

ORIGINAL ARTICLE**Asymptomatic *Plasmodium falciparum* infection and poor school performance in primary school children in the Volta Region of Ghana****Orish Verner^{1*}, Amegan Aho Kokou², Ofori-Amoah Jones³, Osei-Yobah James⁴, Jamfaru Ibrahim¹, Afeke Innocent⁴, Mac-Ankrah Lennox¹, Adzaku Festus⁵****OPEN ACCESS**

Citation: Orish Verner, Amegan Aho Kokou, Ofori-Amoah Jones, et al. Asymptomatic *Plasmodium falciparum* infection and poor school performance in primary school children in the Volta Region of Ghana. *Ethiop J Sci.* 2018; 28(6):749.

doi:<http://dx.doi.org/10.4314/ejhs.v28i6.10>

Received: February 25, 2018

Accepted: April 5, 2018

Published: April 20, 2018

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Funding: Nil

Competing Interests: The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ABSTRACT

BACKGROUND: This study aimed to evaluate the association between asymptomatic *Plasmodium falciparum* infection and poor intellectual development in primary school children in the Volta Region of Ghana.

METHODS: This was a cross-sectional study conducted among children from 5 primary schools in 3 districts in the Volta region of Ghana. Questionnaires were administered, and blood samples collected for malaria investigation using Rapid diagnostic test (RDT) and microscopy. School performance was used to assess intellectual development in the children. Arithmetic was the subject of choice for the standardized test. Pearson chi square test was used to evaluate the association between *Plasmodium falciparum* and poor school performance. Multivariate analysis was used to identify factors independently associated with risk of poor school performance.

RESULTS: Out of 550 children, 305(55.45%) tested positive for malaria with RDT and 249(45.27%) positive with microscopy. Children from the Evangelical Presbyterian (EP) primary school in Afegame had the highest prevalence of *Plasmodium falciparum* infection with both RDT (92, 74.80%) and microscopy (73, 59.35%). Two hundred and fifteen students (39.09%) failed the arithmetic school test. EP primary school in Afegame recorded the highest frequency of poor school performance among the children (53.66%). School performance was significantly associated with RDT malaria diagnosis with failure rate higher among children who were RDT positive (135, 62.79%, $p=0.005$). Lower mean scores were seen in children with positive RDT result (47.35, [SD 30.85], $p=0.021$). *Plasmodium falciparum* infection (RDT) was independently associated with increased risk of poor school performance (AOR, 1.92, $p=0.003$).

CONCLUSION: An urgent scale-up of malaria control program targeting school-going children in this region is needed to mitigate the possible negative impact of *Plasmodium falciparum* infection on their intellectual development.

INTRODUCTION

Malaria poses a great threat to the wellbeing of children living in endemic areas (1,2). Aside contributing a great deal to mortality in children, it also contributes immensely in impacting negatively on the physical and intellectual development of children (3-6). Existing research works indicate that infections from *Plasmodium falciparum*, which is the deadliest and the most predominant species of *Plasmodium*, causes severe malaria and repeated uncomplicated malaria in many countries; and have also been implicated for the depreciating poor intellectual development in children (7-11). However, few studies have linked asymptomatic *P. falciparum* infection to poor intellectual development in children in sub-Saharan Africa (12).

Many studies have employed school performance as a proxy for intellectual development, using standardized school test in arithmetic and local language (13,7,8,9). Other tools like Denver Developmental Screening Test and Ravens Matrices that also assess mental and intellectual development of children have also been used in fewer studies (14,12).

Despite gains in malaria control in Ghana, malaria infections still pose a serious threat to children in the country, especially those living in rural areas (15). Ghana has a vibrant school health program, which involves school feeding program and periodic deworming exercise targeting intestinal helminths and *Schistosoma* infections in school aged children (16). However, in terms of malaria control, neither the school health program nor the national malaria control program targets school-going children. Very little information can be found on the evaluation of the impact of malaria on the intellectual development of school-aged children in Ghana. This study, therefore, sought to determinethe the association between asymptomatic *P. falciparum* infection and poor intellectual development in primary school children in the Volta Region of Ghana.

METHODS

Study area: This study was carried out in two districts and one municipality of the Volta Region of Ghana. The Volta Region is one of the ten regions in Ghana located between latitudes 50 45"N and 80 45"N in the south eastern part of the country, bounded by Togo on the east and Lake Volta on the west. The study area included Ho municipal area (regional administrative capital), as well as Adaklu, and Agotime-Ziope districts. Adaklu is predominantly a rural district; while Agotime-Ziope has about 25% of its population living in the capital of the district which is urban. Ho municipality on the other hand is predominantly an urban area, with about 30% of the population living in rural areas.

