IMPACT OF SEVER PLASMODIUM FALCIPARUM INFECTION ON PLATELETS PARAMETERS AMONG SUDANESE CHILDREN LIVING IN AL-JAZIRA STATE

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ABSTRACT

Background: Falciparum malaria remains one of the most global infection among children particularly in communities with poor resources. Falciparum malaria associated with several hematological changes that affect the major blood cell lines such as platelets lead to platelets parameters (platelets count and indices) abnormalities. **Objectives:** The aim of this study was to evaluate the effects of falciparum malaria on platelets parameters (platelets count and indices) among Sudanese children. In addition to study relationships and correlation between platelets parameters and malaria parasitemia and parasite count. **Methods:** A case control study was conducted in Wad Medani Pediatric Hospital. Among 100 children with severe falciparum malaria (mean age 8.63 ± 3.40 years; 61% males), 100 children with uncomplicated falciparum malaria (mean age 8.83 ± 4.20 years; 45% males) and 100 children with normal healthy children controls (mean age 10.08 ± 3.58 years; 50% males). Parasitemia and parasite count (%) was determined directly from thick and thin blood films respectively. The platelets parameters (platelets count and indices) measured by using Sysmex XP 300 N automated analyzer, and platelets count was confirmed and assessed using stained thin blood film. SPSS software (V 20.0) and Stat disk software (V 13.0) were used for data analysis. **Results:** 72 % of severe falciparum malaria (SM) have hyperparasitemia, while 18 % among uncomplicated falciparum malaria (UM). The thrombocytopenia account for 43 % (SM: 30.5 %; UM: 12.5 %), low PCT account for 35.5 % (SM: 27 %; UM: 8.5 %) and high PDW account for 46.5 % (SM: 23.5 %; UM: 23 %) in falciparum malaria cases. The mean PLTs count and PDW were statistically significantly differences between falciparum malaria cases and normal healthy control (P value 0.000 and 0.008 respectively). The mean PLTs count and PCT in severe falciparum malaria cases were lower than uncomplicated falciparum malaria cases (P value 0.005 and 0.000 respectively). The PLTs count and PCT had significant negative correlation within malaria parasitemia (P value 0.000; r -0.286; P value 0.004; r -0.205 respectively) and malaria parasite count (P value 0.000; r -0.450; P value 0.000; r -0.270 respectively). **Conclusion:** The study concluded that thrombocytopenia, low PCT and high PDW were observed as most platelets parameters changes in falciparum malaria. PLTs count along with PCT to be recommended as hematological diagnostic markers and prognostic tool to assess the disease severity and to improve the management of falciparum malaria among patients.

Keywords: Platelets count; Platelets indices; Thrombocytopenia; Falciparum malaria; Sudanese children.

INTRODUCTION

Falciparum malaria is the most virulent and pathogenic form of malaria [1], it is stills an important threat to public health in sub-Saharan Africa, and outside of Africa, particularly in young children, pregnant women and non-immune adults in communities with poor resources [2,3]. Falciparum malaria accounting for up to 80% of malaria cases globally [4] and 87.6% in Sudan [5].

Falciparum malaria associated with several hematological changes that affect the major blood cell lines such as red blood cells, white blood cells and platelets [6], which play a significant role in severity of falciparum malaria [5,7]. Malaria hematological changes arising from hemolysis, host immune (inflammatory) response, bone marrow suppression, and splenic pooling [8]. Thrombocytopenia (platelet count less than 150 x 10^9/L) is common platelets abnormalities and hematological changes [9] as well as a common feature of malaria due to all plasmodium species particularly in falciparum malaria (occurs in up to 70% of falciparum malaria patients) [9,10]. Platelet survival is reduced to 2-4 days in severe falciparum malaria lead to changes in platelets indices as mean platelets volume (MPV), plateletcrit (PCT), platelets distribution width (PDW) and platelet-large cell ratio (P -LCR). Thrombocytopenia and reduced platelet survival rate may result due to enhanced splenic uptake or sequestration and DIC (platelets may be removed from the circulation at sites of fibrin deposition) [11].

DOI: 10.31878/ijcbr.2020.62.02

eISSN: 2395-0471
pISSN: 2521-0394

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Previous studies have shown a consistent inverse correlation between parasitemia and the platelet count [3, 12-14]. In the Sudan still a need for simple and readily available parameters for the early identification and prognosis of patients at risk for severe or complicated malaria. Evaluation of hematological parameters as platelets parameters may be beneficial for monitoring malaria-infected children as well as determining the relationship between clinical and platelets changes among Sudanese children with Plasmodium falciparum malaria.

Therefore, the present study report on assessment effects of falciparum malaria among Sudanese children on platelets parameters (platelets count and platelets indices) to asses in the diagnosis, prognosis and management of falciparum malaria.

