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# The silent burden of anaemia in Tanzanian children: a community-based study

D. Schellenberg,<sup>1,2</sup> J.R.M. Armstrong Schellenberg,<sup>1,3</sup> A. Mushi,<sup>1</sup> D. de Savigny,<sup>4,5</sup> L. Mgalula,<sup>5,6</sup> C. Mbuya,<sup>5</sup> & C.G. Victora<sup>7</sup>

**Objective** To document the prevalence, age-distribution, and risk factors for anaemia in Tanzanian children less than 5 years old, thereby assisting in the development of effective strategies for controlling anaemia.

**Methods** Cluster sampling was used to identify 2417 households at random from four contiguous districts in south-eastern United Republic of Tanzania in mid-1999. Data on various social and medical parameters were collected and analysed.

**Findings** Blood haemoglobin concentrations (Hb) were available for 1979 of the 2131 (93%) children identified and ranged from 1.7 to 18.6 g/dl. Overall, 87% (1722) of children had an Hb <11 g/dl, 39% (775) had an Hb <8 g/dl and 3% (65) had an Hb <5 g/dl. The highest prevalence of anaemia of all three levels was in children aged 6–11 months, of whom 10% (22/226) had an Hb <5 g/dl. However, the prevalence of anaemia was already high in children aged 1–5 months (85% had an Hb <11 g/dl, 42% had an Hb <8 g/dl, and 6% had an Hb <5 g/dl). Anaemia was usually asymptomatic and when symptoms arose they were nonspecific and rarely identified as a serious illness by the care provider. A recent history of treatment with antimalarials and iron was rare. Compliance with vaccinations delivered through the Expanded Programme of Immunization (EPI) was 82% and was not associated with risk of anaemia.

**Conclusion** Anaemia is extremely common in south-eastern United Republic of Tanzania, even in very young infants. Further implementation of the Integrated Management of Childhood Illness algorithm should improve the case management of anaemia. However, the asymptomatic nature of most episodes of anaemia highlights the need for preventive strategies. The EPI has good coverage of the target population and it may be an appropriate channel for delivering tools for controlling anaemia and malaria.

**Keywords** Anemia/epidemiology/prevention and control/drug therapy; Malaria, Falciparum/complications; Antimalarials/therapeutic use; Iron, Dietary/therapeutic use; Blood transfusion; Immunization programs; Child, Preschool; Cost of illness; Cluster analysis; United Republic of Tanzania (*source: MeSH, INSERM*).

**Mots clés** Anémie/épidémiologie/prévention et contrôle/chimiothérapie; Paludisme plasmodium falciparum/complication; Antipaludique/usage thérapeutique; Fer alimentaire/usage thérapeutique; Transfusion sanguine; Programmes de vaccination; Enfant âge pré-scolaire; Coût maladie; Sondage en grappes; République-Unie de Tanzanie (*source: MeSH, NLM*).

**Palabras clave** Anemia/epidemiología/prevencción y control/quimioterapia; Paludismo falciparum/complicaciones; Antimaláricos/uso terapéutico; Hierro en la dieta/uso terapéutico; Transfusión sanguínea; Programas de inmunización; Infante; Costo de la enfermedad; Análisis por conglomerados; República Unida de Tanzania (*fuente: DeCS, BIREME*).

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Voir page 588 le résumé en français. En la página 588 figura un resumen en español.

انظر صفحة 589 للإطلاع على الكلمات المفتاحية والمخصص باللغة العربية

## Introduction

More than 100 million African children are thought to be anaemic (1), and community-based estimates of anaemia prevalence (blood haemoglobin concentration (Hb) <11 g/dl) in children in settings where malaria is endemic range between 49% and 76% (2–5). The consequences, in terms of years of life lost, of such a high level of anaemia are hard to quantify, although the burden of malaria-associated anaemia has been estimated at 190 000–974 000 deaths per year in children under 5 years of age (6). Certainly, children admitted to hospital with severe anaemia (Hb <8 g/dl) are more likely to die than children admitted without anaemia, and anaemia is

one of the largest killers of children admitted to hospital in sub-Saharan Africa (7–9). Even where blood transfusions are available there is a significant case fatality rate of 6–18% (7, 10, 11). However, most children at high risk of severe anaemia live beyond the easy reach of a hospital, the most common type of health facility that can perform blood transfusions.

The causes of anaemia are often multifactorial and are interrelated in a complex way. First, the relative importance of each factor — for example, hookworm or malaria — varies in different settings (12, 13). Anaemia may be chronic — for example, secondary to iron deficiency, infection with human immunodeficiency virus (HIV), or intestinal

<sup>1</sup> Ifakara Health Research & Development Centre, PO Box 53, Ifakara, United Republic of Tanzania (email: dmschellenberg@aol.com). Correspondence should be addressed to Dr D. Schellenberg.

<sup>2</sup> Unidad de Epidemiología, Hospital Clinic, Barcelona, Spain.

<sup>3</sup> Swiss Tropical Institute, Basel, Switzerland.

<sup>4</sup> International Development Research Centre, Ontario, Canada.

<sup>5</sup> Tanzania Essential Health Interventions Project, Ministry of Health, Dar es Salaam, United Republic of Tanzania.

<sup>6</sup> WHO Country Office, Dar es Salaam, United Republic of Tanzania.

<sup>7</sup> Federal University of Pelotas, Pelotas, Brazil.

worms — or it may be acute, owing to a sickle-cell crisis or *Plasmodium falciparum* infection, or chronic anaemia may be acutely exacerbated. The situation is complicated further because anaemia in childhood can result not only from events in childhood but also from maternal iron deficiency and anaemia, which are associated with impaired fetal development and iron-deficient and anaemic babies (14–17). Socioeconomic status may also affect the risk of anaemia by affecting nutritional status, family size, and birth interval, as well as intensifying problems of affordability and accessibility of preventive and curative measures.

Studies in east Africa have shown that *P. falciparum* malaria and iron deficiency account for much of the anaemia seen in young children (18, 19). One randomized study concluded that approximately 60% of anaemia in infancy could be prevented by antimalarial chemoprophylaxis, illustrating the importance of malaria as a cause of anaemia in this setting (18). The same study also found that iron supplementation reduced the incidence of anaemia by about 30%. In the same area, the prevalence of helminths in children under 5 was only 2% (20), and genetic causes of anaemia, such as sickle-cell disease, were present, but at relatively low prevalences (18, 21). The public health importance of anaemia resulting from HIV infection is not yet clear and is difficult to quantify.

The control of anaemia depends largely on the diagnosis and treatment of anaemia cases, rather than on the prevention of anaemia. However, clinical examination for detecting anaemia in young children is only moderately sensitive (24–74% for an Hb <11 g/dl and 37–81% for an Hb <8 g/dl) (22–29) and may be particularly problematic in very young children examined by relatively poorly trained staff in the primary care setting (4–20%) (30). Various diagnostic tests exist but all reliable approaches require some equipment that is not readily available in many settings. In terms of prevention, insecticide-treated mosquito nets (ITNs) have been shown to improve haemoglobin concentration in children living in malarious areas (31), but only recently has a potentially sustainable approach to the distribution of ITNs been shown to have similar effects (32). It will take some considerable time before systems for the delivery of ITNs are functional on a large scale. The WHO/UNICEF (United Nations Children's Fund) iron supplementation policy recommends daily iron supplements starting at age 6 months for most children and continuing up to 2 years (33). However, this policy is rarely implemented due to the non-availability of a liquid ferrous sulfate preparation and the absence of a mechanism to deliver supplements to the target group.

