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The Relationship between Haemoglobin Levels and Platelet Counts of Malaria Infected and Non-Infected Children in Offinso, Ghana

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Authors' contributions

This work was carried out in collaboration among all authors. Authors EKP and LAO conceived and designed the study. Authors EKP and CWA supervised sampling plan, data collection and analysis. Author EKP drafted the manuscript. All authors edited, reviewed and revised the manuscript.

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ABSTRACT

Malaria is known to have significant effects on the body. This study, investigated the relation between platelet and haemoglobin levels of malaria positive and negative children (age range = 1-14 years). Out of the 1049 children (4.1± 3.3 years), comprising 493 females and 556 males who were tested for malaria parasites, the prevalence of malaria was 35.3%. Children aged one year with malaria recorded the least hemoglobin concentration of 8.0 ± 2.4g/dL. As the age of the children with malaria infection increase, the haemoglobin concentration also increased. The prevalence of anemia (<10 g/dL) in malaria infected children was 55.4% compared to 28.0% in children without malaria. Children with malaria infection were up to 4.0 (OR) times more likely to have severe anemia (<7 g/dL) than those uninfected. Furthermore, only 5.6% of malaria negative patients had thrombocytopenia (platelet <150$\times 10^9/\mathrm{L}$); while 49.5% of malaria positive children had thrombocytopenia. There was a significant weak positive correlation (rho=0.277) between haemoglobin and platelet count of malaria positive children, but a weaker negative correlation (r = -

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0.088) in those without malaria. The haemoglobin levels and platelet counts of children without malaria followed the normal distribution, while those with malaria did not. Therefore, haemoglobin and platelet data from malaria negative and positive children should be analysed differently to improve diagnosis and treatment.

Keywords: Full blood count; thrombocytopenia; anaemia; hematological parameters.

1. INTRODUCTION

Malaria is an avoidable and curable disease and to avoid it, several interventions have been proposed and implemented, notable among them is the use of insecticide treated bed nets [1]. Nonetheless, it continues to kill between 367,000 and 755,000 individuals yearly and known to be the third leading cause of death in children globally [2]. In Africa, more than a quarter of deaths in children less than 5 years can be attributed to malaria [2]. The disease is most prevalent in Sub-Saharan Africa where temperature and humidity conditions foster the growth of the female Anopheles mosquitoes [3].

Changes in haematological indices due to malaria are well known and children between the ages of 1-14 years suffer the most from these changes [4]. Platelets and haemoglobin are part of the haematological parameters worst affected by the disease; hence, most malaria related deaths are caused by anaemia and thrombocytopenia [5,6]. Children and pregnant women appear to be at increased risk of getting thrombocytopenia and anaemia because of reduced immunity [7]. Yet, the role of platelets and their relationship with other haematological parameters during malaria infection is not fully understood. As a result, malaria related anaemia and thrombocytopenia continue to be an enormous public health problem that needs immediate attention.

A study conducted by Berad and Gurbani [8] on healthy subjects established a relationship between low and high levels of haemoglobin concentration on platelet count. However, despite low haemoglobin and platelet count being the most reported haematological changes observed among malaria positive children, little is known about the interactions between these important predictors of the disease. Therefore, we investigated the relation between platelet count and haemoglobin levels of malaria positive and negative children (age range = 1-14 years) by determining their distribution and correlation.

2. METHODS

2.1 Study Design

The cross-sectional secondary data used in this study were obtained from the Laboratory Unit of St. Patrick's Hospital, Offinso, Ghana. The institution granted permission before the anonymized data were used for this study.

2.2 Data Collection

Malaria and Full Blood Count (FBC) results of children (age range = 1–14 years) who reported at the facility between January 2018 and June 2018 were included in this study. Automatic cell counter (Mindray BC - 3000 plus) was used after careful calibration to measure their haemoglobin and platelet levels. Identification of malaria parasites was done using a Rapid Diagnosis Test (RDT) and confirmed by blood film smear examination.