MATERIAL AND METHODOLOGY

Study design: Case control hospital-based study

Ethics approval: All study procedures were approved by the Researches and Ethics Committees of Ministry of Health, Gezira State and Faculty of Medical Laboratory Sciences, University of Gezira, Sudan. Informed consent was written from each participant parents.

Locus of study: Conducted in Gezira State, Sudan at Wad Medani Pediatric Hospital in collaboration with Faculty of Medical laboratory Sciences, University of Gezira as part of a wider research project studying the role of TNF-α levels and TNF-α 238 alleles polymorphisms in malaria severity, malaria anemia and malaria thrombocytopenia.

Inclusion criteria: The study included sick children with falciparum malaria aging 1 month to 18 years old, from both genders and residing in Gezira state who were admitted to Wad Medani pediatric teaching hospital.

Exclusion criteria: The study excluded sick children with mixed malaria or Vivax malaria, those aging ≥18 years old, those residing outside Gezira State, those suffering from recent infection, malignancy, and thrombosis, and those on anticoagulant and anti-inflammatory medication.

Sample size: Three hundred children suffering from falciparum malaria

Methodology:

The samples were collected from 100 children previously diagnosed as severe falciparum malaria (SM) by blood film and WHO criteria [15], 100 children previously diagnosed as uncomplicated falciparum malaria (UM) by blood film or ICT and 100 normal healthy controls according to inclusion and exclusion criteria.

A 2.5 ml venous blood samples were collected by clean venipuncture in K_3EDTA containers. Thin and thick films were prepared immediately. Parasitemia was determined from thick blood films using plus system [16]. Parasite count (% of parasitized red cells counting) was counted from thin blood film [15]. Platelets parameters (platelets count and indices) were determined using the Sysmex XP 300 N automated hematology analyzer (Sysmex, Kobe, Japan). The platelets count was confirmed and assessed using stained thin blood film. Thrombocytopenia was defined as a platelet count of less than 150×10^9/L [17]. The data were analyzed using SPSS software (V 20.0) and Stat disk software (V 13.0).

RESULTS

100 Sudanese children with severe falciparum malaria (mean age 8.63 ± 3.40 years; 61% male), 100 Sudanese children with uncomplicated falciparum malaria (mean age 8.83 ± 4.20 years; 45% male) and 100 normal healthy children controls (mean age 10.08 ± 3.58 years; 50% male) were participated in this study. 72 % of severe falciparum malaria have hyperparasitemia, while 18 % among uncomplicated falciparum malaria (Table 1).

Table 1: Demographic characteristics of study participants

Factors	Uncomplicated malaria	Severe malaria	Control
Age (years)	8.83 ± 4.2	8.63± 3.4	10.1± 3.6
Age (years)			
Less than 5	24	19	7
6 – 10	41	47	20
11 – 15	29	33	58
>15	6	1	15
Gender			
Male	45	61	50
Female	55	39	50
Parasitemia			
+	43	4	
++	25	3	
+++	14	21	
++++	18	72	
Parasite count (%)	0.39 ± 0.3	0.88± 0.4	

The mean of PLTs, PCT, MPV, PDW and P-LCR in falciparum malaria cases were (191.01 ± 142.47 × 109/L, 0.24 ± 0.54 %, 10.18 ± 1.14 fl, 13.51 ± 3.05 fl and 27.36 ± 8.90 % respectively) (Table 2). On the other hand, the thrombocytopenia account for 43 % (severe 30.5 %; uncomplicated 12.5 %), low PCT account for 35.5 % (severe 27 %; uncomplicated 8.5 %) and high PDW account for 46.5 % (severe 23.5 %; uncomplicated 23 %) in falciparum malaria cases (Table 3).

Table 2: Platelets parameters among UM and SM.

Factors	Uncomplicated malaria	Severe malaria	Falciparum malaria (N = 200)
PLTs× 10^3/L	221.1 ± 98.7	160.9± 186.2	191.0± 151.7
PCT %	0.22 ± 0.09	0.15 ± 0.10	0.19 ± 0.10
MPV fl	10.17 ± 1.02	10.19 ± 1.26	10.18 ± 1.14
PDW fl	13.40 ± 2.95	13.62 ± 3.15	13.51 ± 3.04
P-LCR %	27.06 ± 7.77	27.65 ± 10.02	27.36 ± 8.95

Table 3: Frequency of platelets parameters among UM and SM

Parameters	Low	Normal	High
PLTs × 10^3/L	86 (43 %)	110 (55 %)	4 (2 %)
PCT %	71(35.5%)	96 (48 %)	33(16.5%)
MPV fl	4 (2 %)	184 (92 %)	12 (6 %)
PDW fl	4 (2 %)	103(56.5%)	93(46.5 %)
P-LCR %	16 (8 %)	148 (74 %)	36 (18 %)

The mean PLTs and PDW in falciparum malaria cases were (191.01 ± 142.47 × 10^9/L and 13.51 ± 3.05 fl respectively) versus normal healthy control (290.91 ± 97.77 × 10^9/L and 12.61 ± 2.11 fl respectively), giving statistically significant differences (P value 0.000 and 0.008 respectively); while there was no significant difference in PCT, MPV and P-LCR between them (P value 0.264, 0.394 and 0.872) (Table 4).

