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Malaria pattern observed in the highland fringe of Butajira, Southern Ethiopia: a ten-year retrospective analysis from parasitological and metrological data

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Abstract

Background. Studying the magnitude of highland malaria is necessary to implement effective control measures in highland fringes of Ethiopia. Since repeated epidemics were reported in Butajira, this study hypothesized autochthonous transmission in the highland fringes of Butajira. Thus we aimed to determine the malaria occurrence and its association with meteorological variables in the highland fringe of Butajira, Southern Ethiopia from parasitological and metrological data.

Methods. Retrospective monthly malaria case data was collected from monthly outpatient morbidity reports of the Butajira Health Center, for January 2000 to December 2009. Monthly total rainfall and average temperature (maximum and minimum), which was recorded in Butajira weather station, was obtained from National Meteorological Agency, for the same period. Spearman correlation coefficient was used to quantify the strength of linear relationships between meteorological variables and malaria cases. The effect of each independent variable on malaria cases was assessed using multiple linear regression.

Results. During the study period, a fluctuating trend of malaria cases was observed with *Plasmodium vivax* (62.5%) dominancy. The highest occurrence of malaria was recorded in 2003, 2004, 2008 and 2009 and the least was recorded in 2000-2002. None of the meteorological variables was positively correlated with monthly malaria cases at zero months lag. However, minimum temperature was positively correlated with total malaria cases, *P. vivax* and *P. falciparum* with one month lag. Correlation analysis showed that all of the meteorological variables, except maximum temperature at one month lag, were not significant with total monthly malaria cases and each species of malaria (P-value >0.05) at zero and one month lag effect. Nevertheless, after adjusting for the effect of other variables the linear regression analysis indicated that cumulative monthly rainfall (Beta= -0.24; 95% CI: -0.47, -0.02) at zero months lag and maximum temperature (Beta= -12.13; 95% CI: -23.43, -0.82) at one month lag had a significant negative effect on the total malaria count.

Conclusion. There was no significant association between malaria occurrences and meteorological variables between January 2000 and December 2009; therefore non-climatic factors together with climatic variables should be assessed to know the spread and intensity of malaria in the highland fringe of Butajira. This report also warrants the Ministry of Health to include highland areas in its current malaria controlling campaign so as to address those non-endemic foci of the country.

1. Introduction

Malaria is thought to be the disease of antiquity in Ethiopia and its distribution is affected by altitude, topography and climatic factors [1]. The epidemiology of malaria at higher altitude, particularly above 1800 m above sea level, is unstable [2]. In these areas, transmission is highly seasonal and follows the end of both light rains (February to March) and heavy rains (June to September). In contrast, in humid lowland areas with suitable breeding sites transmission is usually perennial with slight seasonal variation in magnitude [3]. In general, the length of the transmission season is believed to progressively decrease with increasing altitude, and with no transmission at 2000 m above sea level though with few exceptions of epidemics [4].

The unstable nature of highland malaria has high potential for epidemics due to absence or low levels of immunity of people that reside at this altitude. However, this picture appears to be changing with evidence indicating increased stability of transmission in highland fringe areas of East Africa [5]. Meteorological and non-meteorological factors such as land use change, anti-malarial drug resistance, pop-

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ulation movement and degradation of health care infrastructure [6-10] are responsible for this apparent change in epidemiology.

Zones of unstable malaria, such as the East African highlands are more sensitive to climate variability [11, 12]. Temperature and precipitation in the highlands are expected to rise above the minimum temperature and precipitation thresholds of malaria transmission at cyclical patterns [13]. Rainfall peaks in East Africa correspond to El Niño southern oscillation (ENSO) years [13, 14]. For instance, the 1958 catastrophic malaria epidemic in Ethiopia was associated with unusually heavy and prolonged rains combined with abnormally high temperature and humidity [5].

