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Shigellosis remains an important problem in children less than 5 years of age in Thailand

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SUMMARY

This is a review of existing data on the burden of shigellosis in Thailand to determine trends, vulnerable groups, predominant species and serotypes, and antimicrobial resistance patterns. Diarrhoea and dysentery morbidity and mortality data from 1991 to 1999 was collected from the routine surveillance system and demographic data from the government census. International and local literature published between 1988 and 2000 was systematically reviewed. Based on the routine surveillance system, the annual incidence of bacillary dysentery decreased from 1·3 to 0·2/10 000 persons per year. The remaining burden is highest in children <5 years of age at 2·7/10 000 persons per year. In comparison, a prospective study utilizing active surveillance found an incidence in children <5 years of age that was more than 100-fold higher at 640/10 000 persons per year. Despite the decrease in morbidity and mortality based on routinely collected data, shigellosis remains an important problem in children <5 years of age in Thailand.

INTRODUCTION

Diarrhoea is a major public health problem but the combined influence of multiple factors has reduced its impact in several countries around the world [1]. These factors include home-based interventions such as encouraging breastfeeding, childhood nutrition, and oral rehydration; health centre-based strategies on diarrhoea case management, measles immunization, and provision of vitamin A; and national improvements in socio-economic status, water supply, and sanitation. In particular, oral rehydration therapy is credited with the reduction in childhood diarrhoea mortality from 4·6 million in 1980 to 1·5 million in 2000 [2].

As the morbidity and mortality from diarrhoeal diseases decrease, more attention has turned to bacillary dysentery (shigellosis), since its treatment is complicated by the emergence of antimicrobial resistance [3]. Antimicrobial agents previously used as first-line therapy such as ampicillin and cotrimoxazole have become ineffective against *Shigella* spp. The organism is rapidly becoming resistant to nalidixic acid, leaving few treatment options.

As Thailand makes its transition from a developing to an industrialized country, the shift from rural to urban living, increased life expectancy and other demographic changes are transforming the health

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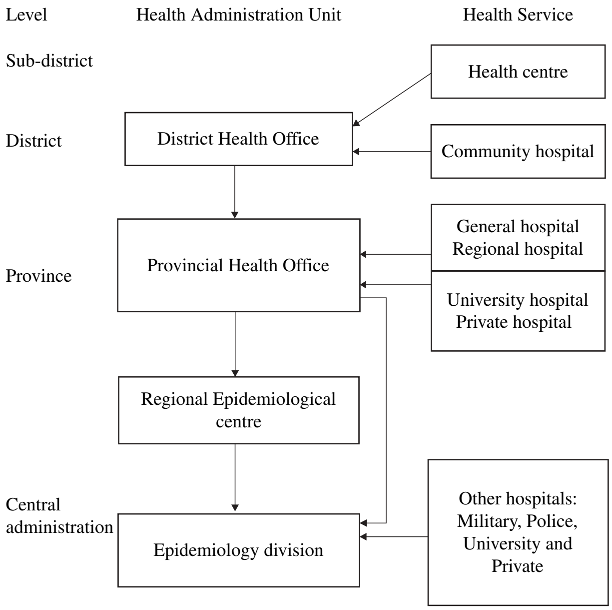

Fig. 1. Health Information System of Thailand.

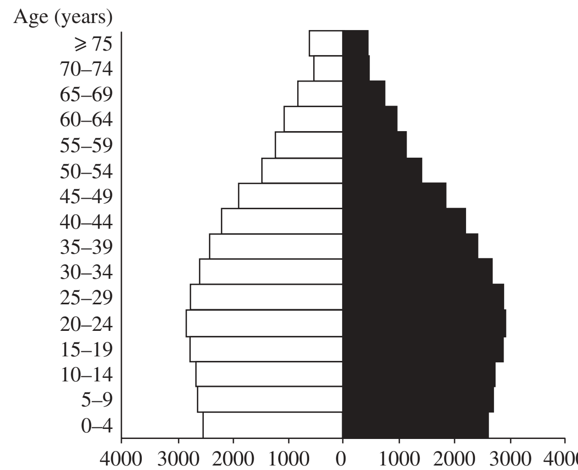

Fig. 2. Total population by age group, Thailand, 2000 [6]. □, Female; ■, male.

problems of its population. A critical analysis of the burden of specific diseases could be useful in developing targeted control measures towards continued improvement of health conditions. This is a review of the burden of shigellosis in Thailand, based on existing data sources from the past decade to determine trends in morbidity and mortality, vulnerable groups, predominant species and serotypes, and antimicrobial resistance patterns.