Documenting the epidemiology of anaemia in United Republic of African communities may offer fresh insights into potential control strategies. With this in mind we report a community-based survey in four districts of south-eastern United Republic of Tanzania.

## Methods

The survey was conducted in the Kilombero, Morogoro Rural, Rufiji, and Ulanga districts of south-eastern United Republic of Tanzania. The area has been described in detail elsewhere (34). Briefly, the predominantly low-lying area extends west from the Indian Ocean south of Dar es Salaam, punctuated by the Uluguru and Udzungwa mountains,

which rise in a crescent through the area. A long rainy season from March to June is followed by dry and dusty months until November/ December when light rains return. The area is holoendemic for malaria. The multi-ethnic people are predominantly subsistence farmers of rice and maize. Infant mortality ranges from 93 to 117 per 1000 live births and the under-five mortality risk (5q0) is 124–183 per 1000 children (34).

This survey was the baseline household survey of the WHO Multi-Country Evaluation (MCE) of the Integrated Management of Childhood Illness (IMCI) in the United Republic of Tanzania. At the time of this study Rufiji and Morogoro Rural districts were in the early stages of implementing IMCI. Cluster samples were taken from the whole of the four districts, and the probability of choosing a particular village was proportional to the size of its population. In accordance with sample size calculations for the IMCI evaluation, 30 rural clusters were chosen from each of the Rufiji, Morogoro Rural, Kilombero, and Ulanga districts; in Kilombero, five additional clusters were selected from the semi-urban centre of Ifakara. Within each selected village 20 households were chosen according to a standardized procedure that gave every household the same probability of being included (details available on request). The purpose of the study was explained to at least one member of each household and verbal consent was requested to proceed with the interview. A standard questionnaire was completed for all children under 5 years of age. The questionnaire developed by WHO for the IMCI MCE (35) was locally adapted and is available on request. The first section documented details of all children in the household, information on household socioeconomic status, and the educational level and occupation of the household head. Mothers were interviewed at home about their educational level and that of the household head, breastfeeding practices, exposure to nutritional counselling, knowledge of caring for a sick child, and about any illness the child had experienced during the two weeks before the survey, including the mother's subjective assessment of its severity and any action she took. The use of a mosquito net for the child, and the child's vaccination history and vitamin A supplementation status were also documented. For children who had been sick, additional modules documented detailed information about the use of health services and drugs.

Children were then invited to attend a measuring station set up in the middle of the cluster where they were weighed on digital scales (Seca Vogel & Halke GmbH, Hamburg, Germany) and their height ( $\geq 2$  years) or length (<2 years old) was measured using purpose-made instruments. The location of the measuring station was documented using a handheld global positioning system (Garmin GPS 12, GARMIN International, Lenexa, KS, USA), enabling the distance from the cluster to the nearest transfusion centre to be estimated. A finger-prick sample of blood was collected and haemoglobin concentration measured using a battery-powered HemoCue photometer (HemoCue AB, Angelholm, Sweden). Children found to be anaemic (Hb <11 g/dl) were dispensed the standard Tanzanian IMCI anaemia treatment (a 14-day course of ferrous sulfate, treatment courses of sulfadoxine-pyrimethamine/chloroquine and mebendazole, depending on age, whether febrile, and treatment history). All anaemic

Table 1. Descriptive data and risk factors for anaemia in Tanzanian children<sup>a</sup>

Variable	No. of children	Mean Hb <sup>b</sup> (g/dl)	No. of children with:	
			Hb <8 g/dl	Hb <5 g/dl
<b>Gender (n=1979)</b>				
Male	996 (50.3) <sup>c</sup>	8.5; 0.10 <sup>d</sup>	405 (41) <sup>c</sup>	28 (2.8) <sup>c</sup>
Female	983 (49.7)	8.6; 0.10	368 (38)	37 (3.8)
		<i>P</i> =0.26	<i>P</i> =0.18	<i>P</i> =0.2
<b>Age (n=1979)</b>				
<1 month	40 (2)	13.5; 0.40	1 (2)	0 (0.0)
1–5 months	221 (11.2)	8.5; 0.18	89 (40)	11 (5.0)
6–11 months	226 (11.4)	7.6; 0.16	133 (59)	22 (9.7)
1 year	403 (20.4)	8.0; 0.14	207 (51)	18 (4.5)
2 years	377 (19.1)	8.3; 0.13	157 (42)	9 (2.4)
3 years	389 (19.7)	9.0; 0.13	112 (29)	3 (0.8)
4 years	322 (16.3)	9.2; 0.11	75 (23)	2 (0.6)
		<i>P</i> =0.009	<i>P</i> <0.00001	<i>P</i> <0.00001
<b>Time taken to travel from home to health facility (n=1860)</b>				
90 minutes	1437 (77)	8.6; 0.09	569 (40)	42 (2.9)
>90 minutes	423 (23)	8.6; 0.17	166 (39)	18 (4.3)
		<i>P</i> =0.9	<i>P</i> =0.9	<i>P</i> =0.25
<b>Fully vaccinated (n=401)</b>				
Yes	328 (82)	7.9; 0.14	172 (52)	14 (4.3)
No	73 (18)	8.1; 0.27	35 (48)	4 (5.5)
		<i>P</i> =0.5	<i>P</i> =0.5	<i>P</i> =0.6
<b>Socioeconomic score (n=1928)</b>				
Most poor	386 (20)	8.4; 0.14	165 (45)	18 (5.0)
Very poor	383 (20)	8.4; 0.14	153 (42)	12 (3.3)
Poor	386 (20)	8.6; 0.18	132 (38)	12 (3.4)
Less poor	385 (20)	8.7; 0.15	136 (37)	2 (0.5)
Least poor	388 (20)	8.6; 0.16	126 (37)	13 (3.8)
		<i>P</i> =0.07	<i>P</i> =0.029	<i>P</i> =0.23
<b>HAZ<sup>e</sup> tertile (n=1873)</b>				
Top	613 (33)	8.8; 0.12	212 (35)	21 (3.4)
Middle	639 (34)	8.5; 0.10	263 (41)	14 (2.2)
Bottom	621 (33)	8.4; 0.11	256 (41)	25 (4.0)
		<i>P</i> =0.01	<i>P</i> =0.02	<i>P</i> =0.6
<b>WAZ<sup>f</sup> tertile (n=1947)</b>				
Top	639 (33)	8.9; 0.11	203 (32)	14 (2.2)
Middle	658 (34)	8.6; 0.12	255 (39)	19 (2.9)
Bottom	650 (33)	8.2; 0.11	301 (46)	28 (4.3)
		<i>P</i> <0.00001	<i>P</i> <0.00001	<i>P</i> =0.02
<b>WHZ<sup>g</sup> tertile (n=1893)</b>				
Top	623 (33)	8.6; 0.12	224 (36)	9 (1.4)
Middle	644 (34)	8.7; 0.11	238 (37)	21 (3.3)
Bottom	626 (33)	8.3; 0.11	282 (45)	29 (4.6)
		<i>P</i> =0.004	<i>P</i> =0.004	<i>P</i> =0.006
<b>Mosquito net (n=1970)</b>				
Treated	237 (12)	8.8; 0.17	71 (30)	3 (1.3)
Untreated	421 (21)	8.7; 0.15	150 (36)	7 (1.7)
None	1312 (67)	8.5; 0.10	551 (42)	55 (4.2)
		<i>P</i> =0.043	<i>P</i> =0.005	<i>P</i> =0.03
<b>Altitude (n=1979)</b>				
<1000 m	1791 (91)	8.5; 0.09	719 (40)	64 (3.6)
≥1000 m	188 (9)	9.1; 0.28	56 (30)	1 (0.5)
		<i>P</i> =0.045	<i>P</i> =0.20	<i>P</i> =0.02
<b>Distance to transfusion centre (n=1979)</b>				
<10 km	359/1979 (18)	9.0; 0.18	101 (28)	3 (0.8)
10–49 km	1340 (68)	8.5; 0.11	547 (41)	50 (3.7)
≥50 km	280 (14)	8.3; 0.25	127 (45)	12 (4.3)
		<i>P</i> =0.0085	<i>P</i> =0.001	<i>P</i> =0.03

