water collections after the rains. A suitable water temperature is also required for breeding which if either too cold or too hot inhibits development of the aquatic stages of the vector. Furthermore, the development (extrinsic incubation) of the *Plasmodium* parasite in the *Anopheles* vector is sensitive to ambient temperature. It is 22 days at 20 °C, 15 to 17 days at 23 °C, and 9 to 11 days at 25-28 °C. The longevity of the *Anopheles* vector seems to be dependent on a suitable relative humidity, and 70-80% relative humidity is thought to be ideal ( Bruce-Chwatt, 1985).

From the foregoing, it is clear that the density and longevity of *Anopheles* vectors as well as the distribution of malaria are all sensitive to changes in climatic conditions. Furthermore, the livelihood of rural subsistence farmers is very much dependent on

the availability of the rains each season for planting crops. Both planting and harvesting seasons may increase the human-vector contact due to increased human activity on the farms, coupled with increased density of vectors. This is known to have increased the incidence of malaria during these seasons as discussed in Chapter 3. Thus, it was thought that a more detailed study of the climatic pattern in Debre Zeit sector was necessary to shed some light on the specific climatic factors associated with the increased incidence of malaria in the past two decades.

## ***5.2 Objectives***

Over the past four decades, this section aims to:

- a) describe the seasonal pattern in day-time (maximum) and night-time (minimum) temperature, rainfall and relative humidity
- b) describe long term trends in maximum temperature, minimum temperature, rainfall, and relative humidity

## ***5.3 Data sets and methods of analysis***

A total of 1,500 monthly records from four weather stations obtained from the National Meteorology Service were examined; namely Bole, Debre Zeit, Mojo and Nazareth. But, due to irregularity of records and incompleteness of data it was

decided to use data from Debre Zeit station which was the most complete. Monthly records of mean maximum temperature and mean minimum temperature in degrees Celsius, relative humidity in per cent, and rainfall in millimetres collected during the January 1951 to April 1993 period were analysed. The total number and percentage of missing monthly records out of the expected total 507 records from January 1951 to April 1993 for each of the four climate variables is shown in Table 5.1 .

**Table 5.1 Missing records for each of the four climate variables at Debre Zeit weather station**

<i>Climate variable</i>	<i>Number of missing records</i>	<i>% missing (N = 507)</i>
Day-time temperature	19	3.7
Night-time temperature	15	2.9
Rainfall	11	2.2
Relative humidity	81	15.9

A series of steps were followed to examine the monthly data for each of the four climatic variables. Firstly, a histogram was plotted to see the frequency distribution of observed values of the relevant climate conditions. Secondly, the long term monthly means over the past 42 years were calculated and plotted to describe the seasonal pattern during the twelve months of the year. Thirdly, missing values were replaced with the mean of each series in SPSS/PC+ Trends. Fourthly, time-series plots of consecutive monthly values were done to observe if there was any evidence of periodic fluctuations of climate conditions over the long term. Finally, positive and negative deviations of the observed values from the long-term monthly mean were plotted to look for any evidence of changes over a longer term, i.e. during the past 42 years. These deviations (anomalies) of the observed values in each month were calculated relative to the 1951-80 mean of each climatic variable to standardise the data and observe the magnitude of increase based on the standard used by the IPCC Scientific Assessment (IPCC, 1992).

## **5.4 Results**

### **5.4.1 Monthly mean day-time (maximum) temperature**

Some 488 monthly records of mean maximum temperature observed from January 1951 to April 1993 with 96.3% coverage of the period were used . The overall mean monthly maximum temperature was 26.19 °C. The median monthly maximum temperature was 26.2 °C. The standard deviation was 1.74 °C. The frequency of

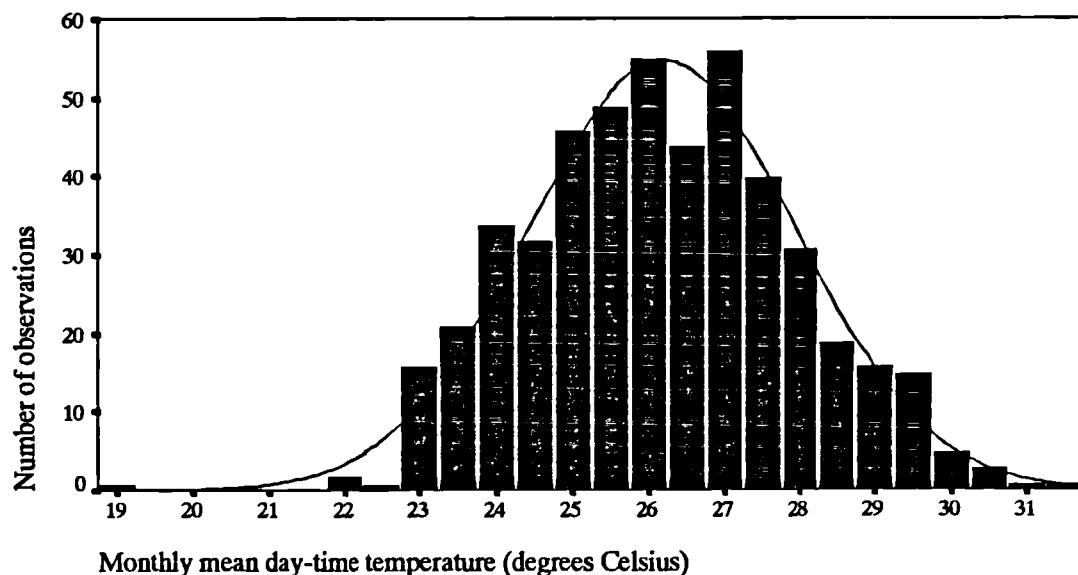
monthly mean day-time temperature seen over 42 years is depicted in the histogram in Figure 5.1.

A monthly mean day-time temperature of about 26 °C was the most frequent observation. It is also notable from the histogram in Figure 5.1 that monthly mean day-time temperatures below 23 °C and above 30 °C were relatively rare although a range of day-time temperatures between 19 °C to more than 31 °C were observed. But, the month and year during which such extreme monthly mean day-time temperatures occurred, particularly those changes towards warmer days may be important in terms of the transmission of malaria in the presence of small water collections created after the rains in the study area. The overall seasonal pattern of day-time temperature is depicted in Figure 5.2. In general, day-time temperatures were high during the months of March, April, and May. The month of May is the warmest month. In contrast, the months of July, August, and September are cool months with August being the coolest. It is also suggested in the figure that the peaks in monthly mean day-time temperature are bimodal with the greatest peak occurring in May followed by a less pronounced peak in October.

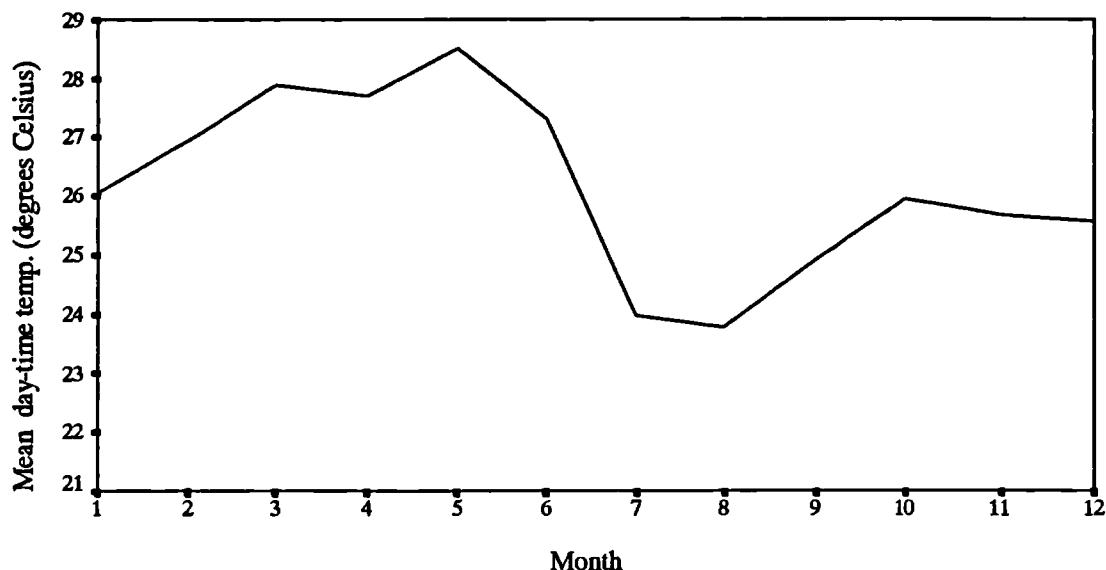
The overall pattern of the monthly mean maximum temperature was plotted as shown in Figure 5.3 which depicts the fluctuation in the monthly mean day-time temperature in the past four decades in Debre Zeit. The characteristic feature in the figure is the abnormal increase during certain years with high day-time temperatures

recorded with greater frequency since 1989. But, it is also notable that an abnormally low temperature of about 19 °C occurred particularly in July 1992. The warmest month / year during the January 1951 to April 1993 period was May 1989 with a record high monthly mean day-time temperature of 31.4 °C. Abnormally high monthly mean day-time temperature values of 30 °C and above were recorded in 1958, 1973, 1984, 1989, 1991, and 1992 in the months of March, April, May and June. It may be worth noting here that the interval during which such abnormally high maximum temperature values were observed has been progressively getting shorter from 15 years, 11 years, 5 years, 2 years and to only 1 year most recently as shown in Figure 5.3.

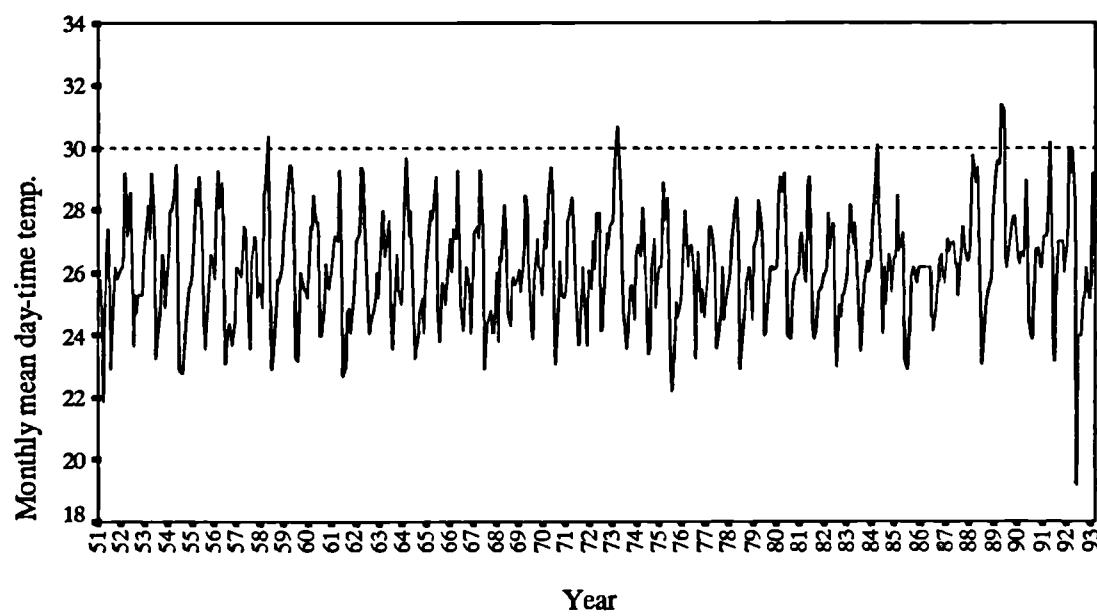
**Figure 5.1 Histogram of monthly mean day-time temperature in Debre Zeit**



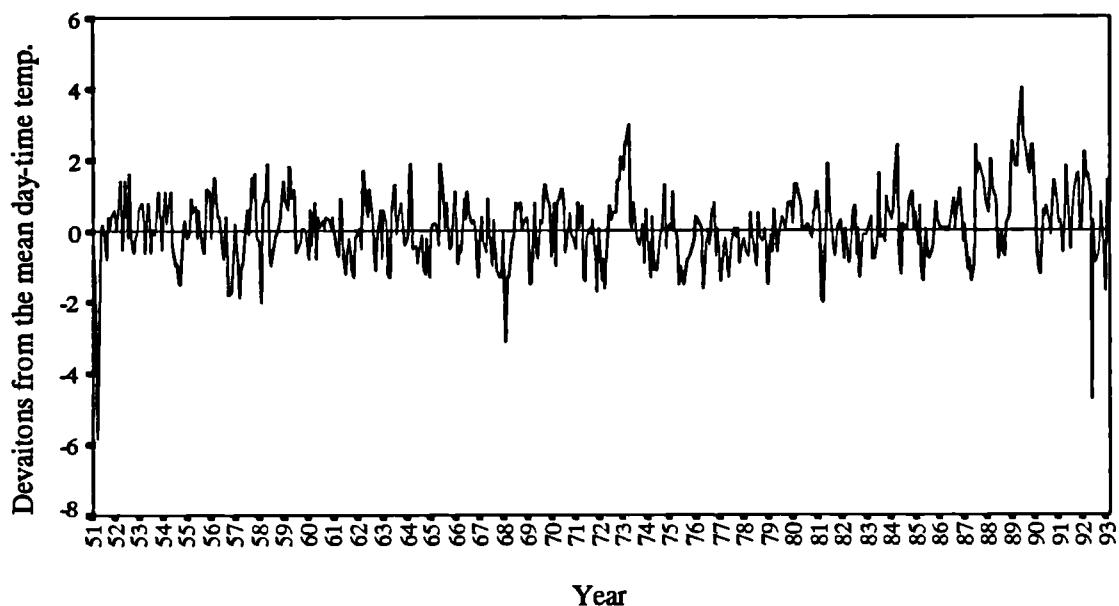
**Figure 5.2 Seasonal pattern of day-time (maximum) temperature in Debre Zeit**



**Figure 5.3 Day-time (maximum) temperature pattern in Debre Zeit**



**Figure 5.4 Deviation from the norm of monthly mean day-time temperature**

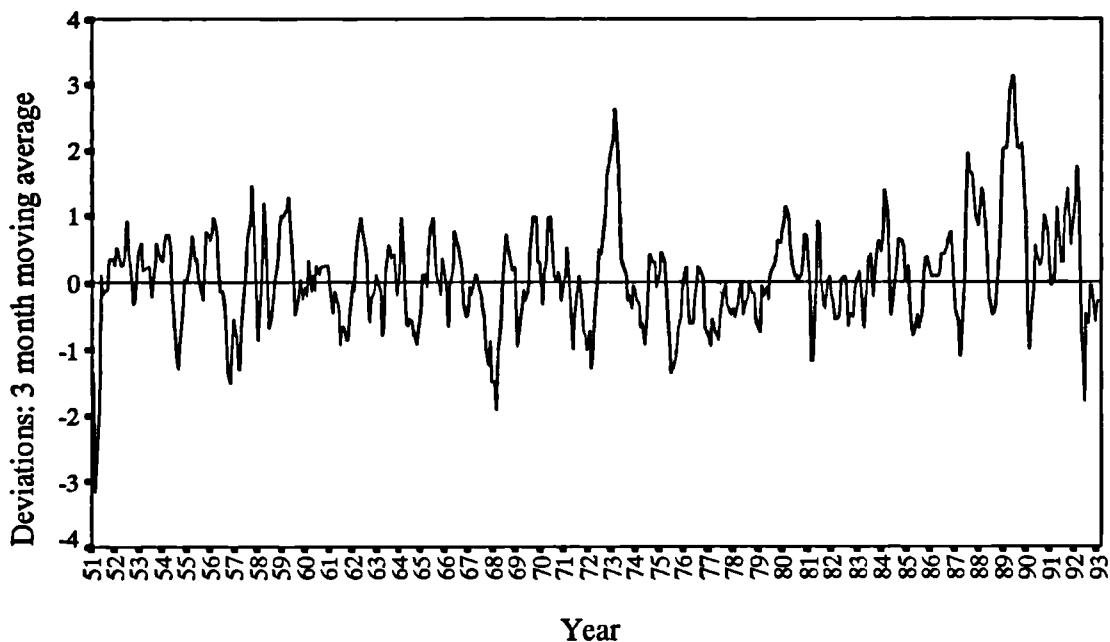


A further analysis of the data was carried out to see the pattern of deviation from the norm for each month relative to the monthly mean for that particular month from 1951 to 1980 according to the standard set by the Scientific Assessment of the Intergovernmental Panel on Climate Change (IPCC, 1992). The result of the deviation is plotted in Figure 5.4. Abnormally high positive deviations from the monthly mean of about 3 & 4 °C, which occurred in 1973 and 1989 respectively , are the most prominent features of the plot. Furthermore, an abnormally low temperature with negative deviation from the mean for the month of about -5 °C to -6 °C occurred in 1951 and 1992.

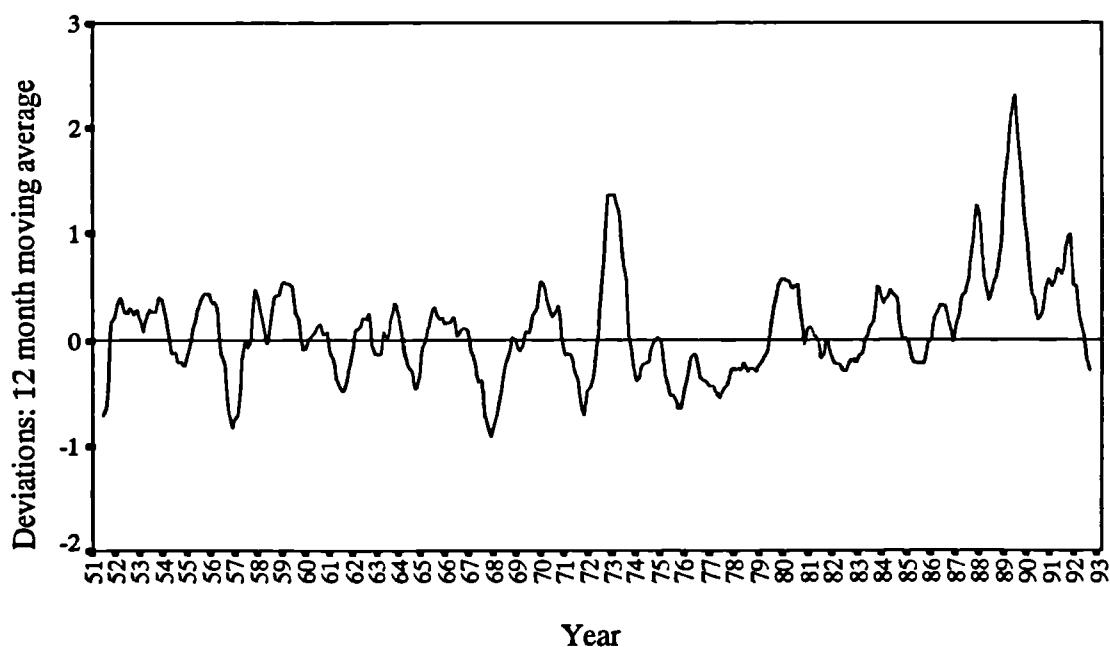
A further attempt was made to smooth the data by computing the moving average of the deviations from the mean in monthly mean day-time temperature with a span of 3 and 12 months separately. This was done to examine whether there was any underlying long term trend in day-time temperature . The results are plotted in Figures 5.5 and 5.6.

Figure 5.5 depicts that there was an abnormally hot day-time temperature in the years 1973 and 1989 in the study area. A similar trend is also shown in Figure 5.6 which confirms that these years were abnormally hot. This was generally true for most of the country in which the year 1973 was characterised by drought and severe food shortages in most of the highlands of Ethiopia as discussed in the introductory section.

**Figure 5.5 Deviations : 3-month moving average of monthly maximum temperature**



**Figure 5.6 Deviations : 12-month moving averages of maximum temperature**



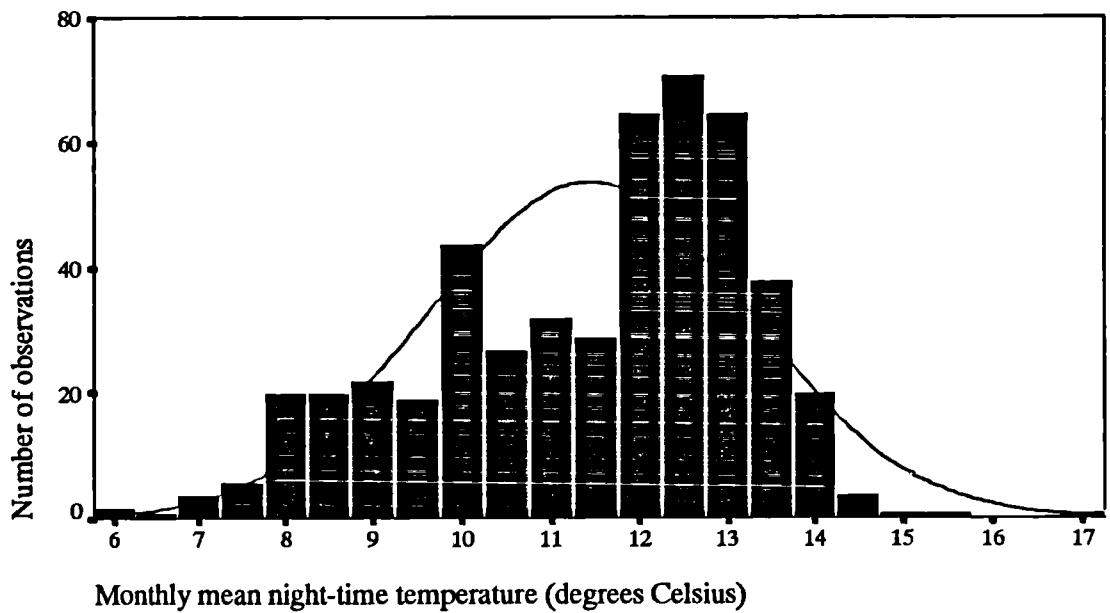
#### **5.4.2 Monthly mean night-time (minimum) temperature**

A total of 492 monthly mean night-time temperature records were used for the study.

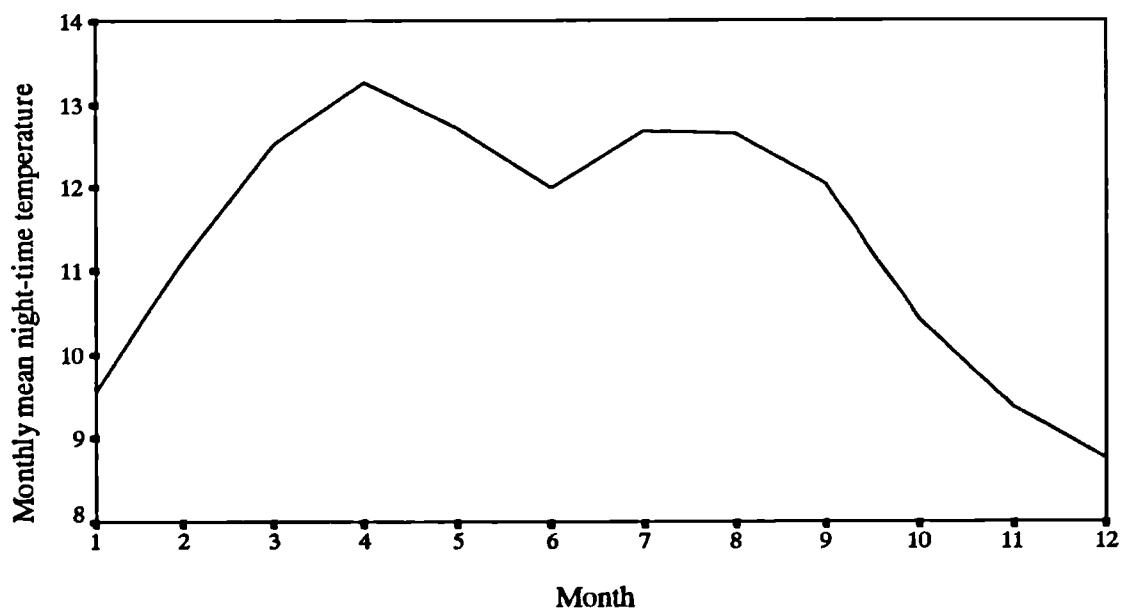
The coverage was about 97 % during the January 1951 to April 1993 period. The overall monthly mean minimum temperature was 11.43 °C, the median was 12.0 °C with a standard deviation of 1.79 °C. The general distribution of night-time temperatures observed in Debre Zeit is depicted in a histogram as shown in Figure 5.7. As seen here, night-time temperatures from 12 to 13 °C were the most frequent observations. Furthermore, although night-time temperatures ranging from about 6 to 17 °C were recorded, monthly mean night-time temperatures exceeding 14 °C and evenings below 8 °C were observed only on a few occasions.

The seasonal pattern of mean night-time temperature is depicted in Figure 5.8 by calculating the long term mean for each month. High night-time temperatures were recorded from March to August with a peak in April reaching about 13.5 °C on average. Low night-time temperatures were recorded in October, November, December and January. The month of December was the coolest with night-time temperatures of about 9 °C on average.

**Figure 5.7 Histogram of monthly mean night-time (minimum) temperature in Debre Zeit**



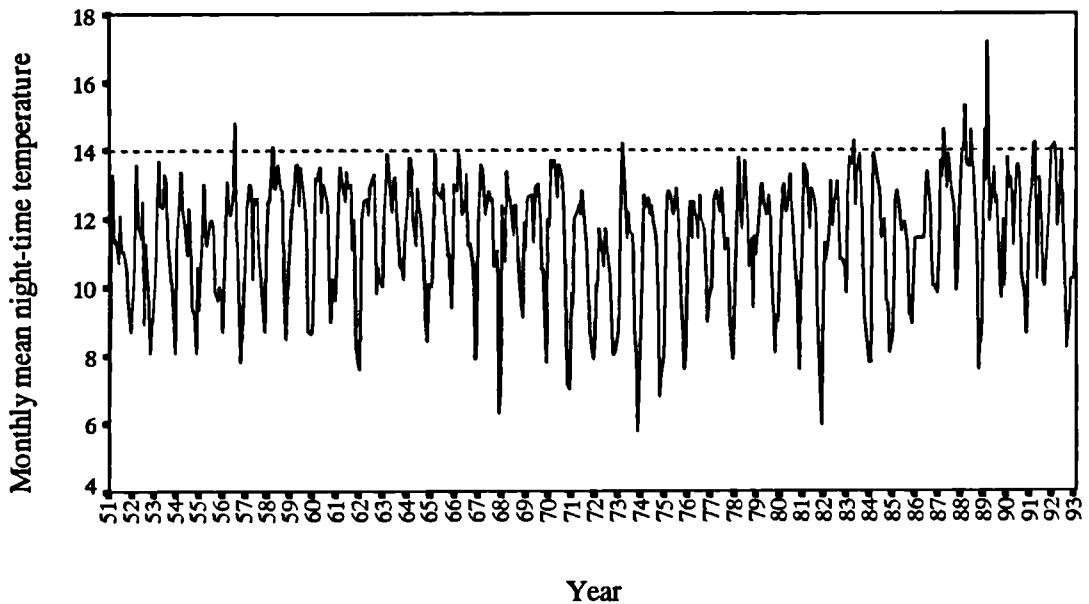
**Figure 5.8 Seasonal pattern of night-time temperature in Debre Zeit**



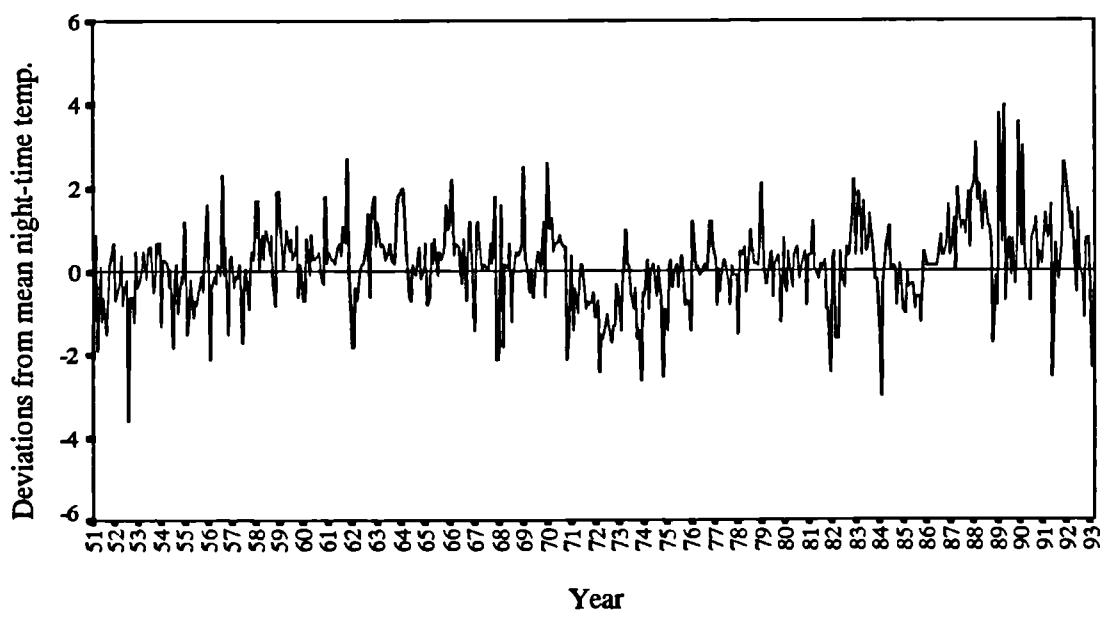
The monthly mean night-time (minimum) temperature varied a lot between the months and years. The warmest month with peak night-time temperature was April 1989 with a record high of 17.2 °C. An abnormally high night-time temperature of 15.3 °C was also recorded in April 1988. But, other abnormally high night-time temperatures of 14 °C and above occurred in 1956, 1958, 1973, 1983, 1987, 1988, 1989, 1991 and 1992 mostly in the month of April as shown in Figure 5.9.

It may be worth noting here also that the interval during which such warmer evenings occurred has been progressively getting shorter particularly since the 1980's and 1990's from 4 years to as frequent as 1 year. The 14 °C threshold temperature, which seems to be critical in the sporogonic development of *P. vivax*, was exceeded only three times over three decades from 1951 to 1980. But, this threshold temperature was exceeded on some thirteen occasions from 1981 to 1993.

**Figure 5.9 Monthly mean night-time temperature pattern in Debre Zeit**



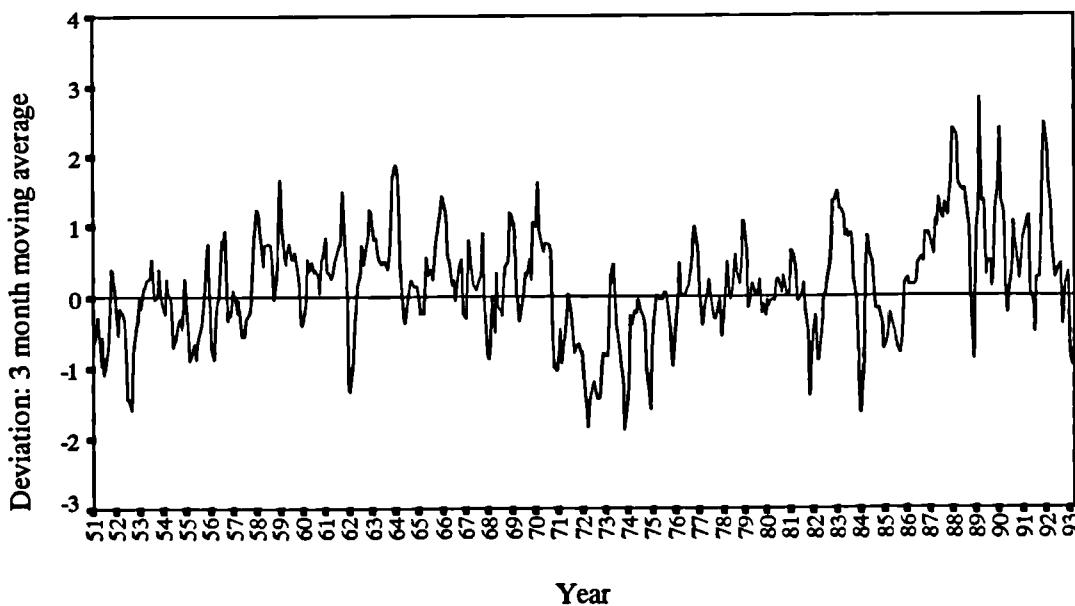
**Figure 5.10 Deviation from the mean of the monthly mean night-time (minimum) temperature**



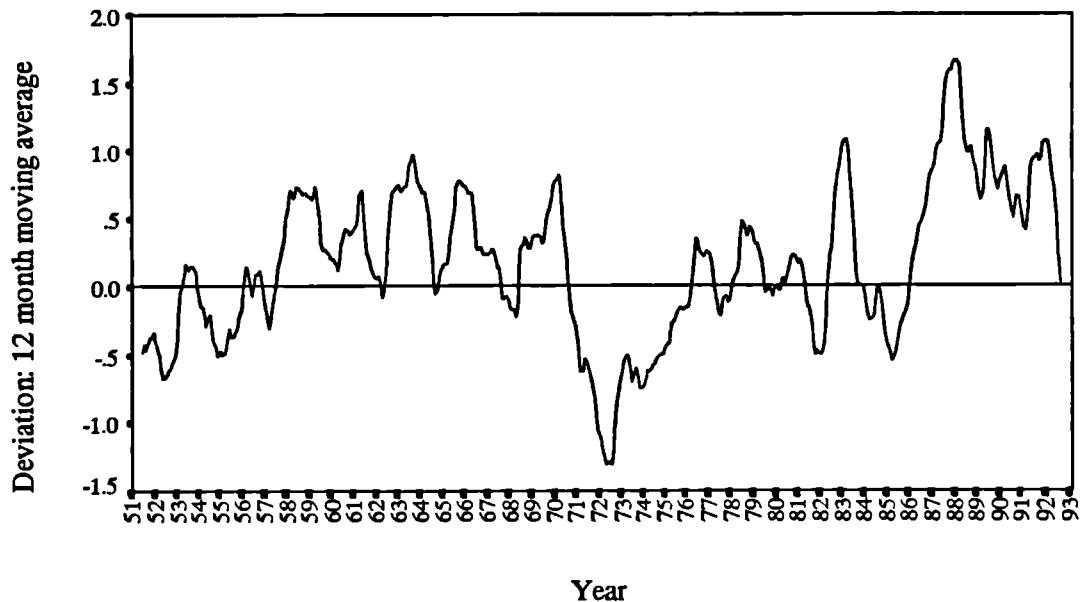
A further analysis was done to see the deviation from the mean for each month relative to the period from 1951 to 1980. The result was plotted in Figure 5.10 which depicts a trend of negative deviations in the early 1950's followed by positive deviations in the late 1950's and 1960's, negative deviations in the early 1970's, and finally largely positive deviations reaching up to 4 °C, most notably in 1988 and 1989.

Although a general pattern was observed, the underlying trend was not very clear from the above figures. Moving averages of the deviations from the mean were then calculated with a span of three and twelve months as for maximum temperature. These results are plotted in Figures 5.11 and 5.12.

**Figure 5.11. Deviations from the norm in monthly mean night-time temperature: 3 month-moving average**



**Figure 5.12. Deviations from the norm in monthly mean night-time temperature: 12 month-moving average**

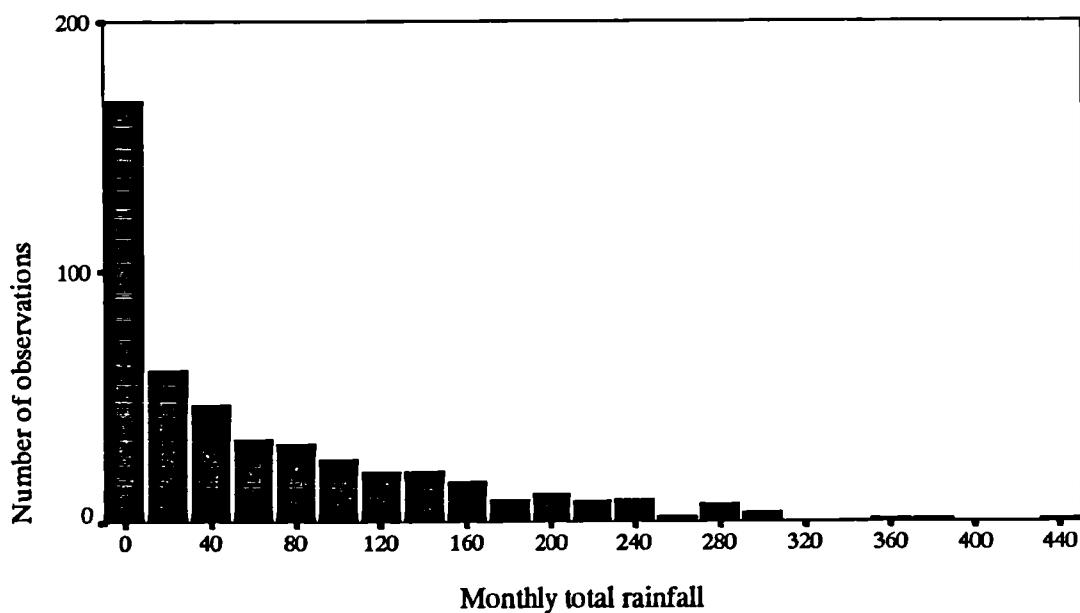


As shown in both the 3-month and 12-month moving averages of deviations from the long term mean for each month in night-time temperatures plotted in Figures 5.11 and 5.12 above, there were largely negative deviations in the 1950's followed by positive deviations in the 1960's , abnormally cool evenings in the early 1970's followed by abnormally warm night-time temperatures with positive deviations with a peak in 1988-89 that persisted with night time temperatures well above the long term mean for each month.

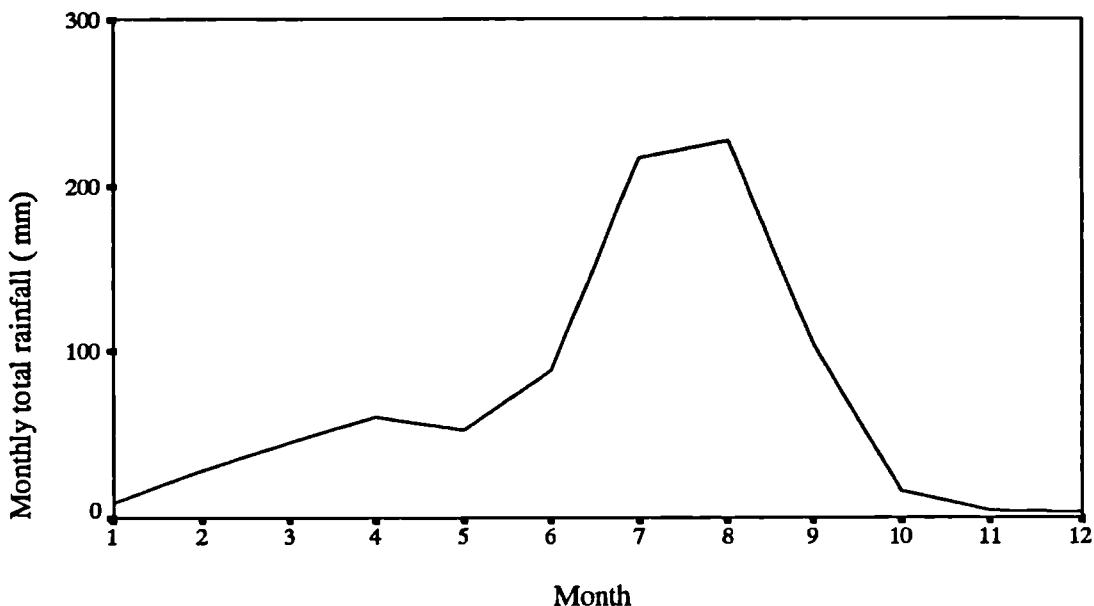
### **5.4.3 Monthly total rainfall**

A total of 496 monthly records from January 1951 to April 1993 were examined with a coverage of 97.8%. The average monthly rainfall was 71.2 mm with a standard deviation of 85.98. The overall frequency of the monthly total rainfall is depicted in Figure 5.13. The histogram of rainfall in this figure depicts a highly skewed distribution which is suggestive of a long dry season with no amount of rainfall recorded during most of the months and a short wet season, but with some abnormally high rainfall exceeding 300 mm that was observed during a few months over the past 42 years.