MATERIALS AND METHODS

The flow of information in the routine national health surveillance system of Thailand is shown in Figure 1. Standard forms for notifiable diseases are completed by the health service units and submitted at the district, provincial, or central level. The reported cases are diagnosed following ICD-10 definitions [4]. The data is collated and analysed in the Epidemiology Division of the Ministry of Public Health and published annually [5]. We abstracted the number of cases and deaths from diarrhoea and dysentery from the 1991–1999 annual reports. Demographic data from the government census [6] was used to calculate incidence per 10 000 persons per year and age group. The data were entered and graphs created in Microsoft Office Excel 2003 (Microsoft Corporation, Redmond, WA USA). Standard deviation for incidence by age group was calculated using SAS (SAS Institute Inc, Cary, NC, USA). χ^2 test for trend was calculated to assess the decrease in case-fatality rate over time using Epi-Info 6.0 [Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA].

International and local literature published between 1988 and 2000 was systematically reviewed using various combinations of the key words: diarrhoea, dysentery, bacillary dysentery, shigellosis, and Thailand. This was done to compare and supplement the data from the national health surveillance system. Emphasis was placed on epidemiological studies and review articles, which were included if they met predetermined criteria. Cohort studies were included if they described at least 1 year's prospective surveillance, with at least weekly visits to detect diarrhoea, appropriate clinical case definitions or culture confirmation using standard microbiological methods, and a clear population denominator. Outbreak investigations were excluded. Case-control studies and case series were included if they described at least 25 cases and utilized standard methods for serotyping and antimicrobial susceptibility testing. The selected articles were reviewed and data extracted on to a standardized form. The data was entered and graphs created in Excel.

RESULTS

Government data

In the year 2000, the total population of Thailand was approximately 62 million. Approximately 5 million (8 %) were <5 years of age (Fig. 2). The current population represents an increase from 56 million in 1991, or a growth of approximately 620 000 per year (1·1 %).

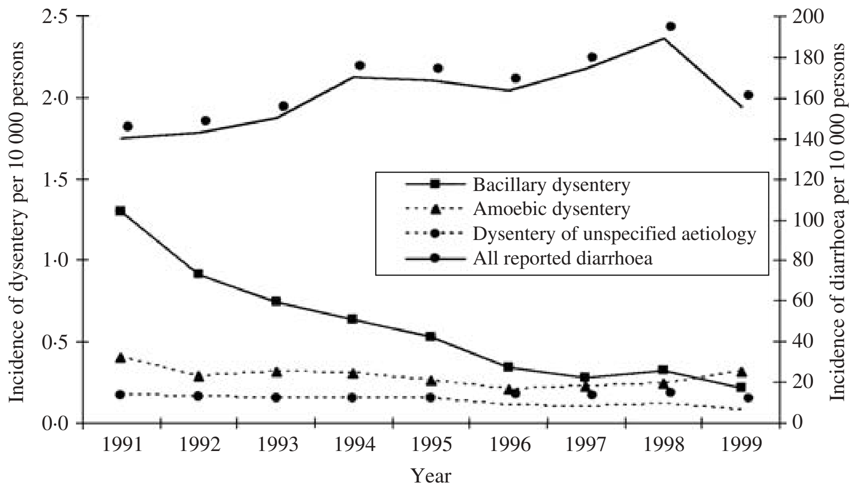

Fig. 3. Annual incidence of reported acute diarrhoea compared with dysentery, Thailand, 1991–1999 [5].

The reported annual incidence of acute diarrhoea and dysentery (bacillary, amoebic, and of unspecified aetiology) from 1991 to 1999 based on the government's routine national surveillance system is shown in Figure 3. The incidence of reported acute diarrhoea remained stable over time, ranging from 140 to 190/10 000 persons. The incidence of amoebic dysentery was similarly stable, ranging from 0·2 to 0·4/10 000 person. In contrast, the reported incidence of bacillary dysentery decreased more than sixfold from 1·3 to 0·2/10 000 persons.

The incidence of bacillary dysentery fell in all age groups. However, the burden remains highest in children <5 years of age. Over the last decade, the average annual incidence of bacillary dysentery in those aged <5 years was 2·7/10 000 persons per year compared to 0·4/10000 persons per year among those aged $\geqslant 5$ years (*P* value $<0{\cdot}01$). Although children <5 years of age make up only 8% of the total population, they accounted for 43% of bacillary dysentery cases. The incidence of bacillary dysentery is lowest in middle life and increases among those over 45 years of age, producing a U-like curve (Fig. 4). The reported case-fatality rate of bacillary dysentery from 1991 to 1999 ranged from 0% to 0·16% (Table 1). Most recently, the reported case-fatality rate has been nil.