2.3 Statistical Analysis

Data collected were checked for errors in excel (2016) and analysed using R software version 4.0.3. Haemoglobin and platelet levels were summarized into means (standard deviations) and median (Interquartile range); also, bar chart was used to visualize malaria infection rate in children. Line plots, histograms and scatter plots were used to determine the relationship between haemoglobin concentration and platelet levels of both malaria positive and negative children. Group means of haemoglobin and platelets were compared using Student's t-test and association between them were determined using Pearson's rank correlations in the case of malaria negative children and Spearman correlation for malaria positive children. Odds ratio (OR) were computed to determine the risk of a child with or without malaria getting anemia or thrombocytopenia. At 95% confidence interval, significant levels were measured and significant differences set at $p<0.05$.

3. RESULTS

3.1 Characteristics of Participants

Out of the 1049 children with mean age of 4.1± 3.3 years, comprising 493 females and 556 males who reported at the facility and were tested for malaria parasite, the prevalence of malaria was determined to be 35.3%. A total of 206 (55.7%) of the malaria positive cases were recorded in children less than 5 years, whilst the 10 to 14 years age group accounted for only 11.1% of the malaria positive cases (Fig. 1).

3.2 Relationship between Haemoglobin and Platelet

Generally, as the age of a child with malaria increases his or her haemoglobin concentration likewise increases; however, for those without malaria infection their haemoglobin levels remained fairly constant (Fig. 2). Patients with malaria and aged one year recorded the least hemoglobin concentration of 8.0±2.4 g/dL, whilst patients without malaria aged 11 years recorded the highest mean haemoglobin concentration of 12.1±0.7 g/dL (Fig. 2).

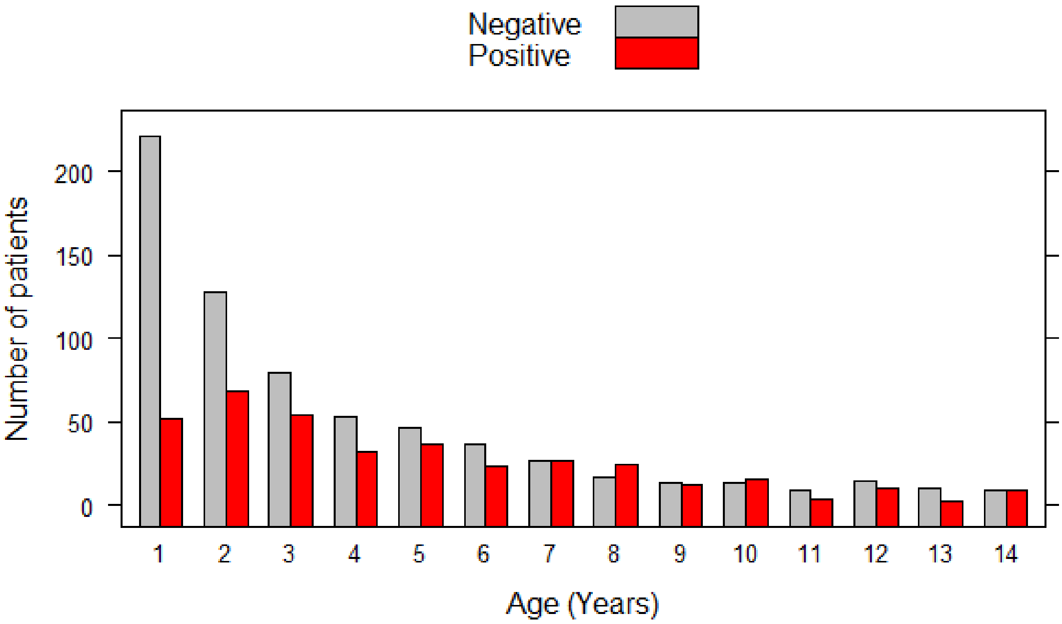

Fig. 1. Malaria positive and negative cases in children (age range = 1-14 years)