**Figure 5.13 Histogram of monthly total rainfall in Debre Zeit**



**Figure 5.14 Seasonal pattern of monthly total rainfall in Debre Zeit**

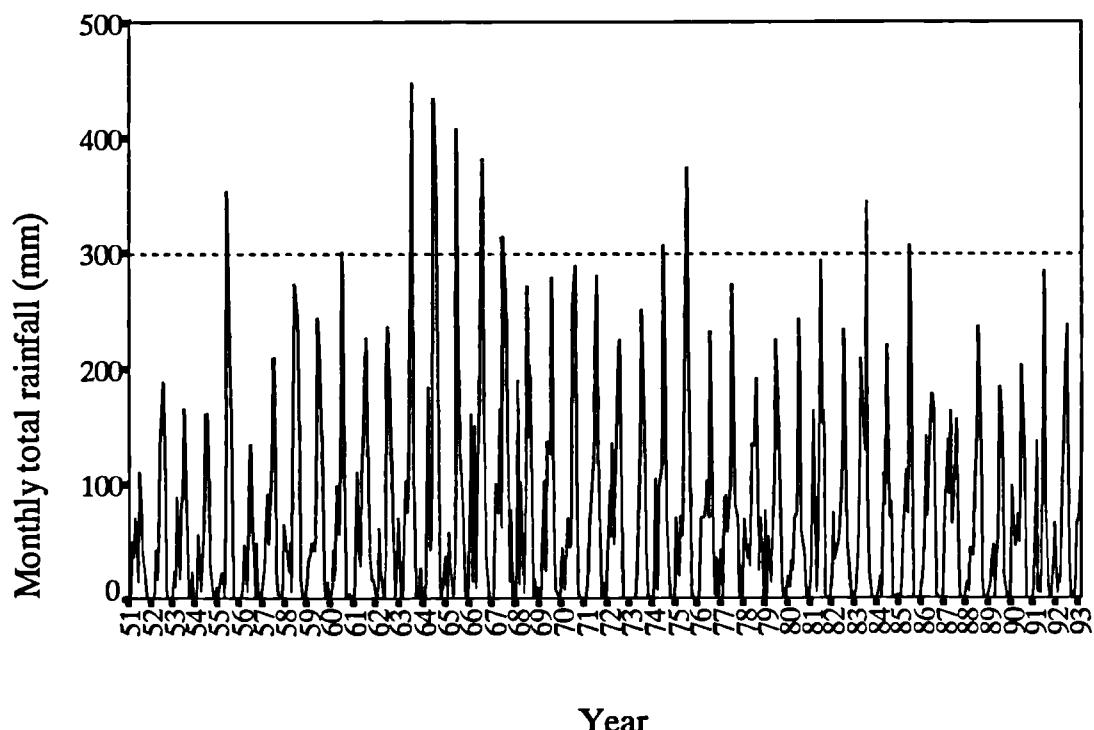


The overall seasonal pattern of monthly total rainfall over the past 42 years was plotted by taking the long term average for each of the twelve months in the year as depicted in Figure 5.14. Here, it is seen that relatively heavy rains start in June with a peak during the months of July and August, then decline in September followed by an abrupt fall to virtual cessation in October, November, December and January.

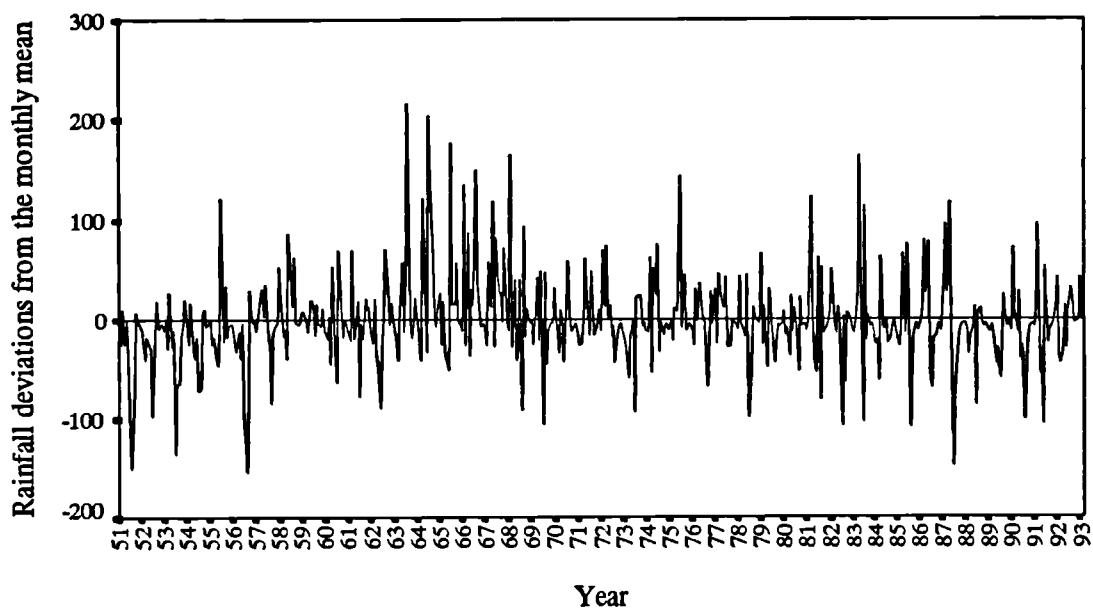
As with temperature, the monthly total rainfall was characterised by a marked fluctuation over the months and years. The wettest month was August 1963 during which a record monthly total rainfall of 448 mm was observed. Other relatively peak

monthly total rainfall was recorded in 1964 and 1965 both in the month of July. The observed monthly total rainfall was plotted as shown in Figure 5.15. It is seen in the figure that the monthly total rainfall was generally low in the 1950's followed by relatively heavy rains in the 1960's and then reduced rainfall throughout the 1970's and 1980's and early 1990's except in about 1975 and 1983. It may be worth noting here that in contrast to temperature patterns, monthly total rainfall seems to have decreased over the past decade.

*Figure 5.15 Monthly total rainfall pattern in Debre Zeit*

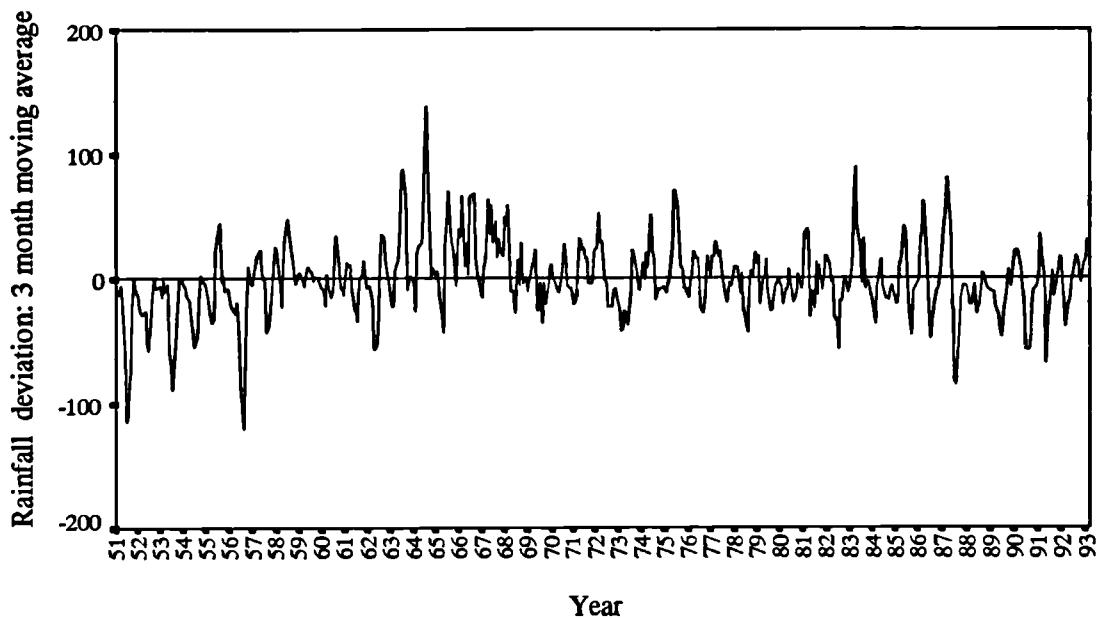


**Figure 5.16 Deviation of rainfall from the mean for each month**

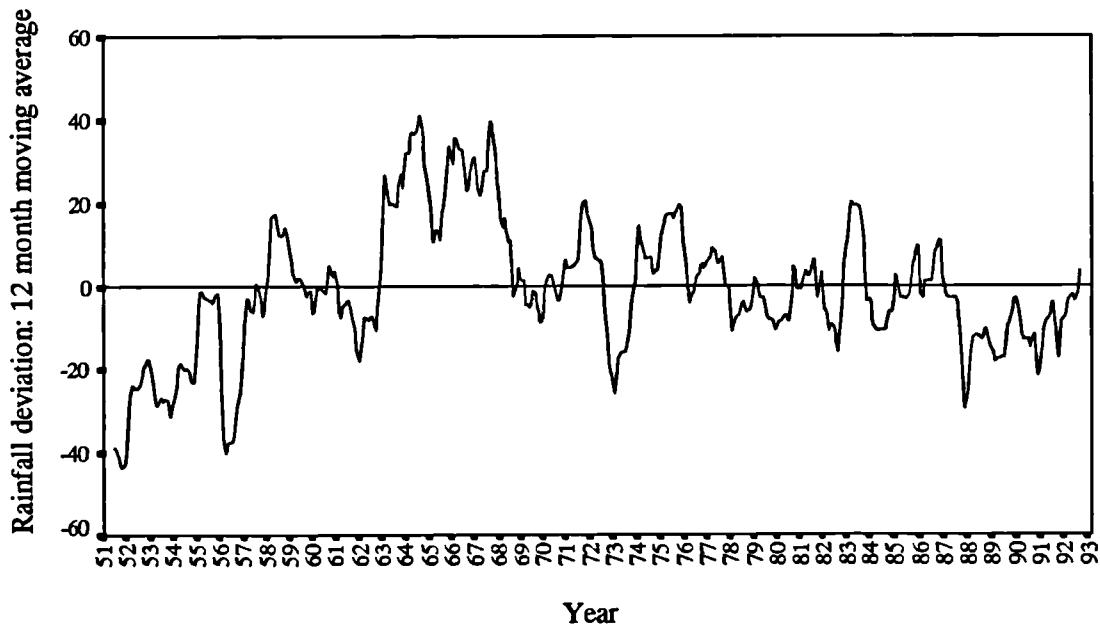


A further attempt was made to see the pattern of rainfall by looking at the deviation from the mean for each month relative to the 1951-80 period. The result was plotted as shown in Figure 5.16. Here, it is seen that the 1950's were largely characterised by negative deviations, followed by largely positive deviations in the 1960's but with progressively decreased positive deviation thereafter. In contrast to the pattern in both day-time and night-time temperature, the years 1987, 1988, and 1989 seem most characterised by largely negative deviation of rainfall from the norm. This pattern of progressively decreased rainfall in the latter half of the 1980's is further clearly illustrated when the 3-month and 12-month moving averages of the deviations from the norm were calculated and plotted in Figures 5.17 and 5.18 below.

**Figure 5.17.** Three month-moving averages of deviations of rainfall from the mean for the month



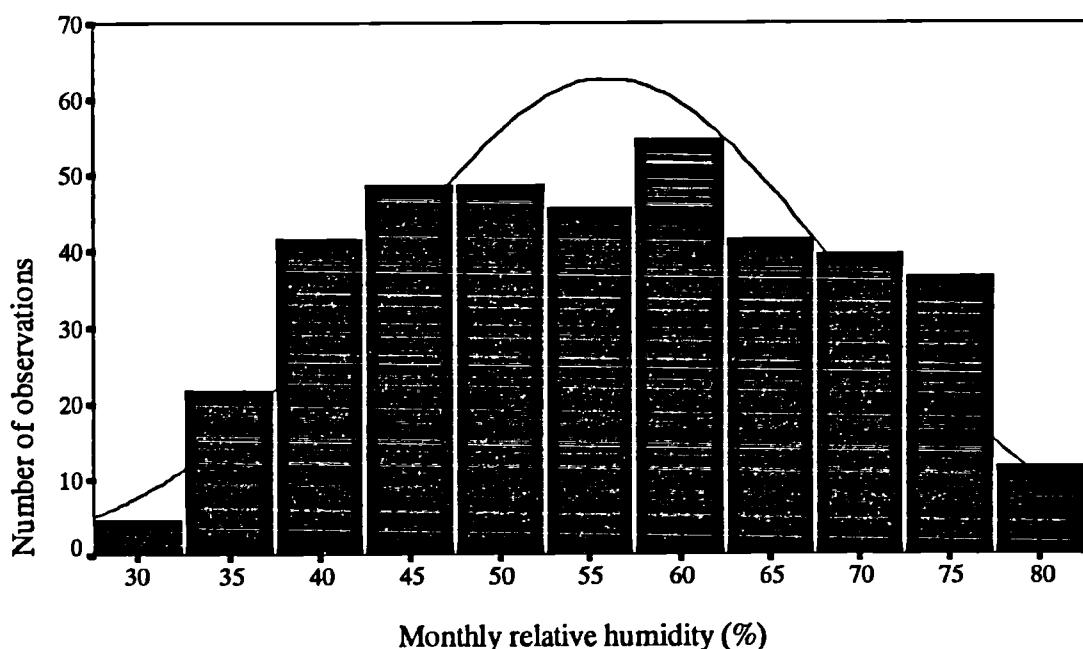
**Figure 5.18.** Twelve month moving averages of deviations of rainfall from the norm for the month



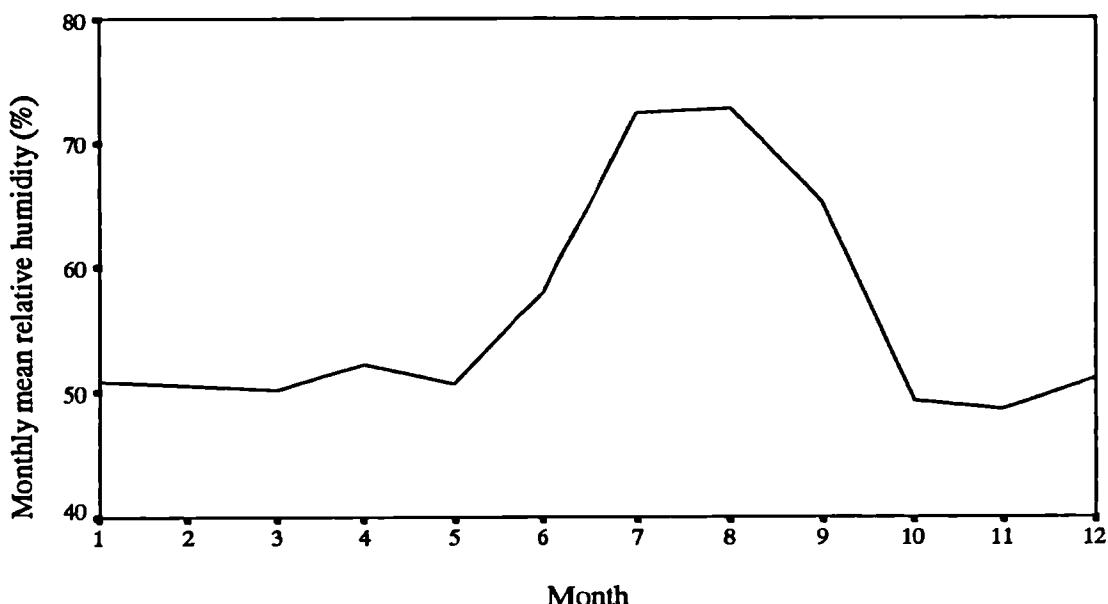
#### **5.4.4 Monthly relative humidity**

A total of 426 monthly records were complete with a coverage of about 84% from January 1951 to April 1993. Records were missing from January 1985 to December 1990. The overall monthly relative humidity was 56.1% with a standard deviation of 11.47. The general pattern of monthly relative humidity is depicted in Figure 5.19. This histogram shows that the most frequent monthly relative humidity is about 55%. Relative humidities less than 35% and greater than 75% seem rare in the study area.

**Figure 5.19. Histogram of monthly relative humidity in Debre Zeit**



**Figure 5.20 Seasonal pattern of monthly relative humidity in Debre Zeit**

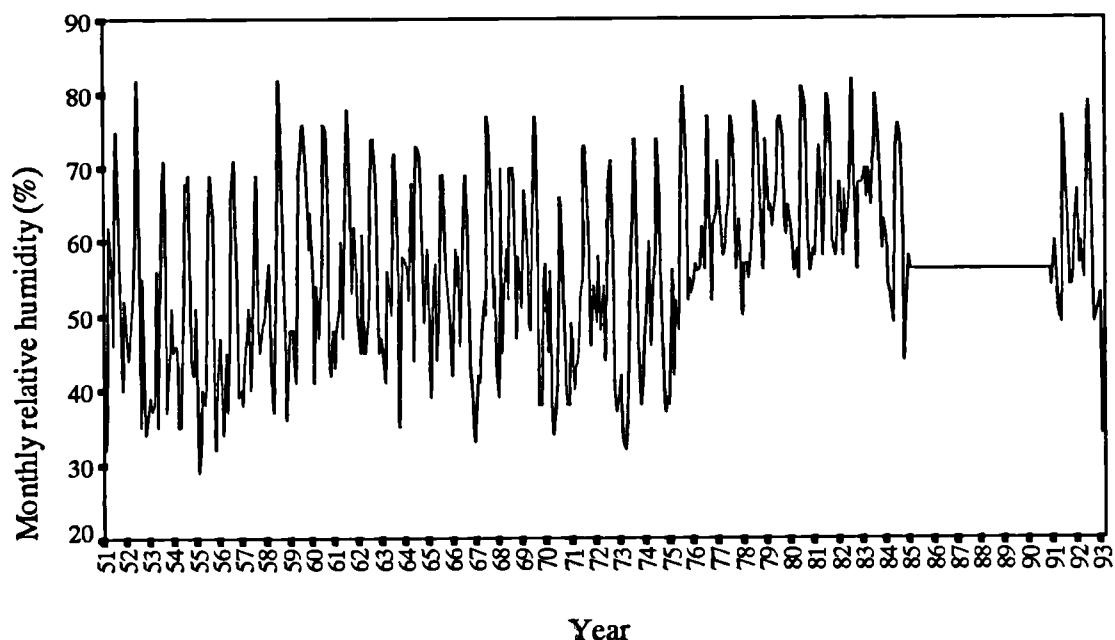


The overall seasonal pattern of relative humidity in the study area is depicted in Figure 5.20 after calculating the long term mean for each month. Here, it is seen that high relative humidity occurs from June to September with a peak during the months of July and August. This was also a pattern characteristic of monthly total rainfall as described earlier.

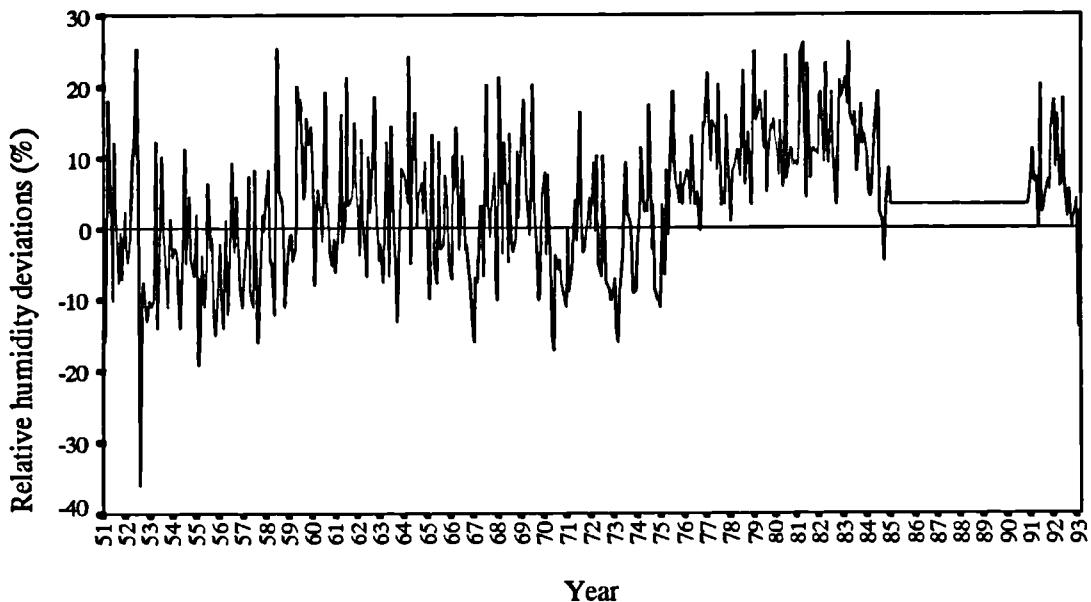
Peak relative humidity was 82%, recorded in July 1952, July 1958 and August 1982. But, abnormally high relative humidity of 80% and above for the study area was recorded in August 1975, July 1980, July 1981, and August 1983. The general pattern of monthly mean relative humidity was plotted to see the pattern as shown in Figure 5.21. The observed pattern of relative humidity does not show any characteristic

feature here. It is to be noted that the horizontal straight line from 1985 to 1990, as shown in the figure is indicative of missing values that were replaced with the long term mean. An attempt was also made to see the deviation from the mean for each month relative to the 1951-80 period as was done for other variables. The result is shown in Figure 5.22 which depicts a very marked positive deviation since 1974.

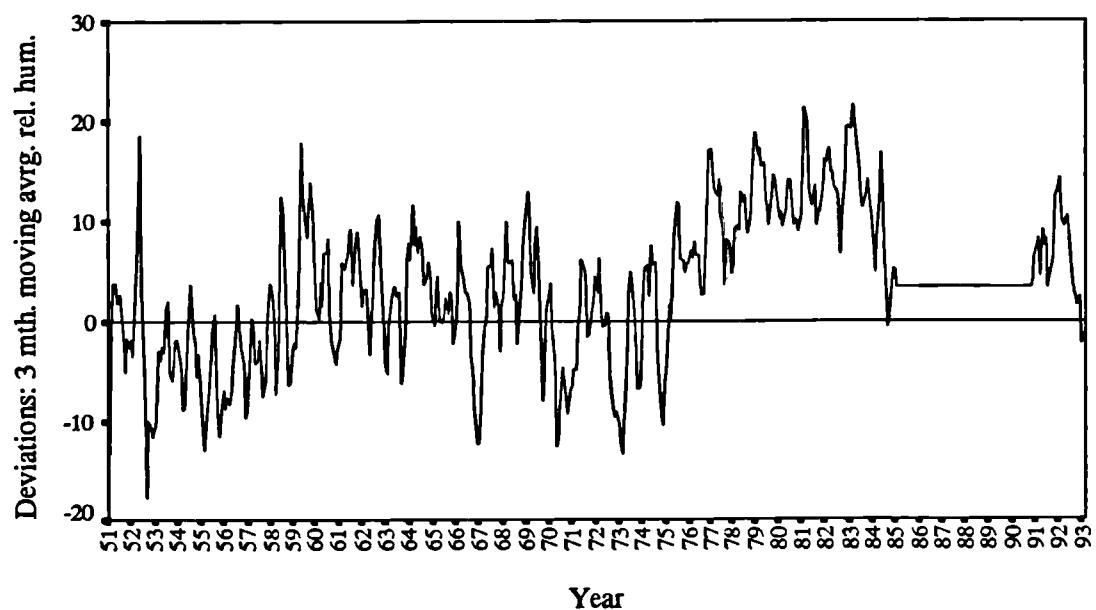
**Figure 5.21 Pattern of monthly relative humidity in Debre Zeit**



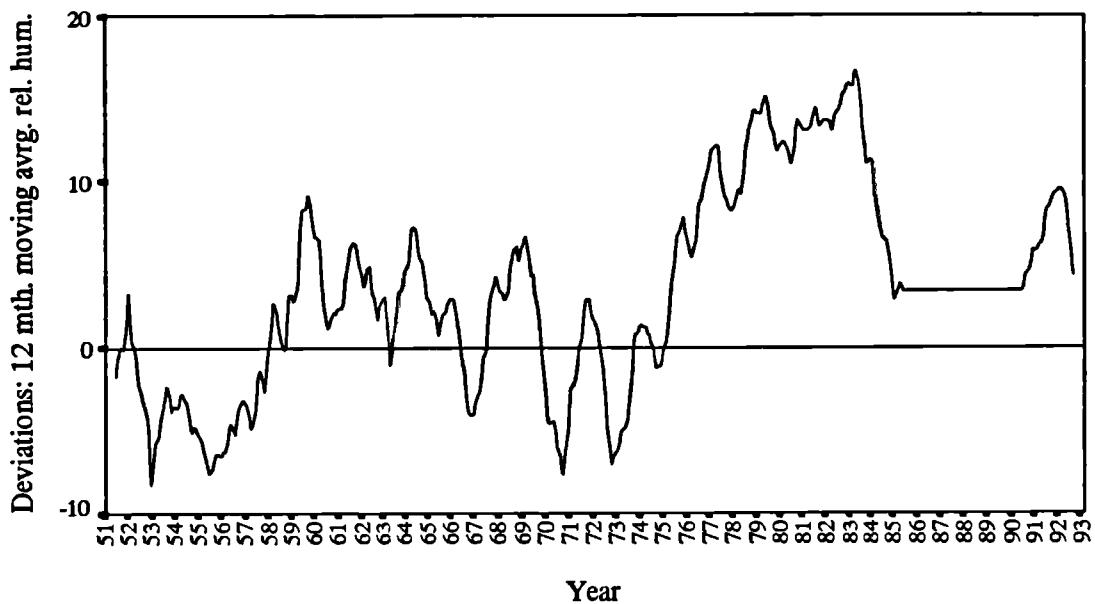
**Figure 5.22 Deviation of relative humidity from the mean for each month**



**Figure 5.23. Three month-moving average of deviations in relative humidity from the mean**



**Figure 5.24. Twelve month-moving average of deviations of relative humidity from the mean for the month**

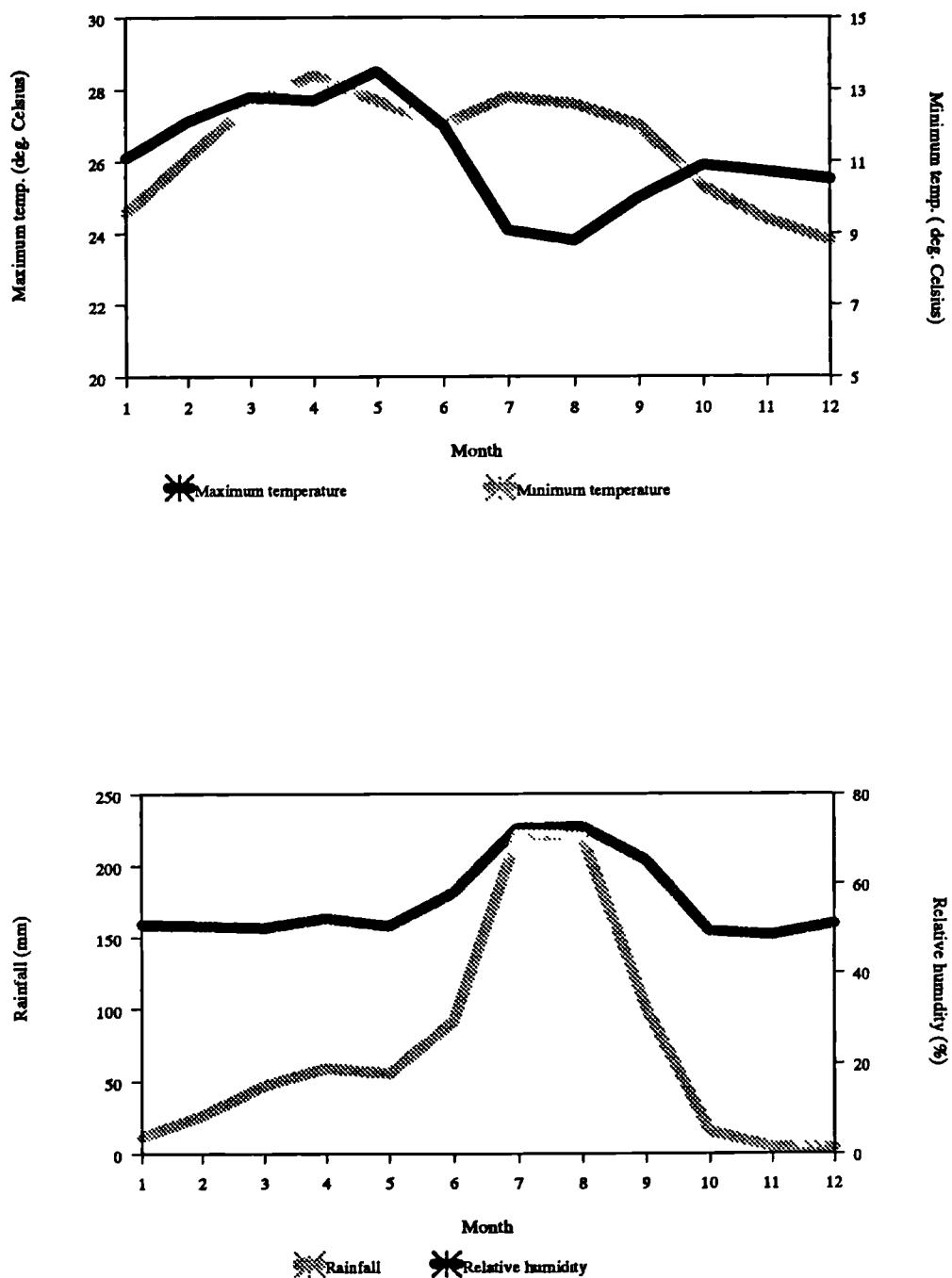


As shown in the plots of the deviations from the mean for each month in relative humidity in Figures 5.22, 5.23, and 5.24 it is clear that a largely positive deviation in relative humidity occurred most markedly in the early 1980's. The plots of deviations in relative humidity from the mean for each month as shown in Figures 5.22, 5.23 and 5.24 further confirm that there was a persistently positive deviation since 1974.

The seasonal relationship of the four climatic variables discussed separately before, is further summarised in the following two plots in Figure 5.25. As shown in Figure 5.25, the peak in minimum temperature is in April while that for maximum temperature is in May. Furthermore, there is a very close relationship between the peak in rainfall and relative humidity both occurring in July and August. In contrast to

maximum temperature which is shown to decrease during the peak for rainfall, minimum temperature actually rises. Similarly, during the dry months of October, November and December, the minimum temperature decreased following the pattern in rainfall and relative humidity. However, this pattern was not shown in maximum temperature.

**Figure 5. 25 Seasonal pattern of temperature, rainfall and humidity**



## **5.5 Discussion**

An increase in ambient temperature (climatic warming) has been noticed over the past century. The global mean surface air temperature has increased by 0.3 to 0.6 °C over the last 100 years. Time series plots of combined land, air and sea temperature deviations (anomalies) relative to the 1951-80 period, from 1861 to 1991 collected from various stations in both Northern and Southern Hemispheres, indicate a pattern of negative deviations from 1870 to 1930 followed by a brief period of positive deviations of up to 0.2 °C between 1930 and 1950, negative deviations from 1950 to late 1970's, and then a marked positive deviation up to 0.5 °C from 1980 onwards (IPCC, 1992). However, the magnitude of this observed warming could be either due to natural climatic variability or due to some other factors which could increase temperature. Increased emission of greenhouse gases such as carbon dioxide, methane, chlorofluorocarbons and nitrous oxide has been proposed as a causal mechanism by experts in climate modelling (IPCC, 1992).

Frequency distribution of climatic conditions examined in the study area show that the most frequently observed day-time and night-time temperatures were 26 and 12.5 °C respectively. Furthermore, rainfall distributions show a characteristically long dry season with a short wet season. Peak day-time temperatures occurred in May while peak night-time temperatures were observed in April. The wet season extended from

June to September. Time series analysis of climate data in Debre Zeit revealed a trend towards a warmer and drier climate in the late 1980's. An abnormally cool monthly mean day-time temperature was also recorded in July 1992. This was thought to be due to the emission of sulphur dioxide into the stratosphere by the eruption of Mount Pinatubo that ultimately resulted in the cooling of the surface of the lower troposphere (IPCC, 1992). But, as shown by subsequent largely positive deviations from the norm in the monthly mean day-time temperature in the data from this study, and as has been predicted earlier by climate experts mentioned above, the cooling effect seems to have been very short-lived.

In contrast, a gradual but progressive decrease was observed in the pattern of rainfall over the past four decades. It is also particularly notable that the months and years during which abnormally high day-time and night-time temperatures were seen seem to have been characterised by abnormally low rainfall. In spite of the progressive decrease seen in the volume of monthly total rainfall, relative humidity seems to have increased since 1980 which may be indicative of a warmer and more cloudy climate but without much rain. Furthermore, it was noted that the interval between observations with particularly warm months and years was progressively getting shorter from 15 years to 11 years, and then to 5 years and ultimately to one to two years.

Time series analysis of climate data from 1875 to 1978 in Southeast Africa revealed that there were 28 El Niño years 22 of which were accompanied by below normal rainfall (World Climate Programme, 1984). El Niño, literally “The Christ Child” in English, was a term used by Peruvian fishermen in the 19th century to describe the warm water that appeared in the coastal regions in late December. In some years during which intense El Niño occur, extremely warm waters displace nutrient-rich waters in the ocean which in turn affects fish stocks along the coast as well as the livelihood of fishermen. This was later known to be a rather global phenomenon also linked to the Southern Oscillation (thus, the term El Niño-Southern Oscillation) in which high atmospheric pressure is associated with low pressure in the Indian Ocean from Africa to Australia. This affects the pattern of both temperature and rainfall in these areas including Ethiopia.

The years 1958, 1972-73, and 1982-83 were all characterised by strong El Niño events. More recently, the years 1987 and 1991-92 were also characterised by conspicuous El Niño events. A closer look at the observed pattern of abnormally high day-time temperature and night-time temperature in the past four decades in Debre Zeit, the present study area, also matches the period during which these El Niño phenomena were observed with the exception of 1956, 1988 and 1989. Particularly high night-time (minimum) temperatures of 14 °C and above, were recorded in 1956, 1958, 1973, 1983, 1987, 1988, 1989, 1991, and 1992. This was 2.5 to 5.9 °C higher

than the standard relative to the monthly mean night-time (minimum) temperature between January 1951 and December 1980.

The frequency during which abnormally high night-time (minimum ) temperatures were recorded over the past four decades from January 1951 to April 1993 is shown in Table 5.2 (at the end of this section). The most conspicuous observation in the table is that the frequency at which the 14 °C threshold mean minimum night-time ambient temperature, below which the completion of the sexual phase of the development of *P. vivax* in the *Anopheles* vector is thought to be unlikely was exceeded on thirteen occasions over the past decade alone since 1983 as compared to only three times over the three previous decades. An upward trend since 1989 with high positive deviations was also observed in the mean monthly day-time (maximum) temperature as shown in the results of time series analysis in the present study area in the past four decades.

As discussed in Chapter 3, it was also noted that the monthly incidence of malaria in the study area was particularly high since the latter half of the 1980's and it seems to have reached epidemic proportions relative to the preceding period. The monthly incidence of both *P. falciparum* and *P. vivax* was increasing although the relative contribution of the former species to this increase was much more marked than the latter. Furthermore, it was also noted that the proportion of hospital admissions due to malaria and the proportion of hospital deaths ascribed to malaria has increased dramatically since 1988. The year 1958 was the time during which a nation-wide

epidemic of malaria in the highlands of Ethiopia claimed 150,000 lives among 3 million estimated cases as discussed in Chapter 1. In fact, this is thought to be a great contributing factor for the establishment of the Malaria Control Programme and the launching of a national campaign to eradicate malaria from the highlands of Ethiopia, which as we now see it could not be achieved due to many reasons.

Although no data exist to allow of comment on other health effects of climate extremes in the present study area, the abnormally warm night-time temperatures in 1973 were associated with drought and famine in the northern and eastern highlands of Wollo and Hararghe respectively. About 50,000 excess deaths were attributed to the famine in Wollo province alone (Miller & Holt, 1975). About 20% of all children under-five were estimated to have died in Hararghe province (Seaman & Holt, 1975). This was seized upon by political activists, local and international media to overthrow the then Imperial government of Haile Selassie in 1974. Similarly, after some ten years, in 1983, the year during which particularly high night-time temperatures were observed in the present study area, there was drought and famine over large areas of the northern and central highlands of Ethiopia that seems to have largely contributed to the rapid and often forced mobilisation of some 600,000 non-immune people in 1984-85 into peripheral lowlands in the west and south-western sections of the country that are known to be endemic for malaria. This is known to have actually increased the vulnerability of the settlers to illness and death from malaria in spite of intensive control efforts as discussed in the first chapter.

The transmission of malaria in an area is governed by many factors amongst which the presence of a suitable water body for the breeding of vectors, a suitable ambient temperature for the development of the vector and for sporogonic development of the parasite, and the presence of susceptible hosts seem essential. Rain pools created during the wet season provide suitable breeding sites for *An. arabiensis*. The duration of the developmental cycle from egg to larva, pupa and imago is also very sensitive to temperature. It may vary between 7 days at 31 °C, and 20 days at 20 °C . Furthermore, the sexual phase of development of the malaria parasite inside the mid-gut of the female *Anopheles* vector is also very sensitive to temperature. In the case of *P. vivax* it may take from 16 days at 16 °C, to as short as 8 -10 days at 28 °C for the completion of the sexual cycle after exflagellation of the male and fertilisation of the female gamete (Bruce-Chwatt, 1985) .

The minimum temperature below which the malaria parasite does not develop inside the *Anopheles* vector is 14.5 °C for *P. vivax* and 16 ° C for *P. falciparum* (Detinova, 1962). But, it is notable that this threshold temperature below which extrinsic development of *P. vivax* is inhibited seems not to have been agreed upon since other authors indicated that it may be 15 °C (Macdonald, 1952, Gilles, 1993). The other problem with this figure is that the authors do not specify whether this critical temperature that may have been observed in laboratory-based experiments could also be a limiting factor at that same threshold temperature in the environment outside,

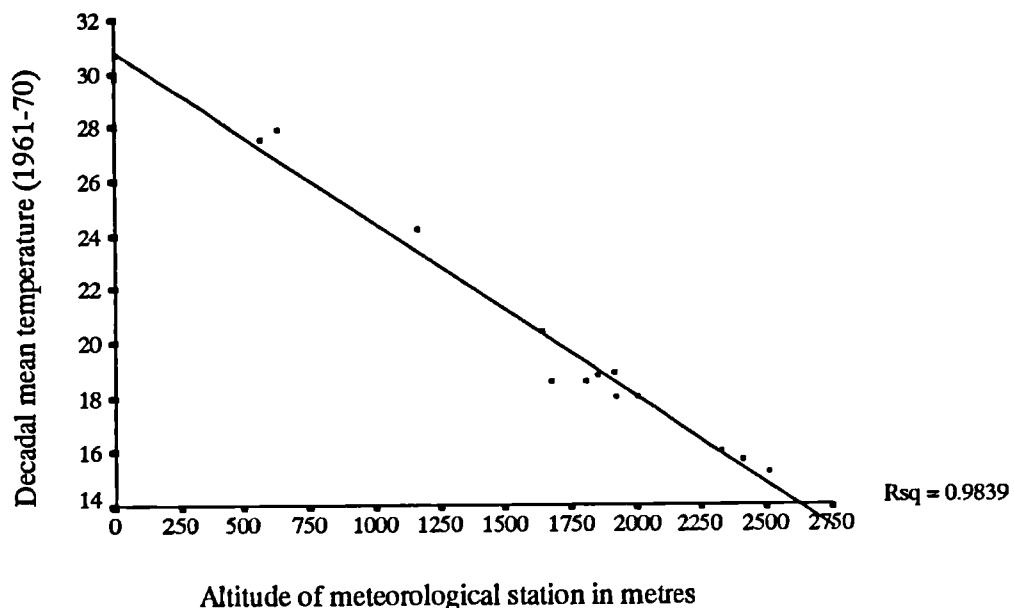
where both the female *Anopheles* and the *Plasmodium* parasites are known to thrive. The longevity of the vector is also thought to be dependent on relative humidity, with relative humidity of 60% and above being preferred. A mean ambient temperature greater than 35 °C and a relative humidity of less than 50% is associated with drastic reduction in the longevity of the vector (Bruce-Chwatt, 1985).

