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Clinical situation of endemic malaria in Yemen

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Abstract. Malaria remains a major public health problem causing mortality and morbidity in tropical and subtropical countries. A cross-sectional study was carried out to determine malaria prevalence and its clinical pattern during malaria season in Yemen. Blood samples were collected from 511 patients with fever who voluntary participated in this study, of them 268 were males and 242 females. Malaria was screened using Giemsa-stained thick and thin blood films. Clinical profile was recorded through physical and laboratory examinations and biodata were collected by pre-tested standard questionnaire. The overall prevalence was 15.3%. Three malaria species (*Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium malarae*) were detected with the predominance of *P. falciparum* (83.33%). People living in the rural areas had higher infection rate compared to urban areas ($p < 0.005$). Children were at higher risk of developing severe malaria compared to adults ($p < 0.05$). Severe anaemia, respiratory distress, jaundice, convulsion and bleeding were more apparent among younger age groups of malaria cases compared to older children. The study indicates that malaria is still a public health problem with children being at high risk of developing severe malaria which may lead to death.

INTRODUCTION

Although it is more than 125 years since the discovery of the malarial parasite, today malaria still remains a devastating global public health problem in more than 100 countries (WHO, 1996). Around 3.2 billion people are at risk of malaria annually (WHO, 2005), with around 300–500 million people contracting the disease each year (WHO, 2008), resulting in 2-3 million deaths (Snow *et al*., 2005). This includes 1 million children of less than five years of age (Sachs & Malaney, 2002; Dyer *et al*., 2007; Joubert *et al*., 2009). In addition, malaria represents a medical emergency because it may rapidly progress to complications and death without prompt and appropriate treatment (Trampuz *et al*., 2003).

In Yemen, malaria remains a significant health problem. Of the total population of 20 million, 60% live in malarious areas (Alkadi *et al*., 2006), placing Yemen after Afghanistan with population at high risk in the WHO Eastern Mediterranean region (WHO, 2009a). *Plasmodium falciparum* is the predominant species which is responsible for 90% of the malaria cases followed by *Plasmodium vivax* and *Plasmodium malariae* (NMCP, 2002). Although *Anopheles arabiensis* is the main vector of malaria in Yemen, *Anopheles culicifacies* and *Anopheles sergenti* have been reported to play an important role in transmission of malaria (Knight, 1953; Thuriau, 1971; Kouzetsov, 1976; NMCP, 2002).

The clinical pattern of severe and complicated malaria varies in different parts of the world. Several studies carried out in Africa showed severe malaria in children below 5 years of age but was less common in older children and adults (Gay-Andrieu *et al*., 2005; Khier *et al*., 2005;

Obonyo *et al.*, 2007; Oduro *et al.*, 2007; Bassat *et al.*, 2008; Opoka *et al.*, 2008). Not much is known about the clinical pattern of malaria in Yemen, a country that culturally, socially, economically and geographically is different from that in Africa. Furthermore, the main malaria vector is different in Yemen. A recent study carried out in Yemen on pediatric malaria showed that severe malaria constituted 17% of pediatric hospital admissions. In the same study, the main presentation of severe malaria was respiratory distress (40%), followed by severe anaemia (37%) and cerebral malaria (8%) (Al-Taiar *et al.*, 2006). The current study is a cross-sectional study stressing on the clinical pattern of malaria among all age groups.

MATERIALS AND METHODS

Study areas

The present study was conducted in five governorates with a total population 7.9 million (National Census, 2004). Among the selected governorates Taiz and Hodeidah represent mountainous hinterland and coastal areas respectively, and Raymah, Dhamar and Sana'a are highland areas (Figure 1). These governorates has different climates, altitudes and seasonal transmission of malaria in Yemen. In the coastal areas, peak malaria transmission appears in winter (October-April), in the western mountains however, this peak occurs in the summer (May-September), while in the highland areas transmission occurs throughout the year. The mountainous hinterland normally shows peak transmission between October and March. The majority of the work force is employed in the agriculture, fishing, livestock and handicraft sectors.