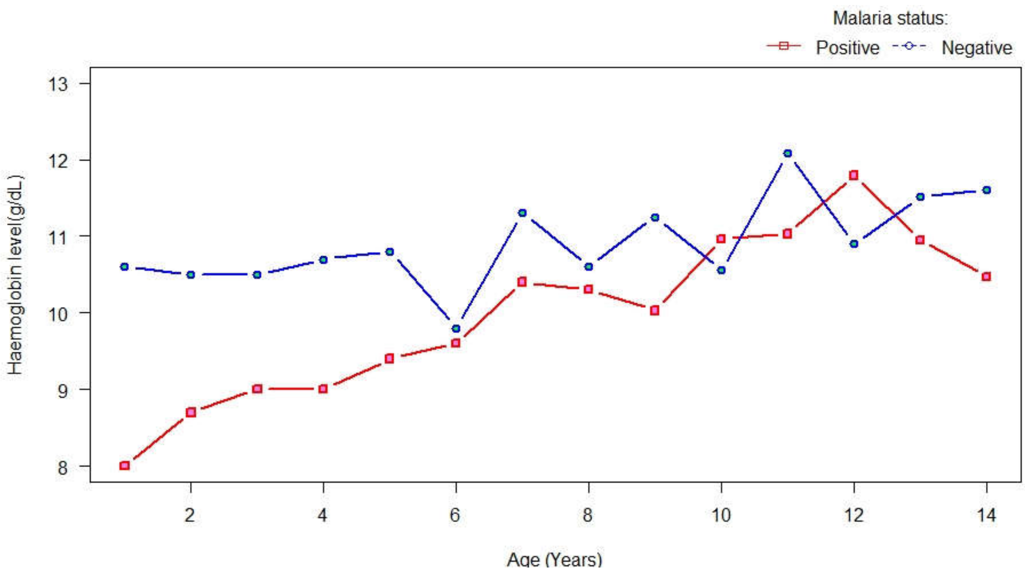

Fig. 2. Mean haemoglobin concentration of malaria positive and negative patients

The mean haemoglobin concentration of all malaria negative children (10.6±1.4 g/dL) was significantly higher than those positive for malaria (9.3±2.3 g/dL) ($p<0.0001$). The prevalence of anaemia (<10 g/dL) among malaria infected children was 55.4% compared to their counterpart without malaria which was 28.0%. Also, children with malaria were up to 4.0 (OR) times more likely to have severe anaemia (<7g/dL) than those without the disease ($p< 0.0001$, 95% CI = 2.4-6.5). Furthermore, Majority (75.9%) of the severe anaemia cases occurred in malaria infected children less than 5 years of age.

For patients with malaria infection, the mean platelet count experienced a downwards trend from age 1 to 10; whilst in children without the infection it was fairly stable, within the levels of $207 \times 10^9/\mathrm{L}$ for age 1 year and 118$\times 10^9/\mathrm{L}$ for age 11 years (Fig. 3).

The grand average platelet count among patients with and without malaria were 173±110 $\times 10^9/\mathrm{L}$ and 346±125 $\times 10^9/\mathrm{L}$ respectively ($p<0.0001$). Only 5.6% of malaria negative patients had thrombocytopenia (platelet <150 $\times 10^9/\mathrm{L}$), nonetheless, almost half (49.5%) of malaria infected children suffered from thrombocytopenia. Furthermore, patients with malaria were 8.8 (OR) times more likely to have low platelet count ($p<0.0001$, 95% CI: 6.1– 12.8).

3.3 Distribution of Haemoglobin and Platelet Count

Majority (71.1%) of the malaria negative children had haemoglobin levels within 9 g/dL and 12 g/dL, whilst 60% of malaria-infected children recorded haemoglobin concentrations within 8.0 to 11.5 g/dL (Fig. 4). The wider spread (SD±2.3 g/dL) of haemoglobin concentration observed in patients with malaria, compared with SD±1.4 g/dL observed in uninfected ones; show that children with malaria have inconsistent hemoglobin concentration.

According to Shapiro-Wilk test, haemoglobin concentrations in malaria negative group followed the normal distribution (W= 0.995, p-value =0.056). However, their counterpart infected with the disease recorded a median haemoglobin value of 9.5g/dL and their data was not normally distributed (W = 0.977, p-value <0.0001).