The impact of climate as a driving force for malaria epidemics in the highlands of East Africa [10, 15, 16] is debated between two groups of scholars. According to Hay *et al.* [15] mean temperature and rainfall did not change significantly at four locations in their study sites where malaria incidence had been increasing. As a result they concluded that the recent increase in malaria in the East African highlands could not attributed to global warming. Instead, the increase in drug resistance was considered a more likely explanation for the observed increase in malaria. Similar studies in Kericho Tea plantations by Shanks *et al.* [17] and Omumbo *et al.* [18] in western Kenya supported the views of Hay *et al.* [15].

On the other hand, Zhou *et al.* [16] found a significant temperature increase in their study sites and concluded that the increased malaria epidemic in 1990s compared to those in 1980s in East African highland was linked with climate variability. They stressed the significance of concurrent analysis on the long-term time series of meteorological and parasitological data to determine the effect. Moreover, short-term variations around the mean climate state on a fine time scale could be epidemiologically more significant than mean temperature increase. According to Pascual *et al.* [19] a half-degree Celsius rise in temperature would increase mosquito numbers between 30% and 100% due to the effect of temperature on their developmental time. Although this increase had a marginal effect in lowland areas where mosquitoes are abundant, it is more likely to be affecting transmission rates highland areas, where the insects are much scarcer [19].

All of the four human malaria parasites species occur in Ethiopia. However, P. falciparum is dominant, accounting for 60% to 70% of the cases while 30-40% is attributable to *P. vivax*, which is rare in sub-Saharan Africa except Eritrea [39]. In recent years the prevalence of *P. vivax* exceeded *P. falciparum* in some parts of the country [30]. Because the nature of malaria in Ethiopia is unstable, the country experiences moderate to severe epidemics periodically [20]. Extensive epidemics showing similar but less pronounced characteristics of the 1958 epidemic occurred in many parts of Ethiopia in 1965, 1973 and 1981/1982 [2]. Epidemic with cyclical patterns of variable magnitudes were observed elsewhere in 1990, 1992, 1997, 1998, and 2002 [22]. Most of the epidemics in Ethiopia followed a period of exceptional meteorological conditions in which unusually high temperatures and humidities created conditions conducive to very high vector proliferation [20, 22].

Studying the magnitude of malaria prevalence in highland areas of different communities would be necessary to implement effective control measures in the highland fringes of Ethiopia. Because parasitological [25, 35] and entomological [25] studies conducted in the highland fringes of Butajira confirmed autochthonous transmission, this study aimed to determine trends in malaria and the correlation of monthly-observed malaria cases with metrological data.

2. Materials and Methods

2.1 Study area

This study was conducted in Butajira district which is located in the Gurage zone, Southern Nations, Nationalities, and People's Regional state (SNNPR). The District borders the Siliti zone to the south, the Mareko District to the east, the Muhur and Akillial District to the west and the Sodo District to the north. The estimated size of the district is 56,200 hectares and it lies at an average altitude of 1900 m above sea level, ranging from 1750 m above sea level in the lowlands to 3400 m above sea level in the mountains.

Annual rainfall in Butajira area ranges between 700-1870 mm. The peak over the last three decades was recorded in 2005. Although the main rainy season is from June to September, light rains are common around March and April. The warmest months are between January and June with a maximum temperature of 30.4 °C in March during the last ten years. During the last decade the annual mean maximum temperature was 26.3 °C and minimum mean temperature was 11.1 °C (National Meteorology Service Agency).

The population of the District is estimated to be 217,575. The district has 40 rural Kebeles (the smallest administrative unit in Ethiopia) and two towns from which Butajira town owned its administration power recently. During the data collection period the District had two hospitals (one private and one government-owned), 3 health centers, 32 functional health posts and 10 registered non-governmental health facilities. The District is characterised by seasonal malaria, with fluctuating annual numbers of malaria cases. A large peak in the number of malaria cases is seen from September to December, following heavy rainfall during June to August. This is followed by a second, less pronounced, peak in April and May. Between these two peaks transmission periods, the level of transmission is more or less constant and low [35].