A negative correlation has been seen between altitude and prevalence of malaria as discussed in Chapter 4 (Figures 4.3b & 4.5b). Furthermore, examination of weather records from 15 meteorological stations (including the present study site using data from world weather records) located at varying altitudes in Ethiopia also showed an inverse relationship between temperature and altitude when the decadal mean temperature from 1961-70 was plotted against altitude as shown in Figure 4.26. Thus, it is highly plausible that an increase in temperature at high altitude could result in new foci of malaria transmission.

As shown in the above discussion, among the climate factors examined, a trend of increased mean monthly values was observed in day-time and night-time temperatures as well as relative humidity while a general trend of progressively decreased total monthly rainfall was recorded. Furthermore, the occurrence of epidemics of malaria and increasingly higher monthly incidence and increased malaria specific mortality was

associated with the occurrence of abnormally high night-time and day-time temperature as well as relative humidity.

**Figure 4.26 Relationship between decadal mean temperature and altitude in Ethiopia (1961-70)**



It is also worth noting that the transmission of malaria among communities in localities lying at higher altitudes in the present study area was also noticed for the first time since the latter half of the 1980's as discussed in the section that dealt with altitude effects on malaria transmission in Chapter 4. Whether this association of increased incidence of morbidity and mortality due to malaria in the highlands and the

observation of increased day-time and night-time temperature as well as relative humidity is causal or not will be the subject of further analysis and discussion in subsequent chapters of the present study. Did the observed warmer and more humid climate in the study area facilitate the transmission of malaria and result in the increased incidence of malaria related morbidity and mortality?

Although not the subject of the present study, it is notable that the progressive decrease in the monthly total rainfall in the past 42 years may have reduced agricultural production in the study area thereby limiting the subsistence livelihood of rural farmers. It is also not difficult to guess the impact of reduced capacity for food production in the light of the presence of a population that grows at a rate of 2.9% per annum as discussed in the second chapter.

### ***5.6 Summary***

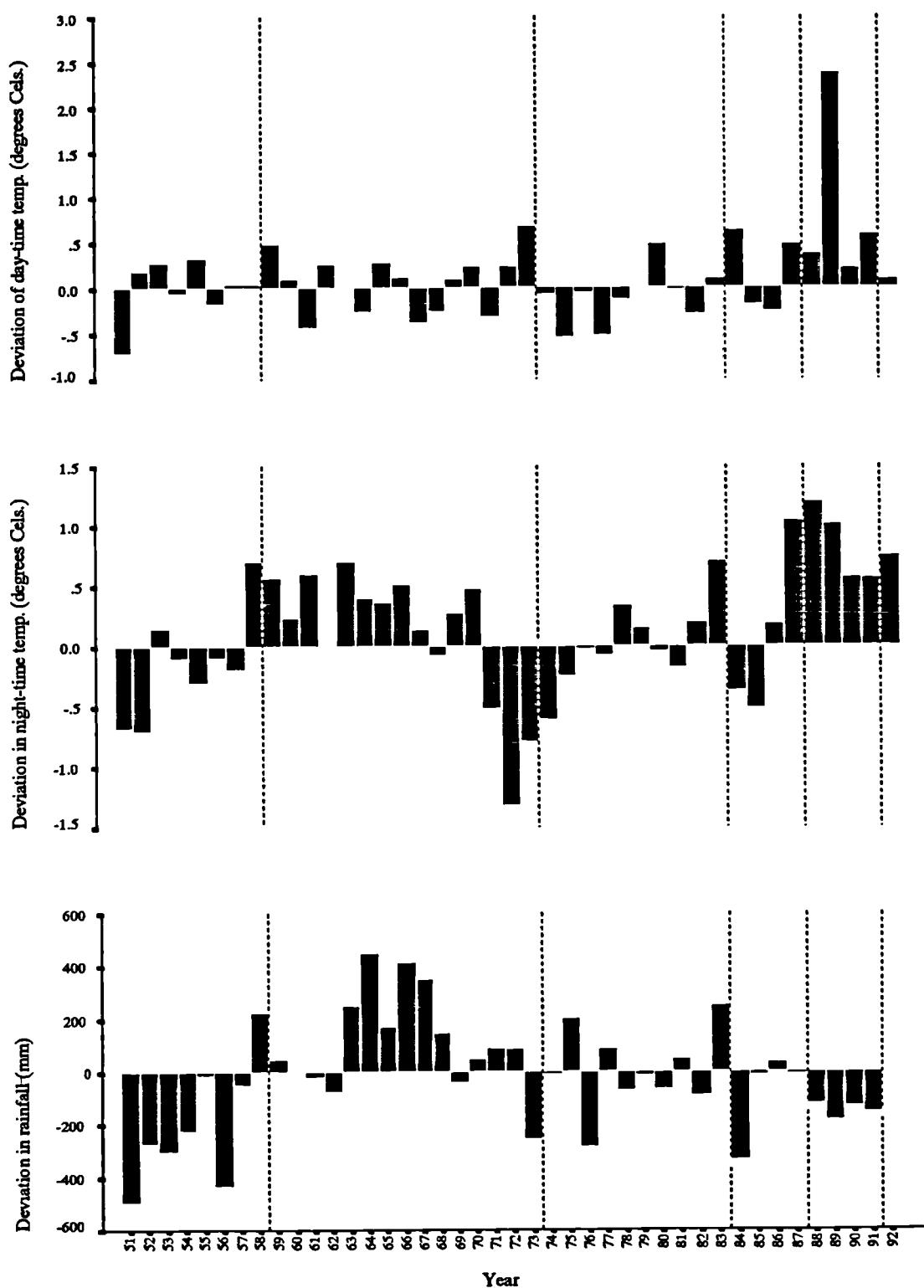
Time series analysis of monthly climate data from January 1951 to April 1993 from Debre Zeit was carried out to see the pattern of climate change and the implication of its association with increased incidence of morbidity and mortality due to malaria in the highlands over the past two decades. A trend of increased climatic warming was noticed in both day-time and night-time temperature particularly since the late 1980's

at which time a very high incidence of malaria was also observed. An upward trend of relative humidity was also observed. In contrast, a trend of progressively decreased total monthly rainfall was observed. Furthermore, the years and months in which abnormally warm temperatures and shortage of rainfall were observed seemed to follow strong El Niño-Southern Oscillation (seen in Table 5.2 and Figure 5.26 at the end of this section). It is not unlikely that these events contributed to serious food shortages and abnormal increases in the incidence of malaria in the highlands of Ethiopia. Further analysis of data will be done to explore whether this trend of increased climatic warming has a causal link with the increased incidence of malaria in the highlands.

**Table 5.2 Periods of increased monthly mean night-time temperature ( $\geq 14^{\circ}\text{C}$ ) from January 1951-April 1993**

Year	Month					
	February	March	April	May	July	August
	Min. temp.					
1956						14.8
1958			14.1			
1973			14.2			
1983				14.3		
1987				14.6		
1988		14.1	15.3		14.6	
1989	14.6		17.2			
1991			14.2	14.2		
1992		14	14.2	14		14

**Figure 5.26** Deviations of day-time temperature, night-time temperature and rainfall from the mean relative to the 1951-80 period associated with intense El Niño Southern Oscillation (seen in dotted lines) from 1951-1992



## **Chapter 6**

### **Effectiveness of treatment in *P. falciparum* & *P.vivax* malaria**

#### ***6.1 Introduction***

As discussed in Chapter 1, a four-fold increase was noted in the slide-positive rate for malaria in the whole of Ethiopia during the 1980-89 period. Furthermore, this increase was even more exaggerated when the level and trend of malaria over the past two decades was examined in a highland where malaria was unstable. A rise in incidence rate of malaria of about 67-fold was observed relative to the October 1973 to October 1991 period in Debre Zeit, the present study area as discussed in Chapter 3. The proportion of hospital admissions attributable to malaria increased from 2.9% in 1981 to 38.6% in 1992. Similarly, the proportion of deaths in Debre Zeit hospital ascribed to malaria increased 13-fold over the same period.

The increase in these indices of malaria was also more apparent among communities residing in localities at higher altitudes in which the transmission of *P. falciparum* seems to have occurred since 1986 for the first time as discussed in Chapter 4. This time during which an abnormal increase in the incidence rate of malaria occurred also was associated with an abnormally high monthly mean minimum and maximum temperatures along with relatively low rainfall as discussed in Chapter 5. An attempt will be made in the present chapter to examine whether a decreased effectiveness of standard treatment regimens to

the two species of malaria prevalent in the area, *P. falciparum* and *P. vivax* could have also played a role in the reported increase in the transmission of malaria in the study area.

The availability of services for proper diagnosis and treatment of clinical malaria remains a priority in both clinical and public health activities aimed at alleviating the suffering of many millions of people from malaria in tropical and sub-tropical countries. This task, however, is also increasingly becoming difficult due to the emergence and rapid spread of drug resistance since the late 1950's in Latin America & Asia, and since the late 1970's in Africa. The problem of drug resistance has been particularly serious in patients with *P. falciparum* malaria.

The first evidence for the emergence of chloroquine resistant *P. falciparum* in Africa was from non-immune travellers who contracted infection while in Kenya and the United Republic of Tanzania (Centers for Disease Control, 1978). However, there were previous studies which suggested that strains of *P. falciparum* in Ethiopia, The Sudan, and Nigeria are less sensitive to chloroquine than are other African strains. This was thought to be due to innate strain variation which were not related to strain selection under drug pressure (Bruce-Chwatt, 1981).

The response of patients with *P. falciparum* to chloroquine in Ethiopia has been evaluated since the early 1970's although the methods of evaluation varied. Research workers at the US Naval Medical Research Unit stationed at Addis Ababa studied the response of acutely

ill patients presenting with a rectal temperature  $\geq 37.8$  °C with evidence of *P. falciparum* in their peripheral blood (Dennis et al., 1974). Chloroquine was administered to 41 patients admitted to St. Paul's hospital in Addis Ababa, at a single dose of 10 mg/kg body weight on the first day. Their response was evaluated by blood samples taken daily for the first seven consecutive days and then twice weekly during subsequent three weeks. Complete clearance of asexual parasitaemia was observed within the first six days and the mean was 3 days. However, 11 of the 41 patients manifested with a recrudescence of asexual parasitaemia while in hospital during the 28 days of observation with a mean of 24.8 days. All patients with recrudescence were treated with standard dose of chloroquine (25 mg/kg over three consecutive days) and there was clearance of asexual parasites within 1 to 7 days. The possible places of acquisition of infection were noted to be the Gibbe and Arba Minch valleys. The response of the parasites was also evaluated by *in-vitro* methods and it was suggested that the level of chloroquine sensitivity of the Ethiopian strain was somewhat intermediate between the Ugandan (African) and Malayan (Asian) strain (Dennis et al., 1974).

Subsequent studies on sensitivity of *P. falciparum* to chloroquine in Ethiopia were done by the same research team. The response of some 150 patients was evaluated in endemic areas in the Awash Valley (Abela & Abadir) and in the Baro-Akobo Valley (Gambela). This study was carried out as a result of a previous report of the presence of "chloroquine" resistant malaria in which 75 deaths were attributed to malaria among newly settled farm workers. A single oral dose of chloroquine, 10 mg/kg body weight, was

administered to all subjects who were either non-immune migrants from the highlands or children in these endemic areas. Serial blood films were obtained from all subjects for seven consecutive days and on the 11th day. Asexual parasites were cleared in all test subjects by day 3. The drug that was initially administered at the time during which the deaths ascribed to malaria occurred was later known to be pyrimethamine and had been mistakenly reported to be chloroquine (Armstrong et al., 1976).

A further *in-vitro* evaluation of chloroquine sensitivity of *P. falciparum* was done in the study sites mentioned above by the same team. This method was thought to overcome the problem of interpretation of results conducted in endemic areas where the response pattern to drugs is affected by the host's immune response, and where seriously ill patients may be excluded in the standard seven-day *in-vivo* field test. Overall, some 58 successful cultures were made and the percent inhibition of maturation of trophozoites to the schizont stage was evaluated under various concentrations of chloroquine. Schizogony was inhibited in 43 experimental samples at 0.5 nmol, in 8 samples at 0.75 nmol and in a further 5 at 1 nmol (Palmer et al., 1976).

The response of *P. falciparum* was also studied by workers at the National Research Institute of Health. The study was conducted in Nazareth town, located at an average altitude of 1,580 metres above sea level and about 100 kilometres east of Addis Ababa. Some 21 patients were successfully followed over seven consecutive days following administration of chloroquine at a dose of 10 mg/kg/day on the first two days and 5 mg/kg

on the third day. Among these patients, 2 had no evidence of parasitaemia after 24 hours, 12 after 48 hours, and 7 after 72 hours since the initiation of treatment. The average clearance time for all patients was 53 hours (Gabre-Mariam et al, 1982). Another 14 patients were subjected to the *in-vitro* test. Maturation of trophozoites to schizonts was not inhibited in 7 at 0.5 nmol, in 2 at 0.75 nmol, and in 1 at 1 nmol. The absence of inhibition of maturation of trophozoites to the schizont stage *in-vitro* in one isolate at the 1 nmol concentration was then suggested to be indicative of refractoriness. However, during subsequent visits about two months after the end of the seven-day test to the three patients who showed retarded inhibition, i.e. growth to schizont stage at 0.75 nmol and above, none of them reported recurrence of fever or other complaints suggestive of malaria.

The first evidence for the emergence of chloroquine resistant falciparum malaria in Ethiopia to a standard chloroquine treatment regimen, i.e. 25 mg/kg over 3 days, came in a study conducted on some 98 patients who acquired infection elsewhere but were successfully followed at a malaria laboratory of the National Organization for the Control of Malaria and Other Vector-borne Diseases in Addis Ababa from June to December 1985. Standard triple dose chloroquine (10 mg/kg/day on the first two days and 5 mg/kg on the third day) was administered to patients. Thick blood films were prepared from samples obtained from patients on the first seven consecutive days during the first week, and once weekly during subsequent three weeks. Clearance of asexual parasitaemia was observed in 76 patients within 1 to 4 days, mean 2.53 days. The remaining 22 patients

failed to clear their asexual parasitaemia during the remaining observation period. Some 8 patients did not clear in the first seven days. Six of these were classified as RII and the other 2 as RIII resistance. The remaining 14 patients cleared within the first seven days but recrudescence was observed in the third week in six cases, and the fourth week in eight cases indicating RI resistance (Teklehaimanot, 1986).

As seen above and in the summary in Table 7.1, the methods that were employed, including recruitment criteria, treatment regimens and response assessment procedures varied greatly between the investigations conducted earlier and during more recent times making comparative evaluation difficult. Furthermore, the studies were conducted in different places at different times which limits one to assess the time during which resistance emerged. Besides, none of the investigators conducted their studies in the highlands where malaria is unstable and the likelihood of epidemics is high.

The incorporation of simple clinical criteria such as fever, which could be an essential tool for the evaluation of the response of patients who were given chloroquine at a primary health facility was not done. Although *P. vivax* was the predominant species in areas with a highland profile in Ethiopia, all the published reports conducted so far were results of laboratory evaluation of the response of *P. falciparum* patients to chloroquine. Thus, the present study was designed to bridge the gap between clinical and parasitological evaluation in a rural primary health care facility and to assess current levels of resistance in

the context of the overall study. The findings of the previous studies may be summarised as shown in Table 6.1.

**Table 6.1 Summary of findings of previous *in-vivo* and *in-vitro* drug sensitivity studies in Ethiopia**

Year	Author(s)	Study site	Finding
1974	Dennis et al.	Arba Minch Gibbe	CQ at 10 mg/kg; 11/41 patients with recrudescence. 3/25 isolates with <u>in-vitro</u> growth at 1 nmol
1976	Palmer et al.	Abadir Gambela Itang	58 <u>in-vitro</u> cultures; 43/58 inhibition at 0.5 nmol, 8/58 inhibition at 0.75 nmol, 5/58 inhibition at 1 nmol
1976	Armstrong et al.	Gambela Arba Minch Abela Abadir	150 patients treated with CQ at 10 mg/kg. All cleared in 3 days.
1982	Gabre-Mariam et al.	Nazareth	21 patients treated with CQ at 25 mg/kg. Clearance in all at 72 hours. Failure of <u>inhibition in-vitro</u> in 1 at 1 nmol.
1985	Teklehaimanot	Gode, Bare Metemma, Pawi Tata, Woyto	22/98 patients not cleared. RII & RIII resistance at Ethio-Somalia & Ethio- Kenya borders. RI at Ethio-Sudan border.

## **6.2      *Objectives***

This section of the study aims to achieve the following objectives in the context of the overall study of determinants malaria transmission in the highlands;

- 6.2.1 Evaluate the response of patients with *P. falciparum* to chloroquine
- 6.2.2 Describe the pattern of chloroquine resistance in Debre Zeit
- 6.2.3 Assess the effectiveness of sulphadoxine-pyrimethamine (Fansidar<sup>R</sup>) in treatment of *P. falciparum*
- 6.2.4 Determine the sensitivity of *P.vivax* to chloroquine *in-vivo*

## **6.3      *Patients and methods***

The study was conducted in an out-patient diagnosis and treatment clinic of the National Malaria & Other Vector-borne Diseases Control Programme in Debre Zeit from April 1993 to March 1994.

### **6.3.1    *Recruitment criteria***

Patients who satisfied the following criteria were recruited for a modified *in-vivo* field test ;

- a) onset of symptoms such as fever, chills and headache suggestive of malaria during the past week
- b) voluntary consent to come to the clinic and submit finger prick blood samples on days 0, 1, 2, and 7
- c) absence of any evidence of cerebral signs
- d) absence of any gastrointestinal disturbances like vomiting and diarrhoea
- e) negative history of antimalarial drug intake during the past seven days
- f) negative history of travel outside the present study area during the last 30 days
- g) evidence for presence of *P. falciparum* or *P. vivax* in peripheral blood

### ***6.3.2 Diagnosis of malaria and treatment regimens***

All patients who satisfied the above mentioned criteria were asked to submit finger prick blood samples. The left ring finger was cleaned with alcohol after which each patient was bled with a sterile disposable blood lancet to obtain blood samples on a slide. Both thick and thin smears were prepared and the slide number was written with an ordinary lead pencil on the thin portion of the blood film. The slides were then stained with Giemsa solution. Diagnosis was then made with an ordinary compound light microscope under high power objective. The species of malaria was identified and asexual parasitaemia was counted until a total of 300 leucocytes were seen. No attempt was made to estimate the densities of asexual parasitaemia per microliter of blood since it may be unwise to do that before the normal leucocyte count in the population of the study area was determined.

Body weight was then measured using a weighing scale and the weight was recorded in kilograms. Axillary temperature was measured with an ordinary clinical thermometer by putting it in the arm pit (axilla) for about 3 minutes. Then, 150 mg base tablets of chloroquine diphosphate were administered at a dose of 10 mg/kg body weight on the first two consecutive days and at another dose of 5 mg/kg body weight on the third day, i.e. a total of 25 mg/kg over three consecutive days. Patients were required to swallow the drug with a cup of water under supervision after which they stayed on the compound of the clinic for about 30 minutes to see that the drug administered was not lost due to vomiting.

Response to treatment was evaluated by observation of asexual parasitaemia and axillary temperature patterns daily during the first 48 hours and then on the seventh day, i.e. during days 0, 1, 2, and 7. The modified *in-vivo* field test (Turaman et al., 1992), adapted with a slight modification by inclusion of fever as one of the evaluation parameters was used. This was done to increase patient compliance by omitting patient-days that could be lost on days 3, 4, 5, and 6. The lack of facilities for the observation of patients for an extended follow-up period during weeks 2, 3, and 4 in an area free of malaria transmission made it impossible to conduct the extended *in-vivo* field test.

The response of some 60 patients due to *P. falciparum* was observed initially to chloroquine in which evidence suggestive of high levels of resistance was seen. Thereafter,

subsequent patients were given a single oral dose of sulphadoxine-pyrimethamine (Fansidar<sup>R</sup>). The response of patients was evaluated by similar methods as for chloroquine.

### ***6.3.3 Definition of fever and resistance in-vivo***

**6.3.3.1 Fever :** All patients with axillary temperature  $\geq 37.5^{\circ}\text{C}$  were defined as suffering from fever related to malaria for the purpose of this study.

**6.3.3.2 In-vivo antimalarial drug resistance:** Drug resistance was defined as the detection of malaria parasites in Giemsa stained blood films indicating the persistence of asexual parasitaemia in the peripheral blood on day 7 in spite of adequate antimalarial treatment at the standard recommended dose and frequency of administration.

#### ***6.3.3.3 Grades of chloroquine resistance***

The interpretation of grades of chloroquine resistance of *P. falciparum* were carried out according to the criteria set by WHO (1981) which are mentioned here.

- a) "If no asexual parasites are found by day 6 and none are present on day 7, the infection may be either sensitive (S) or resistant at the RI level."
- b) "If asexual parasites disappear for at least 2 consecutive days but return and are present on day 7, they are resistant at the RI level."
- c) "If asexual parasitaemia does not clear but is reduced to 25% or less of the original pre-test level during the first 48 hours of treatment, the parasites are resistant at the RII level."

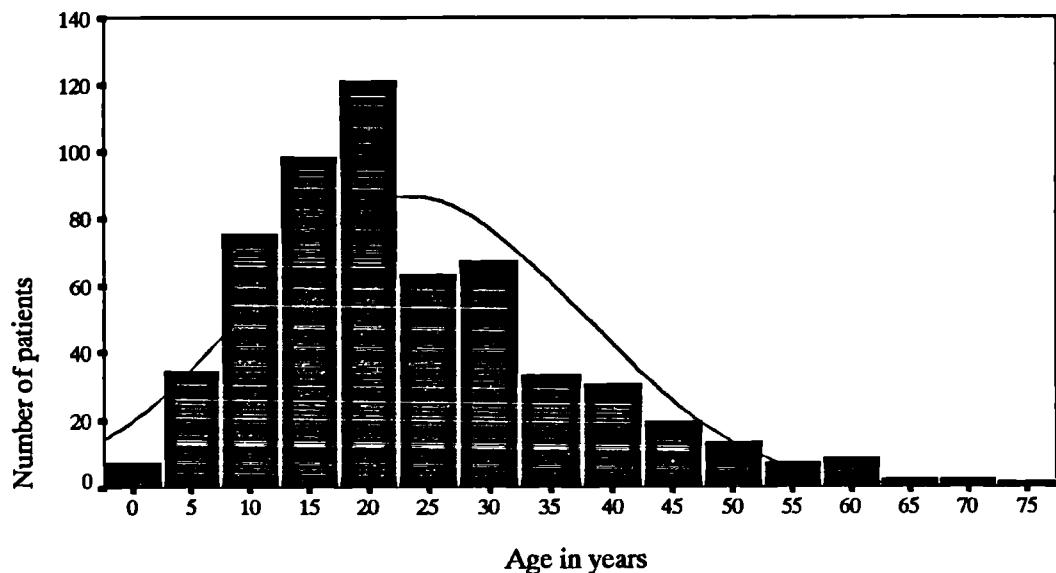
d) “ If asexual parasitaemia is reduced by less than 75% during the first 48 hours or if it continues to rise, the parasites are resistant to the standard dose of the drug at the RIII level.”

## **6.4 Results**

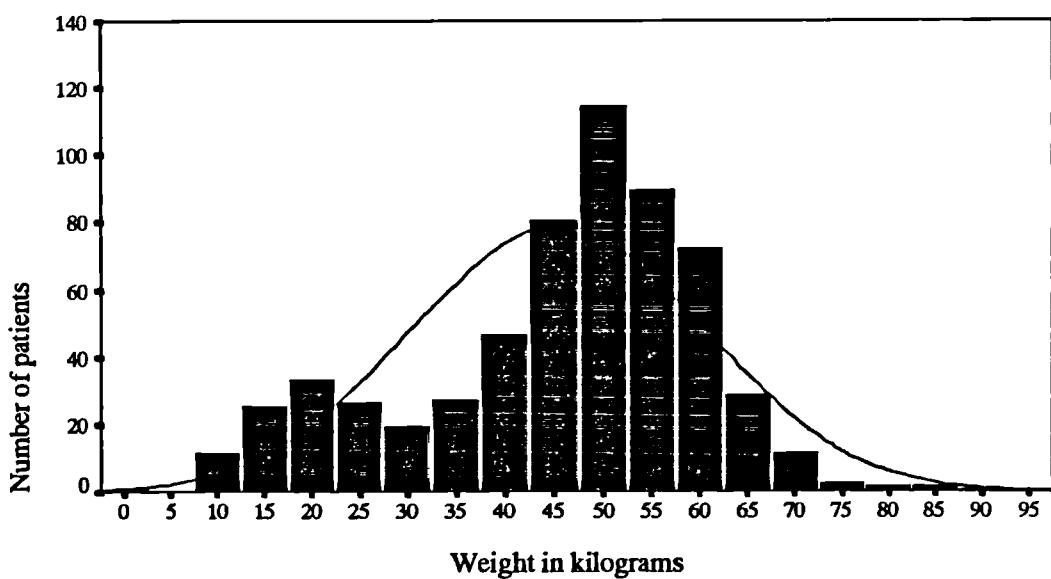
### ***6.4.1 Distribution of age, sex and weight among patients***

A total of 606 patients were recruited on day 0. Among these, 366 (60.4%) were males while 240 (39.6%) were females. Their age ranged from 1 to 76 years with a mean of 23.5 years (s.d. = 13.7). The mean body weight was 45.4 kilograms (s.d. = 15.2). The frequency distribution of age and body weight among the patients who were studied is shown in Figures 6.1 and 6.2. As shown in Figure 6.1, the great majority of patients were young adults, and patients above 55 years and less than five years were relatively few. The body weight of patients also followed a similar pattern.

**Figure 6.1 Age distribution among patients**



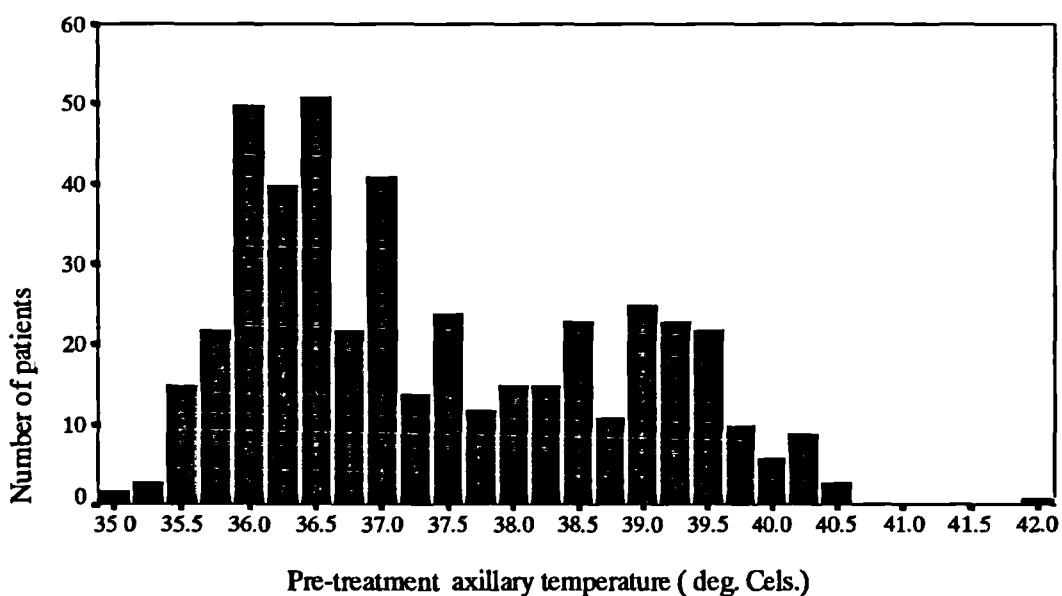
**Figure 6.2 Weight distribution among patients**



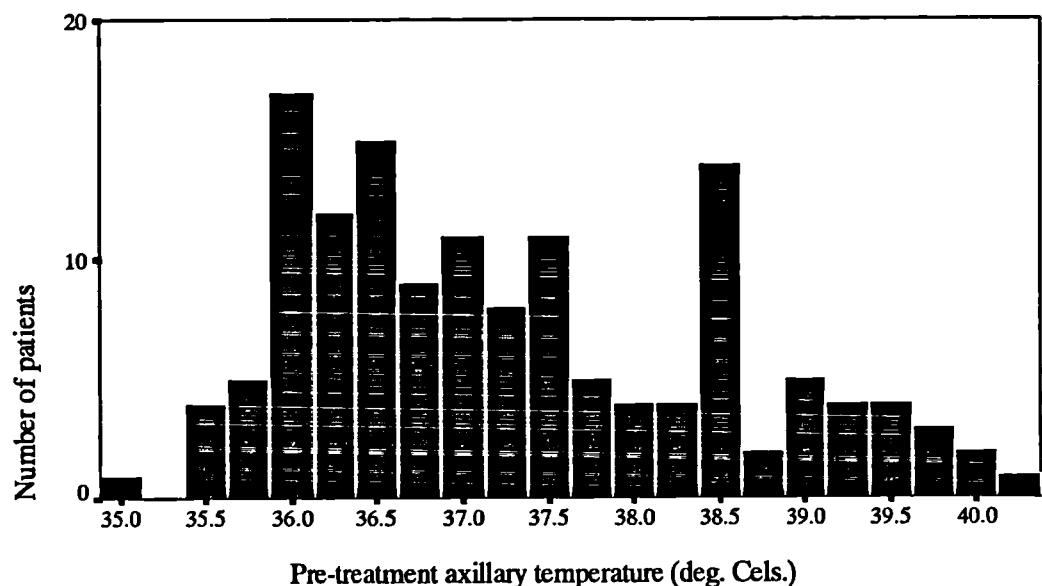
#### **6.4.2 Pre-treatment axillary temperature**

Reliable record of axillary temperature was obtained for 600 patients. Among these, 459 patients were diagnosed to harbour *P. vivax* while 141 were suffering from *P. falciparum*. A total of 190 (41.4%) patients with *P. vivax* had fever, i.e. an axillary temperature  $\geq 37.5$  °C. Furthermore, 53 (37.6%) patients due to *P. falciparum* had fever. The difference in fever risk between the two species was not significantly different ( $\chi^2 = 0.65$ ,  $P = 0.42$ , 1 d.f.). The mean axillary temperature was comparable for the two species of malaria parasites: 37.4 °C and 37.3 °C in *P. vivax* and *P. falciparum* patients respectively. The observed pattern in the frequency distribution of axillary temperature in patients found to be infected with the two species is depicted in histograms shown in Figures 6.3 and 6.4.

**Figure 6.3 Axillary temperature distribution among patients with *P. vivax***



**Figure 6.4 Axillary temperature distribution among patients with *P. falciparum***

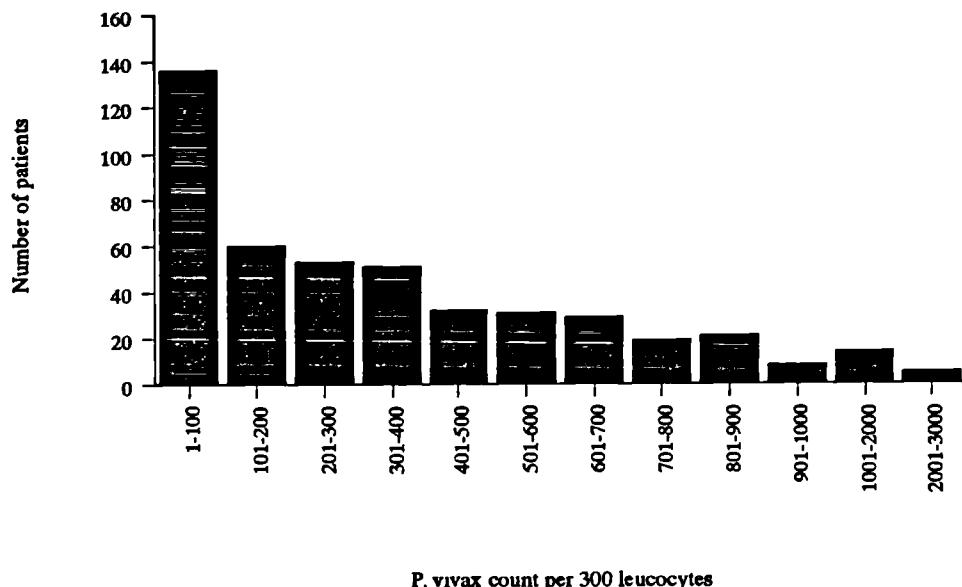


#### **6.4.3 Pre-treatment asexual parasitaemia**

##### **6.4.3.1 *P. vivax***

A total of 459 patients with *P. vivax* submitted blood samples before the initiation of treatment with chloroquine. The median asexual parasite count was 259 per 300 leucocytes (about 6,900 parasites per microliter of blood if the leucocyte count were 8,000/ $\mu$ l). The frequency distribution of the parasite densities is depicted in a histogram as shown in Figure 6.5.

**Figure 6.5 Distribution of *P. vivax* asexual parasitaemia among patients**



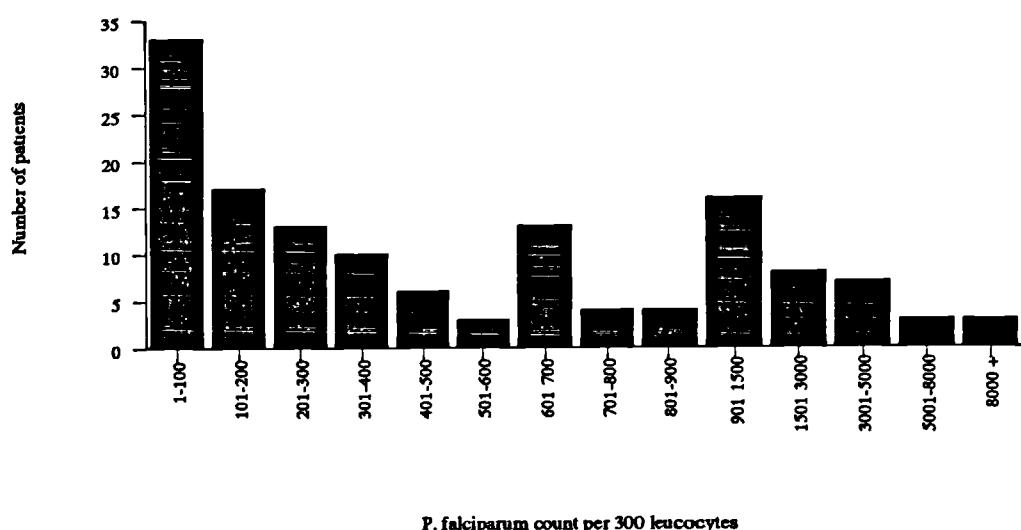
As shown in Figure 6.5, the histogram shows a very skewed distribution of asexual parasitaemia among patients with *P. vivax*. Patients with asexual parasitaemia of *P. vivax* greater than 800 per 300 leucocytes ( $> 21,330 / \mu\text{l}$ ) were relatively rare. Most had parasite counts less than 200 per 300 leucocytes (about  $5,330 / \mu\text{l}$ ).

#### 6.4.3.2

#### P. falciparum

A total of 142 consenting patients with *P. falciparum* were recruited and subjected to the *in-vivo* test. The median asexual parasite count was 330.5 per 300 leucocytes (about 8,810 /  $\mu$ l). The frequency distribution of asexual parasite densities among patients is depicted in a histogram as shown in Figure 6.6. Here also, the distribution of asexual parasitaemia is even more highly skewed than in *P. vivax*. Patients with counts greater than 8,000 parasites per 300 leucocytes were extremely rare. Most patients had less than 4,000 parasites per 300 leucocytes.

**Figure 6.6 Distribution of *P. falciparum* asexual parasitaemia among patients**



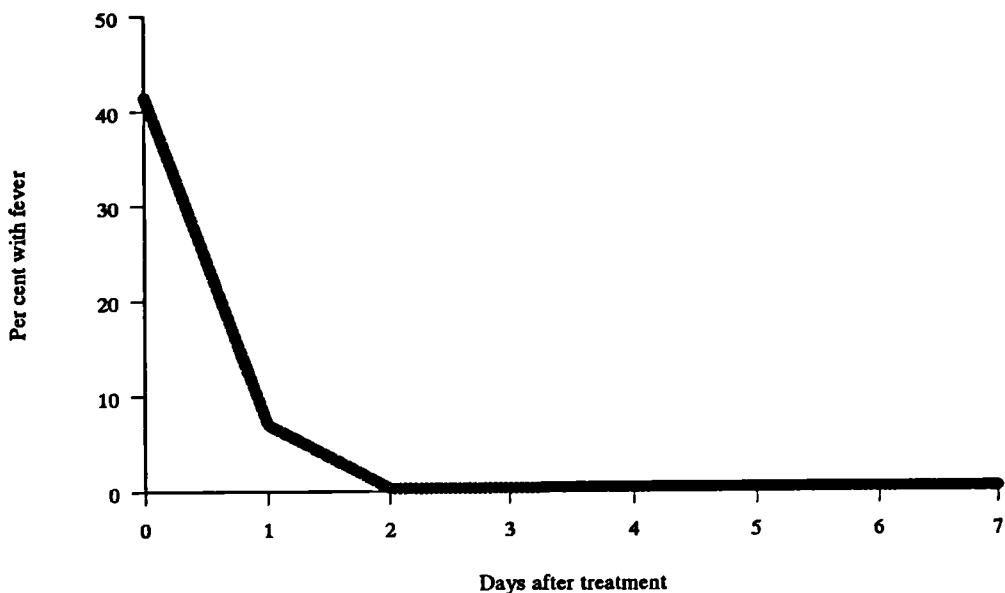
#### **6.4.4 Response of patients to antimalarial treatment**

##### ***6.4.4.1 Response of patients with P. vivax to chloroquine***

###### ***6.4.4.1.1 Remission of fever***

Among the patients who were recruited on day 0 and treated, the number who came on appointment during the subsequent follow-up days dwindled with time. The number of patients who had complete records of axillary temperature was 459 on day 0, 431 on day 1, 389 on day 2, and 244 on day 7. The proportion who completed the follow-up period regularly up to day 7 with respect to the number who were initially recruited was 53.2%. The proportion with fever, i.e axillary temperature  $\geq 37.5^{\circ}\text{C}$  on days 0, 1, 2 and 7 was 41.4%, 7%, 0.3% and 0.4% respectively. Thus, in patients with a diagnosis of *P. vivax* malaria, there was almost complete remission of fever 48 hours after treatment with a standard dose of chloroquine as seen in the absence of fever in 99.7% of those treated. This pattern in the remission of fever in *P. vivax* patients is shown in Figure 6.7.

**Figure 6.7 Remission of fever among patients with *P. vivax* following treatment**



#### **6.4.4.1.2 Clearance of asexual parasitaemia**

The response of patients with *P. vivax* was evaluated by observing the clearance of asexual parasitaemia in the peripheral blood as assessed by serial Giemsa stained blood films on days 0, 1, 2 and 7. On day 0, only 29.6% of patients had asexual parasite counts of less than 100 per 300 leucocytes. But at 24 hours following treatment, some 97.3% had reduced their level of parasitaemia to 100 or less per 300 leucocytes. On day 2, i.e. 48 hours after treatment with chloroquine, only 18.2% of patients had asexual parasites in the peripheral blood, while the remaining 81.8% cleared. By day 7, only 5 of 255 patients

(2%) had evidence of asexual parasitaemia with *P. vivax*. The response of these patients with *P. vivax* to treatment with chloroquine is depicted in Table 6.2.