Study design and procedure: This was a cross-sectional study involving administration of questionnaires and standardized school test, as well as blood sample collection. These activities took place from March 14th to April 14th 2016, between 9:30am and 3pm each day.

School children from the ages of 6 to 14 years were selected from primary schools in the three districts. Primary schools, in both urban and rural settings, were particularly selected for this study (17). A total of five primary schools were selected for this study; namely, Freetown Pimary Shool in the Ho municipality, Dave and Davanu Primary schools in Adaklu district and the Evangelical Presbyterian[EP] Primary schools in Afegame and Kpetoe, both in Agotime-Ziope district.

Sample size calculation: A recommended minimum sample size of 335 was generated using the Cochran formula at 95% confidence interval, 5% margin of error. A prevalence rate of 67.8% was used, being the prevalence of malaria among school children in Adaklu and AgotimeZiopedistrict in Volta region (18).

Ethical clearance: Ethical clearance was obtained from the Ghana Health Service Ethical Committee [ID NO:GHS-ERC: 29/11/15]. Written informed consent was gotten from the parents of children who participated in the study. Assent

forms were signed by the children before they were enrolled onto the study.

Data/sample collection: Data and sample collections were performed using methods and procedure as previously described by Orish et al. (17). Briefly, questionnaires were administered to children recruited for this study to obtain information about their demographic and socio-economic status, vis-à-vis: occupation of both parents, the type of housing they live in, family size, as well as the identity of the guardian they stay with, and if they have been using mosquito net. Blood samples were also collected from each participant by a trained phlebotomist and transferred into ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes. These samples were transported in an ice chest to the laboratory on the same day, and malaria investigation then conducted using Rapid Diagnostic Test (RDT) and microscopy. Bioline SD kit from Standard Diagnostics, INC., South Korea, was used in the detection of histidine rich protein 2 (HRP-2) of *P. falciparum*. All the procedure and tests followed strict observance of the manufacturer's instructions. Microscopy involved 10% Geimsa preparation of thin and thick film on a slide; and the slides were read by two and/or three microscopists where there were discordant results. The presence of asexual forms of the parasite in the blood smear was considered positive. Haemoglobin estimation was also performed using haematology analyzer (Sysmex, Kakogawa, Japan).

Definitions: Asymptomatic *P. falciparum* infection was defined as positive RDT, or microscopy results with no associated clinical symptoms. Anaemia was classified as severe (Hb < 7g/dl), moderate [7-9.9g/dl], and mild [<11g/dl] (19).

Assessment of school performance: School performance assessment was done using standardized school test. Arithmetic was chosen as the subject for assessment. Questions were

gotten from the office of the Volta Region directorate of education. The test was administered to each pupil from the five primary schools, based on their level in school. Ten questions were set for each level, and tests were administered in standard examination setting and condition for 20 minutes. Results of the tests were marked and graded over 100% by a trained educationist from the Ghana Education Service. Pass mark was fixed at 50% and above, while failure was below 50%.

Statistical analyses: A frequency distribution was performed for characteristics like malaria, anaemia and poor school performance. Pearson χ^2 tests analysis was used to investigate the association between poor school performance and *P. falciparum* infection, as well as anaemia and socioeconomic status. Multivariate logistic regression was used to identify factors independently associated with the risk of poor school performance in the primary school children. Analyses were done with 95% confidence interval (CI) and a p value of 0.05 or below (i.e. $p \leq 0.05$) was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistical softwares version 21.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

A total of 550 primary school children were recruited for this study. Figure 1 gives the overview of the study population. It shows the number of children enrolled for each school, available participants and children who successfully participated by answering the questions from the questionnaire taking the standardized test as well as having blood samples collected from them.

