Entomology and Applied Science Letters
Volume 7, Issue 3, Page No: 91-97

Available Online at: www.easletters.com

ISSN No: 2349-2864

Efficacy of *Plasmodium Falciparum* on Hematological Parameters and Coagulation Profile in Children under Five Years Old

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ABSTRACT

Hematological effects are known to be the most frequent problems of malaria and play a significant role in malaria pathogenesis. The objective of this paper was to evaluate the hematological parameters and the coagulation profile of children less than five years of age with malaria. This is a case-control focused on 100 children under the age of five. Fifty children have been diagnosed with malaria as a case group. Additionally, 50 regular healthy children matched the gender and age group as the control group. PT and APTT were carried out using an automated coagulometer. CBC conducted with EDTA anticoagulant blood using an automated hematological analyzer. Based on the age of the patients, this study found that 56 percent of the cases were above three years of age. The present study stated that the male-to-female ratio was male: female 1:1.3. The current research found that hematological parameters were statistically and significantly lower in the patients' group compared to the normal control group with a P-value of less than 0.05, whereas the coagulation profile was significantly higher in the patients' group compared to the normal group (P-value less than 0.05). This study revealed that the hematological profile of children under five years of age with malaria also varies significantly from the control profile of coagulation increased in children with malaria.

Keywords: Hematological parameters, Coagulation profile, *Plasmodium falciparum*, Malaria.

HOW TO CITE THIS ARTICLE: Ragda Khafalla Abdulla, NasrEldeen Ali Mohammed, Sara Abdelghani, Lienda Bashier Eltayeb, Hisham Ali Waggiallah: Efficacy of *Plasmodium Falciparum* on Hematological Parameters and Coagulation Profile in Children under Five Years Old, Entomol Appl Sci Lett, 2020, 7 (3): 91-97.

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Received: 12/05/2020
Accepted: 23/08/2020

INTRODUCTION

Anemia in malaria is induced by hemolysis of the infected RBCs, sequestering of RBCs in the spleen and other deep organs, and inhibition of RBCs development in the bone marrow by the malarial pyrogen-induced cytokines [1-5]. Since malaria parasites attack RBCs, hematological alterations are the major complications and therefore play an important role in the consequence of the disease. Some blood components, including erythrocytes, platelets, and WBCs, are impacted by malaria and extreme anemia is the most frequent problem in children with severe malaria in rural areas of Sudan and other parts of Africa [2] . Alterations in hematological parameters are prone to be impacted by any disorder, particularly infectious diseases such as malaria that can impact human health with various clinical manifestations. Hematological modifications are among the most major symptoms of malaria and play a prominent part in malaria pathogenesis. These alterations include main cell types such as Erythrocytes, WBCs, and platelets [1, 6]

Malaria-infected patients appeared to have considerably lower thrombocytes, White Blood Cells, lymphocytes, eosinophils, RBCs, and Hb levels, while monocyte and neutrophil numbers were significantly greater compared to non-malaria infected people.

Hematological disorders stated to usually follow malaria infection include anemia, thrombocytopenia, splenomegaly, mild to severe atypical lymphocytosis, and rarely distributed intravascular coagulation (DIC) [1].

There were also cases of leukopenia and leukocytosis. Other documented hematological responses to malaria include neutropenia, eosinophilia, neutrophilia, and monocytosis [2].

The numerous findings cited before confirm well-known hematological changes for extreme malaria and acute malaria, especially in adults, and for parameters such as Hb or packed cell volume used for the assessment of anemia and leucocytes [7].

In addition, studies have shown patients with higher leucocytes counts relative to population controls. Thrombocytopenia is the most common side effect during malaria infection. People with platelet counts <150,000/μL were 12-15 times more probable to develop malaria infection than people with platelet counts >150,000/μL [6].

While there is an indication that malaria may influence the profile of circulating cells in peripheral blood, this result may not be compatible across all geographical regions [8-11] Malaria-related hematological variations are prone to heterogeneity based on the degree of endemicity of the disease, nutritional status, hereditary factors, socio-demographic status, race, and immunity [6].

