ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 02, pp.1030-1033, February, 2019

DOI: https://doi.org/10.24941/ijcr.33869.02.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EFFECTS OF CHANGES IN HAEMATOLOGICAL PARAMETERS OF MALARIA INFECTED CHILDREN AND ADULT PATIENTS ATTENDING THE ST. PATRICK'S HOSPITAL, OFFINSO, GHANA

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ARTICLE INFO

Article History:
Received 15th November, 2018
Received in revised form
29th December, 2018
Accepted 05th January, 2019
Published online 28th February, 2019

Key Words:

Haematological, Malaria, Haemoglobin; anaemia, Thrombocytopenia, WBC, Leucocytosis.

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ABSTRACT

***Background*:** Nearly half of the world's population are at risk of being infected with malaria parasite. In Ghana, 3.5 million people get infected with the disease every year and about 20,000 children die from it annually. Haematological changes associated with malaria have been reported but may vary due to age, gender, and demographic factors. ***Objective*:** This study seeks to analyse the effect of malaria on some common haematological parameters of children (1-14 years) and adults (>14 years) patients attending St. Patrick's Hospital, Offinso, Ghana. ***Methodology*:** A total of 2076 full blood count together with malaria test data, comprising of 1200 females and 876 males, were obtained from the laboratory department with 539 (25.96%) testing positive for malaria. ***Results*:** Majority (68.65%) of the malaria positive cases were recorded in children ≤ *14* years. In the 15-44 years category, females recorded significantly high cases of malaria than their male counterpart. There was a significant ($p<0.0001$) difference between the median haemoglobin levels of children with and without malaria. Within the adult population there was no difference between the median haemoglobin levels of malaria positive and negative adults ($p > 0.05$). Significant differences between all studied haematological parameters of malaria infected children and adults were identified. Out of the 370 children with malaria, 14.59% had severe anaemia compared to1.78% from their adult counterpart. The risk of developing severe anaemia was also 8.22 times as high as the risk of severe anaemia in malaria adult.Although 49.46% of children and 38.46% of adult with malaria suffer from thrombocytopenia, the risk of thrombocytopenia among children with malaria was 1.29 times as high as the risk in malaria adult. Median WBC count in children was significantly ($p<0.05$) higher than adult. The study also showed that 87.84%, 56.21% and 22.24% of severe anaemia, leucocytosis and thrombocytopenia respectively that occurred in children with malaria can be attributed to their age. ***Conclusion*:** Children are 2.8 (OR) times more likely to suffer from malaria infection than adults whilst equal cases of malaria occur in females and males. Policy makers and stakeholders should as a matter of urgency develops malaria intervention programs targeting children, whilst health workers should closely monitor the haemoglobin levels, platelet count and WBC of malaria children, since they suffer the worse haematological abnormalities.

Citation: Ellis Kobina Paintsil, Dr. Augustina A. Sylverken and Matthew Glover Addo. **2019.** "Effects of changes in haematological parameters of malaria infected children and adult patients attending the st. patrick's hospital, Offinso, Ghana", *International Journal of Current Research*, 11, (02), 1030-1033.

INTRODUCTION

Globally, it is estimated that, two hundred and sixteen million cases of malaria are reported annually with over 90% recorded in Africa (WHO, 2017). Children less than 5 years are the worst affected, since 70% of all deaths attributable to malaria occurs in this age group (WHO, 2018). Dogbevi (2016) reports that, in Ghana, 3.5 million Ghanaians get the disease every year and about 20,000 children die from it annually. Even though clinical diagnosis is widely used for the diagnosis of malaria in Ghana and most parts of African, fever and other signs and symptoms are known to be sensitive measures of malaria infection. Unfortunately, these signs lack specificity and positive predictive values especially in areas where malaria is less prevalent and therefore difficult to distinguish the sign and symptom of disease from other viral or bacterial infections (Maina *et al*., (2010); Lathia and Joshi (2004). Typically, microscopic slide examination of blood remains the most widely used test and the standard for detecting malaria infection, the drawback is that it requires technical expertise and is time-consuming in smear examinations (WHO, 2011). Since patients of malaria infection normally tend to have significantly lower RBCs, WBCs, platelets, lymphocytes, eosinophils and Hb level, haematological changes have therefore become some of the most common complications in malaria and play a major role in malaria pathogenesis (Bakhubaira (2013); van Wolfswinkel *et al*., (2013); Maina *et al*., 2010). Jairajpuri *et al.,* (2014), also reported that, because majority of the complex life cycle of malaria parasite occurs in the blood, it is not surprising that an infection is expected to

induce some changes in haematological parameters. Changes in haematological parameters are likely to be influenced by any disease condition including endemic diseases, such as malaria, that can affect health of mankind with various clinical presentations (Kotepui *et al.,* 2014). These changes associated with malaria may also vary with age, gender, and demographic factors (Nutan *et al.,* 2015). Therefore, diagnosis and treatment of malaria will greatly improve if the effects of malaria infection on haematological parameters are well known in each geographical area. This study therefore seeks to analyse the changes in some haematological parameters of malaria infected children and adult patients attending the St. Patrick's Hospital, Offinso, Ghana.

