

Seasonal prevalence of malaria, fever, anaemia and factors associated with malaria prevalence among children less than five in an area with prolonged malaria transmission in Ghana

Abstract

Background: Globally, malaria and anaemia are major causes of morbidity and mortality among children. As part of the millennium declaration, countries enjoined themselves to have halted and begun to reverse the incidence of malaria and other diseases by 2015. In 2006, Ghana started implementing malaria control strategies that involved free distribution of Long Lasting Insecticide Nets (LLINs), early detection and prompt appropriate treatment with Artemisinin-based combination therapies (ACTs). This study was set out to assess the prevalence of malaria, anaemia, ownership and use of LLINs at the end of the low transmission (pre-rainy season) and high transmission (post-rainy season) seasons in 2015. It also reported on factors associated with malaria prevalence in the Hohoe municipality of Ghana.

Methods: Two community-based cross-sectional surveys were undertaken among children less than five years in 30 communities. Information was collected on the background of the children, ownership and use of LLINs, history of fever and antimalarial drug used at home. Anthropometric indices and axillary temperature were measured, as well as blood film for malaria parasites and haemoglobin levels. Data analysis was done using z test to compare differences in proportions, t-test to compare differences in means and multiple linear regression to determine association between dependent and independent variables. **Results:** A total of 1915 and 1697 children were screened. The prevalence of malaria by RDT in the pre- and post-rainy seasons were 217 (11.3%) and 676 (39.8%) respectively, and using microscopy were 148 (7.7%) and 451(26.6%) respectively. Malaria parasitaemia prevalence was significantly lower in the pre- compared to post-rainy season (7.7% vs. 26.6%; $p<0.001$). Ownership of LLIN was high, however, similar in the pre- and post-rainy seasons (83.2% vs. 84.1%; $p=0.466$). Usage of LLIN was significantly lower in the pre- than the post-rainy season (68.3% vs. 72.8%; $p=0.003$). Anaemia ($Hb<8.0g/dl$) was significantly higher in the pre- compared to the post-rainy season (11.1% vs. 8.9% $p=0.028$). Gametocyte prevalence was similar in pre- and post-rainy seasons (0.4% vs. 0.3%, $p=0.677$) respectively. Malaria prevalence was found to be associated with fever (temperature $\geq 37.5^{\circ}C$) ($p=0.029$), and ACTs use for suspected malaria during the pre-rainy season ($p=0.027$). **Conclusion:** Gametocyte prevalence is an indication that malaria is transmitted throughout the year though highly seasonal. Treatment of suspected malaria with ACTs can reduce malaria prevalence. Overall, LLIN ownership and use was high but did not meet the millennium targets of 100% ownership and 85% usage. Our findings suggest that in the low transmission season, introduction of systematic detection and treatment of asymptomatic carriers and in the high transmission season, Seasonal Malaria Chemoprevention (SMC) together with the existing interventions could impact on malaria burden to such a level that elimination can be considered. Further studies are required to determine why lower usage of LLINs and higher prevalence of anaemia in the low transmission season.

Keywords: Malaria parasites prevalence, community, children under five, fever, anaemia, transmission season, Hohoe Municipality, Ghana.

Background

46
47 Malaria (fever with any parasitaemia) is a focal problem in Sub-Saharan Africa (SSA), and
48 for that matter Ghana. *Plasmodium falciparum* is one of the six species of plasmodium that
49 causes malaria in humans. This species causes the disease's most dangerous form, falciparum
50 malaria [1]. Rates of infection decreased from 2000 to 2015 by 37%, but increased from
51 2014's 198 million cases [2]. Since 2005, malaria control scale-up has progressed in many
52 African countries using Long Lasting Insecticide treated Nets (LLINs), indoor residual
53 spraying (IRS), intermittent preventive treatment during pregnancy (IPTp) and malaria case
54 management [3, 4].

55
56 A study conducted by Steketee and Campbell (5) indicated that several factors potentially
57 have contributed to recent health improvement in African countries, but there is substantial
58 evidence that achieving high malaria control intervention coverage, especially with LLINs
59 and targeted IRS, has been the leading contributor to reduced child mortality.

60 There have been large reductions in the number of malaria cases and deaths between 2000
61 and 2015 [6]. The number of malaria cases and deaths decreased globally from 262 million
62 and 839,000 respectively in 2000, to 214 million and 438,000 respectively in 2015 with most
63 (88%) of the cases in 2015 occurring in the African Region.

64 Studies have shown that introducing control measures leads to decline in malaria and
65 anaemia prevalence with time. [7] report drastic decline in malaria deaths and confirmed
66 malaria positive cases upon introduction of control measures. It was also found in Bioko
67 (Equatorial Guinea) that having introduced LLINs and Indoor Residual Spraying (IRS), the
68 prevalence of malaria infection was reduced from 40.0% in 2004 to 21.7% in 2005 [8]. The
69 study indicated packed cell volume (PCV) of 41.0% and 39.0%, respectively. According to
70 Goesch et al [9], there is a positive relationship between malaria and anaemia and LLIN use
71 and socioeconomic status. A report from Tanzania shows that LLIN ownership increased

72 from 22.5% in 2005 to 38.3% in 2008 and to 63.4% in 2010 while LLIN use by children
73 under five increased from 15.9% in 2005 to 24.8% in 2008 and to 63.9% in 2010 [10].

