Malaria and severe anemia over eight years at Gambo Rural Hospital, southern Ethiopia

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ABSTRACT

Evolution of incident malaria and frequency of anemia were analyzed over eight years in a rural hospital in southern Ethiopia. Capillary blood samples were tested for hemoglobin concentration, and in some instances for malaria parasites, at Gambo Rural General Hospital between January 2007 and September 2014, and the results recorded. Main demographic data were also recorded in subjects with *Plasmodium* sp. infections. Of a total of 54,493 blood samples taken from 45,096 different patients, 21,723 (39.9%) samples from 19,173 (42.5%) patients were tested for malaria parasites. Malaria was diagnosed in 825 (3.79%, 95% CI 3.55%, 4.06%) instances (58.3% *P. vivax* and 41.7% *P. falciparum*; one episode in 575 patients and two episodes in 125 patients). A sustained decrease in yearly incidence of malaria was observed between 2011 (6.1%) and 2014 (2.4%) ($p < 0.01$). Of all the malaria patients, those with hemoglobin levels less than 8 g/dL, were younger compared to those with levels of 8 g/dL or more (median age of 5 years vs. 18 years; $p < 0.01$) and more commonly infected with *P. falciparum* (57.1% vs. 34.8%; $p < 0.001$). In multivariate analysis, severe anemia (hemoglobin <8 g/dL) in the context of anemia was associated with *P. falciparum* infection (adjusted odd ratio [OR] 2.48, 95% confidence interval [CI] 1.68, 3.65) and younger age (OR 1.06, 95% CI 1.04, 1.07).

KEYWORDS

Malaria; *Plasmodium falciparum*; *Plasmodium vivax*; anemia; Ethiopia

Introduction

Malaria is one of the most deadly infectious diseases affecting countries in the tropics, with around one in two people at risk of infection worldwide, more than 200 million infections and nearly half a million deaths per year. Children below 5 years of age and pregnant women are generally at greater risk of complicated malaria [1].

Ethiopia is endemic for malaria in all areas at altitudes below 2000 m, which accounts for around 75% of the territory affected; both *Plasmodium falciparum* and *Plasmodium vivax* are present at similar relative frequencies all over the country [2]. Incidence of malaria peaks around the rainy season (September–December) and may be as high as four million cases per year [3].

The aim of this study was to determine the characteristics and evolution of incident *Plasmodium* infection and to identify which factors associated with complicated malaria were due to severe anemia in patients attended at a rural hospital in southern Ethiopia.

Material and methods

The study was performed at Gambo General Rural Hospital, which is located in the province of West Arsi (Ethiopia),

245 km southeast of the capital city Addis Ababa, at an altitude of 2250 m above sea level. The hospital provides daily health care and covers nine peripheral health centers serving 23 villages, with a total catchment population of around 98,000 people. Many patients may also come from bordering areas lying at lower altitudes. Other medical facilities within the catchment area of Gambo Hospital are more difficult to access, making the Gambo Hospital a strategically placed center at the population level.

This is a retrospective observational study of all the capillary blood specimens examined at the laboratory in the period between January 2007 and September 2014. The peripheral blood parameters recorded were: hemoglobin only, leucocytes, and thin blood smears for malaria or *Borrelia* infection. Main peripheral blood parameters (hemoglobin and leucocytes) were routinely recorded. Hemoglobin levels were measured by laboratory technicians using a portable digital hemoglobin meter (Hemo Control, EKF-diagnostic GmbH, Barleben/Magdeburg, Germany). Indications for blood tests were always determined by attending health professionals based exclusively on clinical grounds. Anemia was considered severe when hemoglobin concentration was lower than 8 g/dL, irrespective of age.

In some instances, and always in accordance with clinical indications, blood samples were prepared for confirmation of *Plasmodium* infection by microscopic observation of thin Giemsa-stained films. *Plasmodium* species diagnosis was made based on classical characteristics of malaria parasites. In case of possible dual infection, only *P. falciparum* was considered. The main demographic characteristics of the patients tested for malaria parasites were also available for analysis. Only one blood film per episode of malaria was considered in all patients for this study.

Statistical analyses

Demographic data (age and sex), hemoglobin levels and parasite data (*Plasmodium* infection and species) were entered into an electronic database (Microsoft Excel). The data were reviewed and cleaned before being fed into statistical software for analysis (SPSS, v 22.0).

We compared categorical variables by χ^2 test and continuous values using the student's *t*-test; non-parametric tests were applied when needed. We considered any *p* value less than 0.05 to be statistically significant. We included factors associated with malaria plus severe anemia in the univariate analysis in a multivariate analysis.

The study was reviewed and approved by the Ethical Review Board at Gambo Hospital.

Results

A total of 54,493 blood samples from 45,096 different patients attended at Gambo Hospital were examined between January 2007 and September 2014. The average number of blood specimens examined in the laboratory during the period of study was variable (mean 664 SD 216 samples per month). The number of blood samples tested has increased dramatically in recent years, from 4988 samples in 2008 to 9702 in 2012.