**Table 6.2 Pattern in clearance of *P. vivax* asexual parasitaemia**

Parasite density per 300 WBC	Day 0,N = 459	Day 1, N=439	Day 2, N=380	Day 7,N=255
	% of patients	% of patients	% of patients	% of patients
0	0.0	32.3	81.8	98.0
1-100	29.6	65.0	18.2	2.0
101-1000	66.3	2.7	0.0	0.0
> 1000	4.1	0.9	0.0	0.0

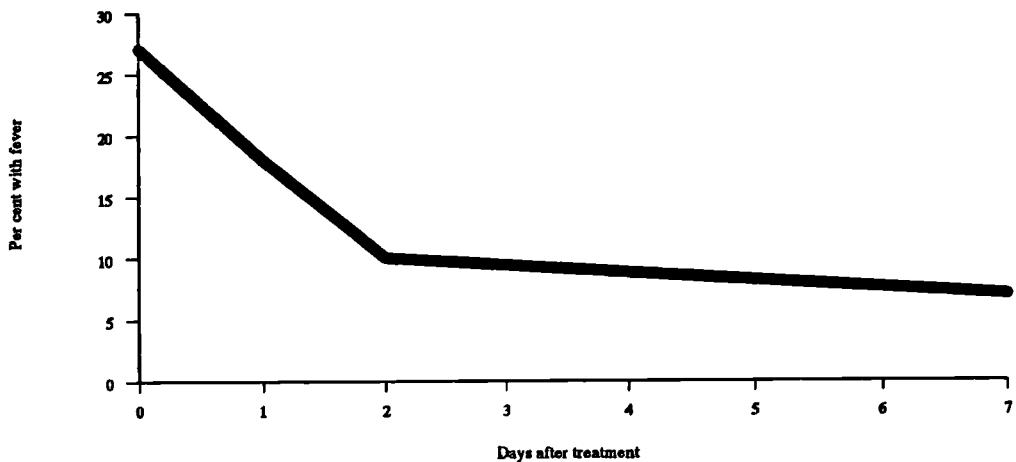
#### **6.4.4.2 Response of patients with *P. falciparum* to chloroquine**

##### **6.4.4.2.1 Remission of fever**

Some 60 patients who satisfied the recruitment criteria and with a diagnosis of *P. falciparum* malaria were treated with a standard dose of chloroquine. The proportion of patients with fever, i.e. axillary temperature  $\geq 37.5$  °C was 27% on day 0, 18% on day 1, 10% on day 2, and 7% on day 7. It is notable that this post-treatment proportion of patients with fever is much higher than that observed in patients with *P. vivax*. The

pattern in the remission of fever among *P. falciparum* patients after treatment with chloroquine is depicted in Figure 6.8.

**Figure 6.8 Response of fever among *P. falciparum* patients**



As shown in the above figure, it is clear that some patients did not show any evidence for the remission of fever in spite of treatment with chloroquine.

#### **6.4.4.2.2 Clearance of asexual parasitaemia**

A total of 60 patients diagnosed to be infected with *P. falciparum* were recruited and treated with chloroquine initially. However, the number of patients who presented for follow-up post-treatment declined with time. The number of patients decreased gradually from 60 on day 0, to 50 on day 1, 34 on day 2, and 29 on day 7. The level of clearance of

parasitaemia on these days as assessed by the proportion of patients with asexual parasite density groups is shown in Table 6.3.

**Table 6.3. Clearance of *P. falciparum* asexual parasitaemia following treatment with chloroquine**

<i>Parasite density per 300 leucocytes</i>	<i>Day 0, N = 60</i>	<i>Day 1, N = 50</i>	<i>Day 2, N = 34</i>	<i>Day 7, N = 29</i>
	<i>% of patients</i>	<i>% of patients</i>	<i>% of patients</i>	<i>% of patients</i>
0	0	12	15	14
1-100	35	40	59	55
101-1000	45	38	15	31
> 1000	20	10	11	0

Thus, as shown in Table 6.3, among the 60 patients who were recruited initially, only 29 (48%) were able to complete successfully the follow-up evaluation. Furthermore, among these 29 patients who were adequately treated with a standard oral dose of chloroquine over three consecutive days, only 4 patients (14%) were able to clear their parasitaemia by day 7. The remaining 25 patients (86%) were unable to clear their asexual parasitaemia by day 7 in spite of treatment suggesting the presence of a high level of *in-vivo* resistance of *P. falciparum* to chloroquine. However, note also that although the proportion of clearance of asexual parasitaemia was low on day 7, the proportion with high parasite densities (>1000 per 300 leukocytes) decreased progressively from 20% on day 0, to 10% on day 1, to 11% on day 2, to 0% on day 7.

#### ***6.4.2.2.3 Grades of chloroquine resistance in P. falciparum strains of Debre Zeit***

The interpretation of grades of chloroquine resistance of *P. falciparum* were carried out according to the criteria set by WHO (1981) which was mentioned in the methods section of this chapter.

Among the 25 patients who failed to clear asexual parasitaemia on day 7, there was no patient who showed any evidence of clearance of asexual parasitaemia for two consecutive days following treatment, thus there was no RI level of resistance. However, the 4 patients (14%) who showed evidence of clearance of parasitaemia on day 7 were not followed during weeks 2, 3 and 4, and therefore may be either sensitive (S) or may have shown delayed recrudescence (RII resistance). It was decided not to conduct the extended field test since there was no way of distinguishing between reinfection and genuine recrudescence in the study area because of ongoing transmission.

A total of 18 of 29 (62%) patients showed evidence of reduction of asexual parasitaemia to 25% or less during the first 48 hours of treatment, but were unable to clear by day 7. These patients were infected with *P. falciparum* strains that were resistant to chloroquine at the RII level. The remaining 7 of 29 (24%) patients were able to reduce their parasitaemia by less than 75% after 48 hours of treatment and therefore were classified as

patients infected with *P. falciparum* resistant to chloroquine at the RIII level. A summary of the grades of resistance is given in Table 6.4.

**Table 6.4      Grades of chloroquine resistance in *P. falciparum***

<i>Grade</i>	<i>Number of patients</i>	<i>Proportion (%)</i>
RI / S	4	14
RII	18	62
RIII	7	24
Total	29	100

#### **6.4.4.3      Response of patients with *P. falciparum* to sulphadoxine-pyrimethamine (Fansidar<sup>R</sup>)**

As shown above, there was clear evidence of chloroquine resistance among patients infected with *P. falciparum*. It was therefore unethical to proceed with further recruitment of patients for a study with a treatment regimen of chloroquine. Subsequently, patients who satisfied the recruitment criteria were given a single oral dose of Fansidar<sup>R</sup> according to their age with a maximum dose of 3 tablets for an adult. This evaluation was necessary

as this treatment regimen with Fansidar for suspected or confirmed cases of chloroquine resistant falciparum malaria in Ethiopia was the policy of the National Organization for the Control of Malaria and Other Vector-borne Diseases.

A total of 81 patients confirmed to be ill due to *P. falciparum* malaria were recruited for observation under treatment with Fansidar<sup>R</sup>. The response of these patients was evaluated by monitoring their axillary temperature and asexual parasitaemia on days 0, 1, 2 and 7 as under chloroquine. The results are given below.

#### ***6.4.4.3.1 Remission of fever***

The number of patients with axillary temperature records and the proportion with fever on days 0, 1, 2 and 7 is shown in Table 6. 5.

***Table 6.5 Response of fever to treatment with Fansidar<sup>R</sup> among P. falciparum patients***

Days post-treatment	Number of patients seen	Proportion (%) with fever
		$\geq 37.5^{\circ}\text{C}$
Day 0	81	43
Day 1	70	26
Day 2	63	18
Day 7	35	3

As shown in the above table, the proportion of patients with fever decreased from 43% on day 0 to 18% on day 2, i.e. a reduction by about 60% after 48 hours of treatment with Fansidar<sup>R</sup>. By day 7, there was only one patient with fever among those who completed the follow-up period.

#### **6.4.4.3.2      *Clearance of asexual parasitaemia***

Assessment of the response of *P. falciparum* patients to a single oral dose of Fansidar<sup>R</sup> was also done by observing the density of asexual parasites in the peripheral blood in Giemsa-stained blood films. The asexual parasite count and the proportion observed in each category following treatment is given in Table 6.6.

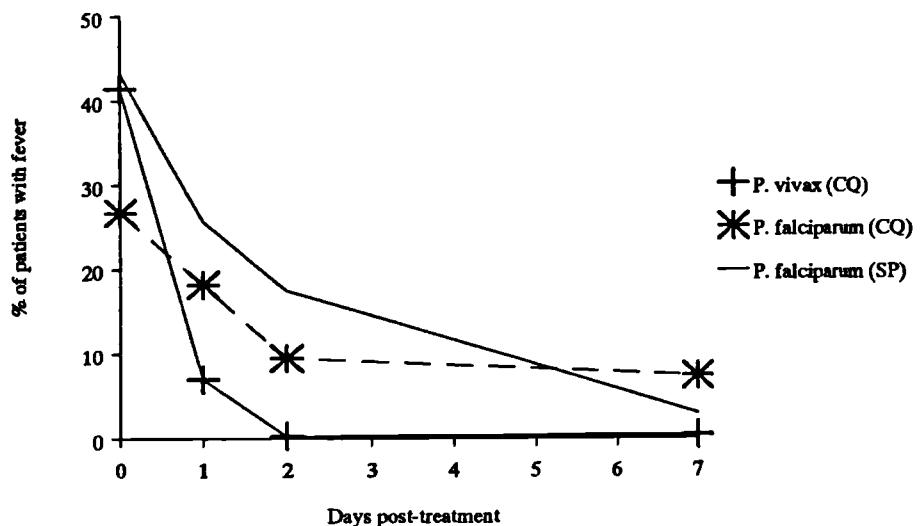
**Table 6.6 *Clearance of P. falciparum asexual parasitaemia after Fansidar treatment***

Asexual count per 300 WBC	<i>Day 0, N = 80</i>	<i>Day 1, N = 64</i>	<i>Day 2, N = 60</i>	<i>Day 7, N = 32</i>
	<i>% of patients</i>	<i>% of patients</i>	<i>% of patients</i>	<i>% of patients</i>
0	0	20	75	97
1-100	15	41	15	0
101-1000	54	28	7	3
> 1000	31	11	3	0

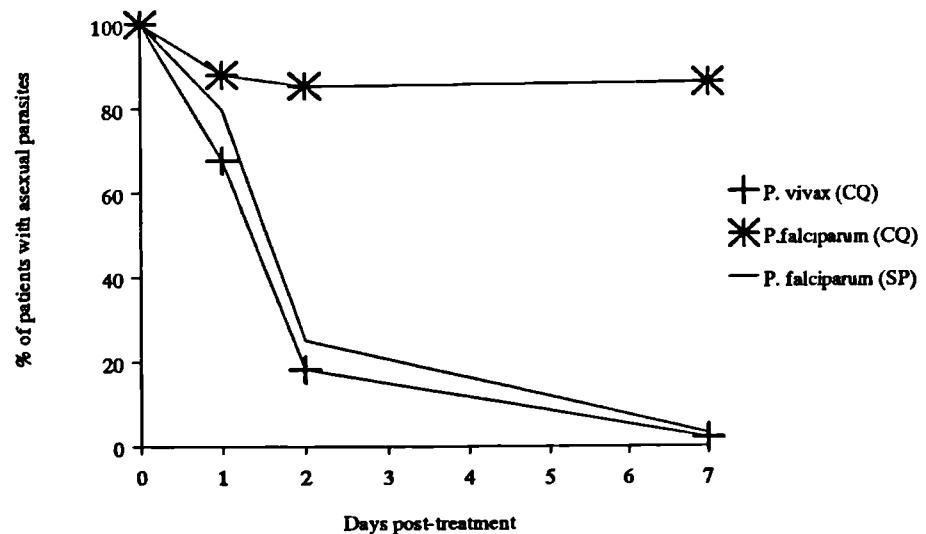
As shown in the table above, in contrast to *P. falciparum* patients who were treated with chloroquine, there was a very marked clearance of asexual parasitaemia following treatment with Fansidar<sup>R</sup>. The proportion of patients with high densities of asexual parasitaemia decreased markedly following treatment. Furthermore, the proportion of patients who showed evidence of complete clearance of asexual parasitaemia was 20.3% after 24 hours, 75% after 48 hours, and 96.9% after one week, i.e. on day 7. However, what is very worrying is the failure of clearance of asexual parasitaemia on day 7 in spite of adequate treatment with Fansidar<sup>R</sup> in one patient.

The following two figures, i.e. Figures 6.9 and 6.10 may give a very general summary of the pattern in the remission of fever and clearance of asexual parasitaemia observed among patients with *P. falciparum* and *P. vivax* following treatment. As shown in Figure 6.9, the remission of fever following treatment was most dramatic among patients infected with *P. vivax* and treated with a standard oral dose of chloroquine. In contrast, the response of patients infected with *P. falciparum* and treated with a standard dose of chloroquine was much less marked in spite of adequate treatment although there was some remission in the first 48 hours. However, the response of patients treated with Fansidar<sup>R</sup> showed a gradual decline in the proportion of patients with fever compared to those of *P. vivax* malaria by day 7.

**Figure 6.9 Pattern in the remission of fever following antimalarial treatment**



**Figure 6.10 Pattern in the clearance of asexual parasitaemia after antimalarial treatment**



Key: CQ= Chloroquine SP = Sulphadoxine-pyrimethamine (Fansidar<sup>R</sup>)

As shown in Figure 6.10, the pattern in clearance of asexual parasitaemia suggests at first glance that patients with *P. falciparum* are not responding to treatment with a standard dose of chloroquine. Furthermore, the pattern in clearance of asexual parasitaemia among patients infected with *P. vivax* treated with chloroquine and patients with *P. falciparum* treated with Fansidar is comparable.

## **6.5 Discussion**

Evaluation of treatment responses of *P. falciparum* and *P. vivax* patients to standard doses of antimalarials in Debre Zeit was conducted by looking at the pattern in the remission of fever and clearance of asexual parasitaemia over the subsequent week. In patients with *P. vivax*, the response to treatment with a standard dose of chloroquine was dramatic in the first 48 hours following treatment. Some 99.7% of patients did not have any sign of fever and 82% did not have any evidence of asexual parasites in their peripheral blood. Furthermore, 98% patients who completed the follow-up period did not show any sign of asexual parasitaemia in their blood by day 7.

There could be two alternative explanations for failure of clearance of asexual parasitaemia among 5 of 255 (2%) patients infected with *P. vivax*. Firstly, the patients may

have been infected with the two species, i.e. a mixed infection of both *P. vivax* and *P. falciparum* in which the latter species escaped detection by standard microscopy. Secondly, it could be the first evidence for presence of *in-vivo* resistance of *P. vivax* in Ethiopia. However, even if the latter scenario is accepted, i.e. the emergence of strains of *P. vivax* resistant to chloroquine in Debre Zeit probably at the RI level, the proportion observed which was only 2%, is likely to be too low to have contributed to the enormous increase in morbidity attributable to *P. vivax* malaria as discussed in Chapter 3. Furthermore, the evidence does not warrant a change in the standard treatment regimen with chloroquine for *P. vivax* malaria. A standard oral dose of chloroquine therefore is recommended in the treatment of *P. vivax* malaria in the study area. Although the response pattern of about 44% of patients who were initially recruited but who failed to show-up on day 7 was unknown, it seems unlikely that the dramatic increase in the incidence of *P. vivax* malaria as discussed in Chapter 4, could be attributed to failure of treatment with chloroquine related to chloroquine resistance.

In contrast to the response of patients with *P. vivax* treated with chloroquine, patients with *P. falciparum* malaria did not show such a marked improvement particularly in the clearance of asexual parasitaemia. Although there was a significant reduction in the proportion of patients with fever by about 64%, only 14% of the patients who completed the follow-up were able to clear their asexual parasites on day 7 suggesting a high level of chloroquine resistance *in-vivo*. The discrepancy between the effect in the reduction of fever and clearance of asexual parasitaemia may be attributed to the strong antipyretic

effect of chloroquine or alternatively to the reduction in the proportion of patients with high parasite counts.

The level of chloroquine resistance observed was classified as RI/S in 14%, RII in 62% and RIII in 24% of 25 patients who failed to clear their asexual parasitaemia. Thus, in spite of common belief that chloroquine resistance is limited to peripheral regions of Ethiopia along the border with Somalia, Kenya and the Sudan (Teklehaimanot, 1986), the findings in this study suggest that there is a high level of chloroquine resistance among *P. falciparum* patients in the highlands of central Ethiopia. This also calls for a further evaluation of the policy of the chloroquine treatment regimen for patients infected with *P. falciparum*. It may be unethical to pursue such a policy in the light of the evidence for the presence of RII and RIII chloroquine resistance in the majority of patients with *P. falciparum*.

Furthermore, it is possible that such resistance has contributed to the presence of recrudescence parasites in the community, facilitating transmission and thus increased morbidity. This may in part explain the observed marked increase in the proportion of patients admitted due to malaria at Debre Zeit hospital as discussed in Chapter 3. The treatment of patients admitted due to *P. falciparum* with chloroquine could also have led to increased mortality attributable to malaria. This may partly explain the 13-fold increase in the proportion of deaths ascribed to malaria which was noted in Chapter 3.

The previous absence of chloroquine resistance in 1980 among 21 subjects who were successfully followed up for seven days in Nazareth, only 50 kilometres east of the present study area (Gabre-Mariam, 1982) suggests that chloroquine-resistance may be of relatively recent onset in Debre Zeit. The ineffectiveness of chemoprophylaxis with chloroquine in preventing at least one episode of malaria among two thousand children in a more recent randomised controlled trial in the Middle Awash Valley (Wolde et al., 1994) may have been due to the emergence of chloroquine resistance in the area. In spite of the previous absence of Fansidar<sup>R</sup> for wider use in the treatment of *P. falciparum*, one of the 32 (3%) patients seemed not to respond to the treatment suggesting the possible presence of *P. falciparum* strains resistant to this drug. This is very worrying as the range of other alternative antimalarials that are safe, effective and that could be afforded at a reasonable cost is very narrow (Bradley, 1991).

The other finding was that in spite of common belief that in such areas with unstable malaria patients with clinical malaria present with fever, only 43.2% of patients with *P. falciparum* malaria and 41.4% of patients with *P. vivax* showed signs of fever, i.e. axillary temperature  $\geq 37.5$  °C. It may be difficult to attribute this to the development of immunity due to the relatively short transmission season and recent onset of transmission in communities living in localities lying at high altitudes as discussed in Chapters 3 and 4. The current level of transmission which has become perennial is of recent onset and even then shows a very marked fluctuation in the incidence of malaria depending on the monthly mean night-time temperature and length of the rainy season as will be discussed in

Chapter 8. Although it is likely that some proportion of patients without fever could be explained by the known periodicity of fever, i.e. patients presenting to the clinic after fever spontaneously subsided temporarily, it is difficult to attribute all the proportion without fever to this factor alone.

In a recent article from work in Tanzania, some 66.5% of malaria-attributable episodes among infants corresponded to axillary temperatures  $< 37.5^{\circ}\text{C}$ , i.e. only some 33.5% of patients that were genuinely ill due to malaria did show any sign of fever (Smith et al., 1995). Although the level of transmission could be very different from that found in the present study area, this finding in infants which could have a similar experience of malaria infection to the adults in this study in terms of duration of exposure to infective bites, is indicative that it may be difficult to rely on fever alone for the diagnosis of malaria as is routinely done in many primary care rural health facilities in Ethiopia. Nonetheless, the monitoring of fever as a complementary tool to laboratory diagnosis seems essential as seen in this study in which failure of clearance of asexual parasitaemia was also followed by persistence of fever in the great majority of patients with *P. falciparum* who did not respond to treatment with chloroquine and in one of the patients treated with Fansidar.

The presence of a very suitable ambient temperature, particularly an increase in the minimum temperature as discussed in Chapter 5, coupled with a high level of chloroquine resistance in *P. falciparum*, could have contributed to a very marked increase in the level of transmission in *P. falciparum* in the present study area. This may also explain the shift

towards a preponderance of this species in relative frequency particularly in localities lying at higher altitudes. In the light of the evidence of chloroquine resistance and possible Fansidar<sup>R</sup> resistance among strains of *P. falciparum* in the study area, there is a very urgent need to intensify efforts in vector control using the most effective tool that could be affordable by the community and the country.

In contrast to the pattern of treatment failures and *in-vivo* resistance to chloroquine in *P. falciparum*, almost all patients infected with *P. vivax* responded dramatically to treatment with chloroquine as shown by the complete remission of fever in 99.7% about 48 hours after treatment and clearance of asexual parasitaemia in 98% seven days following treatment. In the light of this finding, chloroquine resistance does not appear to be an explanatory variable for the observed increase in the transmission of *P. vivax* malaria in this study area. It is therefore likely that some other explanatory variable that could affect the level of transmission of both species did play a more decisive role in the increased incidence of malaria in the study area.

### **6.6. Summary**

A prospective *in-vivo* drug sensitivity study was conducted in a malaria clinic in a highland area of central Ethiopia where malaria is unstable to see whether failure of treatment regimens was responsible for the reported increase in the incidence of malaria . The response to treatment was assessed using remission of fever and clearance of asexual

parasitaemia on days 0, 1, 2 and 7. There was almost complete remission of fever (99.7%) about 48 hours after treatment with chloroquine and 98% showed evidence of clearance of asexual parasitaemia among 255 patients infected with *P. vivax*. In contrast, only 14% of patients infected with *P. falciparum* showed evidence of clearance of asexual parasitaemia although there was reduction in the proportion with fever by 64% after treatment with chloroquine.

The chloroquine resistance levels were RI/S in 14%, RII in 62% & RIII in 24%. However, all but one of 32 *P. falciparum* patients treated with Fansidar<sup>R</sup> cleared their asexual parasites. In the light of this finding, while the high level of chloroquine resistant *P. falciparum* strains in the area may partly contribute to the reported increase in morbidity and mortality attributable to malaria, the effectiveness of treatment with chloroquine in almost all *P. vivax* patients suggests that there must be some explanatory factor other than drug resistance responsible for the increased transmission of malaria in the highlands of Ethiopia. Subsequent chapters will focus on the relative contribution of vector control efforts and favourable climatic changes for the increased incidence of highland malaria.

## **Chapter 7**

### **The use of DDT for the control of malaria in Debre Zeit sector**

#### **7.1 Background**

A resurgence of malaria has been noted in Ethiopia since 1985 as discussed in Chapter 1.

In an attempt to identify the most important determinants of the increased incidence of malaria in the highlands of Ethiopia, an exploratory analysis of both climatic and non-climatic factors was carried out. There was a respective 67-fold and 13-fold increase in morbidity and mortality from malaria when the malaria situation in the highlands of Debre Zeit sector over the past two decades was analysed as discussed in Chapter 3. It was also noted that the altitudinal limit of transmission of both *P. falciparum* and *P. vivax* has extended from less than 2,000 metres to localities up to 2,200 metres above sea level only during the past decade as shown in Chapter 4.

In Chapter 5, the pattern of climatic fluctuation in Debre Zeit and its relation to the El Niño-Southern Oscillation was discussed. The level of effectiveness of antimalarial treatment against *P. vivax* and the pattern of chloroquine resistance in *P. falciparum* was discussed in Chapter 6. In this chapter, an attempt will be made to describe the pattern in DDT (dichloro-diphenyl-trichloroethane) use for the control of malaria in the context of the overall study of determinants of malaria transmission in the highlands of Ethiopia.

Initially, the antimalarial campaign was expected to undergo four phases; namely preparatory, attack, consolidation and maintenance phases although this has not strictly been adhered to in practice as will be seen later in this chapter. The preparatory phase was expected to last for two years and included geographical reconnaissance of potentially malarious localities in which locality maps were prepared, and houses were numbered. The attack phase was expected to last four years and blanket coverage of all premises thought to be resting sites of vector mosquitoes was expected to be undertaken by the DDT spraying operation teams. The consolidation phase was to concentrate on the identification of sources of malaria transmission and prevent reintroduction of infection into an area once it was declared free from malaria. The maintenance phase was expected to be undertaken by the general health services, hoping that malaria would no longer be a problem of public health importance once it was reduced to that level.

A National Malaria Eradication Service was established in Ethiopia by Imperial decree in 1959. Technical sub-professional staff with secondary education were recruited and trained for about 6 months in a National Malaria Training Centre at Nazareth, with the assistance of experts from WHO. The training included basic knowledge of the biology of the parasite and the vector, epidemiology & surveillance and strategies of malaria control. Practical hands-on training was also given in the diagnosis of the malaria parasites, identification of vectors, and collection and interpretation of field data. A certificate was awarded to all those who successfully completed their training. These technicians were the backbone of most of the antimalarial campaigns over the past three decades in Ethiopia. A

few national professional staff with first degrees in biology and agriculture were also recruited and trained in parasitology and entomology to MSc level in the USA as the main funding agency was then USAID. These few national professionals were later posted as senior management staff and were responsible for the co-ordination and supervision of antimalarial activities at the national level.

An extensive intradomiciliary application of DDT was the main strategy with the ultimate objective of the eradication of malaria from the highlands of Ethiopia by 1980 as discussed in Chapter 1. All the 430 localities in the present study area were mapped and census of the population living in each of these localities was conducted in 1965. The strategy was then blanket coverage of all localities irrespective of the level of malaria during the initial stages of the campaign from 1967 to 1973. A change in government occurred in 1974 in which the Imperial Government of Haile Selassie was overthrown to be replaced by a military regime. With this, external funding from USAID & WHO/UNICEF to the national antimalarial campaign stopped. This was further compounded by a change in strategy in which the emphasis shifted from eradication to control following the Alma Ata declaration of "health for all by the year 2000" in 1978. Selective spraying became the main strategy in which cross-sectional blood surveys were carried out annually in selected localities and each locality was categorised in to no spraying , 1 round and 2 round of DDT spraying based on the results of the level of malaria in the seasonal blood surveys.

Spraying activity was organised in small units called squads. Each squad consisted of 4 spray-men and a squad chief. Spray-men were given one week of training on how to mix 75% DDT with water, build a fixed amount of pressure in the Hudson X-pert spray-pump ( about 60 pumps mechanically for each 8 litres), and discharge a certain volume of DDT on a sprayable surface ( a standard of 2 grams of DDT / m<sup>2</sup>). They were also given training on how to clean the spray-pump after each round of spraying during the day. Supervision of spraying activities was carried out first by the squad chief, then by a malaria technician for each of four squads, a malaria operation supervisor for each of 4 malaria technicians, and the whole administrative and technical operation in the sector was managed by a sector chief.

Health education teams went to the villages to persuade residents to co-operate in the spraying activities by taking out all kitchen items and food from the house and refrain from plastering of the sprayed walls for six consecutive months. Spray-men were initially recruited from towns and paid for by the National Malaria Control Programme until 1978. But, with the concept of community participation as one of the strategies in primary health care, each of the peasant associations in the rural areas were asked to select spray-men from each locality. These spray-men were also supported by the communities (who selected them) during training and during the whole period of spraying activities usually lasting about two months each year.

In localities expected to receive one round of spraying with DDT, intradomiciliary spraying was carried out in the months of June and July in the hope of reducing the level of malaria during the peak transmission months of October and November. In those which were to receive two round of DDT, spraying activities were carried out in the months of January-February, and June-July to prevent malaria transmission after the short rains and the main rainy season respectively. Furthermore, all squad chiefs and malaria technicians were given antimalarial drugs so that all patients presenting with symptoms of malaria during the spraying activities could be treated instantly in their own localities.

## ***7.2 Objectives***

Over the past two decades the objectives are to describe the pattern of change in :

- 7.2.1 the amount of DDT used for malaria control
- 7.2.2 the localities that received DDT spraying
- 7.2.3 the coverage of the population expected to be protected directly from malaria and
- 7.2.4 the cost of spraying DDT

## ***7.3 Data set***

Individual records of 430 localities were examined. Historical data on the amount & dose of DDT, number of unit structures (houses) sprayed/unsprayed, and number of people protected /unprotected during each of the two rounds of DDT spraying per year was

extracted from each locality record and entered in the computer. A total of 9,520 records for the past 28 years (1965-93) were entered in this manner. Data on total cost of DDT spraying operations per year was available from 1975 to 1993.

Descriptive analysis was then carried out to see whether a change in the pattern of DDT use was associated with the increased incidence of malaria in the highlands of Ethiopia. This was done by plotting the most important indicators of DDT use for malaria control in the study area against time in years. These were the amount of DDT applied per spray round, the number of houses sprayed and the number of people residing in the houses in each of the 430 localities from 1966 to 1993. A plot was then made to see whether a decreased use of DDT more clearly affected the annual incidence of malaria.

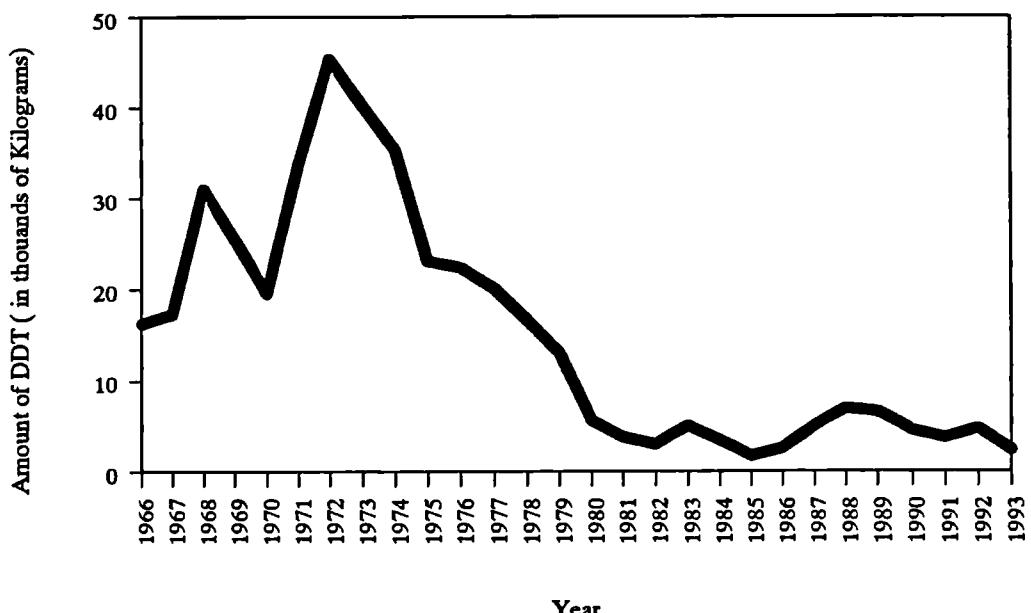
## 7.4 Results

### 7.4.1 *Amount of DDT sprayed for the control of malaria*

Data on the amount of DDT used for indoor spraying for the control of malaria in Debre Zeit sector was calculated from the amount used in each of the 430 localities during each round of spraying operations. The result is plotted in Figure 7.1. As shown in the figure, the period from 1966 to 1979 is characterised by extensive application of DDT for indoor spraying. In contrast, the period from 1980 to 1993 saw much lower levels of DDT used

for indoor spraying for the control of malaria. The most extensive indoor application of DDT was seen in 1972. A total of 45,385.1 kg of DDT was used for the control of malaria in Debre Zeit sector during this year. The smallest amount of DDT was applied in 1985. Only 1,725.8 kg of DDT was applied during this year in the whole sector.

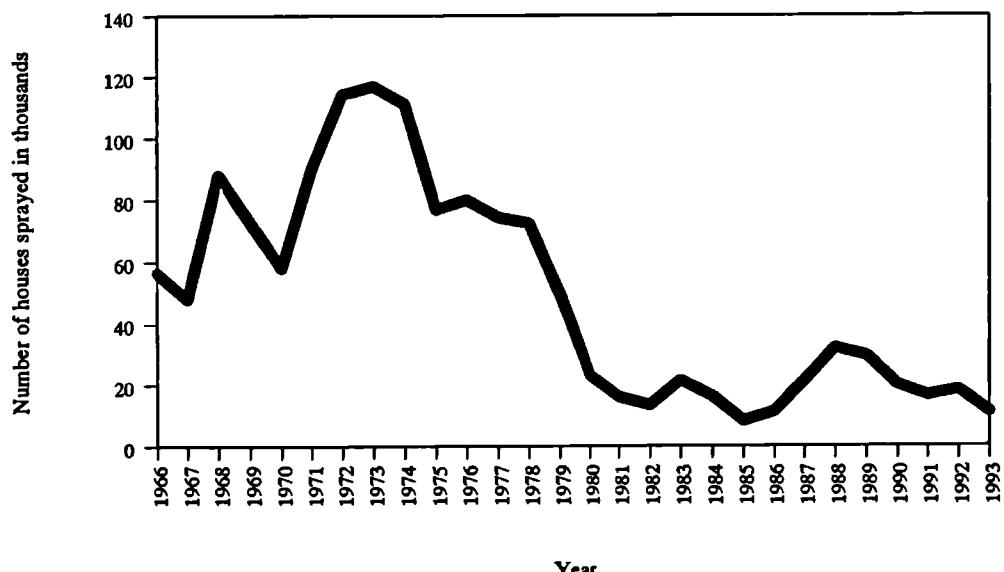
**Figure 7.1      Amount of DDT applied for the control of malaria in Debre Zeit sector**



#### **7.4.2 Number of houses sprayed with DDT for malaria control**

The total number of houses sprayed with DDT during each round of spraying was calculated from 1966 to 1993 for all the 430 localities. The result is plotted in Figure 7.2 which depicts extensive coverage from 1966 to 1979 followed by a very reduced coverage from 1980 to 1993. Peak coverage was in 1974 during which a total of 117,040 houses were sprayed with 75% wettable powder of DDT. The least coverage was in 1985 during which only 8,139 houses in the whole sector were sprayed with DDT.

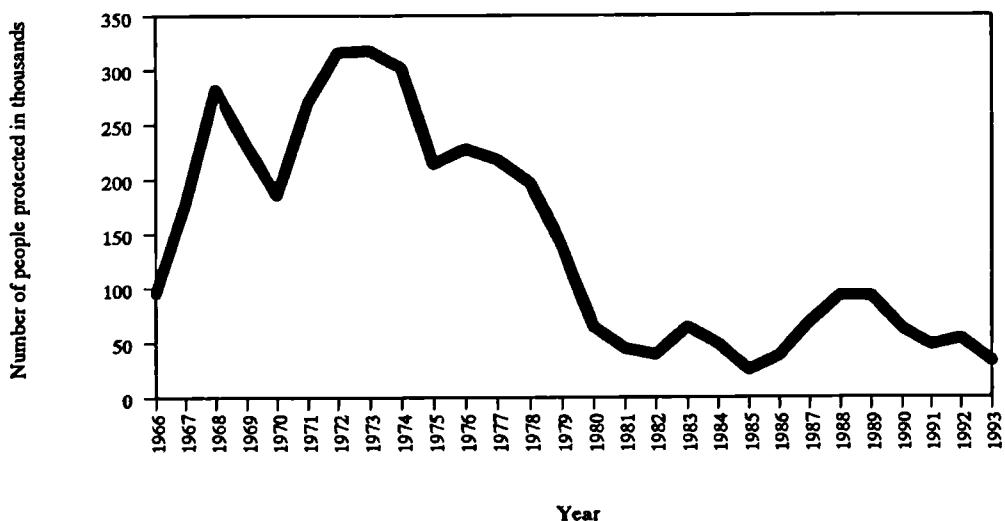
**Figure 7.2      Houses sprayed with DDT for the control of malaria in Debre Zeit sector**



#### **7.4.3 Number of people expected to be protected directly from malaria**

The total number of people expected to be protected directly from malaria by the indoor application of DDT was calculated first by the number of people residing in each house, then in each locality and ultimately for the whole sector by taking the sum. The pattern from 1966 to 1993 is plotted in Figure 7.3. As shown in the figure, the number of people expected to be protected directly by the indoor application of DDT was generally high from 1966 to 1979 followed by a relatively few number of people from 1980 to 1993. The highest number of people expected to be protected directly from malaria by the application of DDT in the whole sector was 317,860 and this was seen in 1973.

**Figure 7.3 Population expected to be protected directly by application of DDT from malaria**



#### **7.4.4 Operational cost of spraying DDT in Debre Zeit sector**

The operational cost of spraying DDT was obtained only for the years from 1975 to 1993.

The cost included an aggregate sum of the expenses for DDT applied, cost of transport, wages of temporary workers and per diem of staff. The total operational cost of spraying DDT from 1975 to 1993 was adjusted to 1992 prices to take account of inflation and plotted in Figure 7.4. Here, it is depicted that in spite of the reduction in the total amount of DDT sprayed, the operational cost in 1992 was the highest during the 18-year observation period. The second most expensive operational year was 1977. The years from 1980 to 1987 saw relatively little expenditures during the spraying operations.

**Figure 7.4 Operational cost of spraying DDT for the control of malaria in Debre Zeit sector**



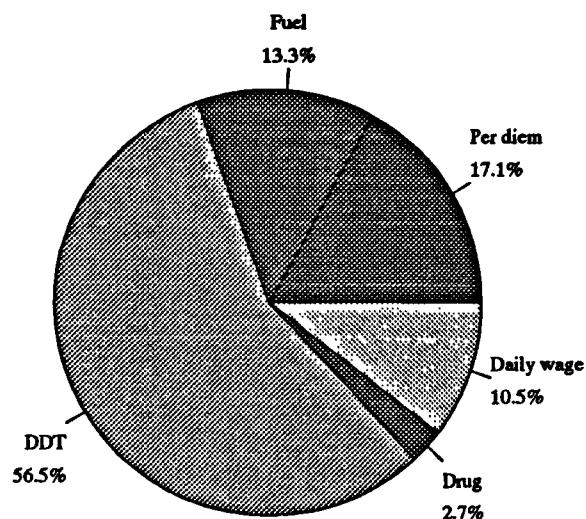
A breakdown of the cost of spraying operations from 1980 to 1991 is shown in Table 7.1. Overall, 56.5% of the cost was spent for the purchase of DDT, 17.1% for per diem of Malaria Control Personnel, 13.3% for fuel, 10.5% for daily wage of labourers (spray-men and camp guards) and about 2.7% for antimalarial drugs to provide treatment to those patients suspected of suffering from malaria during the spraying operation. This is clearer in the pie chart in Figure 7.5.