74

75 Malaria is endemic in Ghana with *Plasmodium falciparum* as the predominant species
76 causing the disease. Malaria has been a major cause of mortality and morbidity in Ghana,
77 especially among children under five years and pregnant women. It remains a public health
78 concern and a leading cause of poverty and low productivity. This is because in 2013, the
79 disease accounted for around 44% of all Out Patient Department (OPD) attendances and 59%
80 of admissions to hospital of children under five years [11].

81 The National Malaria Control Programme (NMCP) has increased coverage and usage of
82 available intervention tools over the past 10 years and indications are that the endemicity
83 levels could be reducing [12].

84

85 According to the WHO: World Malaria Report 2015 [6], Ghana reported 3,415,912
86 confirmed malaria cases with 2,200 deaths, which are however, less than those reported in
87 2013. The NMCP reported that malaria tops most OPD cases and kills 3 children every day in
88 Ghana [12]. The Ghana Demographic Health Survey (GDHS) has shown that malaria is still
89 hyper-endemic in Ghana with prevalence ranging from 11.2% to 40.0% [13]. The prevalence
90 is said to be highest among children living in rural (37.7%) than in urban (15%) areas [13].

91 The 2011 Multiple Indicator Cluster Survey (MICS) in children under five years has shown
92 endemicity ranging from hypoendemicity in the Greater Accra Region, hyperendemicity in
93 the Upper West Region and mesoendemicity in the rest of the country (14% in southern
94 coastal areas, 28% in forest, and 44% in northern and central Savannah) [12].

95 Ghana subscribed to the “Abuja accord of 2000”, that sought to achieve 60% coverage of
96 malaria interventions by 2010. This was to focus particularly on pregnant women and children
97 under five [14].

98

99 As part of the millennium declaration, various countries have enjoined to have halted and
100 reduced the incidence of malaria and other diseases by 2015. In order to achieve this target,
101 Ghana has implemented a malaria control strategy that involves multi and inter-sectoral
102 partnerships, working together to reduce illness and death due to malaria by 50%, increase
103 LLIN ownership to 80% and usage to 60% by 2010, and by 2015, 100% LLIN ownership and
104 85% usage [14]. These strategies include prevention through the use of Long Lasting
105 Insecticides Nets (LLINs), early detection and appropriate prompt treatment with Artemisinin-
106 based combination therapies (ACT’s). The other strategies include use of effective
107 chemoprophylaxis or intermittent preventive treatment (IPT) and indoor residual spraying
108 (IRS).

109

110 Two important Roll Back Malaria (RBM) indicators for monitoring progress towards the
111 target are the proportion of households which own one or more nets and the proportion of
112 under-five children who sleep inside a net. Net ownership is important to assess the
113 effectiveness of the distribution channels of the RBM programme and recommend programme
114 modifications. However, utilization is the crucial indicator that generates the desired
115 epidemiological impact.

116

117 Reports have shown that in Ghana, ownership of LLIN has increased substantially from 18%
118 in 2003 [15] to 78.5% in 2014 [13]. The use of LLIN among children under five has also
119 increased from 4% in 2003 [15] to 56.1% in 2014 [13]. It has also been shown that there is a

decline in malaria and anaemia prevalence in children over the last 10 years in the Hohoe municipality of Ghana. During the high transmission season in 2006 and 2010, anaemia reduced from 12.0% to 4.3% and malaria prevalence reduced from 40.4 to 33.6% respectively [16].

Statistics available indicate that in the Volta region, LLIN ownership was 76.3% in 2014. The percentage of children under five years who slept under LLIN increased from 40.4% in 2008 to 66.3% in 2014 [14,13]. The data also revealed that malaria prevalence among children less than five years using RDT and microscopy was 36.6% and 25.2% respectively whilst anaemia (Hb<8.0g/dl) was 8.4% [13]

Although reports have shown significant improvement in the reduction in malaria cases in Ghana with the introduction of these interventions, malaria and anaemia among children under five are still major health problems in the Hohoe municipality. According to the Hohoe Municipal Health Directorate (HMHD), malaria is still the leading cause of OPD attendance (28%) and the leading cause of deaths (19.4%) in the Hohoe municipality [17]. Out of 40,092 confirmed malaria cases at the Hohoe Municipal hospital (HMH) OPD in 2014, 3,452 (8.6%) were admitted and 1,452 (40.1%) of those admitted were children under five years [17]. In the light of this, this study was undertaken to examine the prevalence of malaria and anaemia as at 2015.

Materials and Methods

Study Area

The study was undertaken in Hohoe Municipality, which is one of the twenty-five administrative districts in the Volta Region of Ghana. The Municipality is located in the

central part of Volta region, with a population of 167,016 inhabitants. Hohoe, the Municipal capital has a population of 63,000 inhabitants [18]. The Municipality has two main seasons: wet and dry. The major wet season is from April to July and the minor one is from September to November. The rest of the year is relatively dry. Records from the Hohoe Municipal Meteorological Department (HMMD) indicate that, the climate is tropical with temperatures varying between 22°C and 37°C. The average annual rainfall in the municipality is 1,592mm with approximately 1,296mm of rain falling between April and October [19]. Malaria is hyper endemic in the study area, but with seasonal peaks. The entomological inoculation rate (EIR) for the study area was approximately 65 (95% CI: 0 - 143) infectious bites per person per year in 2008 [20]. Malaria transmission occurs throughout the year with seasonal peaks, coinciding with the period of the rains (high malaria transmission begins in June and ends in November).

