

Original Article

Malaria and associated co-morbidity in children admitted with fever manifestation in Western Ghana: A retrospective study

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Abstract

Introduction: Children under five years of age are highly vulnerable to malaria infection and often face dire consequences such as severe malaria if they are not promptly and adequately treated with effective anti-malarial medications. We set out to evaluate malaria and associated co-morbidity among children admitted with febrile illness in Sekondi-Takoradi, Ghana.

Methodology: This retrospective study focused on children admitted with fever over a three-year period at the pediatric unit of Effia-Nkwanta Regional Hospital. The children were identified, and the medical records of those who were successfully treated and discharged were searched, retrieved, and reviewed.

Results: A total of 1,193 children were identified and selected for analysis. The mean duration of admission increased from 2.17 days in 2010 to 3.36 in 2012. Conversely, the mean age decreased from 3.85 years in 2010 to 2.74 in 2012. Overall, laboratory-confirmed malaria prevalence decreased; however, this decrease was only observed among children five years of age or younger, while malaria prevalence increased among children one year of age or younger. The proportion of children with severe malarial anemia significantly increased, while the proportion of those with mild malaria decreased significantly.

Conclusions: Despite the general decrease in malaria morbidity seen in this study, children younger than one year of age remain at increased risk of malaria morbidity. With an increase in malaria prevalence among children younger than one year of age over the three years of study, integrated and targeted control measures are highly needed for this age group.

Key words: malaria; anemia; children; febrile; retrospective; Ghana.

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Introduction

Malaria is a serious public health concern in sub-Saharan Africa. People who reside in malaria-endemic regions are at increased risk of infection, especially children and pregnant women [1,2]. However, children under five years of age are highly vulnerable to malaria infection and face dire consequences such as severe malaria if they are not promptly and adequately treated with effective anti-malarial medications [3,4]. As part of achieving the millennium developmental goal of reducing the mortality of children under five

years of age, the World Health Organization (WHO) recommended a three-point approach: (1) the use of insecticide-treated bed nets; (2) prompt and effective treatment of clinical cases of malaria, and; (3) intermittent preventive treatment in pregnant women [5]. These approaches have been widely implemented in several malaria-endemic areas. Over the years, WHO reports indicated a major global reduction in malaria cases due to control efforts [6,7]. These control programs have facilitated the reduction of childhood malaria morbidity and mortality in most

parts of sub-Saharan Africa. In 2013, the WHO World Malaria Report estimated that malaria mortality rates fell by 42% in all age groups, as well as by 48% in children under five years of age [7]. Though the progress made may be grossly uneven in major endemic regions, some regions have made more significant progress than others [8].

In Ghana, malaria accounts for an average of 13.2% of all mortality cases and 22% of all mortalities in children under five years of age [3]. Recently, cases of inpatient malaria deaths dropped nationally, from 3,259 in 2011 to 2,815 in 2012. Malaria deaths among children under five years of age declined, from 1,539 in 2011 to 1,129 in 2012, and also declined in pregnant women, from 918 in 2011 to 476 in 2012, indicating a declining prevalence rate [9].

Anemia in children is an important cause of childhood morbidity and mortality. It accounts for half of malaria deaths among young children in sub-Saharan Africa [10]. Anemia in children with malaria may require blood transfusion and has been associated with high mortality rates [11]. Recently, malaria parasitemia was associated with anemia and its severity in rural Ghanaian children [12]. Anemia has been reported in about 76% of Ghanaian children under five years of age [13], as well as in 73% of Ghanaian children between the ages of two and ten years [14]. Although anemia etiology is multifactorial and context-dependent, it can include malaria, iron deficiency, intestinal parasites, foliate deficiency, malnutrition, sickle cell anemia, and human immunodeficiency virus (HIV) [15,16]. In sub-Saharan Africa, malaria remains a major contributor to anemia [17].

Several initiatives have been undertaken in Ghana through the Roll Back Malaria (RBM) partnership, Global Fund, and the efforts of the Ghanaian National Malaria Control Program. The key aim is to reduce malaria morbidity and mortality by half and to further reduce morbidity and mortality until malaria ceases to be a public health problem. Some progress has been made in improving access to prompt and effective treatment, supply of insecticide-treated nets (ITNs), and the use of intermittent preventive treatment with sulphadoxine-pyrimethamine (SP) in pregnancy (IPTp). With the recent decline in malaria prevalence observed, it is important to conduct more studies at regional and district levels of the country to assess the effectiveness of these control programs. Thus, in this retrospective study, we evaluated malaria and associated co-morbidity among children admitted with

febrile illness to a secondary health facility over a three-year period in Sekondi-Takoradi, Ghana.