Table 4: Comparison of platelets parameters between cases and control

Parameters	Malaria (N=200)	Control (N=100)	P value
PLTs count × 10^3/µl	191.0± 151.7	290.9 ± 97.8	0.000
PCT %	0.19 ± 0.10	0.41 ± 1.20	0.264
MPV fl	10.18 ± 1.14	10.36 ± 1.02	0.394
PDW fl	13.51 ± 3.04	12.61 ± 2.11	0.008
P-LCR %	27.36 ± 8.95	27.56 ± 7.77	0.872

Data was presented as Mean±SD

The mean PLTs and PCT in severe falciparum malaria cases (160.91 ± 186.24 × 10^9/L and 0.15 ± 0.10 % respectively) were lower than uncomplicated falciparum malaria cases (221.10 ± 98.69 × 10^9/L and 0.22 ± 0.09 % respectively), giving statistically highly significant differences between them (P value 0.005 and 0.000 respectively); while there was no significant difference in MPV, PDW and P-LCR between them (P value 0.917, 0.617 and 0.642) (Table 5).

Table 5: Comparison of platelets parameters between UM and SM

Parameters	Uncomplicated malaria	Severe malaria	P value
PLTs × 10^3/L	221.10± 98.7	160.91± 186.2	0.005
PCT %	0.22 ± 0.09	0.15 ± 0.10	0.000
MPV fl	10.17 ± 1.02	10.19 ± 1.26	0.917
PDW fl	13.40 ± 2.95	13.62 ± 3.15	0.617
P-LCR %	27.06 ± 7.77	27.65 ± 10.02	0.642

The mean PLTs count and PCT were significant different between falciparum malaria parasitemia (+, +++, +++ and ++++) (P value 0.000, 0.000 respectively); while there was no significant differences in MPV, PDW and P-LCR (P value 0.643, 0.250 and 0.506 respectively) (Table 6).

Table 6: Comparison of platelets parameters between falciparum malaria parasitemia

Parameters	+ (N=47)	++ (N=28)	+++ (N=35)	++++ (N=90)	P value
PLTs Count ×10^3/µl	272.7±96	208.5±106	136.9±64	164±190	0.000
PCT %	0.27± 0.1	0.21 ± 0.1	0.14± 0.1	0.15±0.1	0.000
MPV fl	10.0± 1.1	10.1 ± 1.1	10.21± 1	10.27±1	0.643
PDW fl	12.7± 2.5	13.8 ± 3.4	13.9± 3.4	13.67±3	0.250
P-LCR %	25.7± 8.4	27.0 ± 7.4	28± 9.4	28.07±10	0.506

PLTs and PCT had significant negative correlation within malaria parasitemia (P value 0.000; r -0.286; P value 0.004; r -0.205 respectively) and malaria parasite count (P value 0.000; r -0.450; P value 0.000; r -0.270 respectively). While MPV, PDW and P-LCR had significant positive correlation within age (P value 0.001; r 0.235; P value 0.042; r 0.144; and P value 0.003; r 0.212 respectively) (Table 7).

Table 7: Correlation between platelets parameters and falciparum malaria parasitemia and parasite count

Parameters		Para-sitemia	Parasite count %	Age
Platelets count × 10^3/µl	Pearson's r	- 0.286	- 0.205	- 0.087
	P value*	0.000	0.004	0.219
PCT %	Pearson's r	- 0.450	- 0.270	- 0.018
	P value*	0.000	0.000	0.802
MPV fl	Pearson's r	0.092	0.004	0.235
	P value*	0.197	- 0.009	0.001
PDW fl	Pearson's r	0.106	0.065	0.144
	P value*	0.135	0.358	0.042
P-LCR%	Pearson's r	0.104	0.008	0.212
	P value*	0.143	0.914	0.003

DISCUSSION

Falciparum malaria is still a major health problem in Sudan, accounts 87.6% [18]. In fact, about 285,000 children died before their fifth birthdays in 2016 in Africa According to the World Health Organization [(7)]. therefore, malaria remains the largest cause of children death in Afric [19]. Furthermore, 75% of population is at risk of developing falciparum malaria. The children are 3 times more likely to get malaria than adults [5]. The treatment outcome of malaria depends on appropriate early diagnosis and appropriate management with the recommended therapy to reduce deaths attributed to severe malaria. The aim of this study was to evaluate the effects of falciparum malaria on platelets parameters (platelets count and indices) among Sudanese children. In addition to study relationships and correlation between platelets parameters and malaria parasitemia and parasite count.