Study population

Sample size calculation was done using the tables of Lwanga & Lemeshow (1991). The sample size was estimated according to previous prevalences reported in Yemen (Alkadi *et al.*, 2006; Al-Taiar *et al.*, 2006; Bin Mohanna *et al.*, 2007). The minimum total sample size required for this study was 196-246. In this study, a total of 511 malarial samples were collected during transmission seasons from June 2008 to

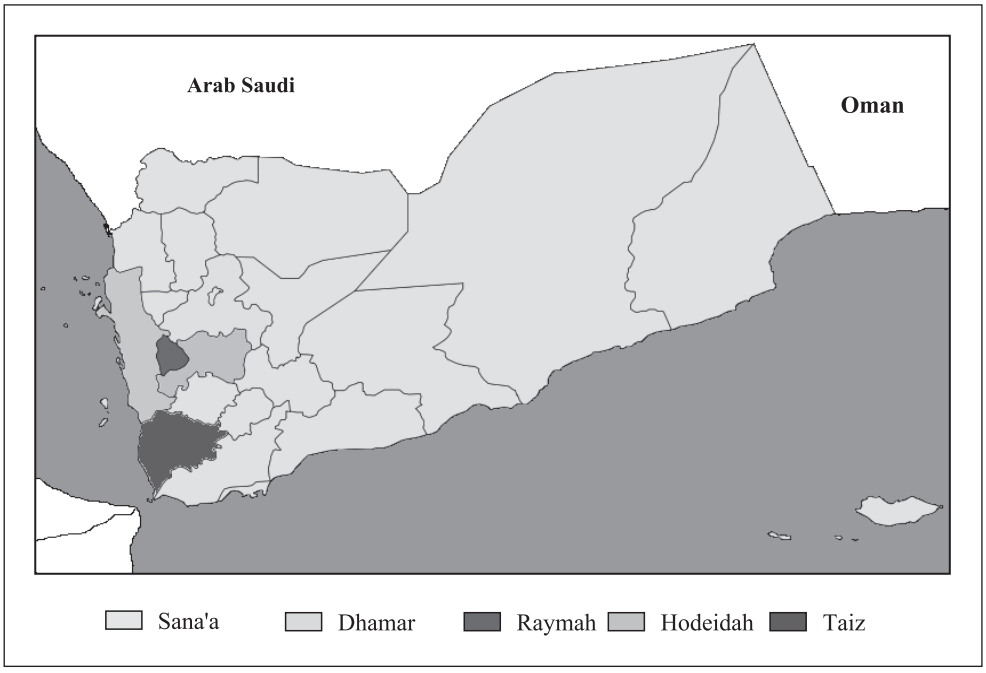

Figure 1. Map of study areas in Yemen

March 2009. Participants with febrile illness who gave written informed consent were included in this study. To study the clinical pattern of malaria, patients with blood films positive for malaria and not other febrile illness only were included in the analysis.

Data collection

Blood was collected from febrile patients attending local public, private health centers or hospitals. A questionnaire was used as a guide by the interviewers. It was pre-tested and translated into the local dialects for better comprehension and easier communication. It included personal details and socio-demographic profile of the subjects, a checklist of clinical symptoms of malaria which may have been experienced by the subjects, and a list of clinical signs observed by the health worker examining the patients. All the data were recorded in the questionnaire by the interviewer. Cases were defined as severe malaria if they met the WHO criteria for severe malaria (WHO, 2000). Symptoms and signs were defined as following; respiratory distress: presence of indrawing of the bony structure in the lower chest wall, abnormally deep breathing, and grunting; convulsion: more than two episodes observed within 24 hours despite cooling; abnormal bleeding: spontaneous bleeding from gums, nose, gastrointestinal tract, etc. and/or substantial laboratory evidence of disseminated intravascular coagulation (DIC); jaundice: detected clinically or defined by a serum bilirubin concentration of more than 3.0 mg/dl. Parasitaemia was graded as low (1–999/µl), moderate (1000–9999/µl) and high (>10000/µl), haemoglobin concentration levels considered as normal (>11 g/dl), low anaemia (9-11 g/dl), moderate anaemia (7-8.9 g/dl) and severe anaemia (<7 g/dl) (Bouyou-Akote *et al.*, 2003).

Laboratory method

Blood from finger pricks was used to prepare thick and thin blood films, air-dried and stained with Giemsa stain. All of the stained slides were examined by local microscopists for malaria parasites. Reexamination and species level identification were performed in a double-blind manner, in two different laboratories by two expert microscopists following standard, quality-controlled procedures. Parasitaemia counts were obtained from thick smears by counting the number of asexual parasites among 200 leucocytes and multiplying the count by the patient's total leukocyte count and divided by 200. A result was recorded as negative only after at least 100 high-powered microscope fields had been scanned. Bilirubin and Hb were measured at the hospitals or medical centers using spectrophotometer instrument.

Data analysis

SPSS version 11.5 was used to analysis the data. A significant level of 0.05 at 95% confidence interval (CI) level was chosen. The associations between proportions were tested using the X^2 test and 95% confidence interval. The significance was defined as $P < 0.05$.