2.2 National protocol of malaria parasite identification

In Ethiopia, blood film investigation for malaria parasite identification is conducted according to standard operating procedure of the country [21]. Before blood sample collection, the finger is cleaned with an alcohol-moistened swab, dried with a piece of dry cotton and punctured with a disposable blood lancet. After wiping off the first drop of blood, the thin and thick blood smears are prepared on the same slide to stain with 10% Giemsa solution for 20 minutes and then air-dried and the thin part fixed with methanol alcohol. The stained slide is examined under an oil immersion microscope for *Plasmodium* species by a certified laboratory technician/technologist. The thick smear is used to detect malaria parasites and parasite quantification, and the thin smear is used to identify the *Plasmodium* species.

2.3 Data collection

Data on malaria cases for the period of 2000-2009 were collected from monthly outpatient morbidity reports of the Butajira Health Center. This Center renders outpatient services mainly for patients that come from Butajira town and highland rural Kebeles, which are situated 2000 m above sea level. The Enseno health center located in Enseno town and Hamus Gebeya health center in a rural Kebele are situated in the lowland area of the district and provide out patient services for the lowland Kebeles. In order to avoid malaria cases from the lowland area and to focus on highlands of the district we used Butajira health center outpatient morbidity reports.

For the period of 2000-2009 monthly cumulative rainfall data and monthly average minimum and maximum temperatures recorded in the Butajira weather station were obtained from the National Meteorological Service Agency in Addis Ababa.

A well-prepared checklist was prepared to collect data on the status of malaria intervention activities and implementation of the new drug artemether/lumefantrine (Coartem) as first-line treatment of uncomplicated malaria and *P. falciparum* in the study area from Butajira District Health office. In addition, information on antimalarial drug resistance within the study area was obtained through Hinari and PubMed and through personal communications.

2.4 Data analysis

Data collected on malaria cases and metrological parameters (*i.e.* rainfall and temperature) over the ten years were managed and analysed using SPPS statistical software package version 16. Spearman correlation coefficient was used to quantify the strength of linear relationships between meteorological variables and malaria cases. The effect of each independent variable on the outcome variable was assessed using linear regressions. To assess the effect of meteorological variables without any lag and at one month lag on malaria cases the monthly malaria cases were considered as the dependent variables, while meteorological variables such as monthly maximum, minimum and mean temperature and total monthly rainfall were considered as independent variables. Metrological variables were included in multiple regression analysis regardless of their statistical significance in the correlation analysis.

2.5 Ethical considerations

Permission was obtained from Butajira Health Office to use the described retrospective malaria morbidity data. The metrological data was permitted and available from the National Meteorological Service Agency, Addis Ababa, Ethiopia.

3. Results

3.1 Malaria distribution pattern

Yearly outpatient morbidity reports of malaria cases treated in Butajira Health Center from 2000-2009 based on parasitological examination is summarized in Table 1. During this time, a total of 9196 microscopically confirmed malaria cases were treated in Butajira Health Center. The annual total malaria cases ranged from 3.1% in 2000 to 26.1% in 2009. Throughout the decade, a fluctuating trend of malaria cases was observed. There was statistically significant inter-annual variation of malaria cases in the study area ($P<0.001$). A decrease in malaria cases was observed from 2003 to 2007 and a notable increase was detected in 2008 and 2009 with peak cases occurring in 2009. Adults aged 15 years and above were more affected (52.3%) compared to the other age groups. Moreover, the proportion of children treated for malaria was 20.9% in the age range of 0-4 years and 26.8% in the age range of 5-14 years (Table 1).

If we combine malaria morbidity data over the ten years, *P. falciparum* accounted for 37.5% and *P. vivax* for 62.5% of cases. Examination of annual data shows the dominance of *P. vivax* over *P. falciparum* in each year except in 2000, 2002 and 2003. A remarkable increment of malaria cases in 2008 and 2009 resulted from *P. vivax* infections rather than *P. falciparum*. In the study area artemether/lumefantrine (Coartem) as first-line treatment for uncomplicated *P. falciparum* malaria was adopted in 2004 resulting in the out-

Table 1. Age and species stratified trend of the number and percentage (in brackets) of malaria positivity based on parasitological data from Butajira Health Center between 2000-2009.