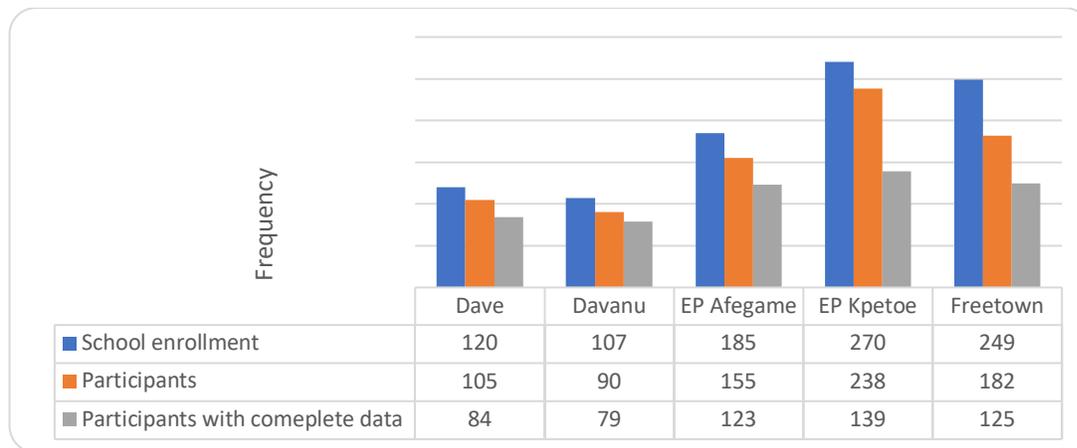


Figure 1: Overview of study population in the 5 primary schools

Table 1 shows the prevalence of *P. falciparum* infection among the primary school children. Rapid diagnostic test (RDT) was positive for 55.45% (305/550) of the children while 45.27% (249/550) was with microscopy. There was a significant difference in the prevalence of *P. falciparum* infection among the children in the 5 primary schools (RDT, $p < 0.001$; Microscopy, $p = 0.007$). Children from EP Afegame school had the highest prevalence of *P. falciparum* for RDT (92, 74.80%) and microscopy (73, 59.35%).

Table 2 highlights the characteristics of the primary school children in the study based on their

school performance in the arithmetic test. Two hundred and fifteen students (39.09%) failed the arithmetic school test. There were no significant association seen between poor school performance and occupation of parents, house type, family size, who child stays with, and sex. However, there was significant association seen with *P. falciparum* infection and anaemia, with higher proportion of children who failed the arithmetic school test being positive with RDT (135, 62.79; $p = 0.001$) and anaemic (48, 47.52%; $p = 0.03$).

Table 1: Prevalence of *P. Falciparum* infection among children in five primary schools in Volta Region

Parameter	Malaria Positive	Malaria Negative	P value
Rapid Diagnostic Test	305(55.45)	245(44.55)	
Freetown (Ho municipality)	60(48.00)	65(52.00)	<0.001
Davanu (Adaklu district)	57(72.15)	22(27.85)	
Afegame (Agotimeziopie district)	92(74.80)	31(25.20)	
Kpetoe (Agotimeziopie district)	58(41.73)	81(58.27)	
Dave (Adaklu district)	38(45.24)	46(54.76)	
Microscopy	249(45.27)	301(54.73)	
Freetown (Ho municipality)	48(38.40)	77(61.60)	0.007
Davanu (Adaklu district)	36(45.57)	43(54.43)	
Afegame (Agotimeziopie district)	73(59.35)	50(40.65)	
Kpetoe (Agotimeziopie district)	54(38.85)	85(61.15)	
Dave (Adaklu district)	38(45.24)	46(54.76)	

Data is presented as frequency with corresponding percentage in parenthesis. p is significant at **0.05**.

Table 2: Characteristics of Children according to performance in the arithmetic school test.

Characteristics	Fail = 215	Pass = 335	p value
Gender			
Male	99(39.76)	150(60.24)	0.43
Female	116(38.54)	185(61.46)	
Occupation of mother			
Trader	128(38.32)	206(61.68)	0.64
Farmer	65(41.67)	91(58.33)	
Civil servant	11(32.35)	23(67.65)	
Unemployed	11(42.31)	15(57.69)	
Occupation of father			
Trader	97(38.19)	157(61.81)	0.97
Farmer	67(39.41)	103(60.59)	
Civil servant	41(39.81)	62(60.19)	
Unemployed	10(43.48)	13(56.52)	
House types			
Family house	77(39.29)	119(60.71)	0.52
Single room	65(39.39)	100(60.61)	
Semi detached	73(38.62)	116(61.38)	
Family size			
2	28(40.58)	41(59.42)	0.5
3	54(45.00)	66(55.00)	
4	38(14.15)	68(64.15)	
5	35(36.46)	61(63.54)	
6	22(33.85)	43(66.15)	
>6	38(40.43)	56(59.57)	
Who child stays with			
Father	12(48.00)	13(52.00)	0.48
Mother	31(38.75)	49(61.25)	
Both parents	121(38.05)	197(61.95)	
Grand parents	31(44.29)	39(55.71)	
Others	20(35.09)	37(64.91)	
P. falciparum infection			
RDT+ve	135(62.79)	170(50.75)	0.001
RDT-ve	80(37.21)	165(49.25)	
MP+ve	103(47.91)	146(43.58)	0.21
MP-ve	112(52.09)	189(56.42)	
Haemoglobin			
<11g/dl	48(47.52)	53(52.48)	0.03
≥11g/dl	167(37.19)	282(62.81)	
Name of school			
Dave	34(17.86)	50(82.14)	<0.001
Freetown	32(25.60)	93(74.40)	
Davanu	32(40.51)	47(59.49)	
Afegame	66(53.66)	57(46.34)	
Kpetoe	51(36.69)	88(63.31)	