Methodology

Study area

Effia-Nkwanta Regional Hospital is a secondary healthcare institution and is the only referral hospital for the whole Western Region, located in the south part of Ghana, in the Sekondi-Takoradi metropolis. It serves all other hospitals within the entire 22 districts of the Western Region and sub-divisions of 13 major districts. Sekondi-Takoradi is within the Shama-Ahanta east and west metropolitan area. It is the administrative capital of the Western Region, with land area of 385 square kilometres, and is located about 242 kilometres to the west of Accra, the capital city. The region is approximately 280 kilometres from Cote d'Ivoire border and has an estimated population of roughly 335,000. It is presumed to be Ghana's third-largest city with respect to industrial and commercial centers and tourist interests.

Data collection

This retrospective study was conducted in the accident and emergency unit of the Effia-Nkwanta Regional Hospital. Pediatric emergencies were seen and, where necessary, were admitted to the children's ward. Admitted patients were recorded in the admissions register. The sampling structure for this study was the admission register of the accident and emergency unit. Only the children admitted with fever as one of the presenting complaints over the study period of 2010, 2011, and 2012 were included in this study. Their medical records were searched and retrieved. Children who were successfully treated and discharged were included in this study. Demographic information and clinical and laboratory findings were collected. Clinical information included other symptoms accompanying fever, the child's weight and temperature, as well as information on sickle cell trait and blood transfusion during admission. Laboratory findings included malaria parasite diagnosis, white blood cell counts, sickling status, and hemoglobin concentration. Treatment histories were also collected, as well as the number of days the patients spent in hospital. Ethical clearance was received from the Ghana Health Service Research Ethical Review Committee, Accra.

Classification of patients with malaria admitted to the hospital was based on WHO criteria for mild and severe malaria [18]. Malaria parasite diagnosis in this facility was done using *Plasmodium falciparum*-

specific rapid diagnostic test kits (Premier Medical Corporation, Nani Daman, India) and microscopy using Giemsa staining. The rapid response kit detects *P. falciparum* antigens; the presence of two lines in the test kit well indicates positivity for *P. falciparum*. Malaria parasites were confirmed with thick and thin smear stained with Giemsa and examined microscopically using 100 power fields under oil immersion. Hemoglobin estimation and white cell count were done as part of the complete blood count from an automated blood cells analyzer machine (Sysmex Hematology Analyzer, Xuzhou Hengda, China).

Definitions

Malaria was defined as the presence of any asexual blood stages of *P. falciparum* species in the thick and thin smear blood film, while malaria-negative samples were confirmed when 100 high power fields were examined using x100 oil immersion objective lens. Anemia was defined based on WHO criteria of hemoglobin (Hb) levels < 11 g/dL [19], categorized as mild anemia (Hb < 11 g/dL), moderate anemia (Hb < 10 g/dL), and severe anemia (< 7 g/dL) [20].

Hemoglobin estimation was performed using the cyanmethemoglobin method [21].

Data analysis

Univariate analyses were conducted and proportions were presented with 95% confidence interval (CI). Statistical significance for cross-tabulations was performed using the Pearson Chi-square test for categorical variables, and analysis of variance (ANOVA) was used for the comparison of mean of the continuous variables. Assessment of whether there were changes in malaria prevalence between 2010 and 2012 was done using the Pearson Chi-square test. All tests were two-tailed, and a p value of 0.05 or less was considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 21.0.

Results

Characteristics of the study population

Table 1 describes the characteristics of the children whose records were used in this study. The average age on admission was 3.16 years. During this study

Table 1. Baseline characteristics of 1,193 children admitted to Effia-Nkwanta Regional Hospital between 2010 and 2012

Characteristics	Years			P value
	2010 n = 343 (%)	2011 n = 395 (%)	2012 n = 455 (%)	
Age (years ± SD)	3.85 ± 3.2	3.04 ± 3.0	2.74 ± 2.9	< 0.001
Age groups*				
0–1 year	105 (31.6)	172 (44.6)	220 (49.4)	
2–4 years	110 (33.1)	111 (28.8)	124 (27.9)	< 0.001
≥ 5 years	117 (35.2)	103 (26.7)	101 (22.7)	
Sex				
Male	204 (60.4)	223 (57.8)	235 (55.6)	0.412
Female	134 (39.6)	163 (42.2)	188 (44.4)	
Mean body weight (kg ± SD)	17.3 ± 10.1	12.5 ± 7.6	12.2 ± 7.4	< 0.001
Mean admission duration, days (SD)	2.17 ± 1.8	3.82 ± 3.2	3.36 ± 3.6	< 0.001
Laboratory diagnosis of malaria				
Positive	81 (23.6)	106 (26.8)	65 (14.3)	
Negative	96 (28)	168 (42.5)	202 (44.4)	< 0.001
Not done	166 (48.4)	121 (30.6)	188 (41.3)	
Sickle cell*				
Hb AA	102 (29.7)	168 (42.5)	191 (42.9)	
Hb AS	13 (3.8)	30 (7.6)	27 (6.1)	< 0.001
Not done	229 (66.6)	197 (49.9)	227 (51)	
Hemoglobin, g/dL*				
< 11 g/dL	90 (45.7)	123 (43.3)	159 (54.6)	
< 10 g/dL	76 (38.6)	91 (32)	80 (27.5)	0.007
< 7 g/dL	31 (15.7)	70 (24.6)	52 (17.9)	