Ethical clearance

This study was given ethical approval by the Sana'a University, Republic of Yemen. Informed consent was obtained from each individual or from the guardian of the participant after explanation of the purpose of the study.

RESULTS

Five hundred and eleven patients presented with fever at hospitals and clinical centers were examined for malaria. They comprised 268 males (52.4%), 242 (47.4%) females. The median of age was 20 with 22 years interquartile range. Overall prevalence of malaria was 15.3%. The study results showed that malaria was significantly associated with younger age group and the infection declined with increasing age ($p < 0.05$). Malaria among children < 5 years was rated at 25%. Males had higher infection rate compared to females (17.9% *vs* 12.4%).

Patients living in rural areas were significantly four times more infected with malaria than those living in urban areas (23.6% *vs* 5.6%) ($p < 0.005$) (Table 1).

The majority (89.7%) of malaria cases were due to *P. falciparum*, followed by cases with *P. vivax* (3.9%) and the rest (6.4%) was classified as mixed infections. Of the mixed infection 5.1% were of *P. falciparum* and *P. vivax*, and 1.3% were *P. falciparum* and *P. malariae*. The mean of malaria parasitaemia was 33156 parasites/microliter (STD 31973 parasite/microliter) with 69% of the cases showing high parasitaemia (Table 2).

Severe malaria was significantly associated with young children while non severe malaria was more common among older children and adults ($p < 0.05$). No significant difference in the severity of malaria between males and females was noted (Table 3). Severe clinical manifestations in the study population were jaundice (43.6%), followed by convulsion (26.9%), severe anaemia (21.8%), respiratory distress (20.5%) and bleeding (3.8%). Among the children aged < 5 years, jaundice (65%), severe anaemia (50%), convulsion (40%), respiratory distress (20%) and bleeding (5%) were recorded (Table 4).

DISCUSSION

Out of 511 blood samples examined in the present study, 78 (15.3%) were positive for malaria. Previous reports showed that malaria prevalence in Yemen ranged between 12.8% and 18.6% (Al-Maktari *et al.*, 2003; Alkadi *et al.*, 2006; Al-Taiar *et al.*, 2006; Bin Mohanna *et al.*, 2007). WHO reported that Yemen is one of the Eastern Mediterranean countries that have not registered a decrease in the number of malaria cases as compared to other countries in the region such as Iraq, Iran and Saudi Arabia, which showed evidence of sustained decrease in malaria cases. These countries have been categorized into

Table 1. Characteristic of study population with malaria in Yemen

Variable	Examined	Infected	P value
Age (years)			
< 5	80	20 (25%)	0.024
5–10	67	11 (16.4%)	
> 10	363	47 (12.9%)	
Gender			
Male	268	48 (17.9%)	0.054
Female	242	30 (12.4%)	
Residence			
Rural	275	65 (23.6%)	0.000
Urban	234	13 (5.6%)	

Table 2. Prevalence of infecting malaria species and parasitaemia levels in the study population

Variable	Percentage
Species	
P. falciparum	70 (89.7%)
P. vivax	3 (3.9%)
P. malariae	0 (0%)
P. falciparum & *P. vivax*	4 (5.1%)
P. falciparum & *P. malariae*	1 (1.3%)
P. vivax & *P. malariae*	0 (0%)
Parasitaemia	
High	54 (69.2%)
Moderate	16 (20.5%)
Low	8 (10.3%)

Table 3. Severity of malaria among patients according to age and gender

Variable	Severe malaria	Non severe malaria	P value
Age (years)			
< 5	6 (30.0%)	14 (70.0%)	0.036
5–10	2 (18.2%)	9 (81.8%)	
> 10	3 (06.4%)	44 (93.6%)	
Gender			
Male	5 (10.4%)	43 (89.6%)	0.197
Female	6 (20.0%)	24 (80.0%)	

Table 4. Clinical pattern of malaria according to age

Variable	Prevalence	P value
Severe anaemia		
All ages	17 (21.8%)	
< 5 years old	10 (50%)	0.002
5-10 years old	2 (18.2%)	
> 10 years old	5 (10.6%)	
Respiratory distress		
All ages	16 (20.5%)	
< 5 years old	4 (20%)	0.972
5-10 years old	2 (18.2%)	
> 10 years old	10 (21.3%)	
Jaundice		
All ages	34 (43.6%)	
< 5 years old	13 (65%)	0.064
5-10 years old	5 (45.5%)	
> 10 years old	16 (34%)	
Convulsion		
All ages	21 (26.9%)	
< 5 years old	8 (40%)	0.286
5-10 years old	3 (27.3%)	
> 10 years old	10 (21.3%)	
Bleeding		
All ages	3 (3.8%)	
< 5 years old	1 (5%)	0.766
5-10 years old	0 (0%)	
> 10 years old	2 (4.3)	

the elimination or pre-elimination stage (WHO, 2009a). However, Yemen has wide scale implementation of malaria control activities. But, still many efforts by the decision makers as well as individuals in the communities are urgently needed. Thus, these preventive measures and control policies should be re-evaluated in order to be effective towards reducing number of malaria infection.