Study Design

The design was cross-sectional, collecting data in the form of interviews and biological samples. The population for the study was all children in the selected communities aged 6 to 59 months who were eligible and their parents/guardians consented to participate (Figure 1). Cross sectional surveys of children aged under five years were carried out in June 2015, thus, the beginning of the high transmission season (pre-rainy season) and at the end of the high transmission season, thus, November 2015 (post-rainy season). It involved asking parents/guardians of the children questions and collecting finger prick blood from the children for laboratory investigations. During the surveys, temperature, weight, height and mid-upper-arm circumference were measured and a finger prick blood sample collected for determination of malaria parasitaemia and haemoglobin (Hb) levels. Information was also obtained on LLIN ownership and use. All children who tested positive for malaria infection

by RDT received a full course treatment with a recommended ACT for first line treatment for malaria). The data obtained in the pre-rainy season survey were compared with those of post-rainy season.

SELECTED COMMUNITIES IN THE HOHOE MUNICIPALITY

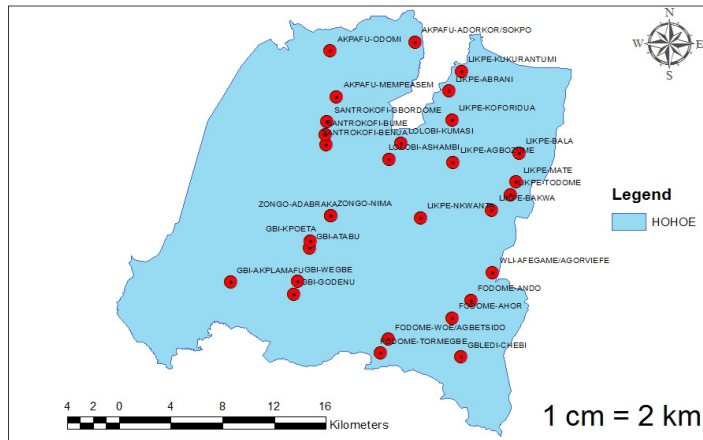


Figure 1: Selected communities for the survey in the Hohoe Municipality

Sampling and Sample Size Determination

Thirty communities were selected by one-stage cluster sampling from a sample frame of all communities in the municipality from the 2010 census (Figure 1). This sampling approach was used to ensure a fair representation of communities in the municipality. The sample size was estimated on the basis of the following: 95% confidence level (Z) and power of 80%, the prevalence (P) of malaria in children aged less than 5 years in June 2006 (end of dry season) as 8.6% [20]. The least acceptable prevalence of malaria was 5.0%. Using Open Epi software version 3 [21], the sample size calculated for each of the cross sectional surveys was 1,648 children aged less than 5 years [22]. However, all children whose parents/guardians reported

for the survey, consented and were willing to participate, were included. Therefore, a total 1,915 and 1,697 were included during the pre and post-rainy seasons respectively.

Laboratory Methods

Malaria Blood Films for Microscopy

Thick and thin blood films were prepared on a glass slide using 10 µL of blood, evenly spread to cover an area of 15 x 15mm of the slide. The smear was stained with 10% Giemsa for 10 minutes, and then examined under oil immersion with a light microscope (magnification x 100). The slides were double read by trained Microscopists. Asexual parasite densities were estimated by counting the number of parasites per 200 white blood cells (WBCs) in the thick film. Parasite counts were converted to parasites per microliter (µl), using relative WBC of 8000 leukocytes per µl of blood.

Similarly, gametocyte rate and density were determined by counting against 500 leukocytes and converted to parasites per microliter as for asexual parasites [23]. A sample was considered negative if no parasite was counted after 200 high power fields had been read. If there occurred discrepancies in the findings in a slide between the two initial technicians (positive or negative or a 50% or more difference in parasite density) a third, more senior microscopist reading was deemed necessary and then adopted. Two senior microscopists from the Noguchi Memorial Institute of Medical Research (NMIMR) and University of Health and Allied Science (UHAS), examined all the positive blood films including a 20% random sample of negative blood slides for quality control.

Haemoglobin and fever measurement

Haemoglobin was measured using URIT-12 Hemoglobin Meter (URIT Medical Electronic Co., Ltd. UK) whilst fever was measured using electronic thermometer (MODE: ZC, SURGILAC Digital Thermometer, UK).

Rapid Diagnostic Testing of Malaria in Human Blood

CareStart™ Malaria HRP2 test kit (Access Bio Inc, New Jersey, USA) was used for the rapid qualitative detection of Malaria Histidine-rich Protein 2 (HRP2) in human blood as an aid in the diagnosis of malaria infection. Using this kit, 5 µL of whole blood was introduced into the sample well with the aid of a pipette after finger pricking. Three drops of assay buffer were added to the buffer well. The result was read within 20 minutes.