**Table 7.1 Itemised cost (in Birr) of spraying DDT for the control of malaria in Debre Zeit sector**

Year	Per diem	Fuel	DDT	Drug	Daily wage	Total
1980	4290.00	3607.84	9567.60	1009.55	6737.70	25212.69
1981	4338.00	3032.77	8583.29	488.90	7422.35	23865.31
1982	10725.50	10723.64	14513.72	1008.11	1729.45	38700.42
1983	8124.25	8141.79	10167.76	318.17	574.68	27326.65
1984	2925.00	1658.74	5105.10	365.46	232.50	10286.80
1985	3608.00	2220.00	13083.00	171.94	308.00	19390.94
1986	5268.00	2440.00	20168.50	262.87	533.10	28672.47
1987	5978.00	5085.00	16888.26	607.53	884.50	29443.29
1988	7225.00	4603.78	37538.76	204.37	1746.00	51317.91
1989	4804.75	4228.50	28477.00	278.00	1573.50	39361.75
1990	3788.00	2224.50	23347.32	1979.45	9155.25	40494.52
1991	7258.50	5137.00	38743.24	3938.91	11312.20	66389.85
Total	68333.00	53103.56	226183.55	10633.26	42209.23	400462.60

Note: 2.07 Birr = 1 US dollar until 1991 and 1 US dollar = 5.30 Birr since 1991

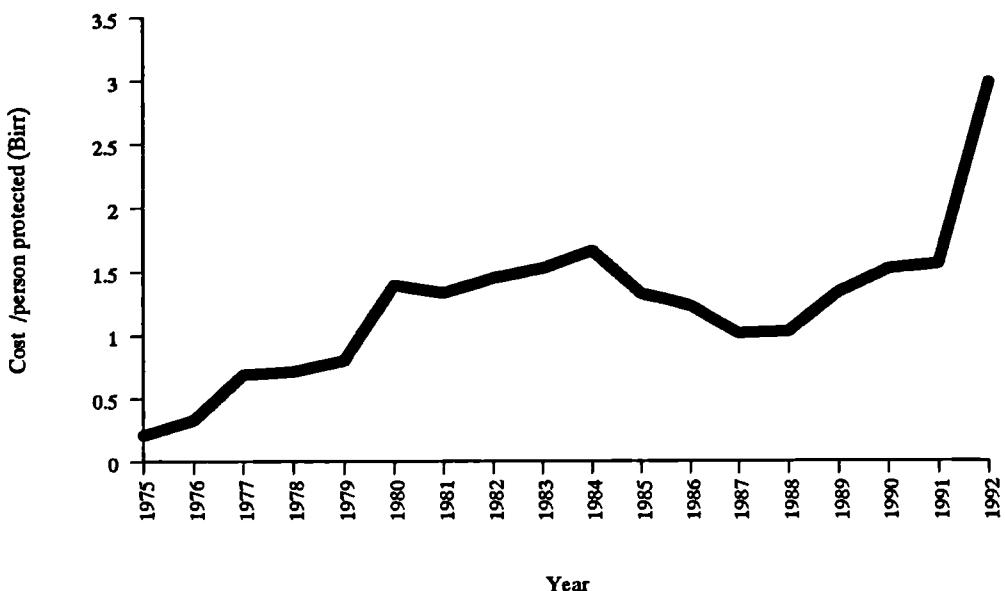
**Figure 7.5 Pie chart of itemised expenses during spraying operations in Ethiopia**



A further attempt was made to see the operational cost of spraying DDT per person expected to be directly protected from malaria. This was done by dividing the total cost of spraying during each spray round by the number of individuals resident in the houses sprayed. The result, after adjusting for inflation according to 1992 prices is plotted in Figure 7.6. The figure depicts relatively little change in the cost per head up to 1991 after which the cost per person expected to be protected increased enormously. The operational cost per person protected was 0.21 Birr in 1975 which soared to 2.98 Birr per person

protected in 1992. This suggested a 14-fold rise in cost of spraying during the 17-year interval.

**Figure 7.6    Operational cost of spraying DDT per person expected to be protected from malaria in Debre Zeit sector**

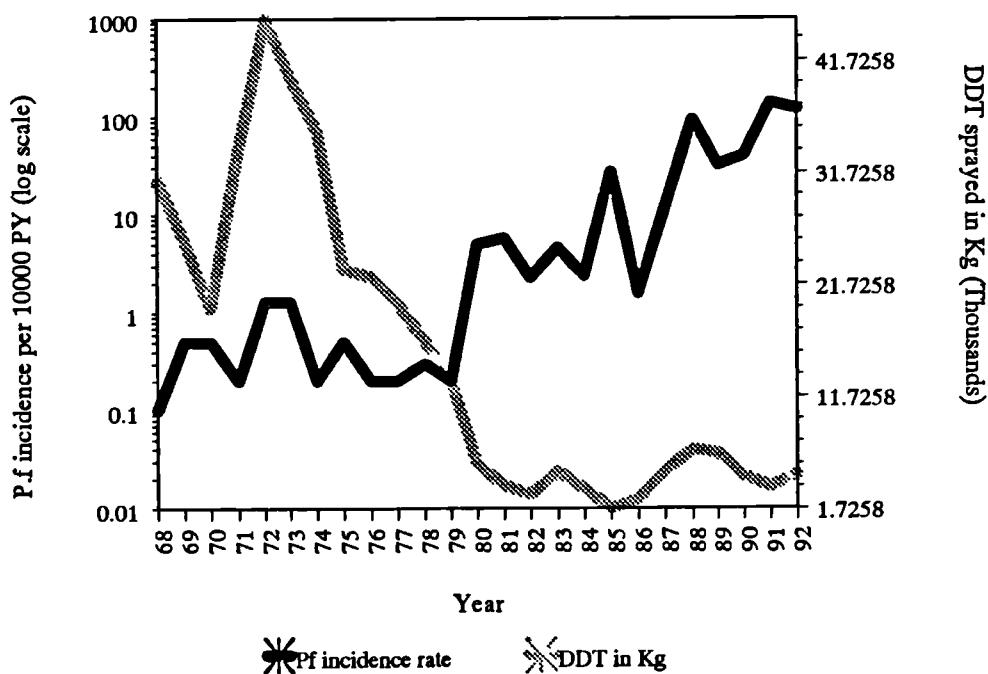


#### **7.4.5    The impact of indoor spraying of DDT on incidence rate of falciparum malaria in Debre Zeit sector**

The relationship between the amount of DDT sprayed per year in Debre Zeit sector and the incidence rate of falciparum malaria was examined by plotting both variables against

time in years. The result is shown in Figure 7.7. The figure depicts that the period from 1968 to 1979 is characterised by extensive application of DDT in the sector and a very low incidence rate of falciparum malaria. In contrast, the period from 1980 to 1992 is characterised by lower levels of application of DDT and a higher incidence rate of falciparum malaria.

**Figure 7.7 Relationship between use of DDT and incidence rate of falciparum malaria in Debre Zeit sector**



## **7.5 Discussion**

The various plots shown in this chapter depicted a consistent pattern in which the years from 1966 to 1979 were most characterised by extensive use of DDT in Debre Zeit sector. Indices of extensive application of DDT were the large amount of DDT used for intradomiciliary spraying, a high coverage in the number of houses sprayed, and the greater number of people expected to be protected directly from malaria by the spraying operations. This was the period also known as the “attack phase” in which the strategy was to achieve a blanket coverage of all localities in the sector irrespective of the level of endemicity of malaria. The main purpose was that every house, building structure, or other premise where vector mosquitoes may rest was properly sprayed with DDT in the correct amounts and at appropriate intervals ( Shafa, 1966). These years also saw a very low incidence of malaria. This extensive coverage in the spraying of DDT probably played a major role in preventing an increased incidence of malaria from 1966 to 1979.

In contrast, the years from 1980 to 1992 were characterised by a very reduced indoor application of DDT for the control of malaria. This was seen in the decreased amount of DDT applied per annum, the small number of houses sprayed and the fewer number of people expected to be protected directly from malaria. The incidence rate of malaria increased several fold during this period. Hospital morbidity and mortality ascribed to

malaria also rose. Amongst other factors such as a favourable climatic pattern and the presence of chloroquine resistant falciparum malaria as discussed in Chapters 5 and 6, the reduced use of DDT for the control of malaria is likely to have contributed to the increased incidence of malaria and simultaneous increase in observed hospital morbidity and mortality ascribed to malaria in the highlands of Debre Zeit.

Despite the reduced use of DDT in the 1980's and early 1990's, the operational cost of spraying DDT increased dramatically, particularly in 1991 and 1992. The total operational cost of DDT spraying rose from 25,212.69 Birr in 1980 to 66,389.85 Birr in 1991. This suggested an estimated 263% rise in total operational cost. Furthermore, the cost per person expected to be protected from malaria rose from 0.21 Birr in 1981 to 2.98 Birr in 1992. This suggested an estimated 1,419% rise in the operational cost of DDT per person protected. This could be explained by the increased cost of daily wage and the devaluation of the Ethiopian currency (Birr) relative to the US dollar from a ratio of 1:2 before 1991 to 1:5 after 1991. The Malaria Control Programme spent relatively little money for daily wage from 1978 to 1989 because of a policy of recruiting spray-men from the peasant associations who also supported the expenses during both training and spraying operations. But, from 1990 onwards this policy was reversed because of difficulty in maintaining the previous relationship with these associations and the daily wage had to be paid by the Malaria Control Programme.

A sustained measure of vector control using DDT and /or bed nets together with an efficient case detection and treatment system at the village level from 1960 to present, has resulted in a very reduced incidence of malaria approaching eradication in Hubei, China ( XU Bohazo et al., 1994). This experience testifies to the fact that when applied regularly and efficiently, vector control methods can achieve spectacular results in the control of malaria. However, a sudden relaxation of control efforts from near total coverage of the population at risk from 1966 to 79 to virtual cessation from 1980 to present appears to have exacerbated the problem of malaria in the highlands of Ethiopia as shown in the findings of this study.

Furthermore, the presence of more conducive climatic conditions especially a more favourable night-time temperature in the 1980's and 90's together with a reduced use of DDT may have encouraged the expansion of the range of distribution of the local vectors to high altitude localities. The emergence of chloroquine resistant *P. falciparum* most probably after 1988 in the study area, as discussed in Chapter 6, has reduced the effectiveness of treatment regimens contributing to a higher number of potential sources of infection as the mosquito vector tries to obtain its blood meal on humans. Once inside the vector, the sporogonic development of the parasite could have been facilitated by the favourable temperature, particularly between 1988 and 1992. This could explain not only the increased morbidity and mortality ascribed to malaria but also the change from a highly seasonal transmission before mid 1988 to more or less perennial transmission of malaria since then in the present study area.

There is growing evidence about the recent resurgence of malaria in many endemic countries and more so about epidemics of malaria in highland areas that border endemic regions. However, most of the published literature presented concentrated on the role of climatic factors ( Loevinsohn, 1994, Bouma and Van der Kaay, 1994) with little regard to the possible role of the level of vector control efforts and chloroquine resistant falciparum malaria. This may be dangerous if not misleading when one considers the interplay of both climatic and non-climatic factors in the dynamics of transmission of malaria in an area. The presence of chloroquine resistance was already confirmed and the application of vector control measures with DDT and malathion was reported to have reduced the incidence of malaria in Burundi, a country that borders Rwanda ( Coosemans, 1989). It is also likely that chloroquine resistance is a problem of public health importance in India as well. Thus, these factors are likely to have contributed to the rise in the incidence of malaria in both Rwanda and India in the articles cited above.

An increase in the cost of spraying operations was observed in 1992 despite a reduction in the amount of DDT sprayed in Debre Zeit sector. This probably is true of all other areas where spraying operations were undertaken for the control of malaria. The rise in the cost of spraying operations could be attributed to the increased cost in daily wage and the devaluation of the Ethiopian currency (Birr) relative to the US dollar. This, together with a continued reduced commitment on the part of the government to allocate the necessary foreign currency required for the purchase of insecticides from abroad may decrease the

coverage of spraying operations further and consequently a worsening of the problem of malaria in the highlands of Ethiopia.

The effectiveness of DDT as a first insecticide of choice for the control of malaria was put under intense critical scrutiny by experts in the field. After an exhaustive review of the literature on the use of DDT for the control of malaria and in the light of the presence of some evidence about the possible link between exposure to DDT and rise in incidence of pancreatic and breast cancers (Garabrant et al., 1992, Wolff et al., 1993), Curtis (1994) concluded that: “ (i) it can no longer be confidently stated that DDT antimalarial spraying is harmless to human health, and (ii) affordable alternatives are becoming available, and DDT should no longer be recommended as the insecticide of choice for malaria vector control”.

Based on the above and other data, a study group of the WHO on vector control for malaria and other mosquito-borne diseases further concluded that: “ (i) at the present time there appears to be no justification on toxicological grounds for changing current policy towards indoor spraying of DDT for vector-borne disease control; (ii) therefore DDT may still be considered on its merits as one of a range of possible insecticides for use in vector-borne disease control; (iii) however, in view of the availability of alternative insecticides, some of which may be equivalent or superior to DDT in epidemiological impact, in public acceptability, in logistical suitability (including ease of application) and in meeting requirements of WHO quality specifications, DDT no longer merits being promoted as the

insecticide of choice" (WHO, 1994). In the light of such recommendations by experts and authorities in the field of malaria vector control, the continued use of DDT should be reviewed and alternatives such as personal protection measures using insecticide impregnated bed nets may have to be explored further to test their effectiveness, cost and acceptability by the communities living in areas at risk of malaria.

The growing problem of chloroquine resistant falciparum malaria as shown by data in the present study area in Chapter 6, and the effect of climatic change towards an increased incidence of malaria as will be discussed in Chapter 8, could be countered more by increased and selective use of vector control methods. In the absence of a safe and effective malaria vaccine, this may be the best tool available at present to reduce the observed morbidity and mortality ascribed to malaria.

## **7.6    *Summary***

The pattern in DDT use for the control of malaria vectors in Debre Zeit sector was examined using data obtained during spraying operations from 1966 to 1993. This revealed that there was an extensive application of DDT from 1966 to 1979 as seen in the large amount of DDT used, number of houses sprayed and coverage of the population expected to be protected directly from malaria. Such extensive use of DDT may have been responsible in preventing increased incidence of highland malaria at the time. In contrast, the period from 1980 to 1993 saw a very drastic reduction in the use of DDT for the

control of malaria in the study area. This, together with a more favourable climatic pattern and the spread of chloroquine resistance in the area may explain the increased morbidity and mortality due to malaria and the change from highly seasonal to perennial transmission. The exact extent of the impact of climatic changes on the increased incidence of malaria will be the subject of the next chapter.

## **Chapter 8**

### **Climatic effects on the transmission of malaria in Debre Zeit sector**

#### ***8.1 Background***

There has been a 67-fold increase in the incidence of falciparum malaria and a thirteen-fold increase in deaths ascribed to malaria in Debre Zeit highlands over the past two decades as discussed in Chapter 3. Abnormally high incidence of malaria due to *P. falciparum* and *P. vivax* occurred particularly in the years 1988, 1991 and 1992. These were also the years during which a peak proportion of hospital deaths ascribed to malaria occurred. Furthermore, transmission of falciparum malaria occurred in localities lying between 2,000 and 2,200 metres only after 1986, as discussed in Chapter 4. The pattern of climate was also characterised by marked fluctuation with a very marked rise in both day-time and night-time temperature and a decrease of rainfall particularly during the years 1988, 1991 and 1992 as seen in Chapter 5. This suggested a strong relationship between climate fluctuation and the level of morbidity and mortality due to malaria in Debre Zeit highlands. In this chapter, an attempt will be made to examine the relationship between climatic fluctuation and monthly incidence of malaria in greater detail.

The relationship between climate and malaria has been known since the time of Hippocrates as one of the oldest epidemiological observations made in establishing the association between the preponderance of patients with fever in humid areas around marshes and swamps (Gill, 1921). Earlier investigations have also suggested a high degree of correlation between the monsoon (July-September) rainfall and the incidence of autumnal malaria in the Punjab (Christophers, 1911). In his analysis of the role of meteorological factors on mortality from "fever" in the Punjab between the years 1901 and 1917, Gill (1921) showed that a monthly mean temperature ranging from 20 °C to 33 °C and mean relative humidity from 61% to 76%, occurring in March, July, August and September were associated with a rise in mortality from fever. No such consistent relationship was found between fever, deaths and rainfall. The fevers, and by implication the deaths, were thought largely to be due to malaria because of the absence of other major causes of fever during those months at the time.

Despite common knowledge about the possible role of climatic factors on the incidence of malaria the subject seems to have been forgotten since the early 1940's when malariologists became preoccupied with insecticides until the more recent resurgence of malaria, particularly since the latter half of the 1980's. This may be because of the success of eradication and control efforts in the 1950's, 1960's and early 1970's. In Ethiopia, the role of climate on the incidence of malaria is well known by local indigenous residents who avoid travel from their homes in the highlands to the lowlands during the months of September, October and November due to fear of acquiring malaria and dying from it.

Although the highly seasonal transmission of malaria in the highlands, and particularly its occurrence after the cessation of the heavy rains in June, July and August is generally known, the precise extent to which climatic factors such as rainfall, night-time temperature and day-time temperature affect morbidity and mortality from malaria has not been studied. Furthermore, the effects of cyclical changes in climatic conditions (yearly cycles) and secular changes over longer periods of time on the incidence rate of malaria has not been estimated. A more detailed study of climate effects became more relevant in the light of the observed increase in morbidity and mortality from malaria in Ethiopia and other countries with a similar highland profile and the possible role of increase in mean ambient temperature ascribed to “global warming” .

## **8.2      *Objectives***

The objectives were :

- (a) to examine the relationship between annual incidence rate of malaria, annual mean night-time temperature, annual mean day-time temperature and annual total rainfall
- (b) to quantify the relationship, during the period from 1968 to 1993, between monthly malaria incidence rate and:
  - monthly mean day-time (maximum) temperature
  - monthly mean night-time (minimum) temperature
  - monthly records of total rainfall

## **8.3 Methods**

### ***8.3.1 Standardisation of dates of malaria incidence and climate data sets***

Monthly data for cases of malaria were collected using the Ethiopian Calendar which has 12 months of 30 days and a thirteenth month which is six days during the leap year and five days at other times. The thirteenth month occurs in the month of September of each year according to the European Calendar which in effect gives an excess of cases for five or six extra days depending on whether it occurred during the leap year or not. The climate data, however, was collected using the European (Gregorian Calendar). It was therefore decided to standardise both malaria incidence data and climate data according to the European Calendar so that malaria incidence rate during a certain month could be compared to the climate in the study area at the same time.

The incidence data was therefore standardised by multiplying the observed number of cases during the month of September by 5/6 during the leap year because  $5/6 \times 36$  days = 30 days. During all other years, the observed number of cases seen during the month of September was multiplied by 6/7 since  $6/7 \times 35 = 30$  days. The leap years from 1968 to 1992 were in 1968, 1972, 1976, 1980, 1984, 1988 and 1992. Although there will still be some slippage of few days in to the next month, it was assumed that the remaining differences of one or two days during all other months were of minor importance.

### **8.3.2 Descriptive analysis**

Monthly malaria surveillance data obtained from Debre Zeit sector for the period from January 1968 to April 1993 in the surveillance data set were used. Incidence of both falciparum and vivax malaria was calculated using the population data from the vector control data set and when missing by projecting the population last seen at a growth rate of 2.9% per annum.

Climate data was obtained from Debre Zeit weather station, and consisted of monthly mean day-time temperature, mean night-time temperature and total rainfall. It was decided to omit relative humidity from the analysis because of missing data for the 1985 to 1990 period.

At first, an attempt was made to see the overall pattern of the relationship between climate and malaria by plotting the annual mean day-time and night-time temperature against incidence rate per year. Then the monthly incidence data and the climatic fluctuation were plotted together. Thereafter, the three climate variables were calculated using SPSS/PC™ release 5 for windows at a lag period of 0 month, 1 month, 2 months, 3 months and 4 months.

It was thought that a direct relationship between the three climatic conditions and incidence rate of malaria beyond a lag period of four months is probably not biologically plausible considering the time it takes for the development of the vector from egg to adult (about 10 days), development of the malaria parasite inside the vector ( extrinsic incubation or sporogonic development from 11 to 20 days depending on the ambient temperature), and the incubation period in the human host (about 10 days on average for falciparum malaria), and the lag period needed to reach a sufficient number of cases of malaria in the community that could be detected by the health services, i.e. the surveillance system of the Malaria Control Service in the study area. All case incidence data were recorded by date of report of the patient to the malaria diagnosis and treatment centre.

### ***8.3.3 Poisson regression analysis***

Firstly, estimation of the effect of each of the three climate variables at lags 0 to 4 months on monthly incidence rate of falciparum malaria was made singly for each climate variable. Secondly, those climate variables which showed significant association with monthly incidence rate of falciparum malaria on bivariate analysis (  $P <0.05$ ) were put in the model and the effect of one of them was estimated by controlling for the other variables at each step. Likelihood ratio tests were used to determine statistical significance throughout the analysis. This was done using Poisson

regression analysis in Stata™ 4 for windows. Poisson regression analysis was used because of the dependent variable being incidence rates per person-year.

The Poisson regression model is represented in the following equation:

$\log \lambda = \alpha + \beta_1 \text{ mintemp} + \beta_2 \text{ maxtemp} + \beta_3 \text{ rainfall} + \text{error}$  ..... 8.3.3.1

where  $\lambda$  represents the incidence rate of falciparum malaria,  $\alpha$  is the intercept term (value of the log incidence rate if minimum temperature, maximum temperature, and rainfall were all 0), and  $\beta_i$ 's represent the log rate ratio associated with a one-unit increase in minimum temperature, maximum temperature or rainfall.

Note that since  $\lambda = \mu / Y$ , where  $\mu$  = cases of falciparum malaria per month and  $Y$  = person-years at risk, then equation 6.3.3.1 can be written as:

$\log \mu = \log Y + \alpha + \beta_1 \text{mintemp} + \beta_2 \text{maxtemp} + \beta_3 \text{rainfall} + \text{error}$  ..... 8.3.3.2

One of the assumptions implicit in such analysis is that the data are not serially correlated. With time-series data this assumption is not correct, as there is strong seasonality and the incidence rate of falciparum malaria in any month is likely to be strongly related to the incidence rate in the previous month. The effect of this on the Poisson regression model is for the strength of associations to be over-estimated; i.e P-values are more extreme than they should be.

Figure 8.1 shows the monthly incidence of falciparum malaria in the study area from 1968 to 1993 while Figure 8.2 shows the total amount of DDT (in Kilograms) used for indoor spraying per annum for the control of malaria in Debre Zeit sector from 1965 to 1993. Analysis was done by splitting the incidence and climate data sets into three distinct phases after looking at the pattern of the monthly incidence of falciparum malaria and the total amount of DDT used for indoor spraying in these two plots.

*a) 1968 to 1979*

This was the period during which biannual indoor spraying of DDT was applied extensively in Debre Zeit sector and the peak incidence rate of falciparum malaria was 0.5 per 10,000 person-years.

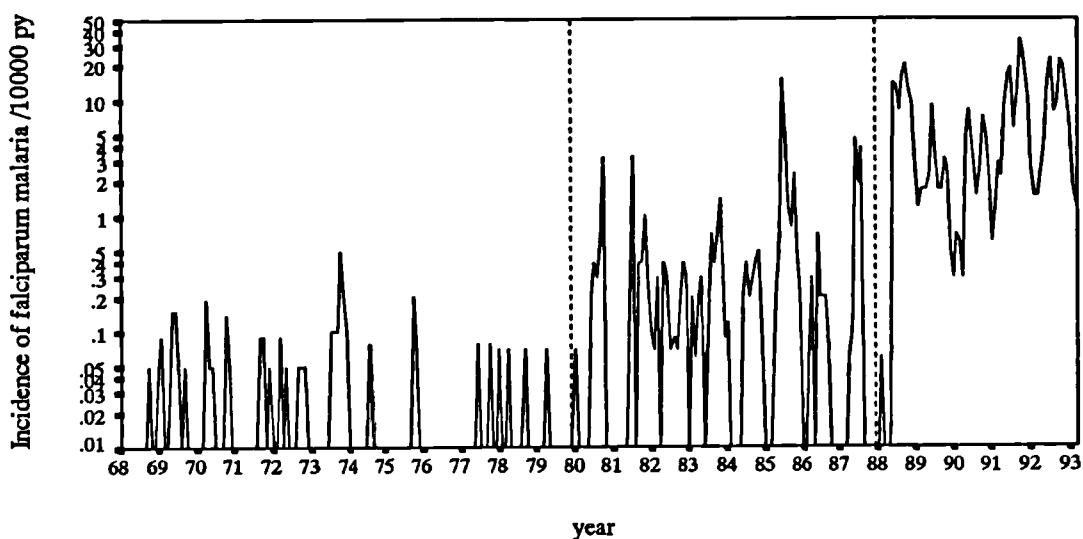
*b) 1980 to 1987*

This was the period during which a drastic reduction in the amount of DDT used for indoor spraying in the sector was seen and the peak incidence of falciparum malaria was about 10 per 10,000 person-years.

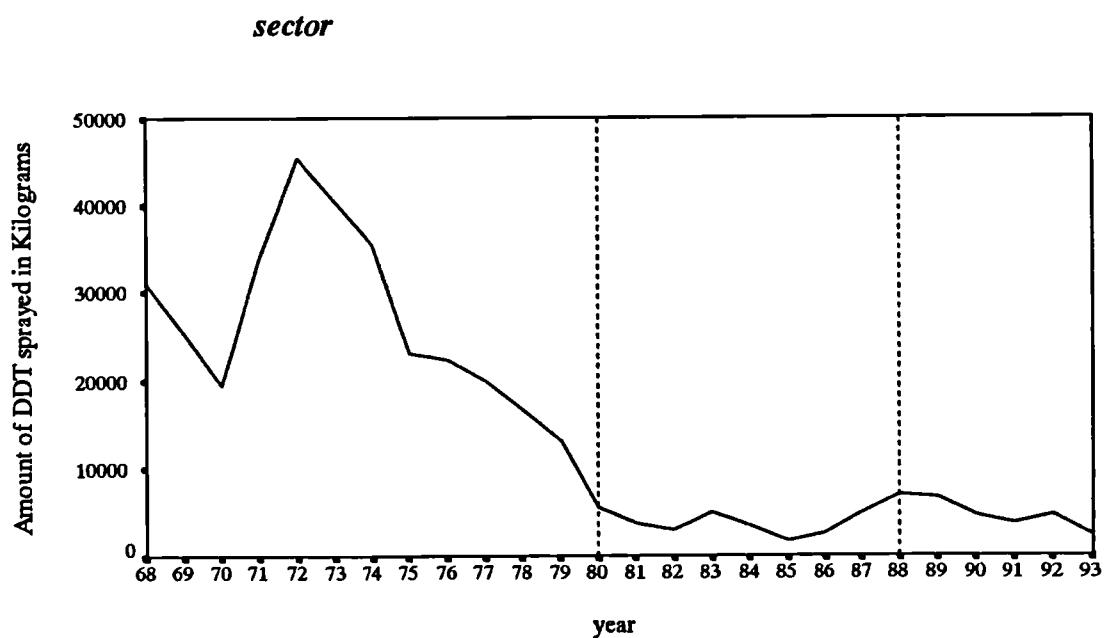
*c) 1988 to 1993*

Malaria incidence occurred all year and peak incidence of falciparum malaria went up to 33.4 per 10,000 person-years since mid 1988. The amount of DDT applied in the sector was virtually unchanged from that seen from 1980 to 1987.

**Figure 8.1     Monthly incidence of falciparum malaria in Debre Zeit**



**Figure 8.2     Total amount of DDT used for indoor spraying in Debre Zeit**



## **8.4 Results**

### ***Effect of long term climatic changes on annual incidence of malaria***

#### ***8.4.1 Night-time temperature effects on annual incidence rate of malaria***

##### ***8.4.1.1 Night-time temperature effects on incidence rate of falciparum malaria***

Annual mean night-time temperatures from 1968 to 1992 per annum were calculated and plotted against incidence rate of falciparum malaria per year to see the overall effect. The result is plotted in Figure 8.3. The figure depicts a positive correlation of annual mean night-time temperature with incidence rate of falciparum malaria per annum that appeared unlikely to have been due to chance, i.e. the higher the annual mean night-time temperature the greater the incidence rate of falciparum malaria per year ( $r = 0.49$ ,  $t = 2.70$ ,  $P < 0.02$ , d.f. = 23).

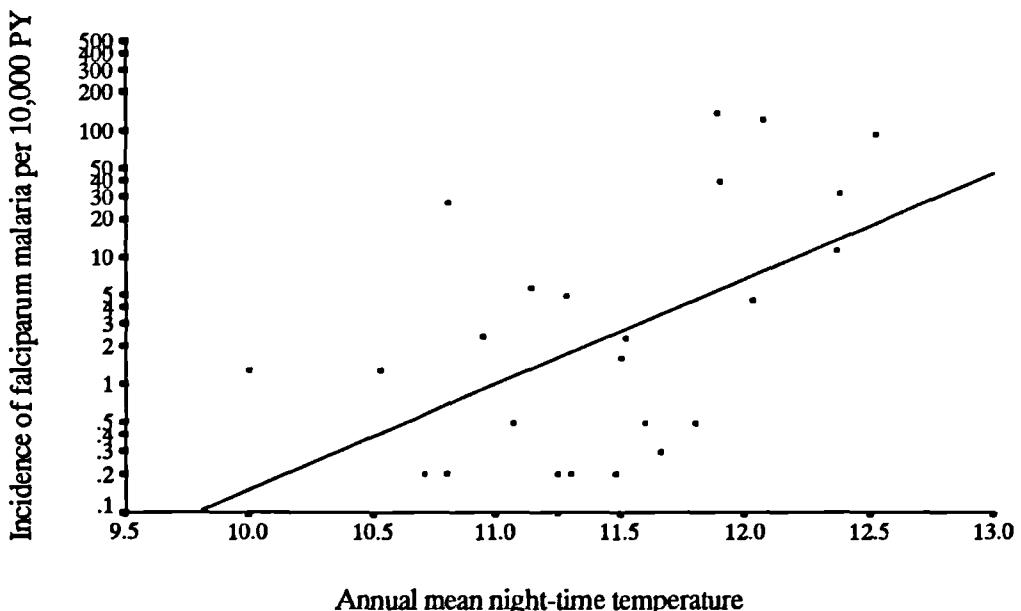
##### ***8.4.1.2 Night-time temperature effects on the incidence rate of vivax malaria***

A similar method of plotting annual mean night-time temperature against incidence rate of vivax malaria was used to see the pattern from 1968 to 1992. The result is plotted in Figure 8.4 which depicts a positive correlation of annual mean night-time temperature with incidence rate of vivax malaria per year that appeared highly unlikely to have been due to chance ( $r = 0.62$ ,  $t = 3.79$ ,  $P < 0.001$ , d.f. = 23).

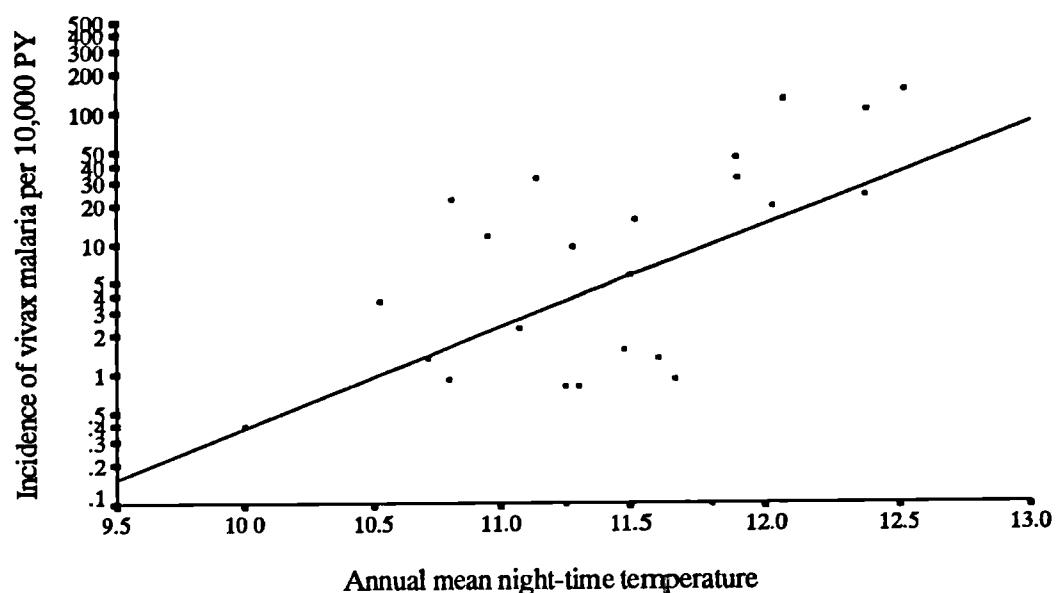
#### **8.4.1.3 Pattern of annual mean night-time temperature and incidence rate of malaria**

The annual pattern of the mean night-time temperature and incidence rate of both falciparum and vivax malaria was plotted against time in years to observe whether the positive correlation depicted in the scatter plots shown in the above two figures persisted. The results are shown in the plots in Figures 8.5 and 8.6. As shown in the plots, there were abnormally cool night-time temperatures in 1972 and peaks in annual mean night-time temperatures in 1983 and 1988. The peak in annual mean night-time temperature seen in 1988 is associated with a peak in the incidence rate of both falciparum and vivax malaria. However, although the drop in annual mean night-time temperatures in 1989 was also associated with a fall in incidence of both falciparum and vivax malaria , the marked drop in 1991 and 1992 was not characterised by such a fall in incidence rate of malaria.

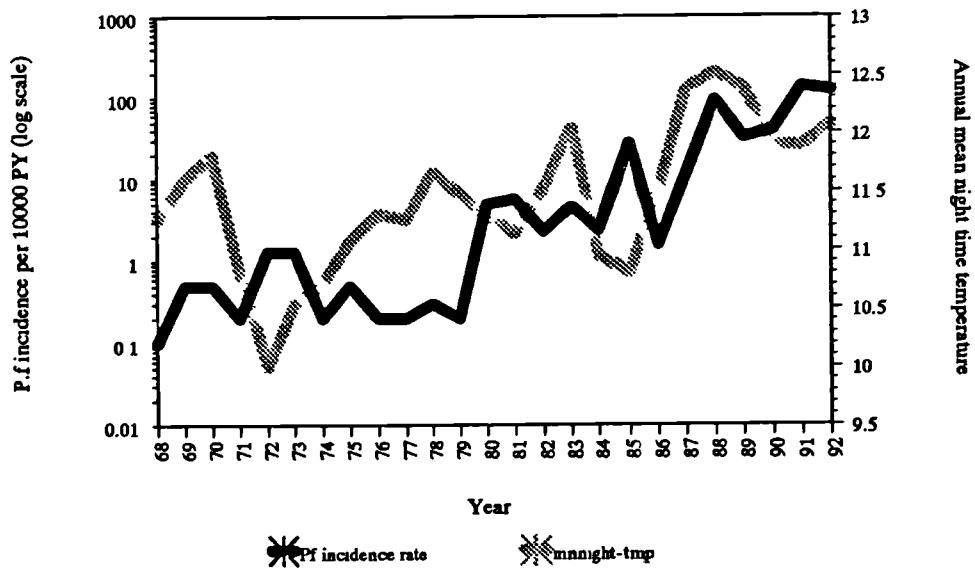
**Figure 8.3      Scatter plot of annual mean night-time temperature and incidence rate of falciparum malaria**



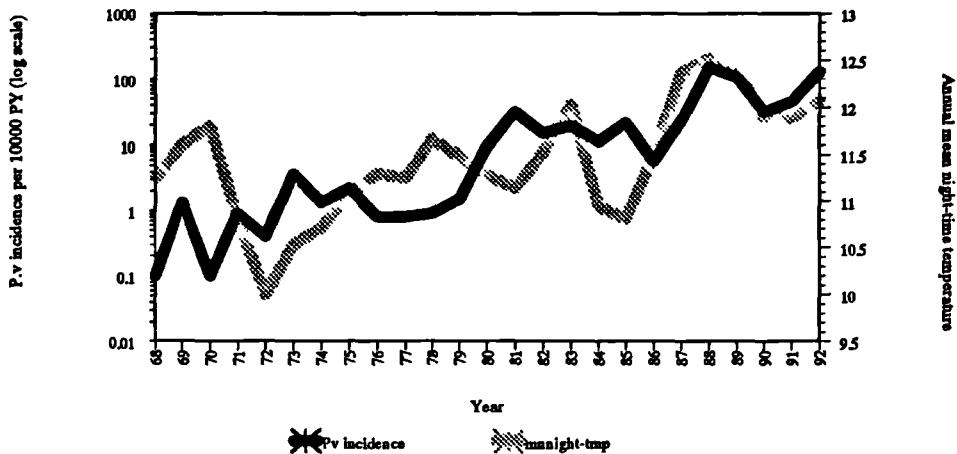
**Figure 8.4** Scatter plot of annual mean night-time temperature and incidence rate of vivax malaria



**Figure 8.5** Annual pattern of mean night-time temperature and incidence rate of falciparum malaria



**Figure 8.6 Annual pattern of mean night-time temperature and incidence rate of vivax malaria**



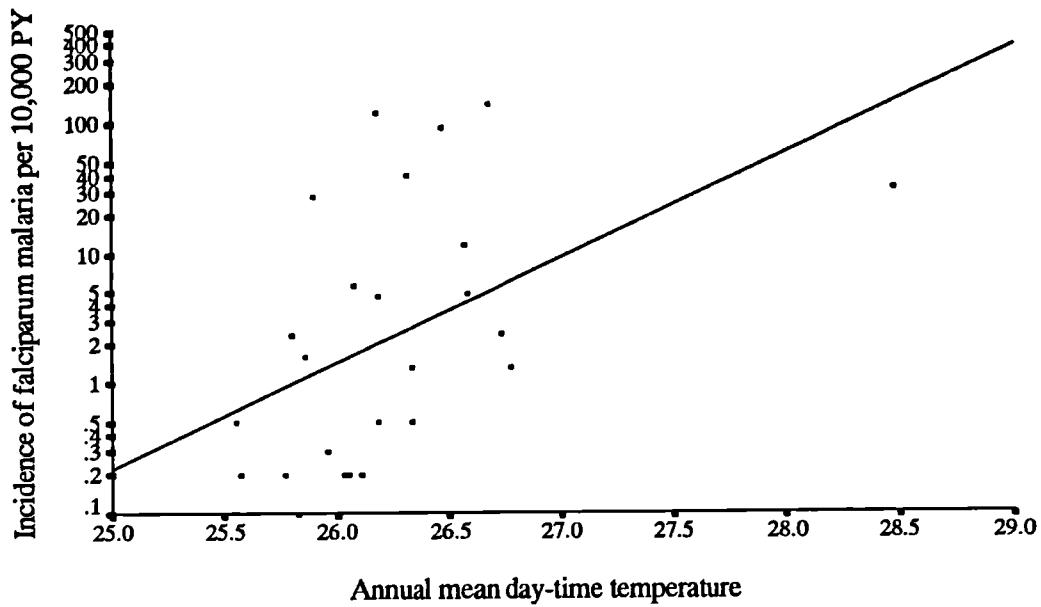
#### 8.4.2 Day-time temperature effects on annual incidence rate of malaria

As with night-time temperature, an attempt was made to see if there was a summary effect of annual mean day-time temperature on incidence rate of malaria by computing the mean day-time temperature per year and plotting it against incidence rate of malaria per year. A scatter plot of this is shown for the two species of malaria prevalent in the area in Figures 8.7 and 8.8.