SD: standard deviation; P values derived from Pearson Chi-square for categorical variables and ANOVA for comparison of the mean of continuous variables;

* Included patients with insufficient data.

period (January 2010 through December 2012), a total of 1,193 children were admitted to the pediatric inpatient department of the Effia-Nkwanta Regional Hospital. The mean admission duration (days) increased significantly, from 2.17 days in 2010 to 3.36 days in 2012 ($p < 0.001$). A total of 497/1,193 (41.7%) children were one year of age or younger, 345/1,193 (28.9%) were between two and four years of age, while 321/1,193 (26.9%) were five years of age or older. The mean age of the study population differed significantly between 2010 and 2012 ($p < 0.001$), with a decrease from 3.85 years in 2010 to 2.74 years in 2012 (Table 1). In addition, the mean age of children with mild, moderate, and severe anemia decreased from 2010 to 2012 with no significant difference ($p = 0.32$) (Figure 1).

When age was categorized into the 0–1, 2–4, and ≥ 5 year age groups, there were significant differences in the proportion of children based on age (Table 1). No statistical differences were observed with respect to the sex of the patients. However, there were significant differences with mean body weight, which decreased from 17.3 kg in 2010 to 12.2 kg in 2012 ($p < 0.001$). Seventy (5.9%) of the admitted children had sickle cell trait (Hb AS).

Prevalence of malaria

In general, 252/1,193 (21.1%) of the children had laboratory-confirmed malaria. When only children with laboratory-confirmed malaria were selected for further analysis, the results indicated a significant decrease in malaria prevalence, from 45.8% in 2010 to 24.3% in 2012 ($p < 0.001$) (Figure 1). The results also showed that malaria prevalence in children 0–1 years of age gradually increased from 20.5% in 2010 to 33.8% in 2012, while it decreased in children ≥ 5 years of age, from 46.2% in 2010 to 26.2% in 2012 ($p = 0.021$) (Figure 2a).

Blood transfusion among malaria-infected children

The proportion of children receiving transfusion decreased from 45% among children 0–1 years of age to 27% among children ≥ 5 years of age (Figure 2a). Furthermore, the proportion of children who received blood transfusions increased from 37.5% in 2010 to 56.3% among children 0–1 years of age in 2012, but decreased among children 2–4 as well as ≥ 5 years of age (Figure 2b).

Malaria and anemia comorbidity among the children

Among the 772/1,193 (64.7%) children classified as anemic during the study period, 372/772 (48.2%)

Figure 1. Prevalence of malaria in children from 2010 to 2012 and mean age of children with anemia. The bars represent 95% CI while mean age bars represent SD.