Anthropometric Measurement

Children under one year were weighed naked while older children above one year were weighed with their pants on Seca weighing scales (Hamburg, Germany) to the nearest 10 grams. The length of children aged less than 24 months were measured using non-stretchable tape to the nearest mm and a locally made measuring board precise to 1 mm. Children aged 24 months or more had their height measured while standing using a locally made measuring board precise to 1 mm. Mid-Upper Arm Circumference (MUAC) was measured on the left arm to the nearest 1 mm using a non-stretchable tape.

Data management and statistical analyses

Data from participants were recorded on specified forms and were checked by field supervisors and a data manager for consistency and accuracy. All data were entered twice into a database using EPI Data software 3.1. The accuracy of data input was checked and

validated using customized validation programs. The cleaned data were converted to Stata version 12 file (Stata Corporation, Texas, USA) by a statistician, prior to analysis.

The primary study endpoints were the prevalence of malaria, fever (defined as axillary temperature $\geq 37.5^{\circ}\text{C}$) and anaemia (defined as an Hb <8.0 g/dl). Proportion of children with malaria parasitaemia, fever and anaemia in the pre-rainy season of 2015 were compared with that of the post-rainy season in the same year. Analysis of the primary and secondary data was carried out on an intention-to-treat basis (this implies that all children who were recruited and screened were included in the analysis). Proportions of data were analyzed using z test for two sample test of proportions. Differences in means were calculated using t-test. Multiple linear regression was used to determine the relationship between dependent variable (malaria parasitaemia) and independent variables (LLIN use, anaemia (Hb <8.0 g/dl), antimalarial drug use, fever (temp $\geq 37.5^{\circ}\text{C}$), history of fever within 48hrs and history of fever within one week). All analyses were done with STATA software version 12.0.

Ethical Issues

The study was approved by the Ethical Review Committee (ERC) of the Ministry of Health/Ghana Health Service, (MOH /GHS), ID NO: GHS-ERC: 14/05/15. Before the commencement of the study, permission was sought from the Municipal Health Management Team (MHMT) and the municipal administration. Permission was also sought from the chiefs and elders in the selected communities. A written informed consent was obtained from the parents/guardians of the children. All the information collected was treated confidentially and used for research purposes only.

Results

A total of one thousand nine hundred and fifteen (1,915) children aged 6 to 59 months were screened in the pre-rainy season and 1,697 in the post rainy season. The mean age of the children was 30.6 ± 15.6 and 30.8 ± 15.9 respectively (Table 1). Overall, mean age, height, weight and ownership of LLIN were similar in both groups. However, Mean Mid-Upper Arm Circumference (MUAC), and sleeping under LLIN the previous night were significantly higher in the post-rainy season compared to the pre-rainy season survey (Table 1).

Table 1: Background Characteristics of the Children

Variable	Pre-rainy season N (%)	Post-rainy season N (%)	p-value*
Number of children enrolled	1,915	1,697	
Age (in months) (mean, SE)	30.6 (15.6)	30.8 (15.9)	0.732 ^a
Weight (mean, SE)	11.8 (3.2)	11.6 (3.3)	0.065 ^a
Height (mean, SE)	84.8 (13.3)	84.3 (14.7)	0.294 ^a
Mid-Upper Arm Circumference (MUAC (mean, SE)	14.8 (1.1)	15.3 (1.7)	<0.001 ^a
Own LLIN	1593 (83.2)	1,427 (84.1)	0.466*
Slept under LLIN last night	1,307 (68.3)	1,235 (72.8)	0.003*

*z=statistics for two proportions ^at test for comparing two means

Prevalence of Malaria

The prevalence of malaria in children age 6-59 months was 11.3% in the pre-rainy season and 39.8% in the post-rainy season as indicated by RDT, and 7.7% and 26.6% respectively using microscopy (Table 2). Gametocytaemia prevalence was slightly higher in the pre-rainy season (0.4%) compared to post-rainy season (0.3%). Proportion of children with high density (>7000 parasites/ μ l) malaria parasitaemia was significantly lower in the pre-rainy season (2.3%) compared to the post-rainy season (4.2%) ($p < 0.001$). All positive thin film blood slides showed only *P. falciparum*.

275

276 **Prevalence of fever and antimalarial drug use**

277 Overall, fever (temperature $\geq 37.5^{\circ}\text{C}$) prevalence among the children was similar in both pre-
 278 rainy and post-rainy seasons (2.6%) and (2.6%) respectively (Table 2). History of fever
 279 within 48 hours was significantly lower (27.4%) in the pre-rainy season compared to 47.4% in
 280 the post-rainy season ($p < 0.001$). The prevalence of history of fever during the one week
 281 preceding the survey differed by season (pre-rainy season (40.1%) and post-rainy season
 282 (56.9%) (Table 2). One in three during the pre-rainy season (13.3% out of 40.1%) and one in
 283 four during the post rainy season (14.7% out of 56.9%) of children with fever took
 284 antimalarial drugs (ACT) (Table 2).