MATERIALS AND METHODS

A total of two thousand and seventy-six (2076) full blood count together with malaria test data were obtained as secondary data from the laboratory department of St. Patrick's Hospital, Offinso, from January 2018 to June 2018. This included 1200 females and 876 males between the ages of 1 to 102 years. The diagnosis of malaria was done using Rapid Diagnostic Test (RDT) and confirmed by blood film smear examination. Full blood count analyses were also done using Mindray BC – 3000Plus auto analyser after careful calibration to measure haemoglobin, white blood cell, platelet, lymphocytes, neutrophils, and mixed cell count. Identification of malaria parasites was done using RDT and confirmed by blood film smear examination. The analyser provides results on 19 haematological parameters and have an internal control that considers neutrophils and lymphocytes as the most important type of WBC. The secondary data obtained was initially entered in Microsoft Excel (2010) and checked for errors after which it was exported to IBM SPSS Statistics 22 software for further analysis. Because all the haematological parameters studied have non-normal distribution, Mann-Whitney test was used to compare groups after determining the medians (interquartile range). Odds ratios (OR), relative risk and attributable risk were computed to determine the risk of children having malaria, risk of having haematological abnormalities and the percentage of abnormalities that can be attributed to age. p-value less than 0.05 was considered significant.

RESULTS

Malaria infection by age and gender: Out of the 2076 patients, 539 (25.96%) tested positive for malaria; majority (68.65%) of the malaria positive cases were recorded in children (Table 1). Moreover, children (1-14 years) were 2.8 (OR) times more likely to suffer from malaria infection than adult (>14 years) ($p<0.0001$, 95% CI: 2.2471 - 3.4060). 539 positive malaria cases recorded 305 (56.59%) occurred in females, while males accounted for 234 (43.41%) of the positive cases. This slightly higher percentage of positive cases recorded in females was however not statistically significant (OR: 0.9350, $p<0.5061$, 95% CI: 0.7669 to 1.1399) (Table 1).

Influence of malaria infection on haematological parameters in children and adult: The least median haemoglobin concentration of 9.5g/dL was observed in children (1-14 years) with malaria infection. Children without malaria recorded highest platelet count of $335 \times 10^9/L$ whilst those with malaria had the minimum median platelet value of $151\times 10^9/L$ (Table 2). Adult with malaria infection recorded the least white blood cell count of $6.7\times 10^9/L$; however, this was not statistically significant ($p>0.05$) compared to the $7.2 \times 10^9/L$ reported in those without malaria. Also, there was no significant difference between haemoglobin concentration and mixed cell count of malaria negative and positive patients in the adult population (Table 3).

Analysis of haematological parameters between malaria positive children and adult, Relative risk (RR)and attributable risk (AR) in malaria infected children: In malaria infected patients, all haematological parameters of children vary significantly from that of adults. Children recorded higher median values for white blood counts, lymphocytes and mixed cell counts; however, for haemoglobin levels, platelet count and neutrophils the median values for adults were significantly more than that of the children population (Table 4).Of the 370 children with malaria 183 (49.46%), 135 (36.49%) and 54(14.59%) had thrombocytopenia, leucocytosis and severe anaemia respectively compared to 65 (38.46%), 27 (15.48%) and 3 (1.78%) respectively in the 169 adult patients with malaria. Children with malaria were 8.22 (95% CI: 2.6077 to 25.9210), 2.28 (95% CI: 1.5759 to 3.3095) and 1.29 (95% CI: 1.0354 to 1.5972) (RR) times as likely to develop severe anaemia, leucocytosis and thrombocytopenia respectively compared to adult with malaria ($p<0.05$). Attributable risk of anaemia in malaria positive children caused by their age (≤14 years) was 87.84%. On the other hand, proportions of leucocytosis and thrombocytopenia in malaria infected children attributable to not being more than 14 years old were 56.21% and 22.24% respectively.