<sup>a</sup> *P*-values are from tests of the association between prevalence of anaemia of different levels or mean haemoglobin and each of the variables in the table.

All tests are adjusted for the clustered nature of the data.

<sup>b</sup> Hb = haemoglobin concentration.

<sup>c</sup> Figures in parentheses are percentages.

<sup>d</sup> Figures in italics are standard errors.

<sup>e</sup> HAZ = height-for-age Z-score.

<sup>f</sup> WAZ = weight-for-age Z-score.

<sup>g</sup> WHZ = weight-for-height Z-score.

Table 2. Frequency and pattern of morbidity by level of anaemia in Tanzanian children aged &lt;5 years

Haemoglobin concentration (g/dl)	Sick in past 2 weeks	Help sought outside the home	Symptomatic at interview	Symptom profile						
				Fever	Cough	Fast breathing	Very sleepy	Vomiting everything	Unable to drink	Denominator <sup>b</sup>
≥11.0	111/257 (43) <sup>a</sup>	67/109 (61) <sup>a</sup>	62/257 (24) <sup>a</sup>	28 (47) <sup>a</sup>	35 (58) <sup>a</sup>	5 (8) <sup>a</sup>	2 (3) <sup>a</sup>	3 (5) <sup>a</sup>	1 (2) <sup>a</sup>	60
8–10.9	477/941 (51)	353/469 (75)	224/941 (24)	120 (55)	147 (68)	28 (13)	8 (4)	25 (12)	10 (5) <sup>c</sup>	217
5–7.9	411/707 (58)	300/409 (73)	227/706 (32)	154 (68)	143 (64)	33 (15)	21 (9)	22 (10)	21 (10) <sup>d</sup>	225
<5.0	44/64 (69)	32/43 (74)	29/64 (45)	24 (86)	26 (93)	8 (29)	4 (14)	7 (25)	4 (14)	28
Overall	1043/1969 (53)	751/1029 (73)	542/1968 (28)	326 (62)	351 (66)	76 (14)	35 (7)	68 (13)	36 (7) <sup>e</sup>	5
Test of statistical association <sup>f</sup>	$F=25.6$ $P<0.0001$	$F=1.7$ $P=0.2^g$	$F=17.1$ $P=0.0001$	$F=21.5$ $P<0.00001$	$F=3.2$ $P=0.076$	$F=4.69$ $P=0.03$	$F=7.5$ $P=0.007$	$F=9.9$ $P=0.002$	$F=9.8$ $P=0.002$	

<sup>a</sup> Numbers in parentheses are percentages. The row percentages exceed 100% as each child may experience more than one symptom.

<sup>b</sup> Unless otherwise stated.

<sup>c</sup> Denominator = 216.

<sup>d</sup> Denominator = 213.

<sup>e</sup> Denominator = 527.

<sup>f</sup> All tests were design-based  $F$ -tests for trend.

<sup>g</sup> Anaemic versus non-anaemic: design-based  $F_{1,123}=8.1$ ;  $P=0.0051$ .

children were given a referral letter for their local health facility. Children with a Hb <5 g/dl were encouraged to attend a hospital urgently and help was given with their transportation where necessary.

The study received ethical clearance from the institutional review board of the Ifakara Health Research and Development Centre (IHRDC) and the national Tanzanian Medical Research Co-ordinating Committee. After two weeks of training, four teams of four interviewers conducted the survey, each with a car, a driver, and a set of measuring devices. In July 1999 the teams started work in Kilombero, at a rate of one cluster per team per day, moving on together through Morogoro Rural, Rufiji, and finally, Ulanga district, where the survey was completed in August 1999. The performance of haemoglobinometers was assessed every day using the manufacturer's checking device: if the check measure was out of range the machine was not used. Apart from daily visual inspections, scales, height sticks, and length boards were cross-checked with each other every two weeks.

### Data analysis

Data were double-entered and verified using FoxPro (version 2.6, Microsoft Corporation, Seattle, WA, USA) at IHRDC. Checks for internal consistency and referential integrity were performed before analysis in Stata (version 6, Stata Corporation, College Station, TX, USA). Weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ) Z-scores were generated using the EPINUT module of EPI-Info version 6.0 (Centers for Disease Control and Prevention, Atlanta, GA, USA). The analysis took into account the clustered nature of the data using design-based  $F$ -tests, and logistic regression for binary outcomes, using standard STATA commands such as "svytab", "svymean", and "svylogit". A relative measure of socioeconomic status was developed, as described in detail elsewhere (36, 37). Briefly, principal components methodology was used to generate a score based on household ownership of assets (radio, bicycle, tin roof, mosquito net, the house itself, livestock), availability of one or more incomes, and the educational

level of the household head and of the child's normal care provider. Cross-validation between the resulting socioeconomic score and height-for-age, known to be strongly associated with socioeconomic status, confirmed that the score was a better predictor of height-for-age than any single component alone. The Haversine formula (38) was used to estimate the distance between the centre of the cluster in which each child lived and the nearest blood transfusion centre.

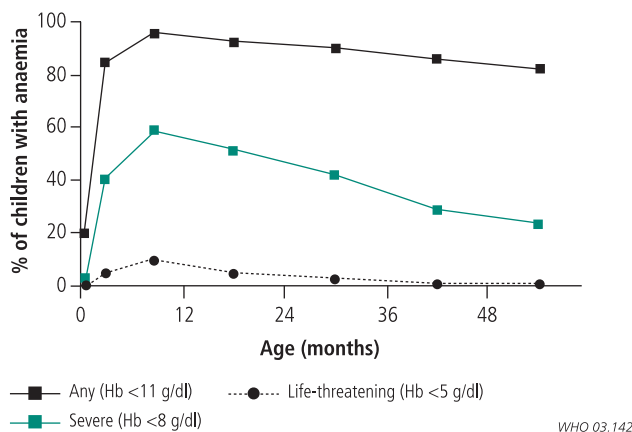
Vaccination coverage rates were calculated for children aged 365–729 days and were based either on documentation in the children's Road to Health card or, where not available, on the vaccination history as reported by the mother. The altitude of each cluster was estimated using MapInfo® to position clusters on a Tanzanian contour map (contour interval of 304 m).