285 **Prevalence of low Haemoglobin Level**

286 During the pre-rainy season, proportion of children with $\text{Hb} < 8.0 \text{ g/dl}$ was significantly higher
 287 (11.1%) than in the post-rainy season (8.9%) ($p = 0.028$) (Table 2). Overall, during the pre-
 288 rainy season only 29.8% of children had normal haemoglobin levels compared to 39.2%
 289 during the post-rainy season and majority suffered from some degree of anaemia. The
 290 difference was statistically significant ($p < 0.001$). Mild Anaemia ($\text{Hb} = 8.0\text{-}10.9 \text{ g/dl}$) was
 291 significantly higher in the pre-rainy season than post-rainy season (59.1% vs 51.9%;
 292 $p < 0.001$). Moderate anaemia ($\text{Hb} = 5.1\text{-}7.9 \text{ g/dl}$) and severe anaemia ($\text{Hb} \leq 5.0 \text{ g/dl}$) though
 293 slightly higher in the pre-rainy season were not significantly different (10.1% vs 8.5%;
 294 $p = 102$) and (0.5% vs 0.2%; $p = 0.131$) respectively (Table 2).

295

296 **Table 2. Prevalence of malaria parasitaemia, fever and anaemia in the seasons**

Variable	Pre-rainy season n (%)	Post-rainy season n (%)	z*	p-value
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Number of children enrolled	1915	1697		
Malaria prevalence				
Proportion with any Parasitaemia by RDT	217 (11.3)	676 (39.8)	-19.85 (-0.31;0.26)	<0.001
Proportion with any Parasitaemia by microscopy	148 (7.7)	451(26.6)	-15.63 (-21.68;-16.88)	<0.001
Mean malaria parasites density (SD)	1078.2 (8408.3)	1877.6 (11213.8)	-3.31 (-3.09; -0.77)	0.015
Malaria with high density (>7000 parasites/ul)	43 (2.2)	71 (4.2)	0.42 (-0.29;0.45)	<0.001
Mean high density parasitaemia	43710.7(36106.4)	38415.8 (0231.7)	-	<0.001**
Gametocyaemia	7(0.4)	5(0.3)	2.19 (0.25; 4.15)	0.677
Fever and history of fever prevalence				
Fever (Temp>=37.5°C)	50 (2.6)	44 (2.6)	0.04 (-1.02;1.06)	0.970
Fever within the past 3-7days	243 (12.7)	161 (9.5)	-0.45 (-3.07; 1.93)	0.655
Fever within 48hrs	525 (27.4)	805 (47.4)	-12.45 (-23.12;-6.92)	<0.001
History of fever within the past one week	768 (40.1)	966 (56.9)	-10.10 (-20.04;-13.60)	<0.001
Anaemia and haemoglobin (Hb) levels				
Anaemia (Hb<8.0 g/dl)	212 (11.1)	151 (8.9)	2.19 (0.00; 0.04)	0.028
Normal (Hb ≥11.0g/dl)	571 (29.8)	665 (39.2)	-5.92 (-0.12- 0.06)	<0.001
Mild Anaemia (Hb 8.0-10.9 g/dl)	1132 (59.1)	881 (51.9)	3.23 (0.03;0.12)	=0.001
Moderate anaemia (Hb 5.1-7.9 g/dl)	194 (10.1)	145 (8.5)	1.64 (-0.00-0.035)	0.102
Severe Anaemia (Hb ≤5.0 g/dl)	9 (0.5)	3 (0.2)	1.51 (-0.00-0.01)	0.131
Mean Haemoglobin (SD)	9.97 (1.67)	10.36 (1.74)	-	<0.001**
Antimalarial drug use at home				
Antimalarial drug use within the past one week	254 (13.3)	250 (14.7)	-0.45 (-0.07;0.05)	0.210

297 *z=test for proportions in two populations; **p-values from t test comparing two means.

298

299 **Factors influencing malaria, fever and anaemia prevalence**

During the pre-rainy season, fever, LLIN use, antimalarial drug use, history of fever within 48hrs and one week were found to have a relationship with malaria prevalence. Fever and Antimalarial drug use at home were strongly associated with malaria prevalence at the time of the survey ($p=0.029$), ($p=0.027$) respectively. There were insignificant relationships between LLIN use, anaemia, history of fever within 48hrs, history of fever within one week and malaria prevalence during the pre-rainy season ($p=0.453$), ($p=0.239$) and ($p=0.065$) and ($p=0.981$) respectively (Table 3). There were insignificant relationships between malaria prevalence and fever, LLIN use, anaemia, antimalarial drug use, history of fever within 48hrs and history of fever within one week during the post-rainy season ($p=0.563$) ($p=0.200$), ($p=0.715$), ($p=0.562$) ($p=0.757$) and ($p=0.200$) respectively (Table 3).