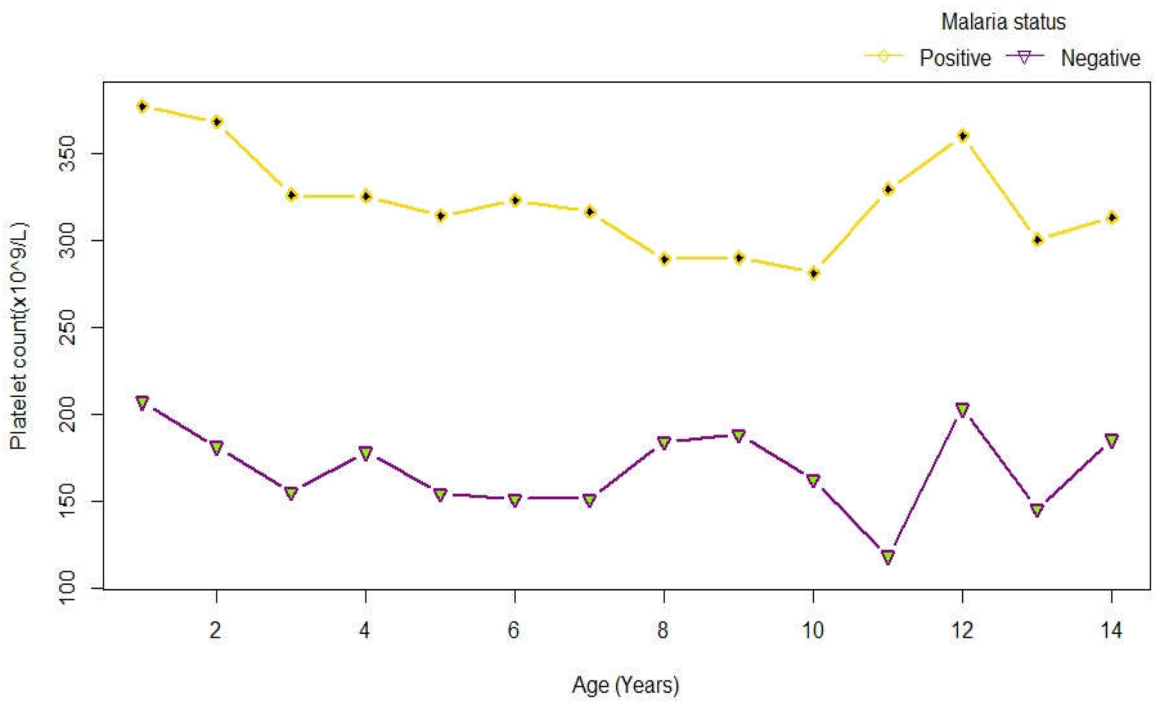

Fig. 3. Mean platelet counts of malaria positive and negative patients

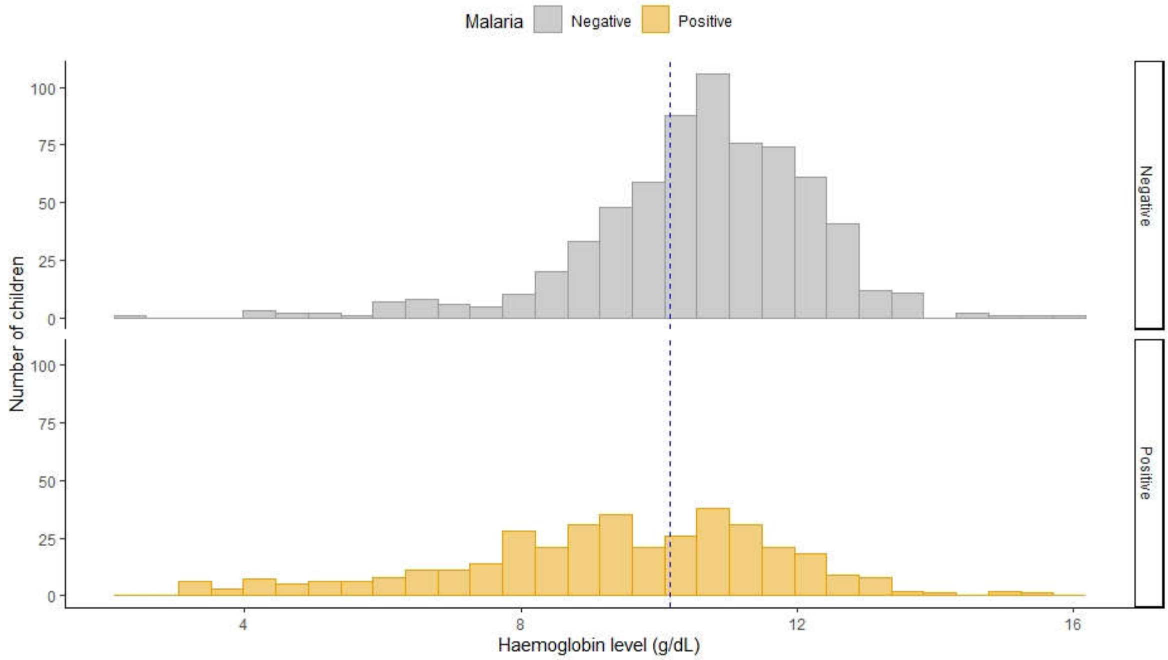

Fig. 4. Histogram of haemoglobin concentration of children with and without malaria infection

In the malaria positive group, 64.6% recorded platelet values below $200 \times 10^9/\mathrm{L}$ whereas 55.1% of the malaria negative patients had platelet counts within 200 to $400\times 10^9/\mathrm{L}$ (Fig. 5). The platelet count data of malaria positive children look skewed to the right; hence confirming that most of them had low platelet levels. In addition, the centers of the two groups were significantly different meaning that their median or mean values are not close to each other. Shapiro-Wilk test of normality indicated that platelet count of malaria negative children were normally distributed (W=0.995, p=0.06), even though their counterpart with malaria had a median platelet value of $151\times 10^9/\mathrm{L}$, it did not follow the normal distribution (W=0.949, P<0.0001) (Fig. 5).

3.4 Correlation Analysis of Haemoglobin and Platelet

The correlation between platelet count and haemoglobin concentration of children with and without malaria is showed in Fig. 6. Based on the distribution of the data (Figs. 4 and 5), Pearson correlation was done for children without malaria and Spearman correlation was run for those with malaria. There was a statistically significant but very weak negative correlation between platelet count and haemoglobin concentration of malaria negative children (r = -0.088, n = 679, p = 0.022). However, children infected with malaria recorded a positive correlation which was also statistically significant; nonetheless, the strength of correlation was weak (rho = 0.277, n = 370, p < 0.05).

4. DISCUSSIONS