This study confirms that malaria in Yemen is age dependent, identifying the younger age as high risk group. This finding is consistent with previous results from Yemen and other countries (Slutsker *et al.*, 1994; Snow *et al.*, 1994, 1997, 2005; Sintasath *et al.*, 2005; Al-Taiar *et al.*, 2006; Bin Mohanna *et al.*, 2007). A previous study indicated that paediatric malaria was responsible for 17% of paediatric hospital admissions in Yemen which resulted in 2.1% – 4.7% deaths (Al-Taiar *et al.*, 2006). Our study has also shown that malaria in Yemen is gender biased with males being more infected. Similar results have been reported in Yemen (Al-Taiar *et al.*, 2006), Saudi Arabia (Malik *et al.*, 1998) and many African countries (Endeshaw & Assefa, 1990; Oduro *et al.*, 2007).

The current study showed high prevalence in rural areas (23.6%) compared to urban areas (5.6%). Findings from this study confirm previous studies that considered malaria as a disease of the rural areas in Yemen (Bassiouny & Al-Maktari, 2005; Al-Taiar *et al.*, 2009). Several factors play important roles in the endemicity of malaria in the rural areas including low income which affects housing, nutrition and health, environmental factors such as uncovered wells and small dams storing rain water which serve as breeding sites for mosquitoes. Furthermore, WHO reported that 75% of rural area population in Yemen does not have easy access to local health services (WHO, 2009b), hence, most of malaria cases may not receive proper clinical management and follow up.

Three *Plasmodium* species (*P. falciparum*, *P. vivax* and *P. malariae*) were reported in this study with *P. falciparum* being the predominant species. Similar results were reported in previous studies (Assabri & Muharram, 2002; Azazy & Rajaa, 2003; AL-Maktari *et al.*, 2003; Bassiouni & AL-Maktari, 2005; Alkadi *et al.*, 2006; Al-Taiar *et al.*, 2006). The WHO Eastern Mediterranean region includes nine countries (Afghanistan, Djibouti, Pakistan, Somalia, Sudan, Yemen, Iraq, Iran and Saudi Arabia). Majority of malaria cases in Afghanistan and Pakistan and almost all cases in Iran and Iraq are due to *P. vivax* while *P. falciparum* is predominant in Somalia, Djibouti, Yemen, Sudan and Saudi Arabia (WHO, 2009a). In this study, majority of malaria cases had high parasitaemia and almost all of them were due to *P. falciparum*.

The current study showed that children < 5 years are significantly at higher risk of developing severe malaria compared to older children. The shift of severe malaria peak to younger age group in Yemen has

also been reported previously (Al-Taiar *et al.*, 2006). In a recent systematic review which included data from Sub-Saharan Africa in the period 1980-2005, showed that hospital admissions for malaria involved mainly children < 5 years old (Carneiro *et al.*, 2010). The bias of severe malaria to younger age group could be explained by the fact that protection against severe malaria may be acquired with age due to repeated exposure in the endemic areas (Carneiro *et al.*, 2010). In this study, severe malaria anemia was reported in 50% of infected children aged < 5 years.

Severe anemia has been noted to be age-dependent in our study, which was also observed in previous studies (Reyburn *et al.*, 2005). Although severe anemia is a common feature of severe malaria among young children, its occurrence is most likely multi-factorial in origin and there is a possibility of association with nutrition and other diseases (Calis *et al.*, 2008). No significant association between respiratory distress, jaundice and convulsion and age was found. In our study, follow-up for severe cases was not done by the research team and there was a possibility that these cases might have developed cerebral malaria and death.

Malaria remains a significant problem in Yemen. Severe malaria puts a high burden on health services in this nation. This study illustrates high prevalence of severe malaria among children < 5 years old. Identification of the age groups at high risk of developing severe malaria in Yemeni communities will enable intervention to be targeted to those at the greatest risk. Thus, age-targeted strategies such as preventive treatment of young children and giving them the priority of getting treated bednets should be implemented.

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