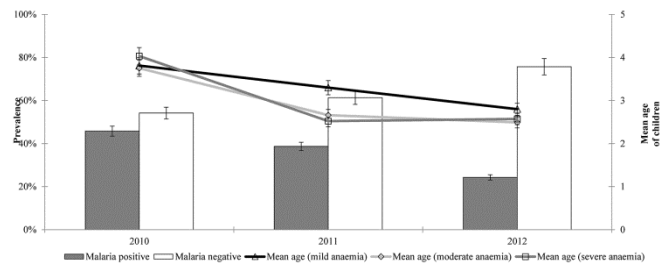
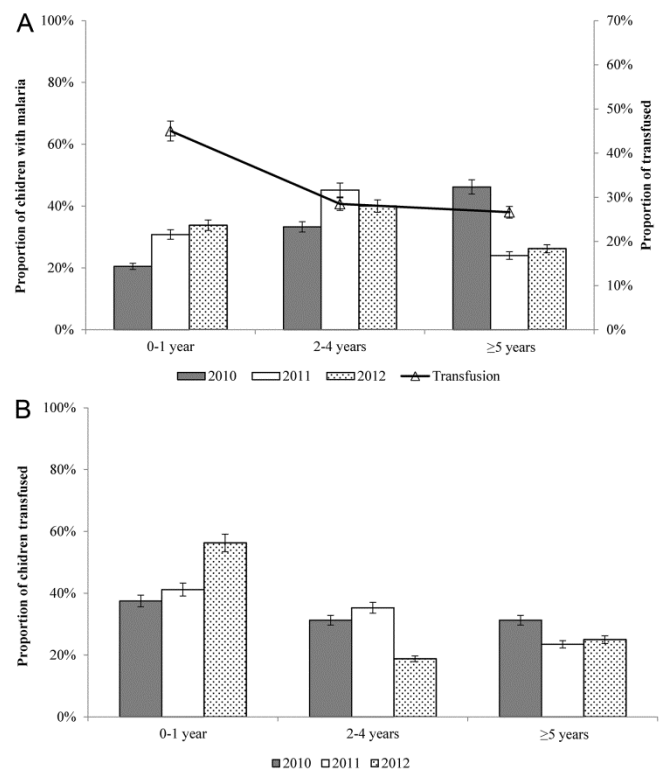
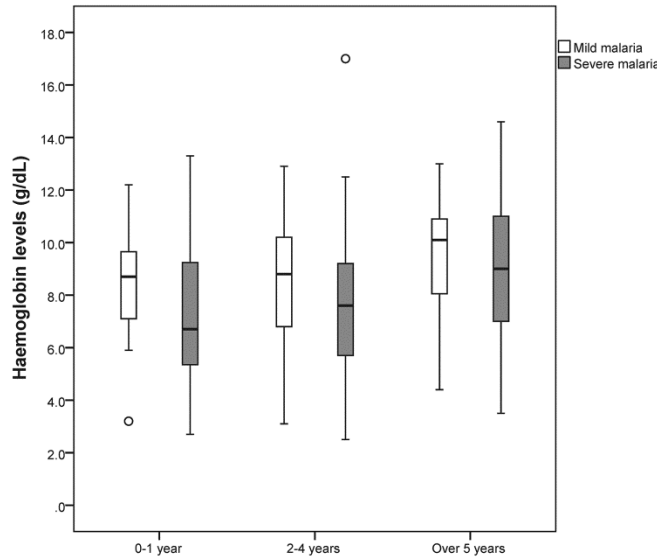


Figure 2. (a) Proportion of children with malaria and transfused children by age groups and year. (b) The proportion of transfused children by age groups and year. The bars represent 95% CI.



had mild anemia (Hb < 11 g/dL), 247/772 (32%) had moderate anemia (Hb < 10 g/dL), while 153/772 (19.8%) had severe anemia (Hb < 7 g/dL). Overall, no malaria-related nor anemia-related deaths were documented in this study period, as all patients were discharged after recuperation. However, the mean hemoglobin levels of the children with both malaria and anemia differed significantly by years and age groups ($p = 0.006$) (Table 2). There were negative correlation coefficients between age and severe malarial anemia ($p = 0.002$). The hemoglobin levels of children with malaria were significantly higher in

Figure 3. Hemoglobin levels (g/dL) of children with co-morbidity. The boxes represent the total observations corresponding to the 25th and 75th percentiles, and the median is represented by the horizontal line. The whiskers represent the 10th and 90th percentiles. The outlier is shown as a circle point outside the 10th and 90th percentile.

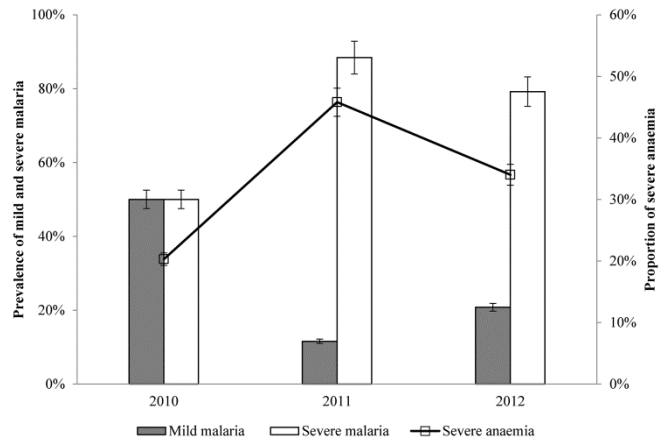


children with mild malaria as compared with those with severe malaria, irrespective of their age groups ($p < 0.001$) (Figure 3). Interestingly, when only children with severe anemia were selected for further analysis, the proportion of children with severe malarial anemia significantly increased, from 50% in 2010 to 79.2% in 2012, while the proportion of those with mild malaria decreased significantly, from 50% in 2010 to 20.8% in 2012 ($p < 0.001$) (Figure 4).