Data is presented as frequency with corresponding percentage in parenthesis. p is significant at 0.05.

There was also a significant difference in the prevalence of poor school performance of the children among the five schools ($p < 0.001$), with

the EP primary school in Afegame having the highest prevalence of poor school performance in the arithmetic school test (53.66%).

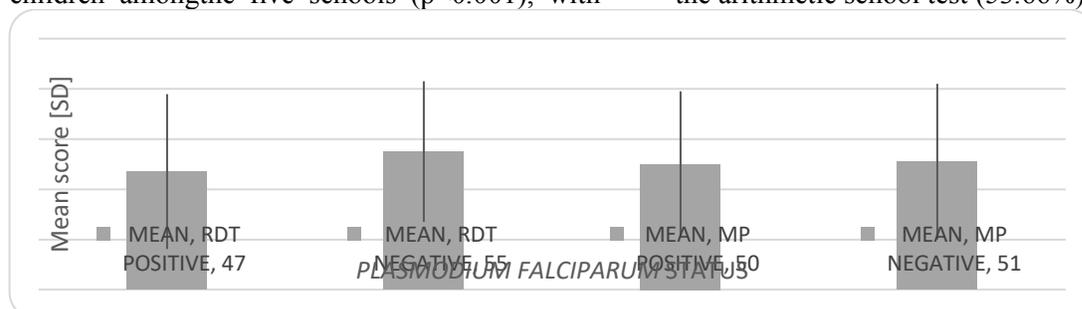


Fig. 2. Mean score and standard deviation of the standardized arithmetic test for children positive and negative for both RDT and microscopy.

Figure 2 shows the mean score and standard deviation of the standardized arithmetic test for children positive and negative for both RDT and microscopy. Children positive with RDT significantly had the lowest mean score (47 [SD 30.85], $p = 0.021$). Those positive with microscopy had a lower mean score (50 [SD 29]) compared to those negative with microscopy (51 [SD 31]), but this finding was not significant ($p = 0.92$).

Table 3 summarizes the factors that predicted the risk of poor school performance in arithmetic among the primary school children in this study. Children attending EP primary school in Afegame had the highest risk of having a poor school

performance with unadjusted OR of 2.86 (95% CI, 1.57-5.20; $p = 0.001$) and adjusted OR of 2.67 (95% CI, 1.44-4.96; $p = 0.002$). *P. falciparum* (RDT) was independently associated with increased risk of poor school performance. Children with *P. falciparum* positive (RDT) had higher risk of poor school performance (Unadjusted OR, 2.01; 95% CI, 1.33-3.06; $p = 0.001$; Adjusted OR, 1.92, 95% CI, 1.25-2.94; $p = 0.003$). Children with haemoglobin level less than 11g/dl were more likely to have poor school performance (Unadjusted OR, 1.76; $p = 0.04$). However, significance was lost ($p = 0.13$) after controlling for confounders like *P. falciparum* and the primary school attendance.

Table 3: Multivariate logistics regression analysis of poor school performance risk among the primary school children .

Variable	Unadjusted OR(95% CI)	p value	Adjusted OR(95% CI)	p value
Gender				
Male	1.05(0.70-1.58)	0.78	1.02(0.67-1.53)	0.95
Female	Ref			
School				
Dave Prim.	1.16(0.57-2.38)	0.69	1.11(0.52-2.36)	0.79
Freetown Prim.	0.70(0.38-1.27)	0.24	0.67(0.36-1.22)	0.19
Davanu Prim.	1.42(0.74-2.75)	0.3	1.39(0.70-2.76)	0.35
Afegame EP	2.86(1.57-5.20)	0.001	2.67(1.44-4.96)	0.002
Kpetoe EP	Ref			
Malaria (RDT)				
Positive	2.01(1.33-3.06)	0.001	1.92(1.25-2.94)	0.03
Negative	Ref			
Hemoglobin				
<11g/dl	1.76(1.02-3.04)	0.04	1.56(0.86-2.78)	0.13
≥11g/dl	Ref			

OR=odds ratio, CI=confidence interval, Ref= Reference. P is significant at 0.05

DISCUSSION

To the best of our knowledge, this is the first work that has attempted to assess the association between *P. falciparum* infection and intellectual development in children in Ghana.