DISCUSSION

In Ghana, about 3.5 million Ghanaians get the malaria disease every year and about 20,000 children die from it annually. Out of the 539 patients who tested positive for malaria parasites 206 (38.22%) and 164 (30.43%) were in the <5 and 5-14 years age group respectively. All the other age groups collectively accounted for only 31.35% of the malaria positive cases. This finding supports a study by Kleinschmidt and Sharp (2001) where they observed a rise in malaria case among children while adults reported only few cases. The World Health Organization reports that children, especially those under five years are most susceptible to malaria infection whilst adults acquire partial immunity due to several years of exposure even though this does not offer them complete protection (WHO, 2018). It is therefore not surprising that in this study, children were 2.8 (OR) times more likely to suffer from malaria infection than adult ($p<0.0001$, 95% CI: 2.2471 - 3.4060). Among the 539 patients who had malaria, 305 (56.59%) and 234 (43.41%) were females and males respectively. Several studies have identified and linked high malaria infection in females to pregnancy (Rogerson, 2017; Brentlinger*et al*., 2006). However, our study reported equal cases of malaria in females and males (OR: 0.9350, $p<0.5061$, 95% CI: 0.7669 to 1.1399). The reason for the current findings could be due to the fact that only 46 (2.22%) of the study participant were pregnant. Contrary to this study and other reports that malaria occurs more in females than males, Ayodele (2006) observed that the severity and prevalence of malaria infection is more common in males compared to females. The current findings presented that there is a statistically significant ($p<0.0001$) difference between the median haemoglobin levels

Table 1. Malaria infection in age groups and gender

Age group	Malaria status in age groups		Malaria positive cases by gender	
	Negative n (%)	Positive n (%)	Female n (%)	Male n (%)
<5	481 (31.29)	206 (38.22)	106 (34.75)	100 (42.74)
5-14	198 (12.88)	164 (30.43)	76 (24.92)	88 (37.61)
15-24	233 (15.16)	69 (12.80)	48 (15.74)	21 (8.97)
25-34	231 (15.03)	37 (6.86)	31 (10.16)	6 (2.56)
35-44	136 (8.85)	22 (4.08)	16 (5.25)	6 (2.56)
45-54	104 (6.77)	16 (2.97)	11 (3.61)	5 (2.14)
55-64	61 (3.97)	11 (2.04)	8 (3.25)	3 (1.28)
≥65	93 (6.05)	14 (2.60)	9 (5.58)	5 (2.14)
Total	1537 (100)	539 (100)	305 (100)	234 (100)

Table 2: Comparison of haematological parameters between malaria negative and positive children (1-14 yrs)

Parameters	Malaria Negative (n =679) Median (IQR)	Malaria Positive (n=370) Median (IQR)	Mann Whitney (U)	p- value
Age (1-14years)	2 (1 – 5)	4 (2 – 7)	95362	<0.0001
Haemoglobin (g/dL)	10.8 (9.8 – 11.7)	9.5 (8 – 11.1)	83036	<0.0001
WBC ($\times 10^9/L$)	9.9 (7.2 – 13.1)	9.8 (7.2 – 13.2)	121771	0.4123
Platelet ($\times 10^9/L$)	335 (250 – 428)	151 (90.25 – 226)	36641	<0.0001
Lymphocyte (%)	39 (27.4 – 50.75)	30.3 (20.6 – 42)	90749	<0.0001
MXD (%)	7.9 (6.45 – 9.8)	7.85 (6.3 – 9.9)	124129	0.7513
Neutrophil (%)	51.9 (39.8 – 64.75)	61.35 (48.7 – 72.7)	92281	<0.0001

IQR = Interquartile range; WBC = White blood cell; MXD = Mixed Cell Count

Table 3. Comparison of haematological parameters between malaria negative and positive adult (>14years)

Parameters	Malaria Negative (n =858) Median (IQR)	Malaria Positive (n=169) Median (IQR)	Mann Whitney (U)	p-value
Age (>14years)	33 (24 – 48)	27 (21 – 43)	60574	0.0007
Haemoglobin(g/dL)	11.9 (10.5 – 13.1)	11.6 (10.2 -12.7)	66195	0.0736
WBC ($\times 10^9/L$)	7.2 (5.7 – 9.8)	6.7 (5.2 -9.7)	65790	0.0569
Platelet ($\times 10^9/L$)	226 (177 – 276)	170 (125 – 214)	43875	<0.0001
Lymphocyte (%)	30.8 (18.6 – 42.9)	21.2 (13.1 – 32.1)	50961	<0.0001
MXD (%)	6.7 (5.5 – 8.3)	6.5 (5.6 – 8)	69743	0.4339
Neutrophil (%)	61.4 (49.1 – 73.8)	71.4 (61 – 79.8)	51317	<0.0001

IQR = Interquartile range; WBC = White blood cell; MXD = Mixed Cell Count

Table 4. Comparison of haematological parameters between malaria positive children (1-14 yrs) and adult (>14 yrs)