The results indicate that there is a relation between platelet count and haemoglobin levels of malaria positive and negative children. Malaria infected children recorded more anaemia cases than non-infected children, this finding is comparable to the findings of similar studies conducted in Nigeria and Uganda [9,10]. Goheen et al. [11] calmed that anaemia offers some kind of protection for children against malaria; this could explain the high occurrence of anaemia noted among children in the study area. Also, the current study observed that children with malaria were more likely to have severe anaemia than those without malaria which is in agreement with several other studies [12,9] and [13]. Increase destruction of red blood cells due to loss of normal shape and interactions with numerous proteins secreted by the parasite could explain why more of the malaria infected children had severe anemia [14].

The current findings noted that half of the malaria positive children suffered from thrombocytopenia. Related results from other studies conducted in

Pakistan and Thailand have reported a higher rate of thrombocytopenia among malaria positive individuals than was observed in this study [15,16]. The seemingly lower percentage of malaria positive children with thrombocytopenia observed in the current study may be due to differences in parasitemia and study population. Even so, a similar study conducted in Cameron identified the rate of thrombocytopenia in malaria infected children to be similar to the current findings [17]. Almost all of the malaria negative children studied had normal platelet count; correspondingly, these children were less likely to have thrombocytopenia, an indication that normal platelet count provide some good evidence against malaria parasite in children.