Published data

The incidence of diarrhoea and shigellosis in children $\leqslant 5$ years of age in a low-income community in Bangkok was measured by a household-based prospective study from 1988 to 1989 [7]. Compared to the government data, the incidence of shigellosis detected

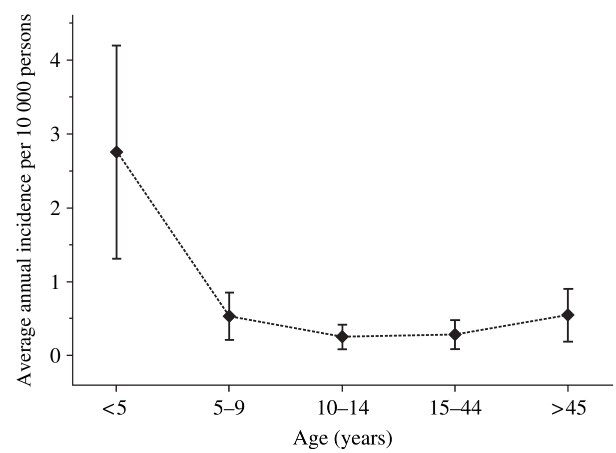

Fig. 4. Average reported annual incidence (with standard deviations) of bacillary dysentery by age group, Thailand, 1991–1999 [5].

by active surveillance in children <5 years of age was more than 100-fold higher at 640/10 000 per year (Table 2). *Shigella* was isolated starting at 6 months of age and 19% of diarrhoeal episodes in children were associated with shigella infections.

At the Children's Hospital in Bangkok, *Shigella* spp. was isolated from 94 (23%) of 410 children with diarrhoea [8]. When only mucoid or bloody stools were considered, isolation rates were higher at 47/91 (52%) and 88/200 (44%) respectively.

Shigella spp. isolation in community-based [9] and hospital-based [10–12] studies is shown in Table 3. In general, the most common shigella serogroup isolated was *S. flexneri* (79%), followed by *S. sonnei* (15%). Only 4% were *S. dysenteriae* and 2% *S. boydii*. *S. sonnei* was relatively more frequent in community- compared to hospital-based studies.

Table 1. *Reported case-fatality rate of bacillary dysentery by age group (%), Thailand, 1991 to 1999* [5]

	1991	1992	1993	1994	1995	1996	1997	1998	1999
Cases	7368	5213	4314	3768	3160	2048	1687	1988	1316
Deaths	7	4	7	3	2	3	1	0	0
Case-fatality rate* (%)	0·10	0·08	0·16	0·08	0·06	0·15	0·06	0·00	0·00

* χ^2 test for trend = 1·7 (P = 0·2).

Table 2. *Incidence of reported diarrhoea and shigellosis from 1988 to 1989, by age group, in a low-income urban community in Bangkok from a household-based prospective study* [7]

	Incidence per 10 000 children		% diarrhoea cases confirmed as shigellosis
Age group	Diarrhoea	Shigellosis	
0–5 months	20 000	0	0
6–11 months	24 000	864	4
1–2 years	12 000	612	5
2–5 years	4000	444	11

Table 3. *Comparison of* Shigella *spp. isolation between a community-based study in 1991* [9] *and hospital-based studies from 1988 to 1994* [10–12]

	Community-based study		Hospital-based study	
Shigella spp.	No.	%	No.	%
S. sonnei	25	28	249	14
S. boydii	1	1	35	2
S. dysenteriae 2–10	4	4	71	4
S. flexneri	60	67	1427	80
Total	90	100	1782	100

As shown in Figure 5, a study from 1985 to 1992 at a rural hospital in Nakhon Nayok, Thailand showed resistance rates of 72–90% to ampicillin and an increase in resistance to cotrimoxazole from 29% to 89% over the years [13]. In this study, no resistance was noted against nalidixic acid or cefotaxime. A study in Bangkok in 1988 showed the pattern of resistance of the four *Shigella* spp. to the commonly used antibiotics (Table 4). Overall, 87% of the shigella isolates were resistant to ampicillin, 84% to cotrimoxazole, and 0·1% to nalidixic acid [8].