Table 3: Factors influencing malaria parasitaemia prevalence (Multiple linear regression)

	Pre-rainy season survey					Post-rainy season survey				
Variable	Coefficient	SE	T	95% CI	p-value	Coefficient	SE	t	95% CI	p-value
Fever (temp $\geq 37.5^{\circ}\text{C}$)	260.43	114.93	2.27	(28.65;492.20)	0.029	-103.70	177.54	-0.58	(-463.4;256.0)	0.563
Use LLIN	122.31	161.64	0.76	(-203.67;48.28)	0.453	83.02	63.59	1.31	(-45.8;211.9)	0.200
Anaemia (Hb<8.0g/dl)	302.94	253.73	1.19	(-208.75;14.64)	0.239	111.20	302.61	0.37	(-501.9;724.3)	0.715
Antimalarial drug use	574.05	250.32	2.29	(69.24;1078.87)	0.027	193.34	330.48	0.59	(-476.3;862.9)	0.562
History fever within 48hrs	-360.62	190.10	-1.90	(-743.99;22.76)	0.065	92.40	296.54	0.31	(-508.5;693.3)	0.757
History of	4.41	184.	0.0	(-)	0.98	150.6	233.1	0.65	(-321.8;	0.20

fever within one week		50	2	367.67;76.49)	1	1	5		623.0)	0
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Discussions

This study has shown that the parasitaemia prevalence rate among children was higher in the post-rainy season than the pre-rainy season. Among the children screened in the pre-rainy and post-rainy seasons, it was (11.3% vs. 39.8%) respectively by RDT and (7.7% vs. 26.6%; $p<0.001$) by microscopy respectively.

High density (>7000 parasites/ μ l) malaria parasitaemia was also significantly lower in the pre-rainy season than in the post-rainy season (2.3% vs. 4.2%; ($p=0.001$). Though ownership of LLIN was similar in the pre-rainy season and post-rainy season (83.2% vs. 84.1%; $p= 0.466$), usage was significantly lower in the pre-rainy season compared to the post-rainy season (68.3% vs. 72.8%; $p=0.003$). Anaemia ($Hb<8.0g/dl$) was significantly higher in the pre-rainy season compared to the post-rainy season (11.1% vs. 8.9% $p=0.028$). Malaria prevalence was found to be associated with fever ($Temp\geq 37.5^{\circ}C$) and antimalarial drugs (ACTs) use at home during the pre-rainy season ($p=0.029$) and ($p=0.027$) respectively.

Parasitaemia prevalence among children screened in the post-rainy season was 39.8% using RDT and 26.6% using microscopy. These findings agree with results of studies conducted in some other communities by GDHS in 2014 which report 36.6% prevalence of malaria by RDT and 25.2% by microscopy. A possible reason for the higher malaria prevalence based on RDT than microscopy could be that the antigens might still be present in the child's blood after the parasites have disappeared [24, 25]. However, the observation that RDT seems to be more sensitive than microscopy is not surprising as RDTs can detect malaria parasites at 200 parasites per microliter at which microscopy cannot [24].

The parasite prevalence was significantly higher during the post-rainy season (26.6%) than the pre-rainy season (7.7%). It implies that even though malaria transmission occurred throughout the year, it showed marked seasonality. It was found in this study that less than 1% of all children surveyed had gametocytes. However, gametocytes presence in the two seasons was an indication that there were carrier reservoirs in the communities throughout the year. The malaria pattern in the Hohoe municipality signifies a possibility of introducing new interventions such as systematic detection and treatment of asymptomatic carriers with ACTs in the low transmission and use of seasonal malaria chemoprevention (SMC) in the high transmission season to further reduce the burden of malaria among children under five years.

Anaemia (Hb<8.0g/dl) in this current study was 11.1% in the pre-rainy season and 8.9% in the post-rainy season. Overall anaemia (Hb<11.0g/dl) during the pre- and post-rainy seasons, 70.2% and 60.8% respectively. This is slightly higher than what was reported by GDHS (2014) for Volta Region 8.4% [13]. It has been shown that anaemia can occur in the presence of low nutritional status (as a result of lack of access to food containing iron and folic acid) [26]. The higher rate of anaemia during the pre-rainy in our study could be as a result of lack of access to food containing iron and folic acid during the pre-rainy season.

It has been shown that malaria incidence positively correlates with anaemia [27]. Therefore, with the higher prevalence of malaria in the post-rainy season, a higher rate of anaemic children should be expected. However, our findings showed a lower rate of anaemia during the post-rainy season compared to pre-rainy season (8.9% vs. 11.1%). This could be as a result of better nutritional status in the post-rainy season (better access to food containing iron and folic acid).

LLIN ownership among children screened in the pre- and post-rainy seasons were similar (83.2% vs. 84.1). This is higher than findings reported by the Ghana demographic health

survey [13], where in the Volta Region of Ghana, ownership of LLIN was 76.3% and ‘use’ was 66.3% among children under five years. Studies have shown increased in ownership and use of LLINs after mass distribution. In Cameroon LLIN ownership in 2013 increased from 41.9% to 68.1% following the free distribution campaign, with 58.3% reportedly sleeping under the net [28]. The higher coverage in our study could be as a result of another mass LLIN distribution in the municipality by the HMHD in 2015. Usage was significantly lower in the pre-rainy season compared to the post-rainy season (68.3% vs. 72.8%) respectively. We observed better usage during the post-rainy season probably because during the rainy season people would want to avoid mosquitoes since they become abundant and also use LLIN to protect themselves against the cold weather due to rains. This finding in our study could be supported by a study conducted by Kunche in 2010 (unpublished) in the study area which found that reasons for non-use of LLIN included absence of mosquitoes (41.5%), LLIN generates heat (17.9%) and hinders comfort (39.0%).