Parameters	1 – 14 years (n =370) Median (IQR)	>14 years (n=169) Median (IQR)	Mann Whitney (U)	p-value
Haemoglobin(g/dL)	9.5 (8 – 11.1)	11.6 (10.2 -12.7)	15621	<0.0001
WBC ($\times 10^9/L$)	9.8 (7.2 – 13.2)	6.7 (5.2 -9.7)	18361	<0.0001
Platelet ($\times 10^9/L$)	151 (90.25 – 226)	170 (125 – 214)	27742	0.0357
Lymphocyte (%)	30.3 (20.6 – 42)	21.2 (13.1 – 32.1)	21540	<0.0001
MXD (%)	7.85 (6.3 – 9.9)	6.5 (5.6 – 8)	22467	<0.0001
Neutrophil (%)	61.35 (48.7 – 72.7)	71.4 (61 – 79.8)	21042	<0.0001

IQR = Interquartile range; WBC = White blood cell; MXD = Mixed Cell Count

of children with and without malaria. Similar to this study, Ewusie*et al.* (2014) analysed demographic and health survey data from Ghana and concluded that the prevalence of anaemia among < 5 years children in Ghana was 78.4%. They argued that the high prevalence could be attributed to the high incidence of malaria cases within this age group. Their report supports the findings of our current study. However, within the adult population there was no difference between the median haemoglobin concentrations of malaria positive and negative patients ($p > 0.05$). Also, this study identified significant difference between platelets, lymphocytes and neutrophils of malaria positive and negative patients in both adult and children. This finding is in agreement with Kotepui *et al.,* (2014) where they identified significant changes in most haematological parameters of patients infected with malaria.

The current study identified significant difference between all studied haematological parameters of malaria infected children and adult. Of these, malaria positive children recorded significantly low haemoglobin levels compared to malaria infected adult. Of the 370 children with malaria, 14.59% had severe anaemia compared to only 1.78% from their adult counterpart; furthermore, the risk of developing severe anaemia was 8.22 times as high as the risk of severe anaemia in adult with malaria. In an earlier study conducted among some Zambian children, severe malarial anaemia was found in 9.5% of them; it was also noted that children with several malarial anaemia recorded deaths similar to those with cerebral malaria (Biemba *et al.,* 2000). According to Lamikanra *et al.,* (2007) severe malarial anaemia is not mainly due to haemolysis and clearance of infected and uninfected red blood cells but also the inability of an infected child to produce enough erythroid response. Although, 49.46% of children and 38.46% of adult with malaria suffer from thrombocytopenia; the risk of thrombocytopenia among malarial children was 1.29 times as high as the risk of thrombocytopenia in malarial adult. A related study conducted in north-western India, by Tanwar *et al.,* (2012), identified that among malaria positive children thrombocytopenia was highest in ≤ 5 years age group and decreased with increasing age. Also, the current finding compares favourably with several other studies conducted across the globe (Shaikh *et al.*, 2011; Khan *et al.*, 2012). Nonetheless, explanations on why malarial patients have low platelet levels differ among researchers. Some believe that platelets directly attack the malaria parasite and kill it, thereby offering a protective role to the patient (McMorran *et al*., 2009). Others are of the view that platelets make malaria infection worse through a process called proinflammatory (Morrell, 2014). Further studies need to be conducted in this

area to clearly determine the role of platelets in malaria infection. During malaria infection, low to normal white blood cell (WBC) count are generally observed (McKenzie *et al*., 2005). Similarly, in this study, for both malaria children and adult normal median WBC count observed, children recorded significantly ($p<0.05$) higher WBC count than adult. Furthermore, malaria children had 128% increase risk of getting leucocytosis over and above the risk adult. This could be due to bacteria co-infection in malaria, which has the tendency of increasing WBC (Nielsen *et al.,* 2015). Our study confirms that children suffer the worse haematological abnormalities compared to adult during malaria attack.

Conclusion

We concluded that children are 2.8 (OR) times more likely to suffer from malaria infection than adults whilst equal cases of malaria occur in females and males. Therewas a significant ($p<0.0001$) difference between the median haemoglobin levels of children with and without malaria. Although, 49.46% of children and 38.46% of adult with malaria suffer from thrombocytopenia; the risk of thrombocytopenia among malarial children was 1.29 times as high as the risk in malaria adult. For both malaria children and adult normal median WBC count was noted; though, children recorded significantly ($p<0.05$) higher WBC count than adult. It is recommended that policy makers and all other stakeholders should as a matter of urgency develops malaria intervention programs targeting children, and health workers should closely monitor the haemoglobin levels, platelet count and WBC of malaria children, since they suffer the worse haematological abnormalities.

Declaration of Conflict of Interest: The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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