Year	Malaria species		Age categories			
	P. falciparum	*P. vivax*	0-4	5-14	>15	Total
2000	130	153	47	84	152	283(3.1)
2001	178	160	73	89	176	338(3.7)
2002	152	93	62	65	118	245(2.7)
2003	1011	362	215	335	823	1373(14.9)
2004	436	749	257	275	653	1185(12.9)
2005	341	483	202	130	492	824(9.0)
2006	391	414	161	175	469	805(8.7)
2007	174	454	172	195	261	628(6.8)
2008	162	951	245	386	482	1113(12.1)
2009	474	1928	487	734	1181	2402(26.1)
Total	3449(37.5)*	5747(62.5)	1921(20.9)	2468(26.8)	4807(52.3)	9196(100)

** Percent total exceeded 100% in horizontal row because the same data is considered in malaria species and age categories.*

numbering of P. vivax over *P. falciparum* in the study area. Over the course of the study period inter-annual variation of *P. vivax* was significant (P<0.001) unlike that of *P. falciparum* (P<0.635; Table 1).

3.2 Monthly distribution of malaria cases in Butajira area, 2000- 2009

In the study area malaria was observed in almost every month of the year although there was significant (P<0.001) fluctuation in the number of malaria cases (Fig. 1). In most years the highest peak of malaria cases was observed during October whereas in 2003 and 2009 the highest number was detected in June.

3.3 Trends of meteorological parameters in Butajira area

Annual variation in total rainfall (P=0.389), minimum temperature (P=0.102), maximum temperature (P=0.185) and average temperature (P=0.801) were not significant. However, there was significance in the inter-monthly variation of maximum and average temperature over the 10-year period (P<0.001). The highest annual mean temperature of 19.1 °C was recorded in 2009 and the lowest annual mean temperature of 18.2 °C was recorded in 2005 and 2008. A slight fluctuating trend in temperature was observed during the study period. However, a high fluctuating trend of rainfall was recorded through the years 2000 to 2009 with maximum total rainfall of 1870 mm recorded in 2005 and minimum rainfall of 491.7 mm recorded in 2009 (Fig. 2).

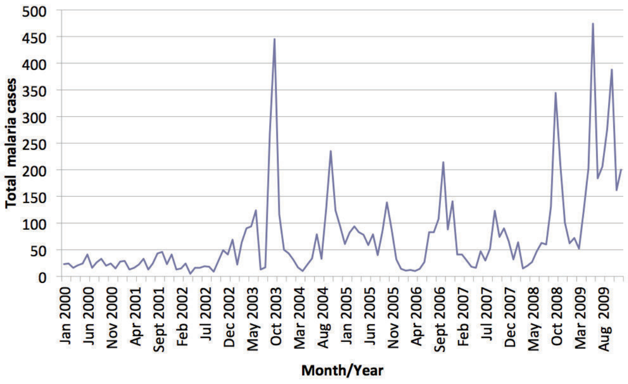

Figure 1. *Monthly distribution of microscopically confirmed malaria cases in Butajira area, 2000-2009. Malaria was observed in almost every month of the the year although there was substantial fluctuation over the different months of the years.*

3.4 Association between malaria cases and meteorological variables

Results from correlation analyses of monthly total malaria cases without lag and at one month lag with meteorological parameters is summarized in Table 2. To observe the relationship between monthly total and each species of malaria cases and meteorological measures (*i.e.* maximum temperature, minimum temperature, average temperature and total rainfall), at a zero months and at one month lag spearman's correlation and linear regression analysis were con-

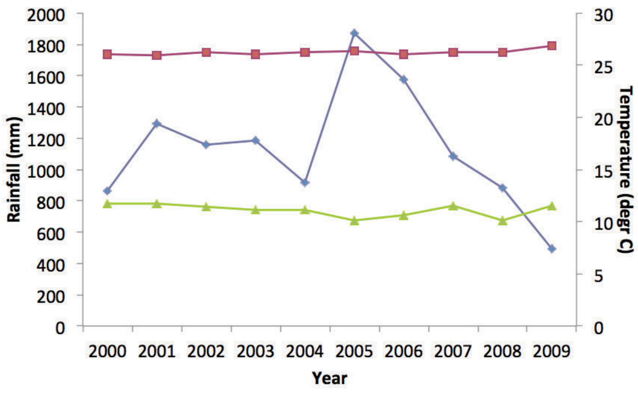

Figure 2. *Annual variations in meteorological indices for Butajira area, 2000-2009, showing high fluctuations in rainfall (blue) but little variation in minimum (green) and maximum (red) temperatures.*

Table 2. Concurrent and one month lag meteorological parameter association with total malaria and *Plasmodium* species in the Butajira area, 2000-2009.