### Results

A total of 2417 households were selected from the 125 clusters. A small number of households declined to take part ( $n = 25$ ; 1%) or were unavailable for interview ( $n = 142$ ; 6%). 2131 children <5 years old were identified in 1405 households, and haemoglobin results were available for 1979 (93%) of them. Half of the children (996) were male (Table 1) and the sample was broadly representative of the population with regard to age and sex of the children included (data not shown).

Table 1 summarizes basic descriptive information and the factors significantly associated with an Hb <11 g/dl. Haemoglobin concentrations ranged from 1.7 to 18.6 g/dl, with the highest Hb recorded in a neonate and the lowest recorded in a child of 2 months. Overall, 87% (1722/1979) of children had some degree of anaemia (Hb <11 g/dl), 39% (775) had an Hb <8 g/dl, and 3% (65) had an Hb <5 g/dl. Fig. 1 shows that the prevalence of all levels of anaemia rose dramatically between 1 and 5 months of age before peaking in children aged 6–11 months. The prevalence of anaemia climbed from 85% (187/221) in the first 6 months of life to 96% (216/226) in the second half of infancy. Of note: 10%

Fig. 1. Prevalence of anaemia in children under 5 years

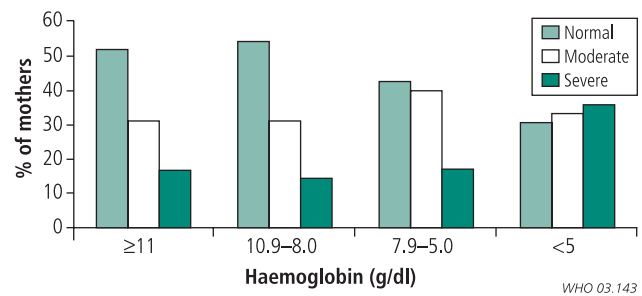


(22/226) of children aged 6–11 months had an Hb <5 g/dl. There were no sex differences in mean haemoglobin ( $P = 0.26$ ) or prevalence of anaemia at any level. Approximately three-quarters of the children lived within 90 minutes of their nearest health facility. Overall, 11% (211/1963) had been admitted to hospital at least once in the previous year and anaemic children were not more likely to have been admitted than non-anaemic children (23/255 (9%) versus 188/1708 (11%),  $F = 0.84$ ,  $P = 0.36$ ). Compliance with the full diphtheria-petussis-tetanus (DPT) and measles vaccination regimen was 82% (327/400) and not associated with risk of anaemia.

The risk of severe anaemia (Hb <8 g/dl) increased as the socioeconomic score decreased, the poorest children being 1.23 times as likely as the least poor to have severe anaemia ( $F = 4.94$ ,  $P = 0.028$ ). Low HAZ, WHZ, and WAZ scores were all associated with an increased risk of anaemia. Only 1 of the 188 children (0.5%) living above 1000 m had an Hb <5g/dl, compared with 64 of the 1791 (3.5%) children living at lower altitudes ( $F_{1,124} = 5.71$ ,  $P = 0.02$ ). Although 86% of children lived within 50 km (approximately one day travelling) of the nearest health facility capable of giving blood transfusions, those living more than 50 km from such a facility were more likely to be anaemic, and this trend was significant (Table 1). Children who spent the night before the survey under a mosquito net, particularly a net treated with insecticide, were up to 29% (95% confidence interval (CI) 7 to 45) less likely to be anaemic than children who had not slept under a net (Table 1).

Table 2 summarizes the frequency and type of symptoms, and pattern of health-seeking behaviour, by level of anaemia. More than half of the children had been unwell during the two weeks preceding, or on the day of, the interview. Children with a history of recent illness were more likely to be anaemic than children with no reported illness, the relative risk being 1.28 (95% CI=1.14 to 1.42) and 1.99 (95% CI=1.17 to 3.40) for Hb <8 g/dl and Hb <5 g/dl, respectively. Increasing severity of anaemia was significantly associated with symptoms at the time of interview, but between half and three-quarters of all anaemic children were asymptomatic. Only 4 of the 762 children (0.5%) with any degree of anaemia and who had not been unwell in the preceding two weeks were symptomatic on the day of the interview.

Fig. 2. Mothers' perceived severity of child's illness (normal, moderate, or severe), by level of anaemia



The minority of anaemic children who were unwell when interviewed had nonspecific symptoms. Fever, cough, fast breathing, being very sleepy, vomiting everything, and being unable to drink/breastfeed as normal were all more frequently reported in children with anaemia than in children without anaemia. Diarrhoea, difficult breathing, and convulsions were reported with similar frequencies for anaemic and non-anaemic children. Increasing anaemia was associated with perceived severity of the episode among children reported to have been ill in the past two weeks. However, 67% (29/43) of mothers of symptomatic children with an Hb <5g/dl, and 81% (365/451) of mothers of symptomatic children with an Hb <8 g/dl, did not think the illness was severe (Fig. 2). Mothers of anaemic children were more likely to seek health care outside the home than mothers of children with no anaemia (Table 2). No assistance was sought for approximately 26% (237/923) of children in each category of anaemia, despite the fact that only 31% (70/225) of these children lived more than 90 minutes away from the nearest health facility.

Table 3 shows that more anaemic children used anti-malarial drugs in the two weeks preceding the interview than non-anaemic children. However, only 19% (320/1720) of anaemic children had received antimalarial treatment and less than 1% had received iron in the preceding fortnight. Only 12% (51/425) of attendances to a formal health provider were to a hospital, including one of the 24 children with an Hb <5 g/dl. None of the remaining 23 children had been referred for hospital care.

## Discussion

Overall, 87% of children under 5 years of age had some level of anaemia (Hb <11 g/dl). We found surprisingly few differences between anaemic and non-anaemic children (apart from anaemia affecting relatively poor and malnourished children), making it hard to identify them as a group for targeted interventions. The most striking observation was the marked age-dependence within the community, the prevalence of anaemia increasing dramatically during the first 6 months of life and reaching maximal levels in the second half of infancy. This pattern was seen for all levels of anaemia and may reflect inadequate fetal iron stores, secondary to maternal anaemia and iron deficiency, which are then compounded by additional insults (14–19). Concerns about the high prevalence of anaemia are heightened by the fact that most

Table 3. Reported use of antimalarial drugs and iron in the previous 2 weeks in Tanzanian children aged &lt;5 years

Haemoglobin concentration (g/dl)	Antimalarial drugs		Iron <sup>a</sup>
	Obtained from formal health sector	Obtained outside formal health sector	
≥11 (n=257)	11 (4) <sup>b</sup>	12 (5) <sup>b</sup>	1 (0.4) <sup>b</sup>
8.0–10.9 (n=946)	100 (11)	50 (5)	4 (0.4)
5.0–7.9 (n=710)	112 (16)	40 (6)	6 (0.8)
<5.0 (n=64)	14 (22)	4 (6)	2 (3)
Total (n=1977)	237 (12)	106 (5)	12 (0.6)
Test of significance <sup>c</sup>	F=32.7 P<0.00001	F=0.43 P=0.5	F=3.0 P=0.08

<sup>a</sup> Only one child (with a haemoglobin concentration <5 g/dl) obtained iron outside the formal health sector.