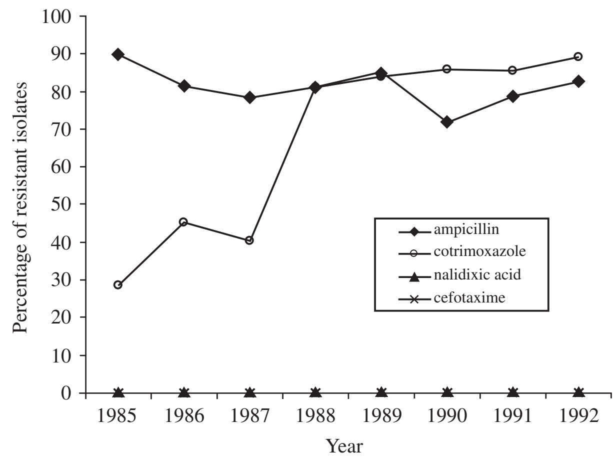

Fig. 5. Percentage of antimicrobial resistance of shigella isolates, Nakhon Nayok, Thailand, 1985–1992 [13].

DISCUSSION

Despite the decrease in morbidity and mortality from shigellosis suggested by the routine national health surveillance system, shigellosis remains an important problem in children < 5 years of age in Thailand. The government data is useful for the detection of trends but comparison with a household-based prospective study using active surveillance suggests that the actual incidence is likely to be several-fold higher. Since the government data relies on passive surveillance, notification rates are affected by whether patients seek medical care, whether the correct diagnosis is made, and whether notification is forwarded to the relevant authority. On the other hand, the prospective study was conducted at a specific site where the disease is believed to be a problem and the results may not be representative of the whole country.

The incidence rates from the household-based prospective study fall between those seen in industrialized and developing countries [3], and are most comparable to those in a newly industrialized country like Israel, which is not surprising considering Thailand's status as a transition country. On the other hand, the

Table 4. *Drug resistance pattern of* Shigella *spp., Bangkok, Thailand, 1988* [8]

	Percentage resistant				
Shigella spp.	Ampicillin	Chloramphenicol	Nalidixic acid	Trimethoprim–sulphamethoxazole	Tetracycline
S. boydii ($n=33$)	18	42	0	27	85
S. dysenteriae ($n=46$)	22	74	0	70	91
S. flexneri ($n=1280$)	98	99	0	88	98
S. sonnei ($n=186$)	42	45	1	72	96

mortality estimate (0–0·16%) is lower than the 0·7% rate that was estimated in a previous paper [3].

S. flexneri is typically the predominant species in developing countries [3]. Probably as a reflection of the transition of Thailand's economy towards increasing industrialization, we found *S. sonnei* to be an emerging species in this review. This finding is supported by a recently completed prospective population-based survey in Keangkoi, a rural area in Thailand. The surveillance identified *S. sonnei* as the predominant species in the study site (Chompook, P., unpublished observations).

The antimicrobial susceptibility patterns confirm increasing resistance of shigella to the commonly used antibiotics [3, 14]. Our data indicate that neither ampicillin nor cotrimoxazole can currently be used for empiric treatment. Although nalidixic acid (given orally four times a day for 5 days), second-generation quinolones such as ciprofloxacin (given orally twice a day for 3 days) and third-generation cephalosporins (given parenterally) are still effective in Thailand, it is probably only a matter of years before the organisms develop resistance to these drugs as well.

Our findings underscore the burden of shigellosis in young children. The increased incidence of shigellosis in older populations is an interesting observation, which to our knowledge, has not been previously reported. In fact, there are few published data addressing the burden of shigellosis in adults [3]. Our findings suggest that this issue should be carefully assessed through prospective research.

A safe and effective vaccine against shigellosis would be a potentially important public health tool. For Thailand, the vaccine would need to be effective against *S. flexneri* and *S. sonnei* and should protect children starting at 6 months of age. Considering that most shigella vaccines under development are designed to provide immunity that is serotype-specific, additional data are needed to determine the distribution of *S. flexneri* serotypes.

Analysis such as this is an example of the possible uses of existing data from routine national reporting systems and published literature. Retrospective analyses are useful to assess the success of disease control programmes, identify priorities, allocate resources, and detect unusual patterns that warrant further attention, such as the apparent vulnerability of the elderly to shigellosis. The accuracy of such data varies depending on the level of development in the country, the resources available, the infrastructure and technical capacity present. Each of these factors influences the quality of routine reporting and research. Notification rates also depend on the type of disease, whether patients seek medical care, whether the correct diagnosis is made, and whether notification is forwarded to the relevant authority. Due to these many variables, it is often not possible to provide conclusive results. Despite its limitations, we believe that the data presented here suggests the importance of shigellosis in young children and the need for a safe and effective vaccine.

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