Of all the blood samples registered in Gambo Hospital, 21,723 (39.9%) were tested for blood parasites. The frequency of blood parasite testing oscillated over each year, with fewer laboratory requests in the months of January, February and September.

Episodes of malaria

A total of 825 episodes of malaria were diagnosed in 700 different patients based on analysis of blood samples. In 575 patients, only one episode of malaria was confirmed, while 125 had two episodes. The overall incidence of malaria in patients tested for malaria parasites at Gambo Hospital during the period of observation was 3.79% (95% CI, 3.55%, 4.06%).

Patients with malaria were younger than those with negative blood films (median 12 vs. 18 years of age, respectively; $p < 0.001$) and had lower hemoglobin levels (median 8.35 vs. 11.90 g/dL, respectively; $p < 0.001$;

Table 1). The proportion of participants under 15 years of age was greater in those with positive (53.9%) vs. negative (47.9%) blood films ($p < 0.01$). No differences in this respect were observed in children under 5 years old or over 15 years old. Distribution between sexes was also similar between people with vs. without malaria (46.8 vs. 47.6% of males [$p = 0.6$], respectively).

Compiling the information from each calendar year showed two peaks in the monthly incidence of malaria, one in July (5.5%) and another in October (6.0%). There were also two periods with nadir incidences, around March (1.4%) and September (2.6%) (Figure 1). The yearly incidence of positive blood films peaked in 2011 (6.1%), then decreased over time to a rate of 2.4%, recorded in the first half of 2014 (Figure 2). The evolution of monthly incidence of malaria over the years of study is shown in more detail in Figure 3.

Among the 825 diagnoses of malaria, 481 (58.3%) blood films were classified as *P. vivax* and 344 (41.7%) as *P. falciparum*. The dominance of *P. vivax* over *P. falciparum* did not change substantially over the months of each year or over the whole period of study.

Complicated malaria

Severe anemia was more common in patients with malaria compared to non-infected subjects (hemoglobin < 5 g/dL in 22.4% vs. 7.1% [$p < 0.001$]; hemoglobin < 8 g/dL in 45.3% vs. 17.0% [$p < 0.001$], respectively) (Table 1).

Within the group of patients with malaria, those with severe anemia (hemoglobin < 8 g/dL) were younger than less anemic patients (median 5 years [range 0.1–60] vs. 18 years [range 1–70]; $p < 0.01$) and were more likely to have *P. falciparum* (57.1% vs. 34.8%; $p < 0.001$), as opposed to *P. vivax* parasitemia. An analysis by age group showed that severe anemia was more common in children under five vs. those aged five or older (48.7% vs. 15.7%; $p < 0.001$), and also under 15 vs. 15 years or older (69.6% vs. 41.2%; $p < 0.001$; Table 2).

Interestingly, there was no difference between sexes in incidence of severe anemia in children with malaria under 10 years old (64.7% in boys and 64.9% in girls, $p = 0.9$). In patients aged 10 years or older, however, malaria with severe anemia was more common in women (34.5%) than in men (21.2%) ($p = 0.01$; Figure 4).

Table 1. Main characteristics of patients with blood films tested.

	With malaria	Without malaria	<i>p</i> value
No. of patients (%)	825 (3.79)	20,898 (96.2)	
Median age (range), years	12 (0.1–70)	18 (0.1–100)	< 0.001
Age (%)			
<5 years old	236 (29.6)	5610 (27.3)	0.2
<15 years old	429 (53.9)	9833 (47.9)	< 0.001
Male sex (%)	377 (46.8)	9818 (47.6)	0.6
Median (range) hemoglobin (g/dL)	8.35 (4.3–17.2)	11.91 (3.6–17.5)	< 0.001
Hemoglobin (%)			
<5 g/dL	114 (22.4)	656 (7.1)	< 0.001
<8 g/dL	231 (45.3)	1569 (17.0)	< 0.001

Figure 1. Aggregated monthly incidence of malaria per blood films tested.

Notes: Y' axis shows average precipitation in Ethiopia according to www.weather-and-climate-com (World Wide Travel Organisation). Addis Ababa Weather Station: latitude: 08–59 N, longitude: 038–48E, elevation: 2355 m.

Figure 2. Combined yearly incidence of malaria per blood film tested.

Figure 3. Monthly incidence of malaria per blood film tested over the period of study.

Table 2. Main characteristics of malaria episodes according to coexistence of severe anemia.