<sup>b</sup> Figures in parentheses are percentages.

<sup>c</sup> Design-based *F*-test on 1124 degrees of freedom.

children were at risk of acute malaria, which may further reduce haemoglobin levels to a point where physiological compromise is inevitable. In particular, the one in ten children aged 6–11 months who were at home with an Hb <5 g/dl would have been at serious risk of life-threatening illness if they became acutely unwell. Illness was common in the communities surveyed, with more than half of the children reporting an illness during the preceding two weeks (36).

The importance of anaemia prevention, rather than cure, is emphasized by first, the huge burden of anaemia; second, its frequently asymptomatic nature, and nonspecific symptoms when they do exist; third, the problems of making an accurate diagnosis; fourth, the inadequate treatment rates, using antimalarials and iron; and fifth, the difficulties accessing transfusion centres and the dangers associated with transfusion. These problems are considered below and approaches to the prevention of anaemia are discussed.

### Lack of clear symptoms

Anaemia is difficult to recognize both at the home and at peripheral health facilities. Most anaemic children (50–75%) were asymptomatic on the day of interview. It is possible that some of these children were recovering from a symptomatic illness that had caused or exacerbated the anaemia. However, very few children (4/762 (0.5%)) with any degree of anaemia and who had not been unwell in the preceding two weeks were symptomatic on the day of the interview, suggesting that their anaemia was not primarily the result of a recent illness and thus supporting the notion that anaemia is usually asymptomatic. This is also in keeping with an earlier study in which a quarter of anaemia episodes in a cohort of children with good access to health care were detected only at cross-sectional surveys (18). When symptoms were reported they were nonspecific: fever, cough, fast breathing, being very sleepy, vomiting everything, and being unable to drink or breastfeed as normal — these symptoms of ill-health are shared with many other diseases. Nevertheless, many mothers sought health care outside the home when their child was sick and there was reasonable access to primary health services.

### Treatment with antimalarials and iron

Difficulty in diagnosing anaemia or inadequate knowledge of treatment guidelines may account for the low antimalarial (13%) and very low iron (1%) treatment rates in anaemic children. Both types of drug are recommended by IMCI for the treatment of anaemia in such settings (39). Although problems of drug prescription, availability, and cost may also account for the low prescription rates, the fact that none of the 23 children with an Hb <5 g/dl who presented to a peripheral health facility was referred to hospital also suggests a problem at an earlier stage in the management pathway. Key areas for improving case management are thus likely to be enhanced diagnosis and improved treatment of cases. IMCI has the potential to improve this by increasing the number of children identified as anaemic, ensuring drug treatment guidelines are clear, and encouraging appropriate referral practices.

### Access to transfusion centres

The assessment of access to transfusion centres suggested that only 19% of children lived within 10 km (approximately 2 hours travelling) of their nearest transfusion centre. Blood transfusion is recommended for children with life-threatening anaemia (Hb <4 g/dl) or less severe anaemia with signs of physiological compromise (40, 41). Transfusions were found to be necessary in 13–20% of general paediatric admissions (10, 42) and almost half the malaria admissions in children aged 1–4 months in one hospital-based study (7). However, such hospital-based data tell us little about the number of child deaths that may be averted by timely blood transfusion, as the majority of child deaths occur in the community (34). Clearly, extended journey times with a child in urgent need of transfusion are likely to increase the risk of an adverse outcome. The increased prevalence of anaemia with increasing distance from transfusion centres was therefore particularly disturbing. Although the reason for this association is not clear, one can speculate confounding associations between socioeconomic status and proximity to malaria-vector breeding sites with increasing distance from transfusion centres, which are typically located in more urban settings.

### Approaches to the prevention of anaemia

There is good evidence that the anaemia seen in this and similar settings is caused largely by malaria or by iron deficiency, or both (18, 19), and hence improved malaria control and iron supplementation programmes could have dramatic anti-anaemia effects.

### Anaemia control in mothers

One approach to preventing anaemia in children is by reducing anaemia and improving iron status in pregnancy and pre-pregnancy. Iron supplementation and intermittent preventive malaria treatment are recommended for women attending antenatal clinics (33, 43), although the transient nature of pregnancy may result in incomplete correction of anaemia or iron deficiency before delivery. Furthermore, women tend to present to clinic relatively late in pregnancy and there is evidence that anaemia in the first trimester reduces fetal growth and birth weight (44). Novel attempts to improve the health of pre-pregnant women — for exam-

ple, by accessing newlyweds at marriage registries (45) — have shown promise in some settings.

### **Iron supplementation in children**

The global guidelines for iron supplementation in childhood may need to be refined if the benefits from iron prophylaxis are to be optimized. With the exception of children of low birth weight, for whom iron supplements are recommended from 2 months of age, WHO/UNICEF/INACG recommend that supplementation should commence only at 6 months; however, by this age anaemia has already affected a large proportion of children. A study from the same area as our survey delivered iron supplements to children aged 2–6 months and showed a 29% reduction in the incidence of severe anaemia (packed cell volume <25% (Hb <8 g/dl)) in the first year of life (18). This supplementation regimen also reduced the prevalence of iron deficiency measured at 12 months of age and the prevalence of anaemia at 4 years of age (C. Menendez, D. Schellenberg, L. Quinto, E. Kahigwa, L. Alvarez, J. J. Aponte, et al., unpublished data).

### **Malaria prevention in children**

Anaemia was less of a problem at altitudes greater than 1000 m, which probably reflects the reduced burden of malaria at such heights. Interestingly, this effect was more marked for life-threatening anaemia than for less severe anaemia. This suggests that malaria may be a relatively important cause of the most severe anaemia but that other causes of less severe anaemia, such as iron deficiency, are still prevalent at altitude. An element of altitude-induced secondary polycythaemia may also be present, although this is unlikely at the altitudes studied. Children sleeping under mosquito nets, especially nets treated with insecticide, had a reduced risk of anaemia, which is a further indication that malaria may be important in causing anaemia. This is in keeping with the results of several randomized studies that showed a mean increase in packed cell volume of 1.4% in children sleeping under an ITN (31). A major challenge is to develop and expand sustainable approaches to the provision of mosquito nets — and net treatment — in endemic settings, and progress in this respect is being made (46). Malaria vector control by residual house-spraying has also been shown to reduce the prevalence of anaemia (47); however, the benefits of this approach over ITN are not clear, especially considering the logistic complexity and expense of house-spraying. Similarly, malaria chemoprophylaxis has been shown to reduce the risk of anaemia by up to 60% (18) but the logistic complexity, expense, concerns over drug resistance, and a rebound increase in malaria and anaemia on stopping chemoprophylaxis render this an impractical public health approach to controlling anaemia.