		Concurrent association		Association of malaria case with one month lag metrological variables	
	Meteorological variables	Correlation coefficient	P. value	Correlation coefficient	P. value
Total monthly malaria	Maximum temp	-0.046	0.614	-0.147	0.109
	Minimum temp	-0.104	0.257	0.100	0.276
	Average temp	-0.109	0.236	-0.024	0.792
	Total rainfall	-0.176	0.054	-0.028	0.757
Monthly *P.vivax*	Maximum temp	-0.030	0.746	-0.082	0.376
	Minimum temp	-0.058	0.531	0.094	0.306
	Average temp	-0.061	0.509	0.016	0.859
	Total rainfall	-0.169	0.064	-0.082	0.372
Monthly *P.falciparum*	Maximum temp	-0.050	0.510	-0.182	0.047
	Minimum temp	-0.128	0.163	0.066	0.475
	Average temp	-0.132	0.150	-0.075	0.413
	Total Rainfall	-0.110	0.231	0.068	0.463

ducted. Correlation analysis using Spearman's correlation coefficient showed that all of the meteorological variables were negatively and non-significantly correlated with both malaria species and monthly total malaria cases at zero months. At one month lag, minimum temperature was positively correlated with both species and with total monthly malaria cases. There was a positive correlation between one month lag monthly total rainfall with *P. falciparum* and monthly average temperature and *P. vivax*. A non-significant negative correlation was observed between *P. falciparum* and maximum temperature at one month lag.

To observe independent effects of monthly cumulative rainfall, minimum and maximum temperature on monthly total malaria cases linear regression analysis was conducted. Results of simple linear regression analysis showed that there was no significant effect of minimum and maximum temperature on concurrent monthly total malaria cases. When all meteorological parameters were entered in a multiple linear regression model the only significant effects were those of cumulative rainfall with no lag (Beta= -0.24; 95% CI: -0.47, -0.02) and maximum temperature at one month lag (Beta= -12.13; 95% CI: -23.43, -0.82). However, the cumulative effect of rainfall, minimum temperature and maximum temperature on total malaria count were not significant at zero month effect (Adj R-squared= 0.0271, P= 0.1033) and at one month lag (Adj R-squared= 0.0283, P= 0.097).

4. Discussion

According to earlier studies reported [4], the upper limit of malaria transmission in Ethiopia was 2000 m above sea level, with few exceptions of frequent epidemics above this limit. Contrary to these earlier reports, recent parasitological and entomological investigations in the outskirts of Addis Ababa indicated autochthonous malaria transmission at an altitude of 2100 m above sea level [24]. The present study, which has documented information about malaria from the highland fringes of Butajira supplemented with recent studies in the same area [25, 35], have provided additional evidence for the existence of locally contracted malaria at high altitudes.

This study showed *P. vivax* to be the dominant species in the study area accounting for 62.5% of the cases. The higher occurrence of *P. vivax* in Butajira is consistent with earlier report of Melville *et al.* [4], which documented the predominance of *P. vivax* at altitudes higher than 1500 m above sea level. This is also in agreement with another report that showed *P. vivax* as the predominant species in towns and highland areas [26] as well as a recent study which reported the dominance of *P. vivax* using parasitological [25,35] and entomological data from the Butajira area [25]. The adoption of artemether/lumefantrine (Coartem®) as first-line treatment for *P. falciparum* malaria at national and local level and the spread of chloroquine-resistant *P. vivax* [36, 37] may be one possible reason for the dominance of *P. vivax* in the study area. There is evidence which shows that artemisinin combination therapies had less impact on vivax malaria [38]. The decrease in malaria cases between 2003 and 2007 in the study area coincided with the introduction of Coartem as first-line treatment in 2004.