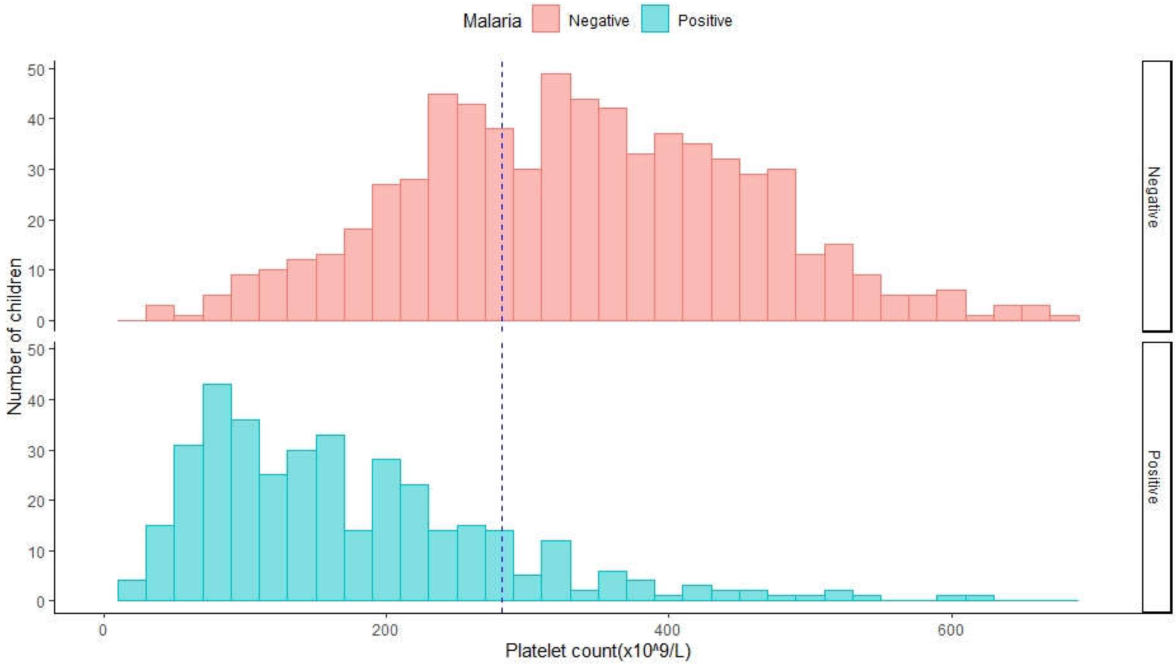

Fig. 5. Histogram of platelet count of children with and without malaria infection