Standard coagulation measures (prothrombin time, partial thromboplastin time, fibrinogen, fibrin degradation products) decreased plasma levels of antithrombin III (AT-III) concentrations were recorded in some normal range studies in all groups and the occurrence was considerably higher in patients with extreme and moderate malaria (83% and 81%) matched with the mild group (37%; P <0.005) [6]. In this context, the research was conducted to assess the alteration in hematological measurements and the coagulation profile among Sudanese children (under five years of age) with malaria.

MATERIALS AND METHODS

Study Design

This is case-control-based research that was performed at Gazira state and Al-Neelain University, Sudan, during 2019. Six ml of venous blood collected from children under five years old known diagnosed with *P. falciparum* malaria and healthy apparent control, three ml were collected in EDTA container for hematological studies, and other three ml were collected in citrate tube for coagulation studies, the ratio of blood to citrate 9:1. Platelets poor plasma was prepared from the citrate tube by centrifugation at 3000xg for 15 minutes and the test was done immediately. The study covered 100 participants, 50 cases, and 50 controls.

Blood is collected and filtered and passed into the tube thin enough that the cells move through one at a time, the features of the cells are tested using lasers (fluorescence flow cytometer) or electrical resistance, the blood is divided via a variety of different channels, the XE-2100 has finely multiple systems. Fully automatic multichannel instruments (sysmex21) require only that an appropriate blood sample is presented to the analyzer and usually measure from 8 to 20 components for the basic CBC and white blood cell differential. Impedance counting system depends on the fact that red cells are poor conductors of electricity, whereas certain diluents are good conductors [12]

The PT tests the clotting time of the re-calcified plasma in the existence of an optimal level of tissue extract (thromboplastin) and shows the overall impact of the extrinsic clotting system. While originally thought to quantify prothrombin, it is now understood that the test also relies on the interactions with factors V, VLL, and X and the plasma level of fibrinogens [13].

The test examines the plasma clotting time after stimulation of the contact factors and addition of phospholipids and Cacl2; however, without the addition of thromboplastin, thus suggesting the overall efficacy of the intrinsic pathway. In standardizing the triggering of the contact factor, the plasma is the first to be pre-incubated for a while with a contact activating agent like kaolin, silica, or allergic acid.

Throughout that phase of the test, factor XIIa is formed, which cleaves factor II to factor XIIa, but

coagulation does not occur after that in the absence of calcium, following recalcification, factor IIa activates factor IX and coagulation occurs.

Standardized phospholipids are given to enable the test to be conducted on low plasma platelets [13]. The test relies not only on the contact factors and factors VIII and factor IX but also on the reactions with X, V, prothrombin, and fibrinogen. It is also responsive to the existence of circulating anticoagulants (inhibitors) and heparin [13].

Ethical Considerations

This study was approved by Al-neelain ethical board, and consent was also obtained from every participant in this study before the samples were obtained.

RESULTS

A total of 100 participants were recruited in this study, 50 were known patients diagnosed by malaria; 28 (56%) were female and 22 (44%) were males; their mean age was 3 years old. Further, 50 normal healthy subjects were matched with the case group and used as a normal control group (Figures 1 and 2).

The analysis of this result showed that WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, LMY, MXD, NEUT, MXDD, and RDW.SD were statistically and significantly different when compared with a normal healthy control group with a P-value less than 0.05. (Table 1).

The present study found that the mean of PT and APTT is statistically and significantly higher in the patients' group in comparison with normal healthy control group MSD (PT 26.36±10.36, PTT58.46±15.65) with P-value 0.00 for both tests. Based on age in this study, our patients were classified into two groups less and more than three years old (Table 2)

The current study showed that there is not any significant difference in PT, and APTT in patients less than three years compared with those more than three years old with a P value more than 0.05 (Table 3)

In current research the result showed that RBC, HGB, HCT, MCV, RDW.C, and PT were statistically significantly different a cross gender when compared with a normal healthy control group with a P- value less than 0.05. (Table 4).