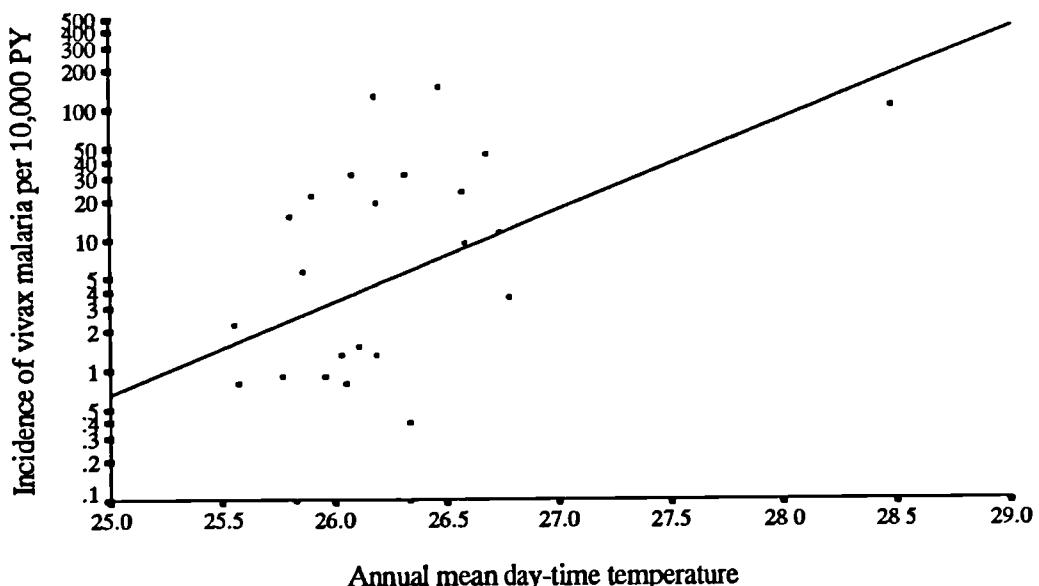
As shown here, the scatter plots in both figures depict a positive correlation between the mean day-time temperature per annum and incidence of both vivax and falciparum malaria. However, the positive correlation between annual mean day-time temperature and *P. falciparum* was weak and not statistically significant ( $r = 0.25$ ,  $t = 1.24$ ,  $P > 0.05$ , d.f. = 23) while the positive correlation with *P. vivax* was greater and appeared unlikely to have been due

to chance ( $r = 0.47$ ,  $t = 2.55$ ,  $P < 0.02$ , d.f. = 23). A further attempt was made to see this pattern more clearly by plotting both incidence rate per year and mean day-time temperature against time in years. The result is plotted in Figures 8.9 and 8.10

**Figure 8.7** *Scatter plot of annual mean day-time temperature and incidence rate of falciparum malaria*

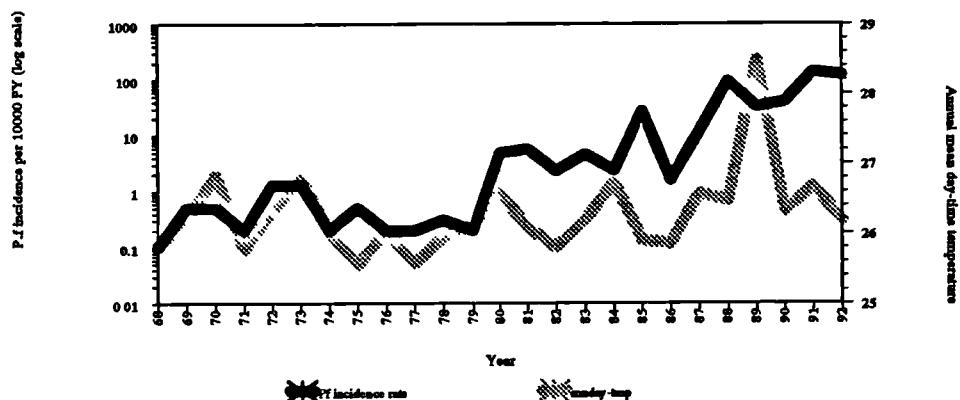


**Figure 8.8** *Scatter plot of annual mean day-time temperature and vivax malaria*

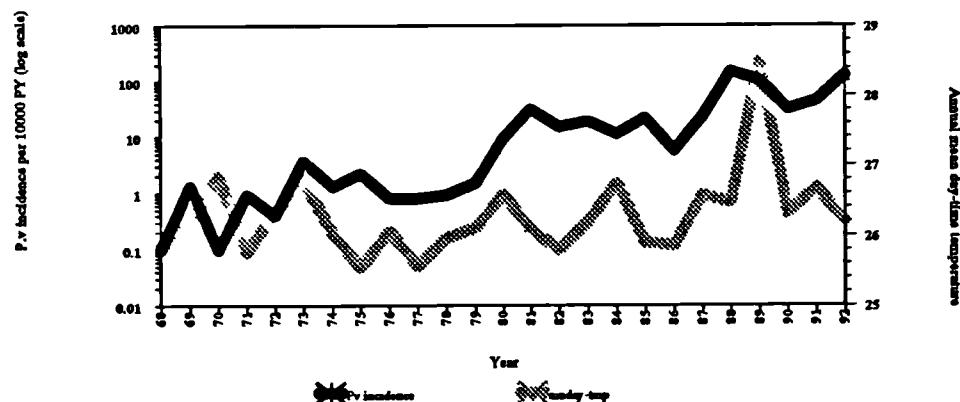


Both figures depict a general relationship between annual mean day-time temperature and incidence rate of falciparum and vivax malaria per year. However, a closer examination of this relationship in both plots reveals that a peak incidence of malaria for both species occurred in 1988 while the peak in annual mean daytime temperature occurred in 1989 at which time the incidence of malaria was falling.

**Figure 8.9** *Pattern of annual mean day-time temperature and incidence rate of falciparum malaria*



**Figure 8.10** *Pattern of day-time temperature and incidence rate of vivax malaria*

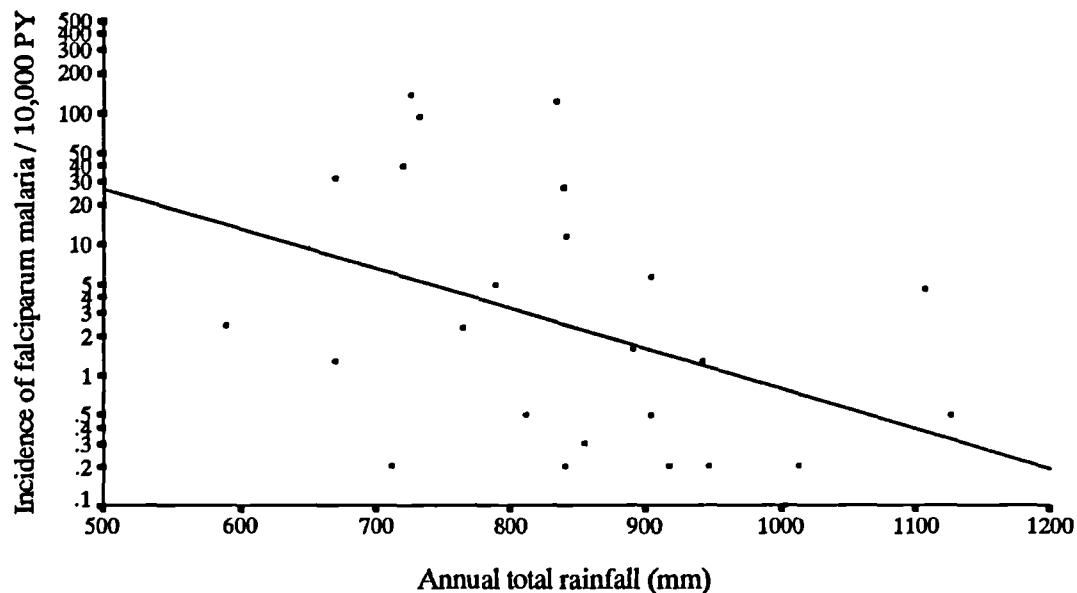


#### ***8.4.3 Rainfall effects on the annual incidence rate of malaria***

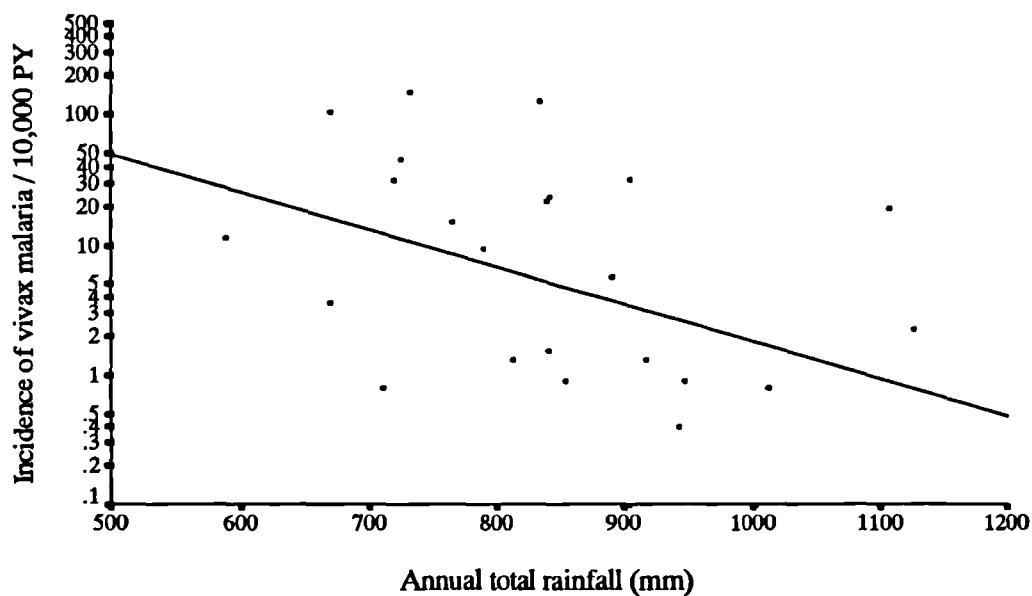
The effect of annual total rainfall on the incidence rate of malaria per year was examined by looking at scatter plots of total rainfall per annum against both species of malaria as shown in Figures 8.11 and 8.12. As shown in the two scatter plots in Figures 8.11 and 8.12, there is a negative correlation between the total amount of rainfall per year and the incidence rate of both falciparum and vivax malaria. However, the observed negative correlation between total rainfall and incidence rate of malaria failed to achieve statistical significance which makes it difficult to assume that the correlation was not due to chance ( $r = -0.31$ ,  $t = 1.56$ ,  $P > 0.1$  d.f. = 23 for falciparum malaria and  $r = -0.33$ ,  $t = 1.67$ ,  $P > 0.1$ , d.f. = 23 for vivax malaria). Thus, it appears that overall, in contrast to annual mean ambient temperature, the amount of annual total rainfall did not appear to have been a major limiting factor in the annual incidence rate of both falciparum and vivax malaria in the highlands of Debre Zeit over the past 25 years.

A further attempt was made to see this relationship more clearly by plotting incidence rate of malaria and total rainfall against time in years as shown in Figures 8.13 and 8.14. As shown in the plots in Figures 8.13 and 8.14, there were two peaks in annual total rainfall in 1975 and 1983. But, the years 1973, 1976, 1980, 1984, and 1989 were characterised by a drop in annual total rainfall. The incidence of malaria showed a peak in 1980, 1985, 1988 and 1991. Thus, over the whole study period, there was a huge rise in incidence rate of malaria per year with some decrease in annual total rainfall.

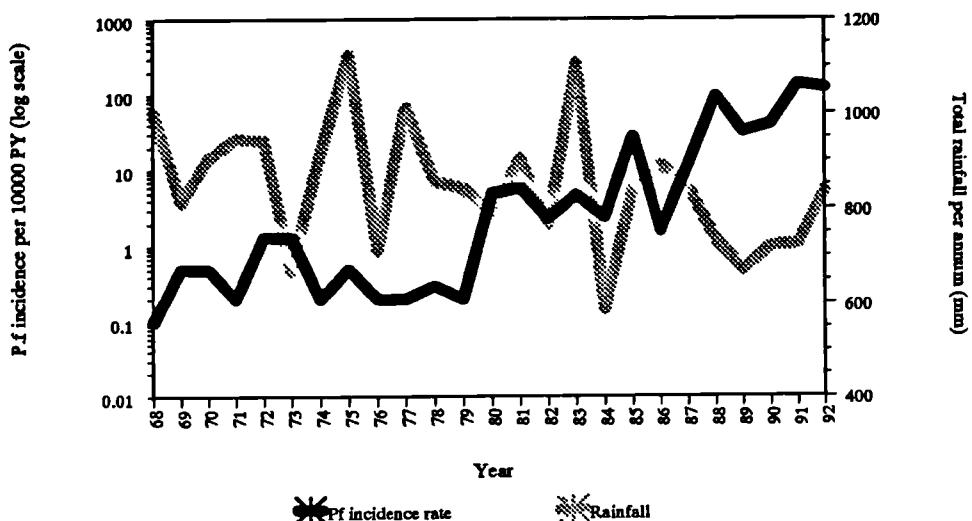
**Figure 8.11 Scatter plot of rainfall and incidence rate of falciparum malaria**



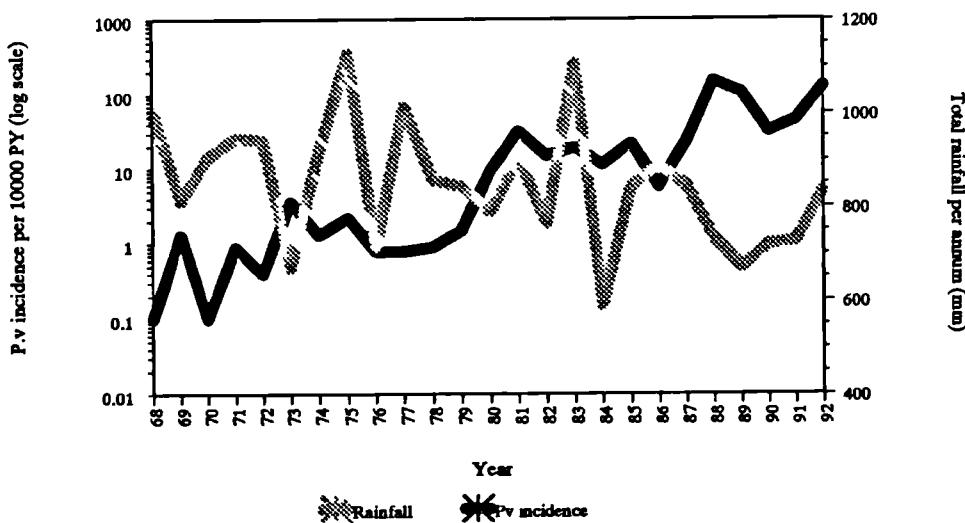
**Figure 8.12. Scatter plot of rainfall and incidence rate of vivax malaria**



**Figure 8.13 Pattern of rainfall and incidence rate of falciparum malaria**



**Figure 8.14 Pattern of rainfall and incidence rate of vivax malaria**



In summary, there was a positive correlation between annual mean ambient temperature and incidence rate of malaria per year. The positive correlation was stronger for vivax than for falciparum malaria. This relationship was more apparent between the annual mean night-time temperature and incidence rate of both falciparum and vivax malaria per year than it was for the annual mean day-time temperature as seen in the greater correlation coefficients and significant "P" values. In particular, a coincident peak in both annual mean night-time temperature and incidence rate of malaria was seen in 1988. In contrast, there was a weak negative correlation between the annual total rainfall and incidence rate of malaria per year that may have been due to chance.

#### ***8.4.4 Effect of short term climatic fluctuations on monthly incidence of malaria***

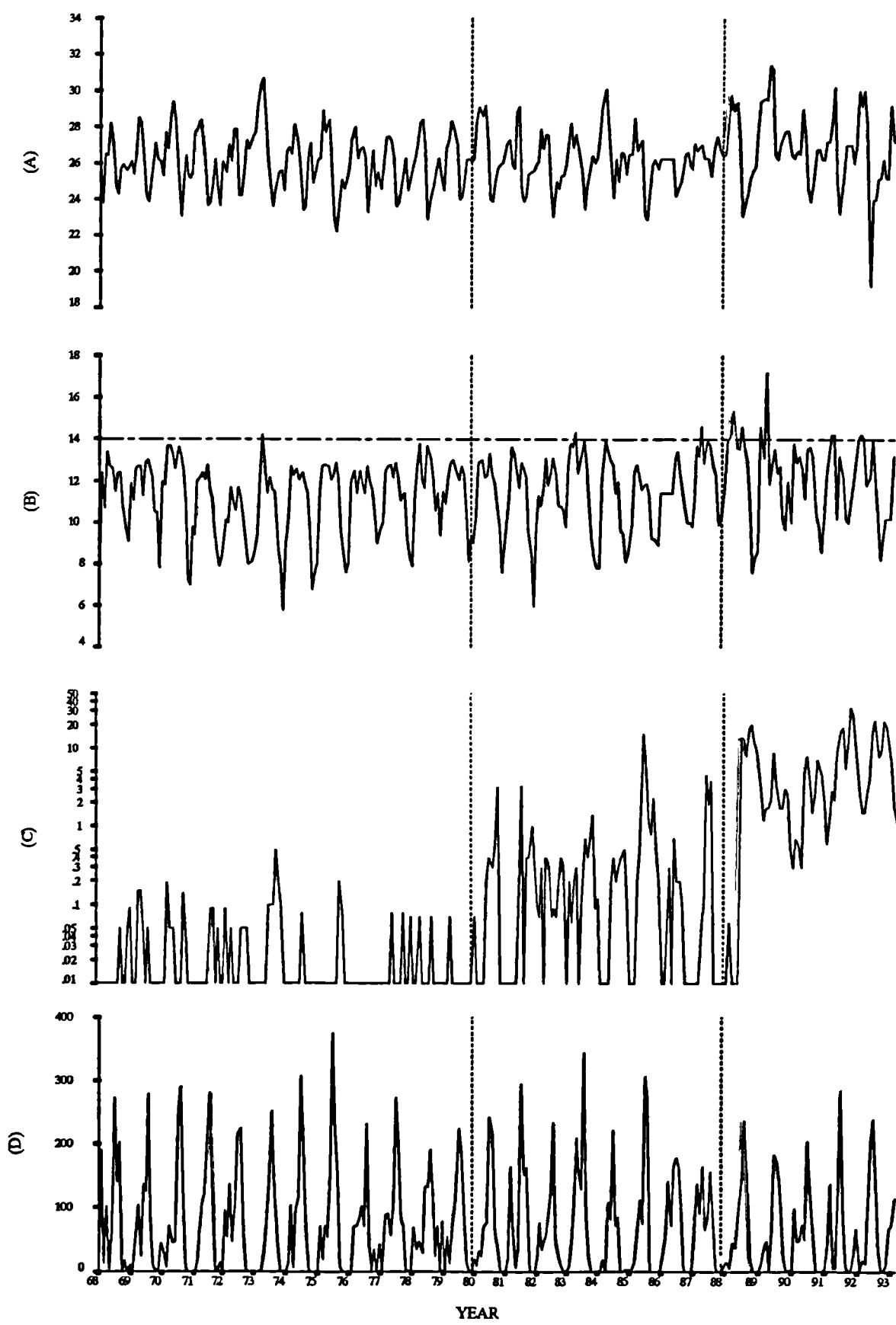
Monthly mean day-time & night-time temperature and monthly total rainfall and monthly incidence of falciparum malaria from January 1968 to April 1993 is plotted in Figure 8.15 . This figure depicts abnormally high monthly mean day-time and night-time temperatures and abnormally low monthly total rainfall in 1973, 1984 and 1989. The period from 1968 to 1979 was the time during which extensive use of DDT for the control of malaria occurred as shown earlier. Furthermore, the 14 °C threshold monthly mean night-time temperature, thought to be more favourable for extrinsic development of the malaria parasite in the *Anopheles* vector, was exceeded only once from 1968 to 1979 ( April 1973) and the incidence of falciparum malaria was minimal. This threshold monthly mean night-time temperature was exceeded on two

occasions from 1980 to 1987 (May 1983 & May 1987), and on eleven occasions from 1988 to 1993 ( three times in 1988, twice in both 1989 & 1991, and four times in 1992).

The period from mid 1988 to 1993 also saw a peak incidence rate of falciparum malaria , i.e. a rise by several folds in monthly incidence rate from 0.5 per 10,000 person-years before 1980 to 33.4 per 10,000 person-years with year round transmission being the characteristic feature from 1988 to 1993. The months during which no cases of malaria were seen, i.e. 0 incidence rates particularly before mid 1988, were replaced with an incidence rate of 0.01 irrespective of the size of the population, to overcome the problem faced during presentation of data on a log scale. Note that the pattern of fluctuation in monthly mean night-time temperature ( shown in "B") observed from mid-1988 to 1993 is approximately a mirror image of the monthly incidence of falciparum malaria (shown in "C") at the same time as seen in Figure 8.15. This pattern was not very obvious for any of the other climatic conditions.

Although a general relationship between climate and incidence rate of malaria is clear from the above results, the extent of these changes in climatic conditions between certain months and years on malaria related morbidity was not immediately apparent. Thus, a more detailed analysis was necessary to estimate the magnitude of the effect of monthly day-time temperature, night-time temperature and rainfall on the incidence rate of falciparum malaria, the cause of the most severe and fatal malaria .

**Figure 8.15:** Pattern of monthly mean day-time (A) & night-time (B) temperature, incidence of falciparum malaria (C) & total rainfall (D) 1968-1993

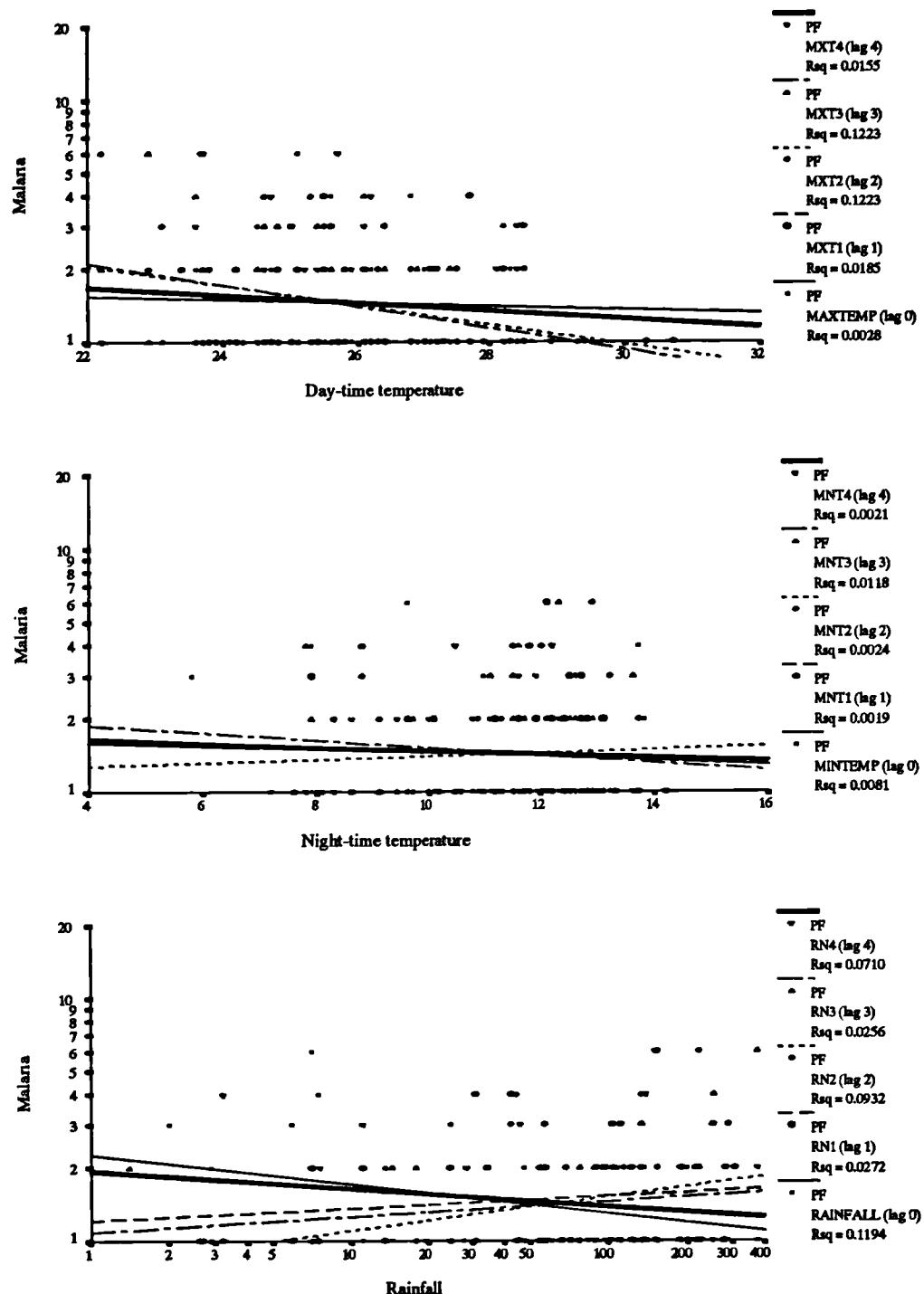


#### ***8.4.4.1 Relationship between monthly climatic conditions and incidence of falciparum malaria in Debre Zeit highlands from 1968-79***

A further attempt was made to see the relationship between monthly climatic conditions and incidence of falciparum malaria. This was done by plotting monthly mean day-time temperature, night-temperature and total rainfall (explanatory variables) against the incidence of falciparum malaria (dependent variable) at current month (lag 0), 1 month later (lag 1), 2 months later (lag 2), 3 months later (lag 3), and 4 months later (lag 4). The result is plotted in Figure 8.16.

Monthly mean day-time temperature showed a clear negative correlation with monthly incidence of falciparum malaria at lags 1-3. This implied that an increase in monthly mean day-time temperature resulted in decreased incidence of falciparum malaria 1 month later, 2 months later and 3 months later. Furthermore, at lags 0 and 4, there was a weak negative correlation between monthly mean day-time temperature and incidence of falciparum malaria. Monthly mean night-time temperature showed a positive correlation with incidence of falciparum malaria at lag 2; i.e. a unit rise ( $^{\circ}\text{C}$ ) in monthly mean night-time temperature resulted in increased incidence of falciparum malaria 2 months later. At other lags, it showed a weak negative correlation. Monthly total rainfall was associated with a rise in incidence of falciparum malaria at lag 1-3. Thus, a unit rise (mm) in monthly total rainfall was associated with an increased incidence of falciparum malaria 1 month later, 2 months later and 3 months later. At lags 0 and 4, it showed a negative correlation. Note that, at all lags, the association between climatic conditions and incidence of falciparum malaria is very weak during this period of extensive application of DDT.

**Figure 8.16 Effect of monthly mean day-time & night-time temperature and total rainfall on incidence of falciparum malaria at lags 0-4 ( 1968-79)**



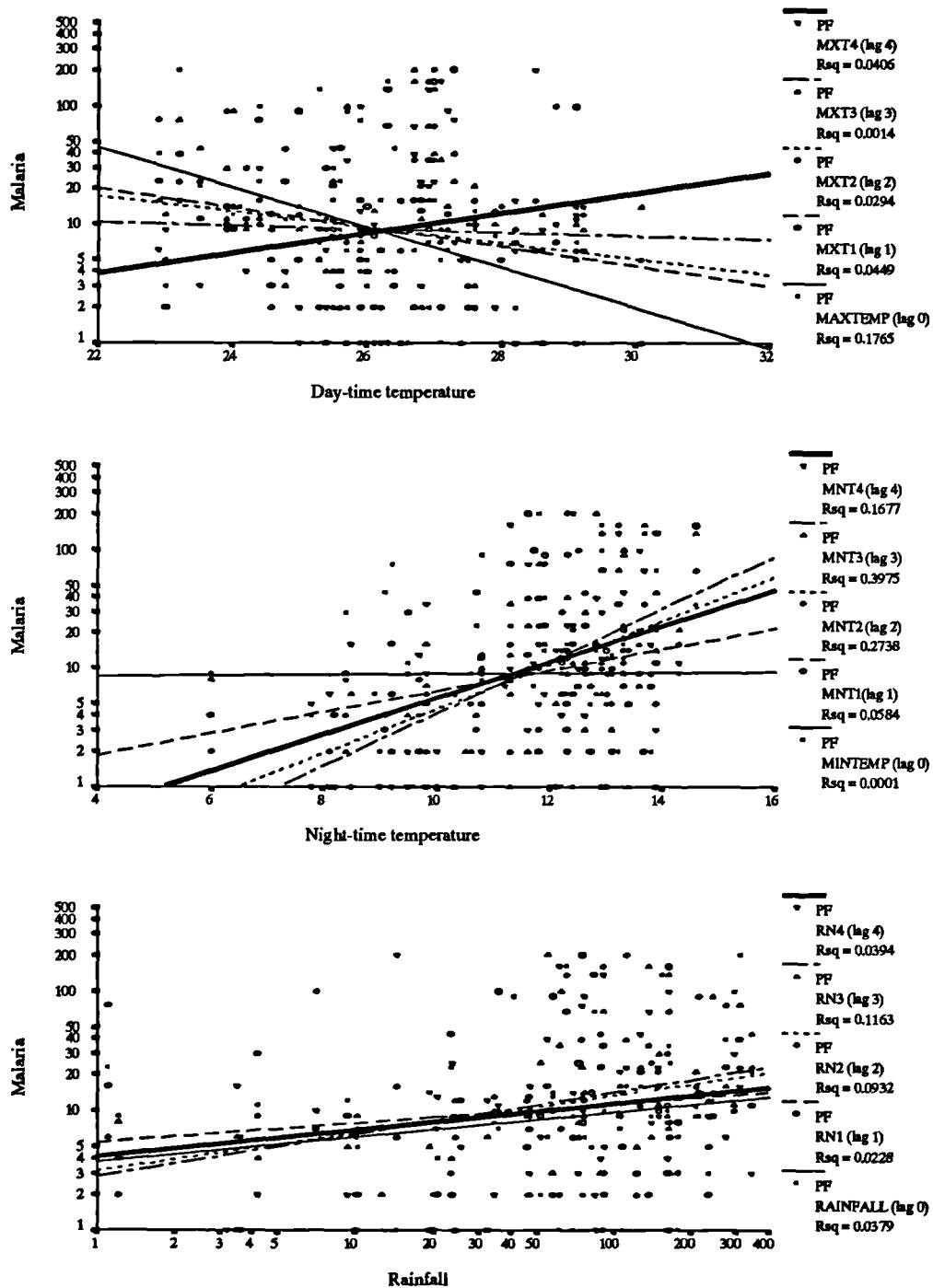
#### ***8.4.4.2 Relationship between monthly climatic conditions and incidence of falciparum malaria from 1980-87***

The effect of monthly climatic conditions on incidence of falciparum malaria was assessed using similar methods as before for the period 1980-87, the time during which the amount of DDT applied for the control of malaria was drastically reduced. This relationship between the dependent variable (incidence of falciparum malaria) and explanatory variables ( monthly mean day-time & night-time temperature, total rainfall) is shown in the scatter plots in Figure 8.17 for lags 0, 1, 2, 3, and 4 respectively.

Monthly mean day-time temperature showed a negative correlation with incidence of falciparum malaria up to lag 2. At lag 3, there was no clear correlation. At lag 4, there was a positive correlation. Thus, an increase in day-time temperature was associated with decreased incidence of falciparum malaria at the same month, 1 month later, and 2 months later. But, 4 months later, it was associated with an increased incidence of falciparum malaria. Monthly mean night-time temperature did not show any clear correlation with incidence of falciparum malaria at lag 0. But at lags 1 to 4, there was a clear and strong positive correlation between monthly mean night time temperature and incidence of falciparum malaria. Thus, an increase in night-time temperature was associated with a rise in incidence of falciparum malaria 1 month later, 2 months later, 3 months later and 4 months later but not during the same month. On the other hand, monthly total rainfall showed a positive correlation with monthly incidence of falciparum malaria at all lags. Thus, an increase in total rainfall was associated with a rise in incidence of falciparum malaria at the same month, 1 month later, 2 months later, 3 months

later, and 4 months later. Note that, the strength of the association between climatic conditions and malaria has increased enormously during this period.

**Figure 8.17      Effect of monthly mean day-time & night-time temperature and rainfall on incidence of falciparum malaria at lags 0-4 (1980-87)**



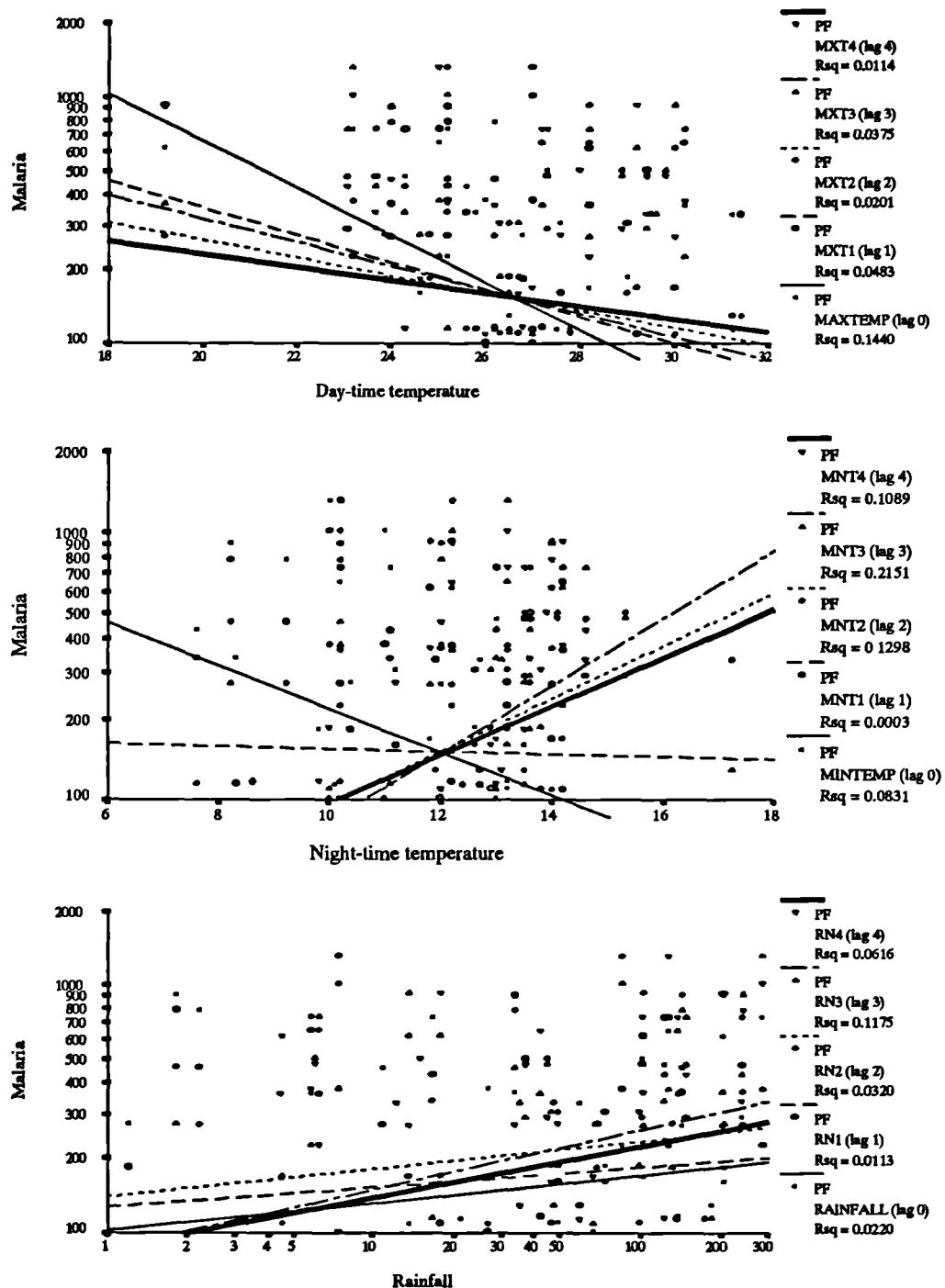
#### ***8.4.4.3 Relationship between monthly climatic conditions and incidence of falciparum malaria from 1988 to 1993***

The effect of monthly climatic conditions on incidence of falciparum malaria was assessed in a similar method as for the previous two time periods. Monthly mean day-time & night-time temperature and total rainfall were plotted against incidence of falciparum malaria during the same month, 1 month later, 2 months later, 3 months later and 4 months later.

The result is plotted in Figures 8.18 for lags 0, 1, 2, 3 and 4 respectively. As shown in the plots, monthly mean day-time temperature showed a negative correlation with monthly incidence of falciparum malaria at all lags. This suggested that for each unit rise in monthly mean day-time temperature there was some decrease in monthly incidence of falciparum malaria. In contrast, monthly mean night-time temperature showed a positive correlation with monthly incidence of falciparum malaria at lags 2, 3 and 4. At lag 1, there was no clear correlation. At lag 0, it showed a negative correlation. This suggested that each unit rise in monthly night-time temperature was associated with an increase in incidence of falciparum malaria 2 months later, 3 months later and 4 months later. But, a unit rise in night-time temperature resulted in a decreased incidence of falciparum malaria during the same month. Monthly total rainfall showed a positive correlation with incidence of falciparum malaria at all lags. This suggested that an increase in monthly total rainfall was associated with a rise in incidence of falciparum malaria at the same month, 1 month later, 2 months later, 3

months later and 4 months later. Note that the positive correlation between night-time temperature and malaria is particularly strong at lags 2, 3, and 4.

**Figure 8.18 Effect of monthly mean night-time & day-time temperature and total rainfall on incidence of falciparum malaria at lags 0-4 ( 1988-93)**



#### **8.4.5 Poisson regression analysis results**

##### **8.4.5.1 Climate effects on incidence rate of falciparum malaria from 1968 to 1979**

A first attempt was made to estimate the effect of each of the three climate variables on the incidence rate of falciparum malaria to see the pattern at a lag period of 0 month, 1 month, 2 months, 3 months and 4 months. Then all the climate variables which showed a significant association on bivariate analysis ( $P < 0.05$ ) were put in the model and the effect of one of them was estimated by allowing for the other variables at each step. Likelihood ratio tests were used to assess significance throughout. Lag periods of 0 month, 1 month, 2 months, 3 months and 4 months were used. The result is shown in Tables 8.1 and 8.2.

Table 8.1 shows results of each climatic condition on monthly incidence of falciparum malaria before allowing for the effect of other climate variables. Almost all climate variables seemed to have an effect on the incidence rate of falciparum malaria with the exception of night-time temperature at lag 1, day-time temperature at lag 0, and rainfall at lag 4. Among the climate variables which showed significant association ( $P < 0.05$ ), a negative correlation with monthly incidence of falciparum malaria was seen in monthly mean night-time temperature at lag 0, total rainfall at lag 0, and monthly mean day-time temperature at lags 1, 2 and 3. The strongest negative correlation with monthly incidence of falciparum malaria was seen in monthly day-time temperature at

lag 2 ( $\chi^2 = 25.91$ ,  $P < 0.001$  and Coefficient = -0.325; and  $e^{-0.325} = 0.723$ ) . This implies that for each °C rise in day-time temperature, there is a 28% decrease in monthly incidence of falciparum malaria 2 months later.

On the other hand, a positive correlation between climatic conditions and monthly incidence of falciparum malaria was seen as follows: monthly total rainfall at lags 1, 2 and 3 & monthly mean night-time temperature at lags 2, 3, and 4. Among these, the biggest positive correlation was seen for night-time temperature at lag 2 ( $\chi^2 = 7.01$ ,  $P = 0.008$  and coefficient = 0.157;  $e^{0.157} = 1.17$ ). Thus, for every °C rise in monthly mean night-time temperature, there is a 17% increase in the monthly incidence rate of falciparum malaria 2 months later.

Poisson regression analysis was then carried out using a likelihood ratio test after allowing for the effect of the climate variables which were significant at the first stage at each lag period. The results are shown in Table 8.2. The climatic variables which showed significant association with monthly incidence of falciparum malaria were monthly mean night-time temperature at lag 0 and 4 months, monthly mean day-time temperature after a lag period of 2 months, and monthly total rainfall after a lag period of 3 months. Among these, a negative correlation with monthly incidence of falciparum malaria was seen in monthly mean night-time temperature at lag 0 and day-time temperature at lag 2. Day-time temperature at lag 2 showed the strongest association ( $\chi^2 = 9.84$ ,  $P = 0.0017$ , and coefficient = -0.286, where  $e^{-0.286} = 0.75$ ). Thus, after

allowing for other climate variables, for each °C rise in monthly mean day-time temperature, there is a 25% decrease in monthly incidence of falciparum malaria 2 months later.

A significant and positive correlation was seen in monthly total rainfall at lag 3 and monthly mean night-time temperature at lag 4. Among these, monthly mean night-time temperature at lag 4 showed the biggest positive correlation with monthly incidence of falciparum malaria ( $\chi^2 = 5.38$ ,  $P = 0.0203$ , coefficient = 0.147,  $e^{0.147} = 1.158$ ). Thus, for each °C rise in monthly mean night-time temperature, there is a 16% increase in monthly incidence of malaria 4 months later.

Thus, during the period from 1968 to 1979 at which time there was also an extensive use of DDT for the control of malaria, monthly mean day-time temperature at lag 2 showed the strongest negative correlation with monthly incidence of falciparum malaria while monthly mean night-time temperature had the strongest positive correlation with monthly incidence of falciparum malaria 4 months later.