Discussion

This study retrospectively assessed the in-hospital morbidity of malaria among children admitted to the children’s ward for fever and other co-morbidities through the accident and emergency unit of a secondary healthcare institution in Ghana. The results of this study showed a significant increase in admission of children younger than five years of age, with a marked increase seen in those younger than one year of age over the three-year study period. Despite the fact that about 40% of children in this study never

Figure 4. The proportion of children with severe anemia as well as mild and severe malaria. The bars represent 95% CI.



had a malaria test, there is a very strong likelihood that malaria would have been the likely cause of the febrile illness that warranted the admission in the first place, since malaria is hyper-endemic in Ghana, accounting for over 50% of admissions of children younger than five years of age [3]. However, with just barely 35% of all children who had a malaria test being diagnosed with malaria, it is important to note that other non-malaria illnesses such as pneumonia, meningitis, typhoid, and other bacterial infections might have been responsible for these admissions [22-24].

Furthermore, mean admission duration (days) increased significantly, by 1.19 days within the study period (2010–2012). Also, the mean age of the study population differed significantly over the study period (2010–2012), with a decrease of 1.11 years. While these results may not have much significance, it is possible that a decrease in the mean age of children who were admitted over the study period could be responsible for the increase in duration of admission that was observed within the study period as well as the increase in the proportion of children one year of age or younger who received blood transfusion within the study period. However, the mean age of children with mild, moderate, and severe anemia decreased over the study period (2010-2012), with no significant difference.

Also observed in the study was an overall

Table 2. Mean hemoglobin levels of children with malaria and anemia comorbidity by year

Age group	Hemoglobin levels (Hb) g/dL ± SD			P value
	2010	2011	2012	
0–1 year	8.00 ± 2.4	7.22 ± 2.9	8.67 ± 2.4	0.006
2–4 years	7.96 ± 2.3	7.61 ± 2.5	8.60 ± 3.2	
≥ 5 years	8.94 ± 2.3	9.13 ± 3.0	9.08 ± 2.5	

SD: standard deviation

progressive decrease of malaria prevalence from 2010 to 2012. This decrease in prevalence was noted among children five years or younger, while children one year of age or younger actually recorded an increase in prevalence. This age-specific discrepancy in decreasing malaria prevalence observed in this study is consistent with several studies that showed peak malaria prevalence with morbidity and mortality in younger children, especially those younger than one year of age in areas of high malaria transmission such as Ghana [25-28].

Taken together, there was a general increase in severe anemia among children admitted to the children's ward during the study period 2010 to 2012. However, children younger than five years had higher rates of anemia compared to children five years of age or older, with children one year of age and younger having the lowest mean hemoglobin levels. Since malaria is a notable indicator for anemia in children, it might not be totally responsible for all the anemia cases in this study, as there are other well-established factors that can also cause anemia [29,20,13]. However, the similarity in age patterns of anemia and malaria prevalence observed in this study shows that malaria might have played a major role in the prevalence of anemia seen in this study.

While severe malarial anemia and blood transfusions increased from 2010 to 2012, especially among children younger than one year of age, mild malaria decreased significantly within the same period. Anemia in children caused by malaria is more common, may require blood transfusion, and has high mortality rates. Furthermore, children admitted with severe anemia are more likely to die than those without anemia [11]. This finding further supports the trend of high malaria transmission in this region with mostly severe malarial anemia presentation in young children [27,30]. The positive correlation between anemia and blood transfusions should be commended, as the regional hospital was able to rise up to expectation in handling the increasing burden of anemia over the three-year period, notwithstanding the various challenges of blood transfusion in this region.

Conclusions

Despite the general decrease in malaria morbidity seen in this study, children younger than one year of age remain at increased risk of malaria morbidity. With an increase in malaria prevalence among children younger than one year of age over the three years of study, augmented control measures are highly needed in this vulnerable population. Hospitals should

be equipped with adequate diagnostic means and manpower to ensure that correct, prompt, and adequate malaria diagnoses are made. This will go a long way in aiding adequate malaria management, monitoring, and evaluation.

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Authors' contributions

VNO and NCI conceived and designed the study. VNO, JYA, IBA, OSO, and AOS searched and retrieved all the study patients from 2010 to 2012. NCI did the statistical analysis and supervised the study. VNO, JYA, IBA, OSO, AOS, and NCI wrote the paper. All authors contributed to the interpretation of results and critical discussion of the conclusion and approved the final manuscript.

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