The use of ACTs for prompt treatment and promotion of home management of malaria could clear parasites and improve Hb. Our study found that ACTs usage was slightly lower in pre-compared to post-rainy season (13.3% vs. 14.7%). Higher usage of LLINs and ACTs could be due to the fact that, during the rainy season individuals in malaria endemic areas tend to be more conscious of malaria, thus complying with preventive measures such as LLIN use and prompt treatment. These could explain why the findings from this current study showed an improvement in anaemia levels in the post-rainy season than the pre-rainy season.

This study however, associated malaria prevalence with other factors such as fever ($\text{Temp} \geq 37.5^{\circ}\text{C}$), history of fever within 48 hours and prompt treatment of suspected malaria with antimalarial drugs (ACTs). Thus, although LLIN use plays a key etiologic role in

malaria prevention in endemic countries, it is clear that other factors such as prompt treatment of children with ACTs by parents at home make important additional contributions.

Limitations of the study

This was a cross-sectional survey at one point of the pre-rainy and post-rainy seasons and not a cohort study that can determine malaria incidence throughout the wet and dry seasons. Information on LLIN ownership and use was obtained from parents of the children without observation to confirm the availability and use.

Conclusions and Recommendations

Malaria is transmitted throughout the year in the Hohoe municipality but with seasonal peaks. Malaria and anaemia prevalence are still high though significant reductions have occurred over the past ten years since the introduction of malaria control measures in the Hohoe municipality. Prompt treatment of suspected malaria cases with ACTs at home has contributed to the reduction of malaria prevalence. Though not all fevers are due to malaria, fever still signifies probable malaria infection. The malaria pattern in the Hohoe municipality signifies that additional interventions in the low transmission and high transmission seasons could impact positively on malaria burden. Efforts by the Hohoe Municipal Health Directorate (HMHD) have significantly increased LLIN ownership and this has actually translated into high LLIN usage. However, the targets set for 2015 were not achieved.

In addition to promoting LLIN ownership and usage, and prompt treatment of malaria with ACTs, we recommend that other approaches including systematic detection and treatment of asymptomatic carriers, SMC and vector control through the use of insecticide paints be encouraged in order to reduce malaria prevalence to such a level that malaria elimination can be considered. In order to improve nutrition in children in general, the HMHD should intensify in

their programmes educating mothers on recommended feeding practices during illness and otherwise.

Further studies are required to determine why LLIN usage is lower and anaemia is higher in the low transmission season. There is also the need to determine the strength of association between malaria prevalence and independent variables

List of abbreviations

RDT, Rapid Diagnostic Test; HTS, High Transmission Season; LTS, Low Transmission Season; LLIN, Long Lasting Insecticide Net ; BMI, Body Mass Index; GDHS, Ghana Demographic Health Survey; GHS-ERC, Ghana Health Service Ethical Review Committee; HRP2; Histidine Rich Protein 2; WBCs, White Blood Cells; ACT, Artemisinin-based Combination Therapy; SMC, Seasonal Malaria Chemoprevention; WHO, World Health Organization; NMCP, National Malaria Control Programme; MICS, Multiple Indicator Cluster Survey; OPD, Out Patient Department.

Declarations

Ethics and consent statement

Ethical clearance was obtained from the Ghana Health Service Ethical Review Committee (GHS-ERC) with the approval identity (GHS-ERC; 14/05/15). Permission was also sought from the chiefs and elders of the communities. Moreover, the parents/guardians of the children consented to be part of the study.

Consent for publication

Written informed consent was obtained from the study participants for publication of this research work. A copy of this form is available for review by the Editor of this journal.