### **Expanded Programme on Immunization**

There is an established channel capable of delivering effective anti-anaemia interventions to the target group. The Expanded Programme on Immunization (EPI) routinely delivers DPT and oral polio vaccines to children aged 1, 2, and 3 months, and measles vaccinations and vitamin A supplements to children aged 9 months. Children with the most severe anaemia were just as likely as others to receive routine EPI vaccinations and overall compliance with the full DPT

and measles vaccination regimen was high (82%). This existing infrastructure already delivers vaccines and micronutrients to the target group for anaemia control. In particular, it has contact with children during the first 6 months of life, when the prevalence of anaemia is rising sharply and may therefore be most amenable to intervention. This principle was confirmed by a study investigating the effects of intermittent malaria treatment delivered at 2, 3, and 9 months of age, in which the incidence of anaemia (Hb <8 g/dl) was reduced by 50% in the first year of life (48). This study also monitored compliance to ferrous sulfate supplements, made available at the time of routine health visits between 2 and 6 months of age, which may be another feasible approach to anaemia control.

### **Study limitations**

This study was subject to the limitations of any retrospective study, such as the reliance on a history of illness and its inherent biases. We related a history of illness and treatments in the two weeks preceding interview to the haemoglobin concentration at the time of the survey. Haemoglobin levels could have fluctuated during the intervening period, thereby crossing the thresholds defining “any”, “severe” and “life-threatening” anaemia in either direction. However, the extremely high prevalence of anaemia at all levels, despite the large number of contacts with the health services (Table 2), suggests that the effects of such misclassifications are likely to be relatively small and that there is considerable scope for improvements in anaemia control. Another limitation of this study is that it was performed over a period of only 2 months in the early dry season, and hence seasonal variations in the pattern of anaemia could not be discerned.

### **Conclusion**

In conclusion, we have documented a very high point prevalence of anaemia in children under 5 years and showed that children less than 6 months of age are already severely affected. Anaemia was usually asymptomatic and when symptoms arose they were nonspecific. Few anaemia cases were managed optimally, despite many children having attended a health facility, and the very high burden of anaemia warrants a concerted approach to its control. Improved availability of diagnostic tests and wider implementation of standard treatment guidelines, including appropriate referral practices and optimizing compliance, are important. However, given the insidious and often undetected nature of anaemia, the difficulties accessing appropriate health care, and the dangers of blood transfusion, increased emphasis on preventive measures is required. The system of EPI contacts may be a suitable means of raising awareness about anaemia and delivering effective anaemia control interventions. ■

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**Conflicts of interest:** none declared.

## Résumé

### L'anémie silencieuse chez les enfants tanzaniens : une étude en communauté

**Objectif** Documenter la prévalence, la répartition par âge et les facteurs de risque d'anémie chez les enfants tanzaniens de moins de 5 ans, en aidant ainsi à l'élaboration de stratégies efficaces de lutte contre l'anémie.

**Méthodes** Un sondage en grappes a été réalisé au milieu de l'année 1999 afin de recenser de manière aléatoire 2417 ménages dans quatre districts contigus du sud-est de la République-Unie de Tanzanie. Des données relatives à différents paramètres sociaux et médicaux ont été recueillies et analysées.

**Résultats** On a disposé du taux d'hémoglobine (Hb) de 1979 enfants sur les 2131 (93 %) recensés et il se situait entre 1,7 et 18,6 g/dl. Dans l'ensemble, 87 % (1722) des enfants avaient un taux d'hémoglobine <11 g/dl, 39 % (775) un taux <8 g/dl et 3 % (65) un taux <5 g/dl. Pour ces trois degrés d'anémie, la prévalence la plus forte a été retrouvée chez les enfants âgés de 6 à 11 mois, dont 10 % (22/226) avaient un taux d'hémoglobine <5 g/dl. Toutefois, la prévalence de l'anémie était déjà élevée chez les enfants âgés de 1 à 5 mois (85 % d'entre eux montraient une Hb

<11 g/dl, 42 % une Hb <8 g/dl et 6 % une Hb <5 g/dl). Cette anémie était en général asymptomatique et lorsque des symptômes apparaissaient, ils étaient non spécifiques et rarement rattachés à une pathologie grave par le dispensateur de soins. Des antécédents récents de traitement par les antipaludiques et de complémentation martiale étaient rares. L'observance du calendrier d'administration du Programme élargi de vaccination (PEV) était de 82 % et n'était pas associée à un risque d'anémie.

**Conclusion** L'anémie est extrêmement fréquente dans le sud-est de la République-Unie de Tanzanie, même chez les très jeunes nourrissons. De plus, la mise en oeuvre de l'algorithme de Prise en charge intégrée des maladies de l'enfance devrait améliorer la prise en charge des cas d'anémie. Toutefois, la nature asymptomatique de la plupart des épisodes rencontrés souligne la nécessité de disposer de stratégies de prévention. Le PEV a une bonne couverture de la population cible et il pourrait constituer un canal approprié par lequel fournir des instruments permettant de lutter contre l'anémie et le paludisme.

## Resumen

### La carga silenciosa de anemia entre los niños de Tanzania: un estudio comunitario

**Objetivo** Documentar la prevalencia, la distribución por edades y los factores de riesgo de la anemia entre los niños tanzanos menores de 5 años, a fin de ayudar a formular estrategias eficaces para controlar la anemia.

**Métodos** A mediados de 1999 se identificaron aleatoriamente mediante muestreo por conglomerados 2417 hogares de cuatro distritos contiguos del sureste de la República Unida de Tanzania. Se reunieron y analizaron datos sobre diversos parámetros sociales y médicos.

**Resultados** Se consiguieron las concentraciones sanguíneas de hemoglobina (Hb) de 1979 (93%) de los 2131 niños identificados, con valores de entre 1,7 y 18,6 g/dl. En términos globales, el 87% (1722) de los niños poseían una concentración de Hb < 11 g/dl, el 39% (775) < 8 g/dl, y el 3% (65) < 5 g/dl. La prevalencia más alta de esos tres grados de anemia se halló en los niños de 6–11 meses, el 10% (22/226) de los cuales presentaba una concentración de Hb < 5 g/dl. Sin embargo, la prevalencia de anemia ya era alta en los niños de 1–5 meses (el 85% presentaba una Hb < 11 g/dl, el 42% < 8 g/dl, y el 6% < 5 g/dl).

La anemia era por lo general asintomática, y en los casos en que había síntomas éstos eran inespecíficos y rara vez conceptualizados como enfermedad grave por el dispensador de atención. Pocas veces se registraron antecedentes recientes de tratamiento con antimaláricos y hierro. El cumplimiento de las vacunaciones dispensadas a través del Programa Ampliado de Inmunización (PAI) era del 82% y no se asoció a riesgo alguno de anemia.

**Conclusión** La anemia es un problema muy común en el sureste de la República Unida de Tanzania, incluso entre los lactantes de muy corta edad. Una más extensa aplicación del algoritmo de la Atención Integrada a las Enfermedades Prevalentes de la Infancia debería redundar en la mejora del manejo de los casos de anemia. No obstante, el carácter asintomático de la mayoría de los episodios de anemia destaca la necesidad de aplicar estrategias preventivas. El PAI, con una buena cobertura de la población destinataria, podría ser un mecanismo apropiado para suministrar los medios necesarios para controlar la anemia y la malaria.