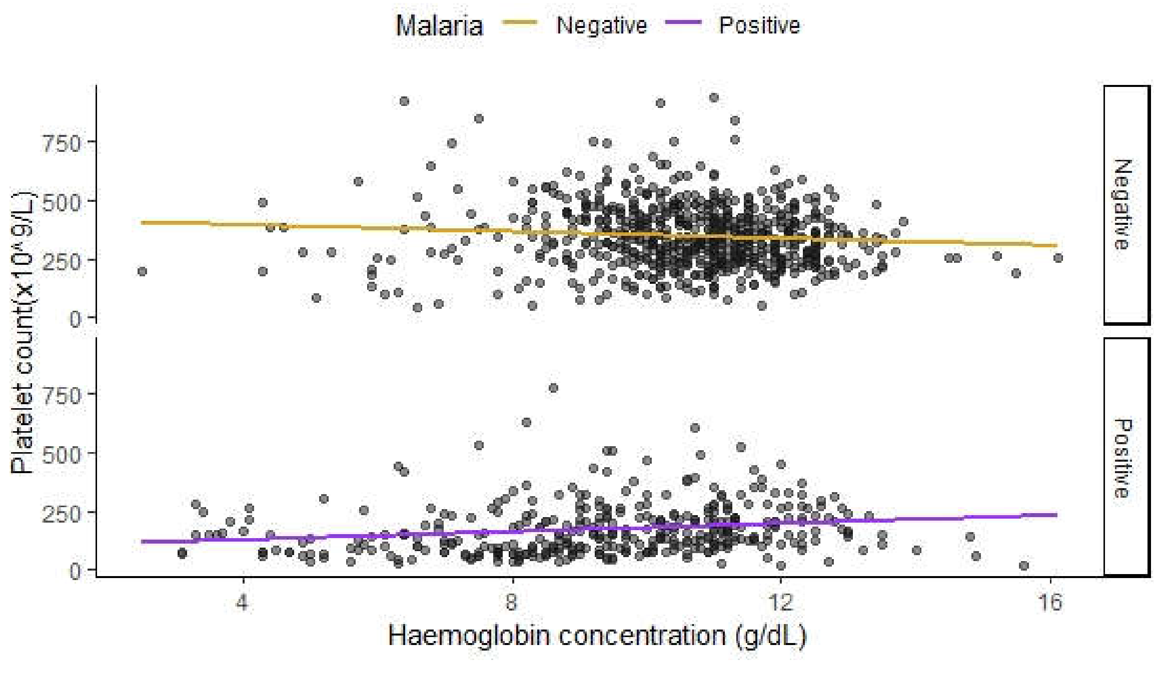

Fig. 6. Correlation between platelet count andhaemoglobin concentration

Haemoglobin and platelet count of children without malaria were found to follow the normal distribution (p>0.05). In concordance to this study, Tufts et al. [18] observed that haemoglobin concentration of healthy men follow the normal distribution. A relatively recent study analysed platelet count in 59 healthy subjects and concluded that they showed a normal distribution [19]. On the contrary, haemoglobin and platelet count data of malaria infected children obtained from this study were not normally distributed (p<0.001). This is consistent with findings from Martínez-Salazar and Tobón-Castaño [20]; they similarly reported that platelets count of those infected with malaria were not normally distributed. The lack of normality in the platelet data could be due to almost half of malaria-infected children recording lower platelet levels. Also the inconsistent nature of haemoglobin concentration of malaria positive children may account for the large standard deviation recorded, leading to the data not following the normal distribution.

Consequently, haemoglobin and platelet data from malaria positive and negative children should not be analysed in the same manner. Non-parametric testing techniques such as median, *Mann –Whitey test, Wilcoxon signed – rank test, Fisher exact* probability test, *Kruskal – Wallis* test, *Friedman test* and *Spearman* correlation should be considered when making meaning out of malaria positive data. Whereas parametric tests such as mean, independent sample t test, paired samples t test, one way analysis of variance (ANOVA) and *Pearson* correlation should be used in the case of malaria negative data [21].

There was a significant positive weak correlation (p < 0.05) between haemoglobin and platelet counts of malaria positive children. Similarly, Morris et al. [22] noted a positive correlation between anaemia and thrombocytopenia; they found that treating anaemia likewise increases platelet count. Nonetheless, there was a significant negative correlation, though very weak, (p = 0.022) between platelet count and haemoglobin concentration in the malaria negative children. This trend is not unusual; a previous related study had reported similar relationship between haemoglobin levels and platelet count in healthy volunteers [8]. However, further studies are needed to determine whether an increase in platelet count is what causes a rise in haemoglobin levels or vice versa.

5. CONCLUSION

The study identified that the relation that exist between haemoglobin and platelet count of malaria infected children differ from that of the non-infected children. This information when further exploited could improve diagnosis and treatment of malaria among children in areas where microscopic or Rapid Diagnostic Test (RDT) are unavailable. However, the explanations offered for the observed difference is unclear so we suggest that further studies need to be done to determine whether a decrease in platelet count is what cause a drop in haemoglobin levels or vice versa.

6. LIMITATIONS OF STUDY

The malaria negative controls used for this study were not healthy individuals; so it is possible some of them might have other infections, which would affect their platelets or haemoglobin levels.

7. FUNDING

The authors self-funded this research. They received no external funding in the collection and analysis of data and writing of the final manuscript.

CONSENT

As per international standard or university standard, patients' guardians' written consent has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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