**Table 8.1      Effect of day-time temperature, night-time temperature and rainfall on incidence rate of falciparum malaria ( without allowing for effect of other climate variables)**

1968-1979

<i>Lag (months)</i>	<i>Variable</i>	$\chi^2$	<i>P</i>	<i>Coefficient</i>	$e^{coef}(IRR)$
0	day-time temp.	1.56	0.213	-.076	0.927
	night-time temp.	9.80	0.002	-.159	0.853
	rainfall	4.71	0.030	-.003	0.997
1	day-time temp.	5.03	0.025	-.139	0.870
	night-time temp.	0.96	0.327	.054	1.055
	rainfall	4.72	0.029	.002	1.002
2	day-time temp.	25.91	<0.001	-.325	0.723
	night-time temp.	7.01	0.008	.157	1.169
	rainfall	23.07	<0.001	.005	1.005
3	day-time temp.	11.22	0.001	-.211	0.809
	night-time temp.	7.26	0.007	.161	1.175
	rainfall	25.54	<0.001	.005	1.005
4	day-time temp.	3.04	0.081	.110	1.116
	night-time temp.	6.74	0.009	.162	1.176
	rainfall	0.43	0.51	.001	1.001

Key :  $e^{coef}$  = exponential of coefficient, and IRR = incidence rate ratio

**Table 8.2      Effect of day-time temperature, night-time temperature and rainfall  
on incidence rate of falciparum malaria allowing for the other  
variables and likelihood ratio test results**

1968-1979

<i>Lag (months)</i>	<i>Variable</i>	$\chi^2$	<i>P</i>	<i>Coefficient</i>	$e^{coef}$ ( <i>IRR</i> )
0	Night-time temp.	5.34	0.0208	-.141	0.868
	Rainfall	0.25	0.6195	-.001	0.999
1	Day-time temp.	1.38	0.2407	-.090	0.914
	Rainfall	1.07	0.3013	.001	1.001
2	Day-time temp.	9.84	0.0017	-.286	0.751
	Night-time temp.	3.22	0.0728	.145	1.156
	Rainfall	0.06	0.8049	.0004	1.000
3	Day-time temp.	0.09	0.7643	-.028	0.972
	Night-time temp.	0.16	0.6894	.034	1.035
	Rainfall	6.31	0.0120	.004	1.004
4	Day-time temp.	1.68	0.1951	.078	1.081
	Night-time temp.	5.38	0.0203	.147	1.158

#### **8.4.5.2 Climate effects on incidence rate of falciparum malaria from 1980 to 1987**

A similar method of analysis was used as for the period from 1968 to 1987 in which the effect of each climate variable was estimated singly and then after allowing for the effect of the other climate variables that were significant in the first stage of analysis.

Table 8.3 shows the effect of each climatic variable at each lag period on the occurrence of falciparum malaria before allowing for the effect of the climate variables. As shown here, all 3 climate variables were strongly associated with the incidence rate of falciparum malaria at all lags.

A significant negative correlation with malaria incidence was seen for monthly mean day-time temperature at lag 0 and monthly total rainfall at lag 4. Monthly mean day-time temperature at lag 0 showed a stronger negative correlation with monthly incidence of falciparum malaria ( $\chi^2 = 134.45$ ,  $P < 0.001$ , coefficient = -0.183,  $e^{-0.183} = 0.833$ ). Each °C rise in monthly mean day-time temperature was associated with an estimated 17% decrease in the monthly incidence of falciparum malaria in the same month.

At other lags, all the three climatic conditions showed a significant and positive correlation with monthly incidence of falciparum malaria. Among all, the strongest association was seen in monthly mean night-time temperature at lag 3, ( $\chi^2 = 1173.48$ ,  $P < 0.001$ , coefficient = 0.539,  $e^{0.539} = 1.714$ ). Thus, each °C rise in monthly mean

night-time temperature is associated with an estimated 71% increase in monthly incidence of falciparum malaria 3 months later.

Then, a likelihood ratio test was conducted at each lag period allowing for the other two climate variables which were significant during the first stage of analysis. The result is shown in Table 8.4. A significant negative correlation between monthly incidence of falciparum malaria and climatic conditions was seen in monthly mean night-time temperature at lag 0 and monthly total rainfall at lag 2. Each °C rise in monthly mean night-time temperature was associated with an estimated 13% decrease in monthly incidence of falciparum malaria in the same month.

On the other hand, the strongest positive correlation remained monthly mean night-time temperature at lag 2 even after allowing for other climate variables ( $\chi^2 = 486.85$ ,  $P < 0.001$ , coefficient = 0.495,  $e^{0.495} = 1.640$ ). Thus, every °C rise in monthly mean night-time temperature is associated with an estimated 64% increase in monthly incidence of falciparum malaria 2 months later. Furthermore, there was an estimated 58% increase in the monthly incidence rate associated with each °C rise in monthly mean night-time temperature 3 months previously. Note also that the strength of the association between the climate variables and the incidence rate of falciparum malaria increased by several folds as seen in the very extreme  $\chi^2$  values, P values, and estimated effects compared to that obtained using a similar method for the 1968 to 1979 period.

**Table 8.3**      *Effect of day-time temperature, night-time temperature and rainfall on incidence rate of falciparum malaria before allowing for other two climate variables*

1980-1987

Lag (months)	Variable	$\chi^2$	P	Coefficient	$e^{coefficient}$ (IRR)
0	Day-time temp.	134.45	<0.001	-.183	0.833
	Night-time temp.	83.66	<0.001	.120	1.127
	Rainfall	534.15	<0.001	.005	1.005
1	Day-time temp.	49.49	<0.001	.109	1.115
	Night-time temp.	445.84	<0.001	.298	1.347
	Rainfall	153.68	<0.001	.003	1.003
2	Day-time temp.	12.35	<0.001	.055	1.057
	Night-time temp.	879.21	<0.001	.449	1.567
	Rainfall	221.42	<0.001	.004	1.004
3	Day-time temp.	254.75	<0.001	.249	1.283
	Night-time temp.	1173.48	<0.001	.539	1.714
	Rainfall	187.39	<0.001	.003	1.003
4	Day-time temp.	334.93	<0.001	.281	1.324
	Night-time temp.	22.38	<0.001	.059	1.061
	Rainfall	27.51	<0.001	-.002	0.998

**Table 8.4      Effect of day-time temperature, night-time temperature and rainfall  
on incidence rate of falciparum malaria after allowing for other two  
climate variables; likelihood ratio test results**

1980-1987

<i>Lag (months)</i>	<i>Variable</i>	$\chi^2$	<i>P</i>	<i>Coefficient</i>	$e^{cof}$ ( <i>IRR</i> )
0	Day-time temp.	40.86	<0.001	.144	1.155
	Night-time temp.	54.65	<0.001	-.144	0.866
	Rainfall	349.96	<0.001	.008	1.008
1	Day-time temp.	63.24	<0.001	.168	1.183
	Night-time temp.	88.36	<0.001	.198	1.219
	Rainfall	36.64	<0.001	.003	1.003
2	Day time temp.	2.14	>0.05	-.031	0.969
	Night-time temp.	486.85	<0.001	.495	1.640
	Rainfall	8.21	<0.001	-.001	0.999
3	Day-time temp.	97.64	<0.001	.208	1.231
	Night-time temp.	391.58	<0.001	.460	1.584
4	Day-time temp.	223.59	<0.001	.312	1.366
	Night-time temp.	0.50	0.478	-.138	0.871
	Rainfall	7.52	0.006	.001	1.001

#### **8.4.5.3 Effect of climate on incidence rate of falciparum malaria from 1988 to 1993**

The relationship between the climate variables and falciparum malaria was examined using similar methods as for the other periods first singly for each variable and then after controlling for the effect of the other variables using a likelihood ratio test. The results are shown in Tables 8.5 and 8.6.

Table 8.5 shows the effect of each climatic variable at each lag period when analysis was carried out without allowing for the effect of other variables. As shown in the table, monthly mean day-time temperature showed a significant negative correlation with monthly incidence of falciparum malaria at all lags. Monthly mean night-time temperature showed negative correlation only at lags 0 and 1, and a positive correlation at lags 2, 3, and 4. Monthly total rainfall showed a significant positive correlation with monthly incidence of falciparum malaria at all lags.

The strongest negative correlation was demonstrated in monthly mean day-time temperature at lag 0 ( $\chi^2 = 3200.48$ ,  $P < 0.001$ , coefficient =  $-0.186$ ,  $e^{-0.186} = 0.830$ ). This implies that there is an estimated 17% decrease in monthly incidence of falciparum malaria for every °C rise in monthly mean day-time temperature in the same month. On the other hand, monthly mean night-time temperature at lag 3 showed the biggest positive correlation with monthly incidence of falciparum malaria ( $\chi^2 = 3190.22$ ,  $P < 0.001$ , coefficient =  $0.232$ ,  $e^{0.232} = 1.261$ ). This suggests that there is an estimated

26% increase in monthly incidence of falciparum malaria for each °C rise in monthly mean night-time temperature 3 months previously.

Subsequent analysis was carried out controlling for the effect of the other climate variables using a likelihood ratio test as before, the result of which is shown in Table 8.6. Here again, it is seen that monthly mean day-time temperature showed a negative correlation with monthly incidence of falciparum malaria at all lags while night-time temperature showed such negative correlation only at lags 0 and 1. The strongest negative correlation was seen in monthly mean night-time temperature at lag 0 ( $\chi^2 = 1451.45$ ,  $P < 0.001$ , coefficient = -0.216,  $e^{-0.216} = 0.806$ ). This suggests a 20% decrease in monthly incidence of falciparum malaria for each °C rise in monthly mean night-time temperature at lag 0.

Monthly total rainfall showed a positive correlation with monthly incidence of falciparum malaria at all lags. However, the strongest association and biggest positive correlation with monthly incidence of falciparum malaria was seen in monthly mean night-time temperature at lag 3 even after allowing for the effect of other climatic variables ( $\chi^2 = 1324.52$ ,  $P < 0.001$ , coefficient = 0.202,  $e^{0.202} = 1.224$ ). This suggests that there is an estimated 22% increase in monthly incidence of falciparum malaria for each °C rise in monthly mean night-time temperature 3 months previously.

**Table 8.5      Effect of day-time and night-time temperatures & rainfall on incidence rate of falciparum malaria before allowing for other climatic variables**

1988-1993

<i>Lag (months)</i>	<i>Variable</i>	$\chi^2$	<i>P</i>	<i>Coefficient</i>	$e^{cof} (IRR)$
0	day-time temp.	3200.48	<0.001	-.186	0.830
	night-time temp.	1924.75	<0.001	-.171	0.843
	rainfall	388.98	<0.001	.002	1.002
1	day-time temp.	1532.41	<0.001	-.132	0.876
	night-time temp.	685.31	<0.001	-.102	0.903
	rainfall	123.06	<0.001	.001	1.001
2	day-time temp.	383.27	<0.001	-.069	0.933
	night-time temp.	774.33	<0.001	.111	1.117
	rainfall	984.06	<0.001	.003	1.003
3	day-time temp.	1033.08	<0.001	-.111	0.895
	night-time temp.	3190.22	<0.001	.232	1.261
	rainfall	4385.36	<0.001	.006	1.006
4	day-time temp.	702.34	<0.001	-.092	0.912
	night-time temp.	1988.67	<0.001	.184	1.202
	rainfall	3411.66	0.006	.005	1.005

**Table 8.6** *Effect of day-time temperature, night-time temperature and rainfall on incidence rate of falciparum malaria after allowing for other two variables*

1988-1993

Lag (months)	Variable	$\chi^2$	P	Coefficient	$e^{coefficient}$ (IRR)
0	day-time temp.	626.17	<0.001	-.130	0.878
	night-time temp.	1451.45	<0.001	-.216	0.806
	rainfall	319.59	<0.001	.002	1.002
1	day-time temp.	461.92	<0.001	-.114	0.892
	night-time temp.	312.89	<0.001	-.097	0.908
	rainfall	243.98	<0.001	.003	1.003
2	day-time temp.	169.02	<0.001	-.067	0.935
	night-time temp.	482.53	<0.001	.117	1.124
	rainfall	26.86	<0.001	.001	1.001
3	day-time temp.	57.95	<0.001	-.038	0.963
	night-time temp.	1324.52	<0.001	.202	1.224
	rainfall	724.41	<0.001	.004	1.004
4	day-time temp.	0.00	1.0	-.001	0.999
	night-time temp.	545.83	<.001	.130	1.139
	rainfall	886.66	<0.001	.005	1.005

## **8.5 Discussion**

### ***8.5.1 Effect of long term climatic changes on annual incidence of highland malaria***

A great increase in the annual incidence of falciparum malaria was seen from 1988 to 1993. An increase in both mean day-time temperature and night-time temperature was also seen during this period. The scatter plots in the results section depicted a positive correlation between mean night-time temperature, day-time temperature and incidence rate of malaria per year over the past two decades. In particular, the positive correlation between annual mean night-time temperature and incidence rate of both vivax and falciparum malaria appeared highly unlikely to have occurred due to chance.

In contrast, there was some decrease in annual total rainfall during this period in the study area. The negative correlation found between total rainfall per year and incidence rate of malaria per year appeared to have been due to chance. The time series plots further depicted that mean night-time temperature and incidence rate of malaria both showed a peak in 1988. There was also some rise in the incidence rate of malaria particularly in 1985 but this rise in incidence rate of malaria was much later than the slight increase in the mean night-time temperature and total rainfall per annum seen in 1983.

### **8.5.2 Effect of short term climatic fluctuation on incidence of highland malaria**

Further investigation using Poisson regression analysis showed that during the period of extensive malaria control with DDT (1968-79), each °C rise in monthly mean day-time temperature was associated with a 25% decrease in monthly incidence of falciparum malaria 2 months later. In contrast, during the same period, each °C rise in monthly mean night-time temperature was associated with a 16% increase in monthly incidence of falciparum malaria. These two variables were the strongest in predicting a change in monthly incidence of falciparum malaria at the time.

During the period from 1980 to 1987, during which there was a drastic reduction in the use of DDT for malaria control, monthly mean night-time temperature showed a negative correlation with monthly incidence of falciparum malaria in the same month. For each °C rise in monthly mean night-time temperature, there was an estimated 17% decrease in monthly incidence of falciparum malaria. However, monthly mean night-time temperature at lags 2 and 3 showed the strongest positive association with monthly incidence of falciparum malaria. For each °C rise in monthly mean night-time temperature, there was an estimated 64% and 58% increase in monthly incidence of falciparum malaria two and three months later respectively. It is worth noting here that the lag period after which an increase in monthly mean night-time temperature resulted in an increase in monthly incidence has shortened from 4 months to 2 months. Furthermore, the estimated increase in monthly incidence of malaria seen for each °C

rise in monthly mean night-time temperature quadrupled from 16% (1968 -79) to 64% (1980-87).

During the years from 1988 to 1993, monthly mean night-time temperature after a lag period of 3 months was the strongest predictor of a rise in the monthly incidence of falciparum malaria. There was an estimated 22% increase in monthly incidence of falciparum malaria for each °C rise in monthly mean night-time temperature 3 months previously. The strength of the association of these climatic variables with a rise in the incidence rate of falciparum malaria also seemed to increase progressively with the strongest association observed during the years 1988 to 1993.

The period from 1968 to 1979 was characterised by a very wide coverage in the application of residual insecticides and a very low incidence rate of both falciparum and vivax malaria. However, given the absence of a marked change in the mean night-time temperature or rainfall during that time it is difficult to conclude whether the observed low incidence rate of malaria was due to the success in vector control using DDT or the absence of a favourable climate for transmission of malaria in the study area or whether it is a combination of both. But, relatively weak relationship between incidence and climatic data during this period would strongly suggest that the extensive use of DDT for malaria control was responsible for the low incidence of malaria.

The years from 1980 to 1987 were associated with the time of drastic reduction in the amount of DDT used for vector control. This period also saw an estimated four-fold rise in monthly incidence of falciparum malaria for each °C rise in monthly mean night-time temperature 3 months previously. It therefore seemed that the removal of DDT enhanced the effect of night-time temperature on the incidence of falciparum malaria.

There was little change in the amount of DDT used for vector control in the study area during the period from 1988 to 1993 as compared to the period from 1980 to 1987. This period saw a very marked fluctuation in both mean night-time and day-time temperature as well as a huge increase in the incidence rate of malaria. Time series plots depicted abnormal peaks in both monthly mean day-time and night-time temperatures in 1988 and 1989. A major peak in the monthly incidence of malaria was also noticed in 1988. The results of Poisson regression analysis suggested that monthly mean night-time temperature in the preceding 2-3 months was most strongly associated with a rise in monthly incidence of falciparum malaria from 1980 to 1993.

There was no such strong relationship between night-time temperature and incidence rate of falciparum malaria from 1968 to 1979, a fact which may be attributed to the extensive use of DDT. Thus, the presence of a very strong positive relationship between night-time temperature and a rise in incidence rate of falciparum malaria 2-3 months later during the period from 1980 to 1993 may in part be due to the removal of

the effect of DDT, as well as the presence of a more favourable climatic condition for the transmission of malaria.

The reasons for the increase in the incidence rate of malaria two to three months later following a rise in monthly mean night-time temperature may be explained by the creation of an optimum temperature for the sporogonic development of the malaria parasite in the *Anopheles* vector and/or a greater density of an efficient anthropophilic vector with increased human-biting habits. A decrease in the extrinsic incubation period of the malaria parasite in the *Anopheles* vector together with increased human-biting habit may have resulted from an increase in mean night-time temperature. Such an increase in monthly night-time temperature could have caused a great increase in the basic case reproduction rate of malaria in the highlands of Ethiopia where immunity of the population to malaria is low.

The explanation for the decrease in incidence rate of malaria following a rise in monthly mean day-time temperature may be due to either the detrimental effects of excessive temperatures for the survival of the adult *Anopheles* vector, i.e. a reduction in the longevity of the vector or due to the desiccation of the aquatic stages of the vector, i.e. egg, larva and pupa as a result of extreme temperatures that dry up breeding habitats or due to both. This is not unlikely when one sees that peak monthly day-time temperatures were observed in May which is generally the month of little or no rain in the study area as discussed in Chapter 5.

An increase in monthly total rainfall was associated with a rise in incidence of falciparum malaria during the same month and up to 1-4 months later. This may be due to the fact that the presence of rain pools, which appear to be preferred breeding sites for *An. arabiensis*, the main malaria vector, was important for the transmission of malaria in the area. This is also in line with the observed peak for rainfall and relative humidity in July and August and the peak in incidence of falciparum malaria in October and November following the cessation of the heavy rains in September.

#### ***8.5.3 The link between climate change and increased incidence of highland malaria***

One of the early observations made in ten districts in the Punjab for 17 years from 1901 to 1917 by Gill (1921) suggested that the highest mean temperature associated with "fever" deaths above the mean in October and November was 33.6 °C. This probably was the most detailed earliest analysis of the relationship between a rise in ambient temperature and deaths due to malaria. As discussed in Chapters 1, 3, 4 and 5, the nation-wide epidemic of malaria that struck the highlands of Ethiopia in 1958, which claimed about 150,000 lives, was also associated with particularly high night-time temperature. There was a positive deviation of about 2 °C in the mean night-time temperature during that year.

A more recent analysis of the relationship between climate and malaria was done using data from Rwanda by Loevinsohn (1994). In this analysis of malaria data from 1976 to 1990, it was suggested that both temperature and rainfall act after a lag period of 1-2 and 2-3 months in affecting the incidence rate of malaria. Although this was biologically plausible, as was suggested, the method used in deriving the equation was not clear in the literature provided. Furthermore, the annual incidence of malaria was about 150 per thousand in 1976 and increased to about 300 per 1000 in 1988. This approximate two-fold rise in incidence was not therefore as abrupt as was seen in the present study area, where incidence increased by about 67-fold. No great effort appears to have been made in explaining other contributing non-climatic human and biological factors such as vector control or drug resistance of *P. falciparum* that could play a role in the rise in incidence of malaria. But, despite these, the simultaneous occurrence of a rise in incidence of malaria in Rwanda which also has a similar highland profile to that seen in Ethiopia suggests the possible role of common factors such as temperature or chloroquine resistance.

A prediction of a rise in the incidence of malaria due to global warming was made by various authorities in the field. A possible expansion of the distribution of vectors of malaria in disease-free highlands such as parts of Ethiopia, Indonesia and Kenya was made by a task force of the World Health Organization when they assessed the potential health effects of climate change (WHO, 1990). As seen in Chapter 5, there is great variability in the climate system as shown in the monthly climate data over the past 42 years which suggest abnormal fluctuations with both positive and negative deviations during certain years rather than a persistent upward trend in ambient temperature. But, it seems also clear that such abnormal fluctuations, particularly large positive deviations from the mean night-time temperature during certain years, may be

very important predictors of an abnormal increase in the incidence rate of malaria as shown in the present study.

The abnormal fluctuations in the climate system are characteristic of the El Niño-Southern Oscillation (ENSO), a complex climate system which originates in the Pacific Ocean along the Peruvian coast and affects much of the global atmospheric pressure system especially those countries that border the Pacific and Indian Oceans. It may be described as the occurrence of a warm ocean current that occurs normally at a frequency of two to seven years and affects the pattern of temperature and rainfall in a particular area (Nicholls, 1993).

In Northeast Africa (Horn of Africa) the occurrence of El Niño events was associated with abnormally high temperatures and below normal rainfall causing drought and famine as well as epidemics of malaria with massive loss of life. The abnormal peak in both ambient temperature and rainfall in 1958 was associated with a strong El Niño event as shown in Figure 5.26 in Chapter 5. This was also the year during which 150,000 people were estimated to have died among 3 million cases of malaria in Ethiopia. The intense El Niño events of 1972-73 and 1982-83 were associated with severe food shortages with consequent famine and massive loss of life in northern and central highlands of Ethiopia. Furthermore, the strong El Niño event in 1987 was followed by an epidemic of malaria in Ethiopia in 1988 as discussed in Chapters 3 and 5. Localities at altitudes between 2,000 metres to 2,200 metres, which were previously free of malaria were affected by the disease for the first time as discussed in Chapter 4. Reported incidence and hospital deaths ascribed to malaria increased by 67-fold and 13-fold respectively as discussed in Chapter 3.

The years 1980-81, 1988-89, and 1991-92 saw peaks in reported outbreaks in higher localities in Debre Zeit sector. The years 1988 and 1989 were especially characterised by peaks in mean ambient temperature and below normal rainfall that was not associated with El Niño event. The year 1988 saw a coincident peak in both monthly mean night-time temperature and incidence rate of falciparum malaria. An abnormal rise in monthly mean night-time temperature appeared to be the most sensitive predictor of a significant rise in the incidence of malaria in the highlands of Ethiopia that occurred two to three months later. The regular monitoring of weather patterns may therefore help to identify such abnormal peaks in ambient temperature that could be of practical importance in public health activities especially in the surveillance and control of malaria in the highlands of Ethiopia and other countries with similar geographic features.

However, it is also not unlikely that the decrease in the intensity of vector control effort as seen by the marked reduction of the amount of DDT since 1980 contributed to the observed increase in the incidence rate of malaria in the study area. This is supported by the increase in the incidence rate of malaria seen in 1985, before the occurrence of an abrupt rise in the monthly mean night-time temperature in 1988. Other possible non-climatic factors such as the failure of treatment especially in those patients infected with *P. falciparum* are also likely to have played a role in the increased morbidity and mortality ascribed to malaria in the study area.

## **8.6 Summary**

Analysis of monthly mean night-time and day-time temperature, monthly total rainfall, and biannual use of DDT for vector control from 1968 to 1993 in Debre Zeit sector was conducted to demonstrate the effect of each of these variables on the monthly incidence rate of malaria. The extensive use of DDT and the absence of favourable climatic conditions from 1968 to 1979 were associated with a very low incidence of malaria. A very drastic reduction in the use of DDT resulted in resurgence of malaria from 1980 to 1987.

The most conspicuous increase in the incidence of malaria was noticed from 1988 to 1993 at which time what had been a highly seasonal transmission became perennial, and the monthly incidence rate of falciparum malaria rose from 0.5 per 10,000 person-years before 1980 to 33.4 per 10,000 person-years. A positive correlation was seen between annual mean ambient temperature and annual incidence of both falciparum and vivax malaria. In particular, the positive correlation between annual mean night-time temperature and annual incidence rate of malaria appeared highly unlikely to have been due to chance. A coincident peak was seen in annual incidence of both falciparum and vivax malaria together with annual mean night-time temperature. Both time series plots and Poisson regression analysis revealed the strongest association of monthly incidence of falciparum malaria with a very marked increase in monthly mean night-time temperature from 1988 to 1993. A rise in monthly mean night-time temperature was the strongest predictor of a rise in monthly incidence of falciparum malaria that occurred two to three months later. The epidemic of malaria in 1958 was associated with a strong El Niño event during the same year. Coincident peaks in both incidence rate of falciparum malaria and mean night-time temperatures in 1988 together with statistical evidence

suggested that climatic warming per se may have played a role in the rise in incidence of both falciparum and vivax malaria in the highlands of Ethiopia that was seen since the latter half of the 1980's.

In 1973 there was a strong El Niño event with abnormal rise in both monthly mean day-time and night-time temperatures with below normal total rainfall in the present study area. But, this year was not associated with any marked rise in the incidence of malaria, probably due to extensive malaria control efforts at the time with DDT and the absence of chloroquine resistance. The following three tentative conclusions may be made based on the current findings; a) the extensive use of DDT from 1968 to 1979 prevented climatic changes causing a rise in the incidence of malaria, b) the reduction in the use of DDT enhanced the effect of climate with a rise in incidence of malaria from 1980 to 1987, and c) the failure of chloroquine treatment in falciparum malaria and the continued reduced use of DDT for malaria control, together with a further climatic change from 1988 to 1993 resulted in year round transmission. The immediate impact was an epidemic of malaria leading to a huge rise in the number of reported cases and hospital deaths ascribed to malaria.

## **Part three :**

Synopsis of findings

Summary

Conclusion

## **Chapter 9**

### **Synopsis of Findings**

An attempt was made to understand the epidemiology of malaria in the highlands of Ethiopia in general and in Debre Zeit (Bishoftu) highlands in particular by exploring the most important determinants of its distribution in space and time in the preceding eight chapters separately. Here, a synopsis of the most pertinent findings in all the previous chapters will be presented.

#### ***9.1 Increased morbidity and mortality ascribed to highland malaria***

As noted in both Chapters 1 and 3, the level and trend of malaria in Ethiopia in general, and Debre Zeit highlands (the present study area) in particular, was characterised by an enormous increase in the incidence of both falciparum and vivax malaria. This great increase in incidence of malaria occurred only since the latter half of the 1980's and especially since 1987. There were a total of 73,065 slide confirmed patients with malaria in 1980-81 among 555,786 patients who submitted finger-prick blood samples (a slide positive rate of 13.1%) in the whole of Ethiopia based on reports compiled by the National Malaria Control Service. This number of slide confirmed cases rose to 408,760 among 967,544 slides that were examined (slide positive rate of 42.2%) in 1987-88. This

suggested an increase of 3.2-fold in the slide positive rate and 5.6-fold in the number of reported cases at a national level during this interval.

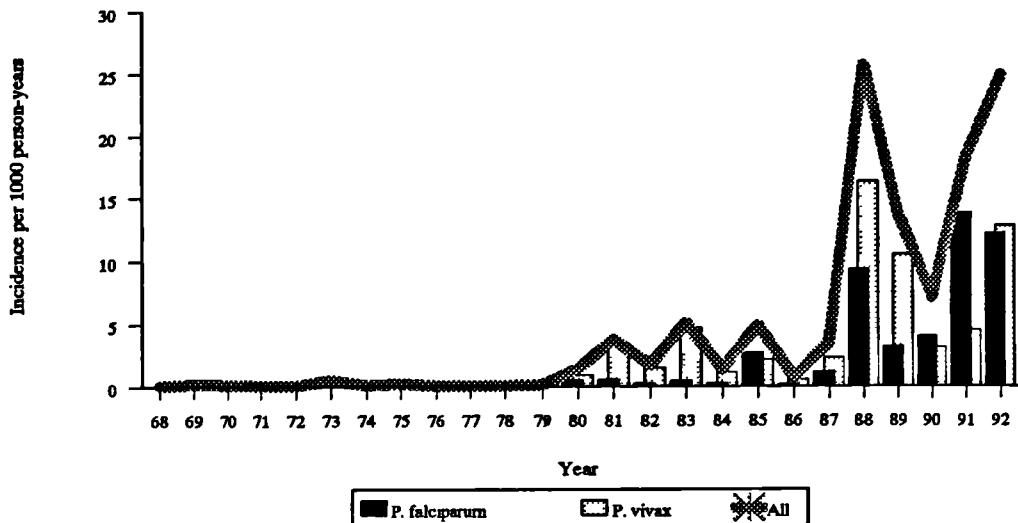
Furthermore, the increased incidence of malaria was much more conspicuous when the pattern over the past two decades was examined in the highlands of Debre Zeit in a relatively stable population. The number of malaria cases rose from only 3 per annum in 1968 to a peak of 9,254 per annum in 1988. This suggested a rise in the estimated incidence rate of malaria from 0.02 per 1000 person-years in 1968 to 25.6 per 1000 person-years in 1988 which suggested an increase of 1,270-fold in the rate of malaria transmission per annum over 20 years assuming a population growth rate of 2.9% per year. This pattern is depicted more clearly in Figure 9.1. As shown in the figure, the annual incidence of malaria started to increase since 1980 but peak incidence occurred in 1988 and 1992. However, when species-specific incidence was considered, peak annual incidence of *P. vivax* occurred in 1988 and that of *P. falciparum* was seen three years later in 1991.

Analysis of age and sex-specific prevalence of malaria showed that children 5-9 years old were most at risk of suffering from highland malaria due to both *P. vivax* and *P. falciparum*. Thereafter, prevalence decreased as age increased. Furthermore, while both genders seemed to share a similar risk up to the age of ten years, males were at a significantly greater risk of morbidity ascribed to malaria than females in all age groups beyond the age of ten years.

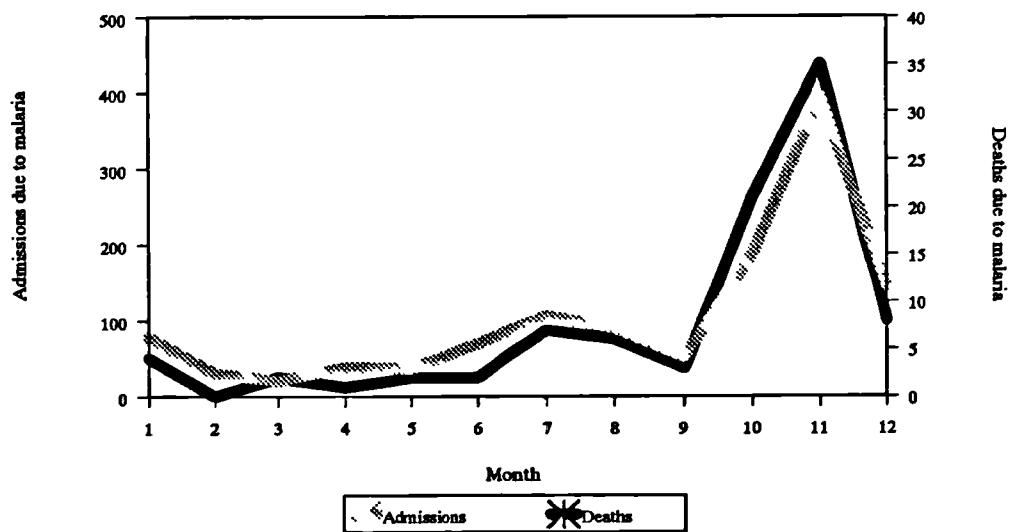
The proportion of hospital admissions and deaths related to malaria also increased sharply when analysis of records of hospital admissions and deaths due to malaria in Debre Zeit hospital was done relative to the 1981-92 period as discussed in Chapter 3. The proportion of deaths ascribed to malaria rose from less than 3% in 1981 to 39% in 1992. This suggested an estimated 13-fold increase in hospital mortality ascribed to malaria over an interval of 11 years. Furthermore, as with data on incidence, peak rate of hospital admissions and deaths ascribed to malaria was observed especially in 1988 and 1992 as shown in Figures 3.10-13.

Analysis of seasonal occurrence of admissions ascribed to malaria in Debre Zeit hospital showed that peak rate of malaria related admissions occur in November accounting for 31.7%, followed by 15.1% in October and 11.5% in December. The lowest number of admissions due to malaria occurred in March and February. Examination of hospital deaths ascribed to malaria further showed a peak in October and November with a respective 23.1% and 38.5% of all deaths related to malaria in Debre Zeit hospital from 1981 to 1992. This is depicted in Figure 9.2 which emphasises the occurrence of the greatest risk of dying from highland malaria in the months of October and November. The above result was obtained by looking at the pattern of a total of 1,247 admissions and 91 deaths ascribed to malaria in Debre Zeit hospital from 1981 to 1992 that suggested an estimated case fatality rate of 7.3%.

**Figure 9.1 Annual incidence of malaria in the highlands of Debre Zeit**



**Figure 9.2 Seasonality of admissions and deaths ascribed to malaria in Debre Zeit Hospital**



## **9.2     Increased transmission of malaria in localities at high altitude**

The effects of altitude on the incidence of highland malaria were discussed in Chapter 4. Some of the main findings in the results were that there was no slide-confirmed case of *P. falciparum* malaria from 1966 to 1980 in localities lying above 1,960 metres. Then, cases of *P. falciparum* were seen in localities lying between 1,965 to 1,995 metres from the years 1981-85. The upper altitudinal limit of transmission seems to have been reached between the years 1986-90 during which time slide-confirmed cases of *P. falciparum* were seen in localities lying up to 2,200 metres. However, with regard to *P. vivax*, this upper limit of transmission was observed between the years 1971-75, about 15 years earlier as compared to *P. falciparum*. The maximum altitude of transmission of malaria due to both *P. falciparum* and *P. vivax* during the 1966-93 period is summarised in Table 9.1 based on current data.

A further observation of altitude effects on peak prevalence of falciparum malaria during reported outbreaks showed that peak prevalence occurred in localities lying at average altitudes of 1,615, 1,840, 1,920 and 1,933 metres in the respective years of 1980, 1981, 1988 and 1992. Thus, it is notable that peak prevalence of reported outbreaks due to *P. falciparum* occurred in localities lying at increasingly higher altitude in more recent times.

**Table 9.1 Maximum altitude of transmission of malaria in the highlands of Debre Zeit from 1966-93**

Year	Maximum altitude of transmission (metres)	
	<i>P. falciparum</i>	<i>P.vivax</i>
1966-70	1,960	1,960
1971-75	1,960	2,200
1976-80	1,960	2,200
1981-85	1,995	2,200
1986-90	2,200	2,200
1991-93	2,200	2,200

### **9.3 Evidence for increased warming of the highlands of Ethiopia**

Time series analysis of monthly mean day-time and night-time temperature records obtained from Debre Zeit Air Force weather station from January 1951 to April 1993 showed that a trend of increased warming has occurred especially since 1988. A record high monthly mean day-time temperature of 31.4 °C was observed in May 1989. This was 5.2 °C higher than the long term monthly mean which was 26.2 °C. However, abnormally high monthly mean day-time temperatures (“heat waves”) exceeding 30 °C have occurred in 1958, 1975, 1984, 1989, 1991 and 1992. It is also notable that the interval during which

such abnormally warm days occurred in these highlands in Ethiopia has progressively shortened from 15 years, 11 years, 5 years , to 2 years and 1 year. Overall, the month of May saw the warmest records in day-time temperature while in August, the lowest values were observed.

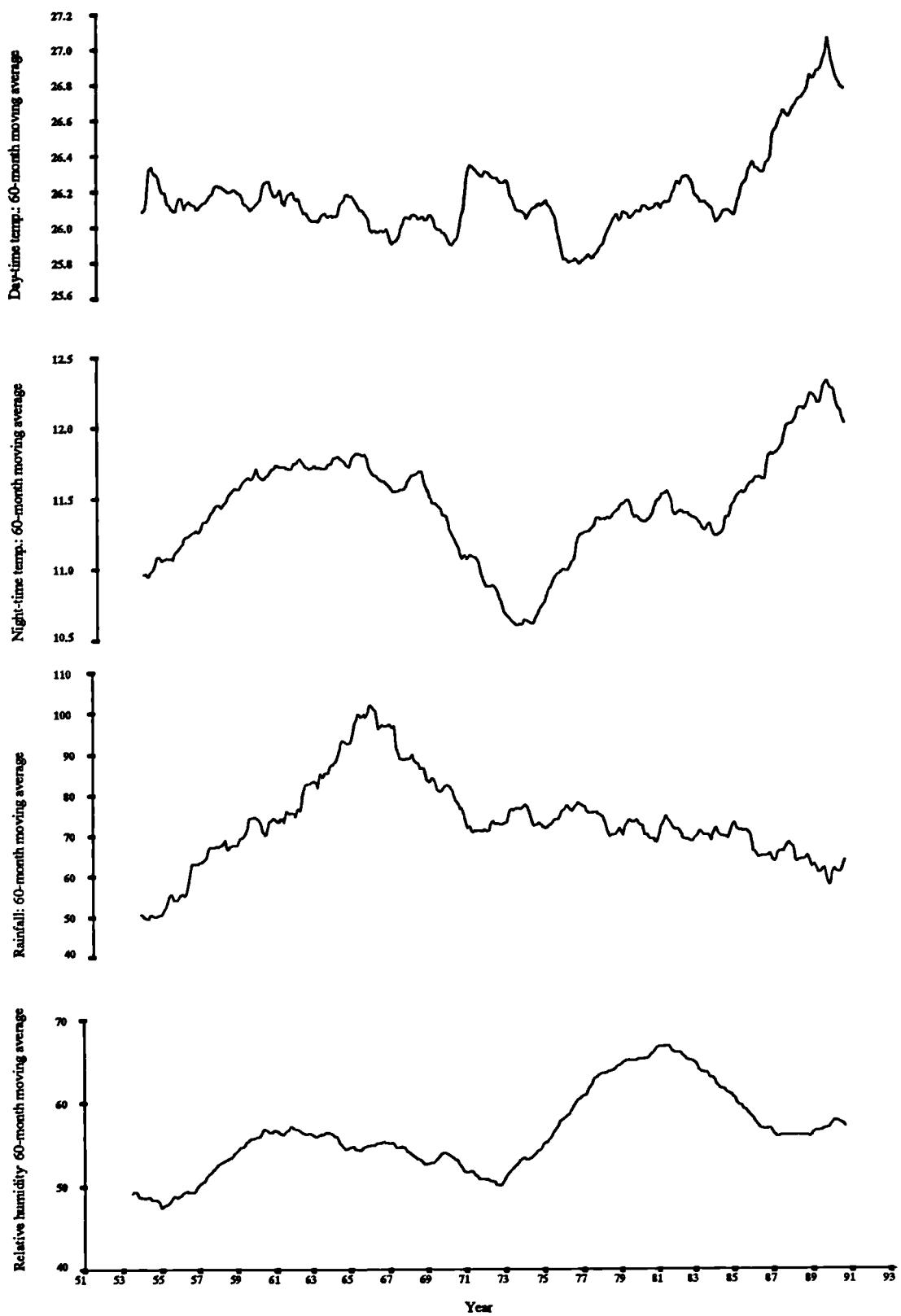
A marked increase was also seen in monthly mean night-time temperature patterns since the latter half of the 1980's and particularly since 1988. Peak record of monthly mean night-time temperature of 17.2 °C was observed in April 1989, one month prior to the peak in day-time temperature mentioned above. This was 5.9 °C higher than the long term monthly mean night-time temperature. Furthermore, although abnormally warm monthly mean night-time temperatures of 14 °C and above, thought to be critical for the completion of the sporogonic development of the malaria parasite (especially *P. vivax*) in the *Anopheles* vector, were observed in 1956, 1958, 1973, 1983, 1987, 1988, 1989, 1991, and 1992, the frequency of such occurrences was especially high since 1988 as discussed in Chapter 5. Analysis of overall seasonal trend of monthly mean night-time temperature revealed that the month of April was the warmest while December was the coolest with respective average temperatures of 13.5 °C and 9 °C. It is also notable that the occurrence of such abnormally warm monthly mean day-time and night-time temperatures during those years was associated with strong El Niño-Southern Oscillation events as discussed previously.