The Study was conducted on 100 children with severe falciparum malaria (mean age 8.63 ± 3.40 years; 61% male), 100 children with uncomplicated falciparum malaria (mean age 8.83 ± 4.20 years; 45% male) and 100 normal healthy children controls (mean age 10.08 ± 3.58 years; 50% male). Study in Sudan showed that malaria infection was higher in male more than female [20]. Similar previous studies were reported from different African countries [21, 22, 23].

The average of platelets count among falciparum malaria cases was lower than controls (P value 0.000); while the average of PDW was higher (P value 0.008). The average of platelets counts and PCT in severe falciparum malaria cases were lower than uncomplicated falciparum malaria cases (P value 0.005 and 0.000 respectively). Previous study finding in Sudan showed that there were significant differences in platelet count, PDW, and PCT between falciparum malaria patients and control [24]. The studies done in Kenya showed the platelets count were significantly lower in malaria-infected children, while MPV were

higher in comparison to non-malaria infected children [25,26]. Martinez-Salazar et al., observed that the most frequently changes were low platelets count and high PDW [27]. Several studies observed platelets count were significantly lower among Plasmodium parasitized subjects compared to controls [13, 28, 29]. Previous report demonstrated that malaria parasite has a direct lytic effect on the platelets [14]. The average of platelets counts and PCT in severe falciparum malaria cases were lower than uncomplicated falciparum malaria cases (P value 0.005 and 0.000 respectively). Furthermore, the average of platelets counts in severe falciparum malaria cases with thrombocytopenia (83.98 × 10^9/L) were lower than uncomplicated falciparum malaria cases with thrombocytopenia (106.88 × 10^9/L) (P value 0.003). Study done in Sudan reported that the children with severe P. falciparum malaria had significantly lower platelets count [30]. Similar studies observed platelets count were lower among severe than in mild cases (Gerardin et al., 2002; Arévalo-Herrera et al., 2015). In contrast study done in Ethiopia observed no differences in platelets count according to malaria severity [22].

There were significant differences in platelet count and PCT between malaria parasitemia (P value 0.000 and 0.000 respectively). Furthermore, malaria parasitemia had significant negative correlation within platelets count (r – 0.468; P value 0.000), and PCT (r – 0.481; P value 0.000). On the other hand, malaria parasite count had significant negative correlation within platelets count (r – 0.205; P value 0.004), and PCT (r – 0.270; P value 0.000). Similar study results showed there were significantly lower in patients with high parasitemia compared to those with low and moderate parasitemia [13]. Many previous studies reported negative correlation between platelet count and malaria parasitemia [14, 31-33]. Malaria thrombocytopenia was common in SM (62%) compared to UM (25%). Platelet survival is reduced to 2 – 4 days in severe falciparum malaria [11]. Several studies in endemic area reported thrombocytopenia were observed in 73.6% [34], 70% (Suh et al., 2004), 85.5% [26]. Thrombocytopenia was significantly more frequent and more profound in those with SM than in those with mild forms [14, 35]. Previous studies concluded thrombocytopenia is associated with peripheral parasitemia levels [26, 36-39]. Thrombocytopenia is a frequent finding in falciparum and possible causes are due to decreased platelets production, increased levels of cytokines and immunological destruction due to antibody and cellular immune responses, removal of platelets from circulation through enhanced splenic uptake and sequestration or by of fibrin deposition [12].

Finally; MPV, PDW and P-LCR had significant positive correlation within age (P value 0.001; r 0.235; P value 0.042; r 0.144; and P value 0.003; r 0.212 respectively).

CONCLUSION

The study concluded that thrombocytopenia, low PCT and high PDW were observed as most platelets parameters changes in falciparum malaria. The PLTs count and PCT were lower in severe compared to uncomplicated cases and in addition were correlated within degree of parasitemia; so PLTs count along with PCT to be recommended as additional hematological markers and prognostic tools to assess the disease severity and to improve the management of falciparum malaria among patients.

Competing interests: The authors declare that they have no competing interests.

Acknowledgements: The Wad Medani Pediatric Hospital and Faculty of Medical Laboratory Sciences is thanked for helping in laboratory working.

Conflict of interest : Nil

Source of funding : Nil

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