432 **Availability of data and material**

433 Available upon request

434 **References**

- 435 1. Perkins DJ, Were T, Davenport GC, Kempaiah P, Hittner JB, Ong'Echa, JM. Severe
436 malarial anemia: Innate immunity and pathogenesis. *International Journal of Biological*
437 *Sciences*. 2011; 7 (9): 1427–1442. doi:10.7150/ijbs.7.1427. PMC 3221949. PMID
438 22110393.
- 439 2. WHO (2014). *World Malaria Report 2014*. Geneva, Switzerland: World Health Organization.
440 pp. 32–42. ISBN 978-92-4156483-0
- 441 3. Roll Back Malaria Partnership: *Global Malaria Action Plan*. Geneva 2008.
- 442 4. Lengeler C: Insecticide-treated bed nets for preventing malaria. *The Cochrane Library*
443 2007, 3.
- 444 5. Steketee RW, Campbell CC. Impact of national malaria control scale-up programmes in
445 Africa: magnitude and attribution of effects. *Malaria Journal* 2010; 9:299.
- 446 6. WHO: *World Malaria Report 2015*, Switzerland, Geneva. Retrieved from
447 http://apps.who.int/iris/bitstream/10665/200018/1/9789241565158_eng.pdf. Accessed 16
448 Mar 2016.
- 449 7. Delacollete C, D' Souza C, Christophel E, Thimasaran K, Abdur R, Bell D, Dai TC,
450 Gopinath D, Lus, Mendoza R, Ortega L, Rastogi R, Tantinimitkul C, Ehrenberg J.
451 Malaria trends and Challenges in the Greater Mekoy Subregion. *Southeast African*
452 *Journal Tropical Medicine Public Health*. 2009; 40(4) 674 – 91.
- 453 8. Pardo G, Descalzo MA, Molina L, Custodio E, Lwanga M, Mangue C, ObonoJ, Nchama
454 A, Roche J, Benito A, Cano J. Impact of Different Strategies to Control *Plasmodium*
455 *Infection and Anaemia* on the Island of Bioko (Equitorial Guinea). *Malaria Journal*.
- 456 9. Goesch JN, Schwarz NG, Decker M-L, Oyakhrome S, Borchert LB, Kombila UD,
457 Poetschke M, Lell B, Issifou S, Kremsner PG, & Grobusch MP. Socio-economic status is
458 inversely related to bed net use in Gabon. *Malaria Journal*. 2008; 7:60.
- 459 10. Telemu K. Prevention and management of malaria in under-five children in Tanzania: a
460 review. *Tanzania journal of Health Research*. Volume 4, number 3, July, 2012.
- 461 11. Singleton G, Osei M. GHANA MALARIA PREVENTION . *Annual Review*. 2014(August).
- 462 12. NMCP: National Malaria Control Programme, Ghana 2016, Ghana. Retrieved from
463 <http://www.ghanhealthservice.org/malaria/>. Accessed 16 Mar 2016.
- 464 13. Ghana Demographic and Health Survey, (2014).
- 465 14. Ghana Demographic and Health Survey, (2008).
- 466 15. Ghana Demographic and Health Survey, (2003).
- 467 16. Kweku M, Appiah EK, Takramah W, Enuameh Y, Norman I, Binka F. Effect of a
468 Malaria Control Program on the Prevalence of Malaria, Fever and Anaemia in Children
469 under Five Years in the Hohoe Municipality of Ghana: A Comparative Analysis of Cross-
470 Sectional Surveys. *Advances In Infectious Diseases*. 2015; 5, 180-188.
- 471 17. Hohoe municipal hospital annual report (2014).
- 472 18. Ghana Statistical Service (GSS), (2012)
- 473 19. Hohoe Municipal Meteorological Department (HMMD) report, (2006)
- 474 20. Kweku M, Liu D, Adjuk M, Binka F, Seidu M, Greenwood B, Chandramohan D. (2008)
475 Seasonal intermittent preventive treatment for the prevention of anaemia and malaria in
476 Ghanaian children: a randomized, placebo controlled trial. *PLoS One* 3: e4000.
- 477

- 478 21. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for
479 Public Health, Version. www.OpenEpi.com, updated 2013/04/06, accessed 2016/10/12.
- 480 22. Fleiss JL, Statistical Methods for Rates and Proportions, formulas 3.18 & 3.19.
- 481 23. Drakeley CJ, Jawara M, Targett GAT, Walraven G, Obisike U, Coleman R, Pinder M,
482 Sutherland CJ,. Addition of artesunate to chloroquine for treatment of Plasmodium
483 falciparum malaria in Gambian children causes a significant but short-lived reduction in
484 infectiousness for mosquitoes. *Trop. Med. Int. Health.* 2004; 9, 53–61.
- 485 24. Faye B, Nath-Chowdhury M, Tine RC, Ndiaye JL et al.: Accuracy of HRP2 RDT
486 (Malaria Antigen P.f®) compared to microscopy and PCR for malaria diagnosis in
487 Senegal. *Pathog. Glob. Health.* 2013, 107:273-278.
- 488 25. Dinko B, Ayivor-Djanie R, Abugri J, Agboli E, Kye-Duodu G, Tagboto S, Tampuori J,
489 Adzaku F, Binka FN, Awandare GA. Comparison of malaria diagnostic methods in four
490 hospitals in the Volta region of Ghana. *Malaria World Journal* 2016; 7:5
- 491 26. de Mast Q1, Brouwers J, Syafruddin D3, Bousema T4, Baidjoe AY5, de Groot PG2, van
492 der Ven AJ6, Fijnheer R. Is asymptomatic malaria really asymptomatic? Hematological,
493 vascular and inflammatory effects of asymptomatic malaria parasitemia. *J Infect.* 2015
494 Nov;71(5):587-96. doi: 10.1016/j.jinf.2015.08.005. Epub 2015 Aug 21.
- 495 27. Owusu-Agyei S, Fryauff DJ, Chandramohan D, Koram KA, Binka FN, Nkrumah FK, Utz
496 GC, Hoffman SL. Characteristics of severe anemia and its association with malaria in
497 young children of the Kassena-Nankana District of northern Ghana. *Am J Trop Med Hyg.*
498 2002 Oct; 67(4):371-7.
- 499 28. Tobias O. Apinjoh, Judith K. Anchang-Kimbi, Regina N. Mugri, Delphine A. Tangoh,
500 Robert V. Nyingchu, Hanesh F. Chi, Rolland B. Tata, Charles Njumkeng, Clarisse Njua-
501 Yafi, Eric A. Achidi. The Effect of Insecticide Treated Nets (LLINs) on Plasmodium
502 falciparum Infection in Rural and Semi-Urban Communities in the South West Region of
503 Cameroon. *PLOS ONE* 2015; 10.1371.