The present retrospective data showed that 20.9% of malaria cases were reported in young children aged 0-4 years against 26.8% of cases reported from the 5-14 years cohort. These findings are also in agreement with a longitudinal study conducted in Butajira area, in which considerable numbers of cases were reported from children aged 0-4 [25]. These reports from parasitological data were confirmed by entomological surveys and the presence of suitable vectors in the area [25]. Moreover, as a stable community, the chance of mobility of these age groups is very unlikely and can be supportive to adequately explain the presence of *P. falciparum* in this area rather than suggesting these cases were imported from surrounding endemic areas.

In this study, malaria occurrence and rainfall variation in the study area over the last ten years was not significantly correlated with zero and one month lag. This is in agreement with a study done in the highlands of Bangladesh [27] in which there was no evidence for association between the number of malaria cases and rainfall. In Burundi, a negative effect was observed in time series analysis of monthly malaria incidences and rainfall in the same month [28]. However, in different parts of the world an underlying relationship between rainfall and malaria transmission is well recognized. For instance, significant and positive correlation was observed between monthly parasite incidences and rainfall in one month lag in India [29], Ethiopia [30], and China [31].

In 2008 and 2009 the annual rainfall was very low compared to the other years but high annual occurrence of malaria was observed in the study area. Although continuous and heavy rainfall disturbs mosquito breeding, however, as soon as the frequency and intensity of rainfall decrease, it is likely that numerous mosquito-breeding sites will be created [5]. On the other hand, when the number of rainy days in a specified period becomes few (and there is an intermittent rainfall) fast created pools become favourable breeding sites [22]. Malaria transmission is also common when the amount of rainfall is much below normal or if there is drought because water bodies such as streams and rivers will create small intermittent pools in the riverbeds, which are favourable for anopheline breeding. When such phenomena are coupled with high air temperature, unusual epidemics may occur in the highlands and/or highland fringe areas [22]. For instance, the droughts in Ethiopia, which occurred in 1958, 1965, 1973-1974 and 1983-1985 overlapped with malaria epidemics in these years [32].

In the current study minimum and maximum temperature were negatively correlated with Plasmodium species and monthly total malaria cases at zero month effect. This finding is in contrast to findings in India [29], China [31], and Kenya [16]. In this study each Plasmodium species and total monthly malaria cases is positively correlated with minimum temperature recorded during the previous month. This is in line with studies conducted in Burundi [28], India [29], Ethiopia [30], and China [31]. Minimum temperature was strongly associated with the occurrence of malaria cases in Rwanda [33] and Tanzania [34]. In contrast to this, our findings showed that there was no association between minimum temperature and monthly malaria cases in the study area, similar to the study conducted in Bangladesh highlands [27]. The lack of significant association between malaria cases and meteorological parameters in the study area indicates that malaria transmission was not predominantly affected by climatic factors over the last decade.

According to the information obtained from Butajira District Health office no systematic malaria control programme has been in place in Butajira town and the highland rural locality in recent years. Distribution of free insecticide treated bed nets (ITNs), indoor residual spraying (IRS) and other malaria control activities were only undertaken in the lowland localities of the district by considering Butajira town and the rural highland fringe localities free of malaria. Some elders interviewed in rural localities of the study area said that IRS was carried out in highland fringe area up to 2100 m above sea level at a time of Emperor Haile Selassie I by the malaria control office, which became integrated with the district health office. Like other parts of Ethiopia, artemether/lumefantrine (Coartem®) (AL) was implemented in 2004 due to the increased resistance of *P. falciparum*. However, chloroquine is still used at present for treatment of *P. vivax* infections in the study area because data on chloroquine resistance in *P. vivax* do not warrant a change.

In conclusion, this parasitological retrospective study from Butajira showed that the rise of malaria is not due to meteorological influences, at least for the period 2000-2009, but may be due to changes in agro-ecology, drug resistance, or absence of malaria control activities. This report warrants the Ministry of Health to include these non-endemic highland areas in its current malaria control campaign, for instance through the provision of insecticide-treated bednets.

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