## ملخص

## التعبء الصمامت لفقء الدم على اطفال تنزانيا: دراسة مجتمعية المرئكز

كان معدل انتشار فقر الدم مرتفعاً في الأطفال الذين تتراوح أعمارهم بين شهر وحمسة شهور إذ كان خضاب اندم يقل عن 11 غرام/ديسي لتر عند 85% منهم، ويقل عن 8 غرام/ديسي لتر عند 42% منهم، ويقل عن 5 غرام/ديسي لتر عند 6% منهم. وكان فقر الدم عادةً لا يرتفق بأعراض؛ فإذا ترتفق بأعراض كانت أعراضها غير نوعية. وناحراً ما كان يضر إليها مقدمو الرعاية الصحية على أنها أعراض وخيمة؛ وكان من النادر وجود سوابق حديثة العهد لعالجة بأدوية مصاددة للملاريا وبالحديد. وقد كان معدل الامتثال للبرامج التمنيع الموسع والتلقاحات التي تعطى من خلاله 82%، ولم يرتفق ذلك بخفض فقر الدم.

النتيجة: إن فقر الدم واسع الانتشار والشيوع في جنوب شرق تنزانيا، حتى بين الرضع الصغار جداً. وسيؤدي تطبيق منهج التدبير العلاجي المتكامل للأمراض الطفولية لتحسين في التدبير العلاجي للحالات المصابة بفقر الدم؛ إن عدم الارتفق بالأعراض في معظم هجمات فقر الدم يستلزم استراتيجيات وقائية. وقد كان للبرنامج الموسع التمنيع نعطية جيدة لتسكين المستهدفين، وقد يكون العناية المناسبة لتقديم أدوات مكافحة الملاريا وفقر الدم عندهم

الهدف: نوثيق معدلات الانتشار، والتوزع حسب العمر، وعوامل حضر فقر الدم بين أطفال تنزانيا الذين تقل أعمارهم عن 5 سنوات؛ فذلك يساعد في إعداد استراتيجيات فعالة لمكافحة فقر الدم.

الطريقة: أخذت عينات عشوائية لاستقصاء 2417 عائلة بشكل عشوائي من أربع مناطق متجاورة في جنوب شرق تنزانيا أواسط عام 1999 وقد جمعت وحللت المحطيات حول مختلف المتغيرات الاجتماعية والاقتصادية والطبية.

الوجودات: تم الحصول على قياسات لتركيز الهيموغلوبين في الدم عند 1979 طفلاً من أصل 2131 الأطفال البالغ عددهم 2131 طفلاً (93%)، وقد تتراوح تركيز الهيموغلوبين بين 1.7 و 18.6 غرام/ديسي لتر. وقد كان تركيز الهيموغلوبين يزيد عن 11 غرام/ديسي لتر عند 1722 طفلاً (87%)، ويقل عن 8 غرام/ديسي لتر عند 755 طفلاً (39%)، ويقل عن 5 غرام/ديسي لتر عند 65 طفلاً (3%). وقد كانت أعلى معدلات انتشار فقر الدم في المستويات الثلاثة جميعها عند الأطفال الذين تتراوح أعمارهم بين 6-11 شهراً، فقد كان خضاب الدم أقل من 5 غرام/ديسي لتر لدى 10% منهم (22 طفلاً من أصل 226 طفلاً)، كما

الكلمات المفتاحية: فقر الدم، وبائيات فقر الدم، الوفاية من فقر الدم ومكافحته، الفعالية الدوائية لفقر الدم، الملاريا، الملاريا المنحلية، مضاعفات الملاريا المنحلية، مصادات الملاريا، الاستخدام العلاجي للمضادات الملاريا، الحديد، الحديد، الحديد، الاستخدام العلاجي للحديد، نقل الدم، برامج التمنيع، الفعول، أطفال ما قبل المدرسة، تكاليف المرض، تحيين عمقودي، جمهورية تنزانيا المتحدة، المصدر: رؤوس الموضوعات الطبية: المكتب الإقليمي لشرق المتوسط

## References

- DeMaeyer E, Adiels-Tegman M. The prevalence of anaemia in the world. *World Health Statistics Quarterly* 1985;38:302-16.
- Premji Z, Hamisi Y, Shiff C, Minjas J, Lubega P, Makwaya C. Anaemia and *Plasmodium falciparum* infections among young children in a holoendemic area, Bagamoyo, Tanzania. *Acta Tropica* 1995;59:55-64.
- Muhe L, Oljira B, Degefu H, Enquesellasse F, Weber MW. Clinical algorithm for malaria during low and high transmission seasons. *Archives of Disease in Childhood* 1999;81:216-20.
- McElroy PD, ter Kuile FO, Lal AA, Bloland PB, Hawley WA, Oloo AJ, et al. Effect of *Plasmodium falciparum* parasitemia density on hemoglobin concentrations among full-term, normal birth weight children in western Kenya, IV. The Asembo Bay Cohort Project. *American Journal of Tropical Medicine and Hygiene* 2000;62:504-12.
- May J, Falusi AG, Mockenhaupt FP, Ademowo OG, Olumese PE, Bienze U, et al. Impact of subpatent multi-species and multi-clonal plasmodial infections on anaemia in children from Nigeria. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2000;94:399-403.
- Murphy SC, Breman JG. Gaps in the childhood malaria burden in Africa: cerebral malaria, neurological sequelae, anemia, respiratory distress, hypoglycemia, and complications of pregnancy. *American Journal of Tropical Medicine and Hygiene* 2001;64(1-2 Suppl.):57-67.
- Schellenberg D, Menendez C, Kahigwa E, Font F, Galindo C, Acosta C, et al. African children with malaria in an area of intense *Plasmodium falciparum* transmission: features on admission to hospital and risk factors for death. *American Journal of Tropical Medicine and Hygiene* 1999;61:431-8.
- Marsh K, Forster D, Waruiru C, Mwangi I, Winstanley M, Marsh V, et al. Indicators of life-threatening malaria in African children. *New England Journal of Medicine* 1995;332:1399-404.
- Slutsker L, Taylor TE, Wirima JJ, Steketee RW. In-hospital morbidity and mortality due to malaria-associated severe anaemia in two areas of Malawi with different patterns of malaria infection. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1994;88:548-51.
- Lackritz EM, Campbell CC, Ruebush TK, 2nd, Hightower AW, Wakube W, Steketee RW, et al. Effect of blood transfusion on survival among children in a Kenyan hospital. *Lancet* 1992;340:524-8.
- Bojang KA, Palmer A, Boele van Hensbroek M, Banya WA, Greenwood BM. Management of severe malarial anaemia in Gambian children. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1997;91:557-61.
- Rewlins SC, Campbell M, Fox K, Bennett F, Gibbs WN, Greene M. Parasitic infections in young Jamaicans in different ecological zones of the island. *Tropical and Geographical Medicine* 1991;43:136-41.
- Hall A, Latham MC, Crompton DW, Stephenson LS, Wolgemuth JC. Intestinal parasitic infections of men in four regions of rural Kenya. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1982;76:728-33.
- Sweet DG, Savage G, Tubman TR, Lappin TR, Halliday HL. Study of maternal influences on fetal iron status at term using cord blood transferrin receptors. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2001;84:F40-3.
- Singla PN, Tyagi M, Shankar R, Dash D, Kumar A. Fetal iron status in maternal anaemia. *Acta Paediatrica* 1996;85:1327-30.
- Singla PN, Tyagi M, Kumar A, Dash D, Shankar R. Fetal growth in maternal anaemia. *Journal of Tropical Pediatrics* 1997;43:89-92.
- Jaime-Perez JC, Herrera-Garza JL, Gomez-Almaguer D. Relationship between gestational iron deficiency and iron deficiency in the newborn; erythrocytes. *Hematology* 2000;5:257-62.
- Menendez C, Kahigwa E, Hirt R, Vounatsou P, Aponte JJ, Font F, et al. Randomised placebo-controlled trial of iron supplementation and malaria chemoprophylaxis for prevention of severe anaemia and malaria in Tanzanian infants. *Lancet* 1997;350:844-9.
- Newton CRJC, Warn PA, Winstanley PA, Peshu N, Snow RW, Pasvol G, et al. Severe anaemia in children living in a malaria endemic area of Kenya. *Tropical Medicine and International Health* 1997;2:165-78.
- Gascon J, Vargas M, Schellenberg D, Urassa H, Casals C, Kahigwa E, et al. Diarrhoea in children under 5 years of age from Ifakara, Tanzania: a case-control study. *Journal of Clinical Microbiology* 2001;38:4459-62.
- Clegg JB, Weatherall DJ. Thalassemia and malaria: new insights into an old problem. *Proceedings of the Association of American Physicians* 1999;111:278-82.