In contrast to the increased warming seen in both monthly mean day-time and night-time temperature, monthly total rainfall showed a trend of decreased precipitation over time. This was particularly obvious especially in those years in which abnormally high records of ambient

temperature was observed. Monthly mean relative humidity also decreased over time. The long-term secular changes in the four climatic variables are summarised more clearly in the time-series plots in Figure 9.3, that were obtained by plotting the 60-month moving averages over the past four decades. Note that the plots in Figure 9.3 clearly depict that both monthly mean day-time and night-time temperature showed a persistent upward trend especially since 1987. This has never been seen at such a scale during the previous three decades. In contrast monthly total rainfall showed a persistent downward trend since 1971 with a marked drop since 1987. Relative humidity also seems to have decreased especially since 1987.

**Figure 9.3**

*60-month moving average of monthly mean day-time & night-time temperature (°C), monthly total rainfall (mm), and relative humidity (%) in Debre Zeit*



## **9.4 Strength of the link between climatic warming and increased incidence of highland malaria in Ethiopia**

### **9.4.1 Temporal association**

Analysis of data on the level and trend of malaria in the highlands of Debre Zeit showed that peak incidence of malaria occurred in 1988, 1991, and 1992 as discussed in Chapter 3 and shown in Figure 9.1. Furthermore, analysis of altitude effects on incidence showed that the transmission of *P. falciparum*, the cause of severe and fatal malaria, has been seen among communities living in localities lying between 2,000 and 2,200 metres from 1986-93. These communities appeared to have been suffering from morbidity and mortality due to *P. falciparum* malaria for the first time. Hospital morbidity and mortality ascribed to malaria also was greatest in the years 1988, 1991 and 1992 as seen in data from Debre Zeit hospital.

Climatic patterns in Debre Zeit, the same study area from which data on morbidity and mortality from malaria were collected, revealed that abnormally high monthly mean day-time and night-time temperatures occurred in 1988, 1991, and 1992 during which time total rainfall decreased. A further search for evidence of secular changes favouring increased transmission of malaria in the highlands showed the occurrence of monthly mean night-time temperatures 14 °C and above (thought to be the minimum threshold for completion of sporogonic development of the malaria parasite inside the *Anopheles* vector) only once from 1968-79, twice from 1980-87, and eleven times from 1988-93. Furthermore, a coincident peak in both annual mean night-time temperature and incidence rate of both falciparum and vivax malaria was seen in 1988. All these suggested the

existence of a very strong relationship between climatic warming and increased incidence of highland malaria.

#### **9.4.2 Statistical evidence**

A search for statistical evidence of long term trends of climatic changes (secular changes) and incidence of falciparum malaria showed a positive correlation between annual incidence rate of malaria and annual mean ambient temperature. Generally, a stronger correlation was shown for annual mean night-time temperature than annual mean day-time temperature, and for vivax malaria than for falciparum malaria as shown below.

<i>Malaria parasite</i>	<i>Annual mean temperature</i>	<i>Correlation coefficient (r)</i>	<i>t</i>	<i>P</i>	<i>Degrees of freedom (d.f.)</i>
<i>P. vivax</i>	Night-time	0.62	3.79	<0.001	23
<i>P. vivax</i>	Day-time	0.47	2.55	<0.02	23
<i>P. falciparum</i>	Night-time	0.49	2.70	<0.02	23
<i>P. falciparum</i>	Day-time	0.25	1.24	>0.05	23

The positive correlation between a rise in both ambient temperature and malaria appeared unlikely to have been due to chance alone with the exception of day-time temperature and falciparum malaria as shown above. In contrast, a weak negative correlation was seen between annual total rainfall and annual incidence of malaria. However, this negative correlation was not unlikely to have been due to chance ( $r = -0.31$ ,  $t = 1.56$ ,  $P > 0.1$ ,  $d.f. = 23$  for falciparum malaria and  $r = -0.33$ ,  $t = 1.67$ ,  $P > 0.1$ ,  $d.f. = 23$  for vivax malaria). This is in line with the general pattern of increased warming in both night-time and day-time temperature as well as decreased annual total rainfall.

A further statistical examination of the relationship between monthly climatic data (explanatory variables) and monthly incidence of falciparum malaria (dependent or outcome variable) at current month (lag 0), 1 month later (lag 1), 2 months later (lag 2), 3 months later (lag 3), and 4 months later (lag 4) was carried out first in scatter plots, and then by Poisson regression analysis as discussed in Chapter 8.

The results showed that the strongest positive correlation was between monthly mean night-time temperature at lag 3 and monthly incidence of falciparum malaria,  $r = 0.63$ . This suggested that a unit ( $^{\circ}\text{C}$ ) rise in monthly mean night-time temperature had the strongest effect on increased incidence of falciparum malaria 3 months later. There was also a strong positive correlation between monthly mean night-time temperature and monthly incidence of falciparum malaria at lag 2,  $r = 0.52$ . In contrast, monthly mean day-time temperature showed the strongest negative correlation with monthly incidence of falciparum malaria at lag 0,  $r = -0.42$ . This suggested that each unit rise ( $^{\circ}\text{C}$ ) in monthly mean day-time temperature had the strongest effect in reducing the monthly incidence of malaria during the same month. Monthly total rainfall showed a weak positive correlation with monthly incidence of falciparum malaria at all lags ( $r = 0.15-0.34$ ). This suggested that each unit (mm) rise in monthly total rainfall is associated with an increased incidence of falciparum malaria during the same month, 1 month later, 2 months later, 3 months later and 4 months later with the greatest effect after 2 and 3 months,  $r = 0.31$  and  $0.34$  respectively.

Following the above observation of the general relationship between climatic conditions and incidence of malaria, a more detailed Poisson regression analysis was carried out to estimate the exact effect of climatic variables on monthly incidence of falciparum malaria. This was done firstly by estimating the effect of monthly mean night-time & day-time temperatures, and then monthly total rainfall at a lag period of 0 month, 1 month, 2 months, 3 months, and 4 months. Secondly, all climatic variables which showed a significant association on bivariate analysis ( $P < 0.05$ ) were put in the model and the effect of one of them was estimated by allowing for the other variables at each step. Thirdly, likelihood ratio tests were used to assess statistical significance throughout all lags.

The results showed that the strongest positive correlation was between monthly mean night-time temperature at lag 2 and monthly incidence of falciparum malaria ( $\chi^2 = 486.85$ ,  $P < 0.001$ , coefficient =  $0.495 e^{0.495} = 1.640$ ). This suggested that every °C rise in monthly mean night-time temperature was associated with an estimated 64% increase in monthly incidence of falciparum malaria 2 months later. The second strongest positive correlation was seen in monthly mean night time temperature at lag 3 which suggested that each °C rise in monthly mean night time temperature was associated with an estimated 58% increase in monthly incidence of falciparum malaria 3 months later. No such positive correlation was seen in either monthly day-time temperature or monthly total rainfall. Thus, based on current data from this study area, a rise in monthly mean night-time temperature remained the single most important predictor of a significant increase in monthly incidence of falciparum malaria.

## ***9.5 Factors that amplify the impact of global warming on increased morbidity and mortality ascribed to malaria in the highlands of Ethiopia***

Morbidity and mortality ascribed to highland malaria has increased by several folds as discussed in Chapters 1, 3, and 4. This appears to have been mainly due to global warming, and more specifically due to a marked rise in the monthly mean night-time temperature as discussed in Chapters 5 and 8. In this section, an attempt will be made to describe the factors that amplified the impact of global warming on the increased incidence of morbidity and mortality ascribed to highland malaria based on current data from the present study area.

### ***9.5.1 Emergence and spread of chloroquine resistant falciparum malaria in the highlands of Ethiopia***

In a study carried out by the National Organization for the Control of Malaria and Other Vector-borne Diseases in 1985 in Ethiopia, the first evidence for the emergence of chloroquine resistant falciparum malaria was reported among patients who acquired the infection in peripheral lowlands along the border with Somalia, The Sudan and Kenya. Overall, 22.4% ( N = 98) failed to clear their asexual parasitaemia among whom a respective 63.6%, 27.3% and 9.1% were resistant to chloroquine at the RI, RII and RIII levels. Furthermore, it was reported that the problem of chloroquine resistant falciparum malaria is limited to peripheral lowlands and the central highlands of Ethiopia were believed to be free.

However, as discussed in Chapter 6, chloroquine resistant strains of falciparum malaria are already widespread in the central highlands of Ethiopia posing a major threat to the successful treatment of patients suffering from this malaria parasite. Among a total of 29 patients who were successfully followed up on days 0, 1, 2, and 7 following treatment with a standard regimen of chloroquine, only 4 patients (14%) were able to demonstrate evidence of complete clearance of asexual parasitaemia by day 7. The remaining 25 patients (86%) were unable to clear asexual parasites by day 7 in spite of treatment suggesting the presence of a high level of chloroquine resistant strains of *P. falciparum* malaria *in-vivo*. Among the latter, a respective 14%, 62% and 24% were resistant to chloroquine at RI, RII and RIII levels.

In spite of the fact that a high level of chloroquine resistance *in-vivo* was observed, the proportion with high asexual parasite densities (>1,000 asexual parasites per 300 leucocytes) decreased progressively from 20% to 10%, 11%, and 0% on the respective follow-up days 0, 1, 2, and 7 after treatment. This suggested that while chloroquine treatment was unable to show complete clearance of asexual parasitaemia, it still had a great effect in reducing the proportion of high parasite densities by an estimated 50% after 24 hours and 100% after 7 days of standard triple dose chloroquine therapy. Furthermore, the proportion of patients with fever, i.e. axillary temperature  $\geq 37.5^{\circ}\text{C}$ , was 27% on day 0, 18% on day 1, 10% on day 2, and 7% on day 7. This showed that despite the failure of complete clearance of asexual parasitaemia, chloroquine treatment had a significant impact

in reducing both the proportion of fever and high parasite densities among patients suffering from falciparum malaria by an estimated 74% and 100% respectively on day 7. Only one of thirty-two patients (3%) treated with sulphadoxine-pyrimethamine (Fansidar<sup>R</sup>) and who completed the follow-up period, failed to clear asexual parasitaemia due to *P. falciparum*.

A total of 255 patients diagnosed to suffer from *P. vivax* malaria were treated with a standard dose of chloroquine and were successfully followed up on days 0, 1, 2 and 7. Among these, only 5 patients (2%) failed to clear asexual parasitaemia. Furthermore, the proportion of patients with fever declined from 41.4% to 7%, 0.3% and 0.4% on the respective days of 0, 1, 2, and 7 post-treatment. This suggested an estimated 98% effectiveness of chloroquine in clearance of asexual parasitaemia and 99% in the reduction of the proportion of fever among patients suffering from *P. vivax* malaria.

#### **9.5.2 *Decreased malaria vector control efforts***

The exact extent of the efforts expended in the control of malaria vectors especially through the use DDT has been discussed in Chapter 7. Overall, the period from 1966-79 was known as the “attack phase” and huge efforts were spent through the extensive application of DDT by blanket coverage of all localities in the sector irrespective of the level of endemicity of malaria. This was mostly because of the then prevailing global strategy of malaria eradication. In contrast, the 1980-93 period was characterised by a marked decrease in the use of DDT for malaria vector control. This is probably

attributable to the change in strategy from eradication towards control in which only selective spraying of localities with high prevalence of malaria was advocated and implemented.

The reduced use of DDT for malaria vector control in the present study area could be indicated as shown in the following indices of coverage; a) an estimated 96% reduction in the amount of DDT used for indoor spraying, b) a reduction by about 93% in the number of houses sprayed, and c) a decrease by 92% in the number of people expected to be protected from malaria. Furthermore, despite such a reduction in the coverage of DDT spraying operations for the control of malaria in the present study area, the total operational cost of spraying DDT has increased by an estimated 263%. Moreover, the cost per person protected rose by 1,417% as discussed in Chapter 7.

### **9.5.3 *Population migration***

An attempt was made to see whether the increased incidence of malaria in the highlands of Debre Zeit was attributable to population migration, i.e. whether the infection was acquired elsewhere despite the diagnosis of cases at Debre Zeit malaria clinic. This was done by looking at individual patient records pertaining to both place of residence and history of travel during the preceding one month prior to the date of reporting at the malaria clinic. Frequency distribution of patients by Administrative Region (Kifle-Hager, Zone) of residence suggested that 99.2% were from Shewa (N = 130,651). Furthermore,

97.2% ( N = 127,311) were from Yerer-Kereyu province. The present study area, that consists of four districts lies in both the province and administrative region mentioned above. A further examination of the distribution of patients by place of possible acquisition of infection by district based on the history of travel during the past month is shown in Table 9.2.

**Table 9.2: District in the study area where malaria infection was probably acquired by species**

District	Examined	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. f &amp; P.v</i>
Adea	77,696	8,966	16,963	79
Akaki	795	84	105	1
Liben	3,820	764	547	8
Lume	44,438	9,105	8,048	40
Total	126,749	18,919	25,663	128
Grand total	131,662	19,786	26,351	132

Thus, as shown in Table 9.2, 95.6% ( N = 19,786) of all *P. falciparum* and 97.4% ( N = 26,351) of all *P. vivax* infections diagnosed in Debre Zeit sector malaria clinic appear to have been acquired inside the four districts of the present study area. Furthermore, 95.5% and 97.5% of those diagnosed to suffer from *P. falciparum* and *P. vivax* respectively seem to have acquired the infection in Adea and Lume, the two nearest districts to the malaria clinic in Debre Zeit. Hence, based on current data, it appeared unlikely that the increased

incidence of malaria in the highlands of Debre Zeit (the present study area), could be attributed to population migration.

However, the problem of malaria attributed to population migration in general, and that of resettlement malaria in particular is a relevant issue for the control of malaria in Ethiopia as discussed in Chapter 1. The actual magnitude of resettlement malaria and the estimated proportion of all malaria in Ethiopia attributable to resettlement malaria for the period 1985-89 is shown in Table 9.3 based on surveillance data of the National Organization for the Control of Malaria and Other Vector-borne Diseases.

**Table 9.3 Proportion (%) of malaria attributable to resettlement malaria in Ethiopia from 1985-89**

Year	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. malariae</i>	<i>P.f + P.v</i>
1985-86	12.9% (64,157)	20.6% (75,201)	3.2% (656)	7.3% (619)
1986-87	35.4% (118,011)	49.9% (114,970)	17.3% (156)	25.9% (375)
1987-88	47.2% (271,089)	45.4% (136,985)	20.5% (117)	29.3% (569)
1988-89	51.3% (233,939)	54.5% (91,504)	16.7% (53)	34.7% (300)

Note: the brackets include the number of all malaria patients in Ethiopia by species

Note that as shown in Table 9.3, more than half (51.3 % & 54.5% of *P. falciparum* and *P. vivax* respectively) of all malaria cases diagnosed in Ethiopia in general were in the resettlements in 1988-89, at which time a coincident peak in both climatic warming and incidence of malaria also occurred. It therefore appeared that these non-immune

populations who were resettled from the northern and central highlands of Shewa, Wello, and Tigray into western and south-western peripheral lowlands in Wellega, Metekel, Metemma and Gambella were at a particularly increased risk of morbidity and mortality from malaria ascribed to global warming. This case from Ethiopia also illustrates the relationship between high population density and deforestation of the highlands with severe land degradation, warming of the highlands, drought, hunger, population migration, resettlement in the lowlands and increased morbidity and mortality from malaria on a wider scale.

Despite the lack of data, it is likely that other forms of migration than resettlement, such as that of seasonal migration of the labour force to malarious areas during the planting and harvesting season, the movement of soldiers, both legal and illegal merchants together with refugees along the borders with Somalia, The Sudan and Kenya, as well as nomadic pastoralists to and from malarious areas also play a role in facilitating the transmission of malaria in Ethiopia. It is likely that the incidence of malaria related morbidity and mortality especially among the non-immune group of the above categories would be high.

## **9.6 Implications of study findings for the control and surveillance of malaria**

### **9.6.1 The link between the Ethiopian malaria situation and other countries with a highland profile**

The increased incidence of malaria has been reported in many Northeast and East African as well as Southeast Asian countries with a highland profile especially since the latter half of the 1980's. These countries consisted of Madagascar (Lepers et al., 1988; Fontenille et al., 1987), Tanzania (Matola et al., 1987; Lines et al., 1991), Kenya (Rees, 1994; Some, 1994), Rwanda (Loevinsohn, 1994), Ethiopia (Tulu, 1989), Indonesia (Anthony et al., 1992) and Pakistan (Bouma et al., 1994). Despite the rarity of reports published elsewhere, it is likely that the occurrence of epidemics of highland malaria was much more extensive and many more countries were probably affected at the same time.

Although many factors were suggested to be the cause of these epidemics, only two authors indicated that climatic factors were responsible for the increased incidence of highland malaria (Loevinsohn, 1994; Bouma et al., 1994). Furthermore, even the latter authors appear to have neglected the role that non-climatic factors could play in amplifying the impact of global warming on morbidity and mortality ascribed to highland malaria. However, as shown in the findings of this study, while climatic factors were mainly responsible for the occurrence of malaria in localities lying at high altitude, non-climatic factors have played a significant role in amplifying the impact of global warming

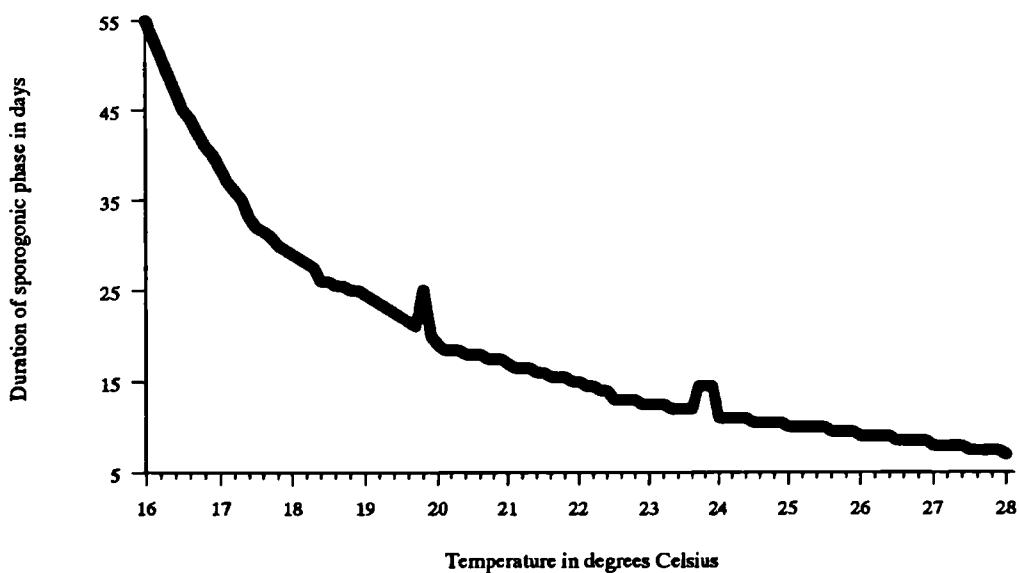
on morbidity and mortality ascribed to highland malaria. These non-climatic factors probably play their amplifying role at some distal points in the causal pathway.

The occurrence of climatic warming mainly through an increase in the monthly mean night-time temperature is expected to facilitate the transmission of malaria mainly through the reduction of the duration of sporogonic development of the malaria parasite in the *Anopheles* vector. This could be especially important in areas at high altitude where the transmission of malaria was either non-existent or very short-lived due to low temperature as seen in many localities in the present study area. There was a very close relationship between altitude and temperature at four weather stations located at different elevations in the present study area. The long term monthly mean night-time temperature was 8.7 °C, 11.4 °C, 12.7 °C, and 13.9 °C in weather stations located at respective altitudes of 2,354, 1,900, 1,870, and 1,622 metres above sea level. Furthermore, there was an estimated 0.65 °C rise in monthly mean night-time temperature for each 100 metres decrease in altitude. This value is close to the 0.50 °C fall for every 100 metres rise in altitude irrespective of latitude or continent suggested by other investigators earlier (Garnham, 1948).

There are two specific stages in the life cycle of the malaria parasite and its vector which are very sensitive to changes in climatic conditions and especially ambient temperature. These are the gonotrophic cycle, i.e. the period between successive ovipositions of the female anopheles, and the sporogonic cycle, i.e. the period between infection of the mosquito when obtaining a blood meal on humans with the malaria parasite and the

development of the sporozoite in its salivary glands. The duration of sporogony of *P. vivax* may vary from 55 days at 16 °C to only 7 days at 28 °C as shown in experiments conducted at various temperatures (Detinova, 1962). This signified that there may be a reduction in the duration of sporogony by about 4 days on average for each °C rise in ambient temperature. However, at the lower range of temperature, the magnitude of decrease was much more dramatic. The duration of sporogonic phase decreased by 16.5 and 9.5 days when the ambient temperature increased from 16 to 17 °C and 17 to 18 °C respectively. This is more clearly depicted in Figure 9.4 which shows an inverse relationship between temperature and the duration of the sporogonic phase in the vector.

**Figure 9.4 Duration of the sporogonic phase of *Plasmodium vivax* in the *Anopheles* vector based on data from Detinova (1962).**



From the foregoing, it is plausible to assume that the reported increase in morbidity and mortality from malaria in countries with a highland profile was due to an increase in ambient temperature. This must have facilitated the transmission of malaria at high altitudes by reducing the duration of the sporogonic phase and possibly by reducing the interval between successive blood meals. Furthermore, despite the rarity of such comprehensive analysis about the factors that could amplify the impact of global warming on highland malaria from elsewhere, it is very likely that spread of drug resistant malaria, relaxation of vector control efforts, and population migration were common denominators in many of these countries, though with varying degree from place to place.

#### ***9.6.2 The relationship of study findings to models on climate change and malaria***

The occurrence of abnormally warm climate over large areas of the planet was characteristic of most meteorological records at numerous weather stations in the past decade. This has caused alarm in public opinion and various study groups including experts on both climate and health have been set up. The Intergovernmental Panel on Climate Change was formed to assess scientifically past events, current data and predict as to what might happen in the future in order to give an informed advice to policy makers.

##### ***9.6.2.1 Models about observed climate variation and change***

A comparison of variations of climate in different parts of the world and analysis of recent trends based on data from 1861 to 1991 showed that the 1980's were the warmest decade

(Jones et al., 1991). Furthermore, the sub-period 1986-90 was the warmest and positive anomalies (deviations relative to the 1951-80 mean) were noticeably larger during December to May than in the rest of the year in both southern and northern hemispheres. Comparative analysis of data on a three decade basis (1931-60 & 1961-90) revealed that rainfall has decreased by 30% in Sahel region of Africa (IPCC, 1992).

Global warming was also thought to be the cause of the recession of mountain glaciers and a decrease in their mass by about 50% in the European Alps since the middle of the nineteenth century as suggested by observations in both aerial and ground surveys (Haeberli, 1990). Furthermore, expanded bleaching of the coral reef was also said to result from the expulsion of algae from the coral due to extremely warm temperatures .

Current findings in time-series of climate data from the present study area in Ethiopia are generally in line with the trends mentioned above. The 1980's was the warmest decade and especially the sub-period from 1986-90 saw peak records in both monthly mean day-time and night-time temperatures. A record peak in monthly mean night-time and day-time temperature occurred in 1989 in the months of April and May respectively. In contrast, both monthly and annual total rainfall decreased during these periods.

### **9.6.2.2**

### ***Predictive models of both climate change and malaria***

There are five climate change scenarios based on atmospheric general circulation models (GCM) that predict global warming depending on a doubling of the concentration of carbon dioxide. These are known as: (a) the Standard Geophysical Fluid Dynamics Model without Q-flux correction (GFDL) GCM, (b) the Geophysical Fluid Dynamics Laboratory with Q-flux correction (GFDLQ) GCM, (c) the Goddard Institute for Space Studies (GISS) GCM, (d) the Oregon State University (OSU) GCM, and (e) the United Kingdom Meteorological (UKMO) GCM. These five models and the scenarios they produce have been described in detail in the two successive reports of the Intergovernmental Panel on Climate Change (IPCC, 1990; IPCC, 1992).

Furthermore, a very recent model has been developed about the potential malaria occurrence zone that could result from global warming based on the five general atmospheric circulation models, the minimum inhibitory ( $15^{\circ}\text{C}$ ) and maximum tolerable ( $32^{\circ}\text{C}$ ) temperatures, a mean moisture index (ratio of precipitation to potential evapotranspiration) of 0.7, and climatic data pooled from 7,500 meteorological stations. The most pertinent findings of this model were that: (a) there will be an estimated increase by 12% (GFDLQ) to 55% (UKMO) of seasonal zones of malaria transmission, and (b) there will be an estimated decrease by 3% (GFDLQ) to 41% (UKMO) in the zone of perennial transmission of malaria (Martin and Lefebvre, 1995).

The problem with the findings in this model is that while it is understandable that there could be an expansion in the zone of malaria transmission to areas where malaria was previously free due to the creation of a more suitable ambient temperature as was seen in the current study in Ethiopia, the reasons for the decrease in the zone of occurrence of perennial malaria predicted by the model are not at all clear. Current findings from the present study in Ethiopia showed evidence for an increased incidence of both seasonal and perennial malaria. Besides, the fluctuations in the incidence of malaria were often associated with the El Niño-Southern Oscillation events which the model appears to have ignored.

Moreover, the model fails to account for the role of non-climatic factors such as biological adaptive responses in both the parasite and the vector such as drug and insecticide resistance, human adaptive responses such as control efforts expended on diagnosis and treatment of malaria as well as vector control, and population migration all of which could either amplify or diminish the impact of global warming on the incidence of malaria (McMichael and Martens, 1995). In fact, although there is a potential for the occurrence of malaria due to global warming in developed temperate zones as predicted by the model, the conclusion that malaria will occur in the developed world is probably unlikely to hold much weight. Findings in the present study area suggest that in the presence of effective vector control programmes and treatment regimens, the incidence of malaria was very low or even non-existent in some of the localities at high altitude despite the presence of a suitable temperature in 1973 associated with El Niño event. Furthermore, past control

efforts have successfully eradicated malaria from the Pontine marshes in Italy and fertile agricultural lands of Southern USA and there is as yet no evidence that malaria transmission is taking place in these areas despite the presence of a suitable climate as well as the vectors of malaria. In the light of these facts, the present author agrees with what has been suggested earlier by mathematical model experts in the field of transmission of vector-borne diseases and global change, “it is probably correct to assume that a vector now confined to the tropics will spread into more temperate regions if global warming occurs but it is much less certain that the diseases they carry will eventually be as prevalent in the newly invaded area as elsewhere” (Rogers and Packer, 1993).

## **9.7      *Limitations of the study***

### **9.7.1    *Limitations inherent in retrospective data***

As discussed in Chapters 1 and 2, it is clear that the study was designed to detect changes in the incidence of morbidity and mortality from malaria in the highlands that could be ascribed to global warming. This aim dictated a retrospective approach since global warming is a slow process that must have occurred over the past several years. Hence, data sets pertaining to both malaria and climate collected in the past had to be used. However, it is clear that such data have inherent problems such as variations in the methods of collection of data between different observers and with the same observer at different times in the past. It is not inconceivable that methods of detection of cases, microscopic diagnosis, hospital management of patients, antimalarial treatment regimens, recording of climate data may have varied over time.

The problem of missing data of relative humidity from 1985-89 in the climate data set was a limitation that hindered the attempt to estimate the amount of malaria attributed to changes in relative humidity although it is clear that relative humidity has an important role in the longevity of vectors. Furthermore, the incidence of malaria was estimated based on data from the diagnosis and treatment clinic in Debre Zeit sector. It is likely that the actual incidence of malaria was grossly underestimated since it is known that only a limited proportion of patients who were within a walking distance were diagnosed, and if they were far away, those who could afford the cost of transport, and those who knew that they may be suffering from malaria and could be treated came to the clinic. In fact, this differential access to the health facility, especially geographic access, may explain the reason why only less than 4% and 2% of respective cases of falciparum and vivax malaria were coming from outside the two nearest districts of the study area. It is therefore likely that the incidence of malaria, as well as mortality ascribed to malaria in the remaining two districts in which there were many localities lying at high altitudes was grossly underestimated.

#### ***9.7.2 Limitations of sample size in in-vivo study***

Only 29 of the 60 patients with *P. falciparum* recruited for the study on the response to chloroquine were able to complete the follow-up period although it has been recommended earlier that at least 30 persons in a given locality are required to obtain information on the base-line sensitivity of local parasites (Bruce-Chwatt, 1986). However, it was seen in the study that 86% of those who completed the follow-period to day 7 were unable to clear asexual parasitaemia suggesting the presence of a high level of chloroquine resistant strains of *P. falciparum*. Thus, it is unlikely that a larger sample size will alter the conclusion about the presence of chloroquine

resistance in the study area. Nevertheless, since these data were based on patients who came to the clinic and the sample was small, it is possible that the actual level of chloroquine resistance in the community may have been overestimated.

### ***9.7.3 Limitations in analysis of data sets***

The amount of malaria attributed to climatic changes and especially global warming has been estimated using both time-series and Poisson regression methods. The occurrence of abnormal increases in both monthly mean day-time and night-time temperature as well as monthly total rainfall and their relationship with incidence of malaria has been known. The lag period between the occurrence of extreme climatic conditions and an estimate of the expected increase in incidence of malaria has also been worked out. However, the exact amount that could be attributed to qualitative changes like antimalarial drug resistance or decreased vector control has not been shown.

## **SUMMARY**

Epidemics of malaria have increasingly been reported in the highlands of Ethiopia and other East African and Southeast Asian countries with a similar geographic profile since the latter half of the 1980's. In Ethiopia, where malaria is unstable in the highlands between 1,500 and 2,500 metres, malaria became the second cause of out-patient attendance and the leading cause of hospital deaths in 1988-89. Earlier studies ascribed this increase in malaria to a massive resettlement programme involving 600,000 non-immune highlanders to peripheral lowlands in the west and Southwest parts of the country.

The present study was planned to look at a stable population with the objective of exploring whether global warming was the main factor in the rise in the incidence of malaria in the highlands and to identify non-climatic biological and human factors that may have amplified the observed morbidity and mortality ascribed to highland malaria. Both retrospective and prospective analytic methods were employed to conduct a study in Debre Zeit (Bishoftu) sector, central Ethiopia with a population of 406,891 living in 430 localities. Nine data sets were collected and these included maximum and minimum altitude, monthly malaria incidence, annual point prevalence during peak transmission, monthly hospital morbidity and mortality, outbreaks of malaria, biannual data on vector control using DDT, monthly climate data about mean day-time and night-time temperature, total rainfall, and relative humidity, and the response of patients suffering

from *P. falciparum* and *P. vivax* to standard doses of chloroquine and sulphadoxine-pyrimethamine.

Morbidity analysis revealed that the incidence of falciparum malaria increased from 0.5 per 10,000 person-years in October 1973 to 33.4 per 10,000 person-years in October 1991, i.e. a 67-fold increase in about two decades. The proportion of deaths ascribed to malaria increased from 2.9% in 1981 to 38.6% in 1992, i.e. a 13-fold increase during the last decade. Analysis of altitude effects showed that *P. falciparum* had a greater advantage of transmission below 1,800 metres while above this altitude, *P. vivax* showed a greater relative frequency. Highland communities living at altitudes between 2,000 and 2,200 metres were affected by *P. falciparum* for the first time since 1986. Children between 5 to 9 years were most at risk.

Time series analysis of climate patterns revealed a trend of increased climatic warming in both day-time and night-time temperatures especially since 1988, at which time a coincident peak in incidence of malaria was also observed. In contrast, a progressive decrease in both total rainfall and relative humidity was seen. Some of the years and months with increased mean ambient time temperature and decreased total rainfall together with high incidence of malaria were associated with strong El Niño events. Further analysis using Poisson regression showed that each °C rise in monthly mean night-time temperature was associated with an estimated 64% and 58% rise in the incidence of falciparum malaria two and three months later respectively.

While climate change and especially increase in monthly mean ambient temperature had a primary role in the transmission of malaria at high altitude localities by affecting factors in the proximal parts of the causal pathway, non-climatic biological and human factors may have amplified the impact of global warming on morbidity and mortality ascribed to malaria in Ethiopia through their effect at more distal points in the causal pathway. These non-climatic that amplified the transmission of malaria included the failure of chloroquine treatment to clear asexual parasitaemia among 86% of patients infected with *P. falciparum*, the drastic reduction in the amount of DDT used for intradomiciliary spraying, and large scale population migration consisting of the movement of more than half a-million non-immune individuals from central and northern highlands to remote peripheral lowlands.

## **CONCLUSION**

From the foregoing, it is plausible to reach at the following conclusions based on data from the present study area and previous work from other parts of Ethiopia.

### ***A. Global warming as the cause of malaria transmission in the highlands***

Data from the present study area suggest a trend of climatic warming in both day-time and night-time temperature. This warming of the climate, and especially the abnormal increase in night-time temperature appears to have facilitated malaria transmission in the highlands of Ethiopia. New foci of malaria transmission have been identified in high altitude localities where malaria was previously absent. Both the rate and duration of transmission also appear to have been enhanced in previously existing foci of transmission. This was the main cause of increased morbidity and mortality from malaria in such areas. This may be true of other East African and Southeast Asian countries with a similar highland profile known to be prone to periodic epidemics of malaria.

### ***B. Association of epidemics of highland malaria with strong El Niño-Southern Oscillation***

The most disastrous epidemic of malaria in Ethiopia that occurred in 1958 in which 150,000 people were estimated to have died among 3 million estimated cases of malaria was associated with an abnormal increase in ambient temperature and rainfall. This year

saw a strong El Niño event. The epidemic of malaria that occurred in 1988 in Ethiopia was also preceded by a conspicuous El Niño event in 1987. The more recent epidemics of malaria in 1991 and 1992 also were El Niño years. Current findings suggest that the frequency of El Niño events has increased very much and it is likely that this also led to an alarming increase in the frequency of epidemics of highland malaria. This has also been the case in many other countries with a highland profile. It may be plausible to assume that global warming led to an increase in the frequency of El Niño events which in turn resulted in increased frequency of epidemics of malaria in countries with a highland profile.

***C. Failure of chloroquine treatment as the cause of hospital mortality ascribed to malaria***

Current data from Ethiopia suggest that failure of chloroquine treatment especially in those patients with *P. falciparum* malaria was the main cause of hospital mortality ascribed to malaria. It is plausible to assume that chloroquine resistance spread from peripheral lowlands on the borders with Somalia, Kenya and The Sudan to the interior of the country affecting large parts of the central highlands of Ethiopia since 1988.

***D. Decreased vector control efforts as an amplifying factor of the impact of global warming on malaria transmission in the highlands of Ethiopia***

Past vector control efforts especially using DDT for malaria control from 1968 to 1979 were extensive and may have contributed to the low incidence of malaria in known foci of malaria

transmission. However, the drastic reduction in the level of vector control from 1980 to 1993 together with the presence of a very suitable ambient temperature especially since 1988 appears to have amplified the impact of global warming on morbidity and mortality ascribed to highland malaria.

***E. Large scale population migration from highlands as the cause of increased morbidity and mortality from malaria in the lowlands***

The movement of non-immune population groups from highlands where the incidence of malaria was either absent or very low to lowlands where there is year round transmission of malaria has created very vulnerable risk groups. The mobilisation of about 600,000 non-immune settlers has particularly aggravated the problem of malaria in Ethiopia at which time a coincident peak occurred in both incidence of malaria and ambient temperature. More than half of all the cases of malaria in Ethiopia were from resettlement sites at that time.

***F. Development of an early warning system for the detection & control of epidemics of malaria***

While long term secular climatic changes may be important to influence policy at the global level about ways of tackling the probable causes of global warming (decreasing the concentration of green house gases, reforestation, seeking alternative and sustainable sources of energy, control of the explosive growth of the population in the Third World, improvement of agricultural practices, etc.) short-term year to year climatic fluctuations associated with El Niño events may be very important for the development of an early warning system for the surveillance and control of malaria at the local level. This could be

especially important in areas prone to epidemics where morbidity and mortality from malaria not only of children but that of adults (bread winners of the family) is high and its prevention and/or reduction is very crucial for the survival of many communities.

Based on current data, it appears that there is at least a lag period of two to three months between the occurrence of high night-time temperature and rainfall and the detection of epidemics of malaria. Although this is clearly a very short interval of time to mobilise resources to very remote areas, it may be sufficient to deploy epidemic control teams to areas already identified as prone to epidemics. The use of emergency air-lifts in the supply of antimalarial drugs and residual insecticides may be especially advantageous in such situations when disaster is declared and both national and international assistance is sought.

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## **Corrigenda**

Page 4, last line missing at end of page:

**Table 2.1 Data sets, frequency of collection and period covered in years**

Page 17, paragraph no.3, line no.1:

...“*An gambiae s.l*” should read as.... *An. gambiae s.l.*

Page 24, paragraph no.2, line no.6:

...“as shown Table 2” should read ...as shown in Table 2

Page 39, paragraph no.2, line no.8:

...“as well” should read ... “as well as”

Page 43, paragraph no. 2, line no. 9:

...“was collected” should read as ...were collected

Page 54, title for Figure 3.2:

...“by age and sex” should read as.... by age and species of malaria

Page 67, paragraph no.1, line no.1:

...“cases fatality rate” should read as ...case fatality rate

Page 94, paragraph no.1, line no.7:

...“up to 1,965 metres” should read as ...up to 1,995 metres

Page 102, paragraph no.1, line no.2:

...“ higher threshold” should read as ...lower threshold

Page 106, paragraph no. 2, line no. 11missing word in sentence:

...“It is 22 days at 20 °C, 15 to 17 days at 23 °C, and 9 to 11 days at 25-28 °C.” should read as... It is 22 days at 20 °C, 15 to 17 days at 23 °C, and 9 to 11 days at 25-28 °C for *P. falciparum*.

Page 136, paragraph no. 1, line no. 8 incomplete sentence:

...“This was later known to be a rather global phenomenon also linked to the Southern Oscillation (thus the term El Niño-Southern Oscillation) in which high atmospheric pressure is associated with low pressure in the Indian Ocean from Africa to Australia” should read as ...This was later known to be a rather global phenomenon also linked to the Southern Oscillation (thus, the term El Niño-

Southern Oscillation) in which high atmospheric pressure in the western Pacific is associated with low pressure in the eastern Pacific and the Indian Ocean from Africa to Australia.

Page 141:

“Figure 4.26” should read as Figure 5.26

Page 145:

“Figure 5.26” should read as Figure 5.27

Page 156, paragraph no.2, line no.9:

...“according to the criteria set by WHO (1981)” should read as ...according to the criteria set by WHO (Bruce-Chwatt, 1981)

Page 167, paragraph no.2, line no.9:

...“(>1000 parasites per 300 leukocytes)” should read as ...(>1000 parasites per 300 leucocytes)

Page 168, paragraph no.1, line no.2:

...“WHO(1981)” should read as ...WHO (Bruce-Chwatt, 1981)

Page 174, paragraph no.2, line no.7:

...“98% patients” should read as ...98% of patients

Page 234, paragraph no. 1, line no. 1:

...“from 1968 to 1987” should read as ...from 1968 to 1979

Page 285, paragraph no. 1, line no. 5:

...“ambient time temperature” should read as ...ambient temperature

Page 286, paragraph no.1, line no. 6:

...“non-climatic that amplified” should read as ...non-climatic factors that amplified

Page 292, missing reference after reference no. 12:

Centers for Disease Control (1978). Chemoprophylaxis of malaria. *Morbidity and Mortality Weekly Reports*, US Public Health Service, 27, No.10 Supplement.

Page 298, reference no. 66:

...“Results of an *in-vivo* test” should read as ...Results of an *in-vitro* test.

Page 301, missing reference after reference no. 83:

World Health Organization (1994). Use of DDT in Vector Control: Conclusions of Study Group on  
Vector Control for Malaria and Other Mosquito-Borne Diseases, 16-24 November 1993. *Medical and  
Veterinary Entomology*, 8: 113.