There was a high prevalence of *P. falciparum* of 45.3% and 55.5% with microscopy and RDT respectively, which is not uncommon within the region and other parts of Ghana (17, 20); although another study reported a much lower prevalence in the region (21). The *P. falciparum* infections in this study were mainly asymptomatic, which is the predominant presentation of infections in malaria endemic environment (22). It is known that older children, especially school-going children are usually asymptomatic with *P. falciparum* infection (23). There was a difference between RDT positive and microscopy positive *P. falciparum* infection in this study. This discrepancy has been widely reported by several other studies (24–26). The strength and weakness of these two malaria diagnostic methods may be responsible for the differences in results (24). Microscopy is regarded as the gold standard, but its availability and high expertise required makes it unsuitable in certain instances (24, 26). For RDT, it requires very little expertise and results are promptly available (24). The downside however for RDT is that it requires a higher parasite threshold (≥ 200 p/μl) to generate adequate titre of antigens to be detected (24, 27). Despite this factor, most RDTs have over 95% sensitivity especially those specific for *P. falciparum* which was used in this study (28, 29). More so, in some studies, RDT has demonstrated to be more accurate and sensitive compared to microscopy, using Polymerase chain reaction (PCR) as standard (26, 30).

Poor school performance was significantly associated with *P. falciparum* infected children (RDT). This finding was supported by the result showing children from the Evangelical Presbyterian (EP) Primary school in Afegame having the highest poor school performance, since this particular school significantly ($p < 0.001$) had the highest prevalence of *P. falciparum* infection. *P. falciparum* and

Afegame EP primary school were independently associated with increased risk of poor school performance in the children. These findings are in agreement with other studies that reported malaria causing poor scores in arithmetic among children who are infected (7, 8). These studies argued that these poor results in the standardized school test is due to the impairment of the intellectual development of the infected children by malaria (7, 8, 9). The mechanisms behind this impairment have been linked to severe, repeated, uncomplicated and asymptomatic malaria (7, 8, 9, 12). It is believed that the cytokines released during malaria infection play a role in depreciating cognitive function in children who recover (7, 31). In the case of asymptomatic and uncomplicated malaria, repeated infection and their adverse impact on cognition have been implicated (4, 7, 12).

Anaemia is another proposed pathway of cognitive impairment from malaria infection (32, 33). Repeated asymptomatic malaria can cause chronic iron deficiency anaemia which has an adverse impact on cognition (34, 35). However, in this study anaemia was not independently associated with increased risk of poor school performance in arithmetic standardized test; probably suggesting that the impairment here might be due to a more direct immunologic pathway (12, 31).

There was no significant association seen with socioeconomic factors such as parents' occupation, house type, who child stays with, and poor school performance in this study. Some studies reported association between socioeconomic factors and poor school performance and cognitive function (7, 12). Other factors which can impair intellectual development in children and cause poor school performance like helminths infections were not mentioned in this study. However, the reported low levels of intestinal helminths infections among primary school children in this region (21, 36), and the periodic deworming exercise targeting intestinal helminths and *Schistosoma* infections (16, 21), make it less likely for helminths infections to contribute significantly to impaired intellectual

development and poor school performance in this study.

This was a cross-sectional study which cannot state in categorical terms the causality between asymptomatic infections and poor school performance. However, reverse causality is very much unlikely to happen between asymptomatic malaria and poor school performance; since poor school performance cannot cause malaria infection(12). Furthermore, this study cannot completely ascertain if the association noted was the lingering effect of previous symptomatic malaria attack on the children or the current asymptomatic status. However, efforts were made to control for other confounders that might have impacted poor school performance in the primary school children, like socioeconomic factors (parent's occupation, family size and parental care) in this study.

Our study reported a significant association between asymptomatic *P.falciparum* malaria and poor school performance in arithmetic standardized school test. Also, children in Afegame, with the highest prevalence of *P. falciparum* infection had the poorest performance in the school test. More studies are needed to throw more light on this association between malaria and intellectual development in school children in Ghana. This will ensure the consolidation of the gains of malaria control and the school health programs.

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