22. Thaver IH, Baig L. Anaemia in children: Part I. Can simple observations by primary care provider help in diagnosis? *Journal of the Pakistan Medical Association* 1994;44:282-4.
23. Luby SP, Kazembe PN, Redd SC, Ziba C, Nwyanwu OC, Hightower AW, et al. Using clinical signs to diagnose anaemia in African children. *Bulletin of the World Health Organization* 1995;73:477-82.
24. Ekwunwe EO. Predictive value of conjunctival pallor in the diagnosis of anaemia. *West African Journal of Medicine* 1997;16:246-50.
25. Kalter HD, Burnham G, Kolstad PR, Hossain M, Schillinger JA, Khan NZ, et al. Evaluation of clinical signs to diagnose anaemia in Uganda and Bangladesh, in areas with and without malaria. *Bulletin of the World Health Organization* 1997;75 Suppl. 1:103-11.
26. Zucker JR, Perkins BA, Jafari H, Otieno J, Obonyo C, Campbell CC. Clinical signs for the recognition of children with moderate or severe anaemia in western Kenya. *Bulletin of the World Health Organization* 1997;75; Suppl. 1:97-102.
27. Weber MW, Kellingray SD, Palmer A, Jaffar S, Mulholland EK, Greenwood BM. Pallor as a clinical sign of severe anaemia in children: an investigation in the Gambia. *Bulletin of the World Health Organization* 1997;75;Suppl. 1:113-8.
28. van den Broek NR, Ntonya C, Mhango E, White SA. Diagnosing anaemia in pregnancy in rural clinics: assessing the potential of the Haemoglobin Colour Scale. *Bulletin of the World Health Organization* 1999;77:15-21.
29. Muhe L, Oljira B, Degefu H, Jaffar S, Weber MW. Evaluation of clinical pallor in the identification and treatment of children with moderate and severe anaemia. *Tropical Medicine and International Health* 2000;5:805-10.
30. Stoltzfus RJ, Edward-Raj A, Dreyfuss ML, Albonico M, Montresor A, Dhoj Thapa M, et al. Clinical pallor is useful to detect severe anemia in populations where anemia is prevalent and severe. *The Journal of Nutrition* 1999;129:1675-81.
31. Lengeler C. Insecticide-treated bednets and curtains for preventing malaria. *Cochrane Database of Systematic Reviews* 2003;(2):CD000363.
32. Abdulla S, Schellenberg JA, Nathan R, Mukasa O, Marchant T, Smith T, et al. Impact on malaria morbidity of a programme supplying insecticide treated nets in children aged under 2 years in Tanzania: community cross sectional study. *BMJ* 2001;322:270-3.
33. Stoltzfus R, Dreyfuss M. *Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia*. Washington: ILSI Press; 1998.
34. Armstrong Schellenberg JRM, Mukasa O, Abdulla S, Marchant T, Lengeler C, Kikumbih N, et al. *The Ifakara Demographic Surveillance System. p. INDEPTH Monograph Series: Demographic surveillance systems for assessing populations and their health in developing countries. Vol. 1. Population, health and survival in INDEPTH sites*. Ottawa: IDRC/CRDI; 2001.
35. UNICEF/WHO. *Child Health/IMCI household baseline survey generic tool*. Available from: URL: <http://www.unicef.org/programme/health/document/generic.pdf> (accessed on: 30 May 2003).
36. Armstrong Schellenberg JRM, Victora CG, Mushi A, de Savigny D, Schellenberg D, Mshinda H, et al. Inequities among the very poor: health care for children in rural southern Tanzania. *Lancet* 2003;361:540-1.
37. Filmer D, Pritchett LH. Estimating wealth effects without expenditure data — or tears: an application to educational enrollments in states of India. *Demography* 2001;38:115-32.
38. Sinnott RW. Virtues of the Haversine. *Sky and Telescope* 1984;68:159.
39. *Handbook of integrated management of childhood illness*. Geneva: WHO/CAH and UNICEF, 2000. p. 50.
40. WHO/CAH and UNICEF. Management of the child with a serious infection or severe malnutrition. Guidelines for care at the first-referral level in developing countries. WHO document WHO/FCH/CAH/00.1. p. 59.
41. Balidin B. KCMC management schedules of some common children's diseases at hospital level, 5th ed. Moshi, Tanzania: KCMC educational committee, 1994. p. 53.
42. English M, Ahmed M, Ngando C, Berkley J, Ross A. Blood transfusion for severe anaemia in children in a Kenyan hospital. *Lancet* 2002;359:494-5.
43. *WHO expert committee on malaria*, 20th report. Geneva: World Health Organization; 2000. (WHO Technical Report Series, No. 892).
44. Turgeon O, Santure M, Maziade J. The association of low and high ferritin levels and anemia with pregnancy outcome. *Canadian Journal of Dietetic Practice and Research* 2000;61:121-7.
45. Jus'at I, Achadi EL, Galloway R, Dyanto A, Zazri A, Supratikto G, et al. Reaching young Indonesian women through marriage registries: an innovative approach for anaemia control. *The Journal of Nutrition* 2000;130;2S Suppl:456-8S.
46. Armstrong Schellenberg JRM, Abdulla S, Minja H, Nathan R, Mukasa O, Marchant T, et al. KINET: a social marketing programme of treated nets and net treatment for malaria control in Tanzania, with evaluation of child health and long-term survival. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1999;93:225-31.
47. Curtis CF, Maxwell CA, Finch RJ, Njunwa KJ. A comparison of use of a pyrethroid either for house spraying or for bednet treatment against malaria vectors. *Tropical Medicine and International Health* 1998;3:619-31.
48. Schellenberg D, Menendez C, Kahigwa E, Aponte J, Vidal J, Tanner M, et al. Intermittent treatment for malaria and anaemia control at time of routine vaccinations in Tanzanian infants: a randomised, placebo-controlled trial. *Lancet* 2001;357:1471-7.