	Hemoglobin level		p value
	<8 g/dL	≥8 g/dL	
No. of patients	231 (45.3)	279 (54.7)	
Median (range) age, years	5.0 (0.1–60)	18.0 (1.0–70)	<0.01
Age (%)			
<5 years-old	109 (48.7)	43 (15.7)	<0.001
<15 years-old	156 (69.6)	113 (41.2)	<0.001
Male sex (%)	89 (38.9)	121 (44.0)	0.2
<i>P. falciparum</i> (%)	132 (57.1)	97 (34.8)	<0.001

Finally, in multivariate analysis, factors associated with malaria plus severe anemia were *P. falciparum* infection (adjusted odds ratio [OR] 2.48, 95% confidence interval [CI] 1.68, 3.65) and younger age (OR 1.06, 95% CI 1.04, 1.07). Being a woman (OR 1.43, 95% CI 0.96, 2.12) and being aged 15 years of age or older (OR 1.82, 95% CI 0.96, 3.45) were risk factors with a statistically borderline association (Table 3).

Discussion

This study found a low incidence of malaria (around 3.8% overall) among approximately 20,000 clinically suspected cases in a rural hospital in southern Ethiopia for an 8-year study period. The first observation to be made concerns the cost-effectiveness of malaria parasite staining, which is a time-consuming procedure [4]. Given the low malaria rate observed, use of rapid malaria tests for initial evaluation could be an alternative. Visual examination of blood films would still be needed to differentiate *Plasmodium* species and assess parasitemia levels.

In 2011, the government of Ethiopia set out a national plan to control malaria, based on better prevention, diagnosis and treatment of the disease [5]. Our study confirms a progressive reduction in incident malaria between 2011 (incidence of 6.1%) and 2014 (incidence

of 2.4%), which suggests this strategy may have been effective. The peak rate observed in 2011 may have been due to the unstable nature of malaria in Ethiopia, where cyclical outbreaks occur as a result of climate variations [6]. Still, the incidence figures observed in our series are significantly lower than those seen in other studies conducted in Ethiopia, which showed proportions of positive slides as high as 17–40% [7,8]. It should be noted that both of these studies were performed in areas of north-western Ethiopia where the low altitude (below 1000 m) facilitates malaria transmission to a greater extent than in the higher location of our site.

The monthly distribution of malaria cases was concentrated in two peaks, one around July and the other around October; this observation reflects an unstable pattern of *Plasmodium* transmission, which is closely related to the rainy seasons and higher temperatures, as previously described [9]. It is important to note that in the last three years of the study, variation between peak and nadir months decreased, reflecting the efficacy of prevention measures based on vector control.

Another aspect of interest is the similar relative frequency of *P. falciparum* and *P. vivax* infection observed in this study. Ethiopia is known to be one of the African countries with the largest proportion of *P. vivax* infection [10], which in recent years has become the main cause of malaria in areas where both types are endemic [11]. It seems that *P. falciparum* is usually more common in areas with bodies of water, such as lakes or dams [12]. In contrast, *P. vivax* prefers dryer areas at altitudes below 1800 m [13]. Although Gambo Hospital is located at an altitude of more than 2100 m, the catchment area expands over West Arsi province, and most of the population lives at around 1800 m. The frequent occurrence of *P. vivax* infection may be a double-edged sword. On the one hand, this malaria species causes milder disease than *P. falciparum* infection; on the other hand, *P. vivax*

Figure 4. Distribution of severe anemia in patients with malaria, by sex and age.

Table 3. Multivariate analysis.

Variables	Adjusted odds ratio (95% confidence intervals)
<i>P. falciparum</i>	2.48 (1.68–3.65)
Younger age (per year)	1.06 (1.04–1.07)
Female sex	1.43 (0.96–2.12)

Note: Risk of hemoglobin <8 g/dL in patients with malaria.

can evolve to relapsing malaria, potentially making it a more endemic infectious agent that poses a challenge to prevention strategies.

As might be expected, patients with malaria were younger and had lower hemoglobin levels compared to subjects without parasitemia. The frequency and severity of anemia in our series seems significantly higher than in other recent studies performed in Ethiopia [14,15]. The authors of those studies explain that this complication is closely related to access to care. In this respect, the location of Gambo hospital, kilometers away from rural areas where malaria is more prevalent, may explain our findings. More severe episodes of anemia among subjects with malaria occurred at younger ages and tended to be more common in women after puberty. Although we do not have information on the coexistence or history of pregnancy among observed patients, this factor may in part explain the latter finding.

Some limitations need to be acknowledged, such as the retrospective nature of the study and the lack of uniform criteria set for the definition of patients with malaria. Important information is missing, such as duration of symptoms, comorbidities (HIV infection, malnutrition, etc.), presence of pregnancy, area of residence, etc. Notwithstanding, the large number of patients observed provides a good picture of the burden and main complications related to malaria in southern Ethiopia. In addition, sampling bias may overestimate incidence of malaria, as this figure was calculated only in tested patients rather than in all individuals visited.

In conclusion, a reduction in incidence of malaria has been observed in southern Ethiopia in recent years, where *P. vivax* is slightly more common than *P. falciparum*. Younger age, *P. falciparum* infection and (close to significance) female sex in adults are associated with greater risk of severe anemia during the episode of malaria.

Disclosure statement

No potential conflict of interest was reported by the authors.

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