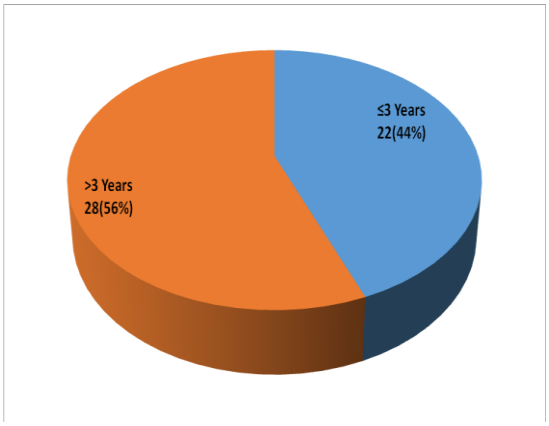

Figure 1: Distribution of Patients according to Age Group

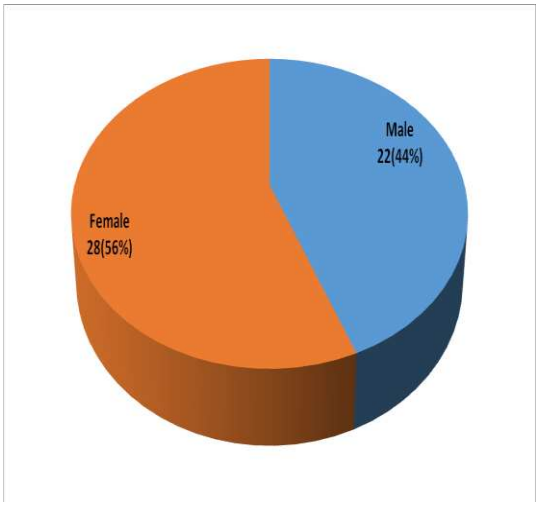

Figure 2: Distribution of Study Group according to Gender (n = 50)

Table 1: Comparison of Study Parameters in Case Versus Control Group (n = 100 = 50 Cases + 50 Controls) (INR=1)

Parameters	Case (Mean ± SD)	Control (Mean ± SD)	*P-value*
WBC	7.77±2.94	6.74±1.82	0.039
RBC	3.83±0.97	4.41±0.42	0.000
HGB	10.40±2.92	12.53±1.10	0.000
HCT	34.02±8.62	37.60±3.57	0.008
MCV	74.18±11.24	84.54±3.41	0.000

MCH	25.30±3.74	27.78±1.11	0.000
MCHC	31.58±3.48	32.98±2.92	0.032
PLT	108.9±29.16	277.8±67.90	0.000
LMY	41.65±17.53	35.44±9.59	0.030
MXD	9.61±3.51	6.46±4.04	0.000
NEUT	50.13±17.51	56.94±12.39	0.026
MXDD	1.01±0.92	0.44±0.25	0.000
NEUT	3.54±1.98	3.96±1.65	0.009
RDW.SD	40.61±3.74	42.64±3.65	0.007
RDW.CV	13.07±2.41	12.98±0.77	0.005
PDW	12.17±2.52	10.50±1.49	0.000
MPV	10.29±1.78	10.08±1.01	0.022
PT	26.36±10.36	13.44±1.77	0.000
PTT	58.46±15.65	32.28±3.47	0.000

Table 2: Comparison of Study Parameters among Patients based on Age Group (n = 50 Cases)

Parameters	≤3 Years (Mean ± SD)	>3 Years (Mean ± SD)	*P-value*
WBC	7.75±2.34	7.78±3.39	0.974
RBC	3.83±1.03	3.83±0.94	0.999
HGB	10.55±3.20	10.29±2.73	0.762
HCT	35.91±8.41	32.54±8.64	0.172
MCV	74.64±14.15	73.82±8.57	0.802
MCH	25.55±4.36	25.11±3.25	0.685
MCHC	31.50±3.81	31.64±3.26	0.887
PLT	115.1±26.97	104.2±30.41	0.195
LMY	41.97±14.87	41.40±19.65	0.910
MXD	9.87±3.99	9.41±3.14	0.654
NEUT	51.79±14.87	48.79±19.50	0.553
LMYY	2.11±1.20	2.53±1.13	0.414
MXDD	1.05±0.84	0.99±0.88	0.807
NEUTT	3.54±1.50	3.53±2.32	0.988
RDW.SD	40.59±3.87	40.62±3.70	0.977
RDW.C	13.68±2.59	12.59±2.19	0.113
PDW	12.55±2.83	11.87±2.27	0.348
MPV	9.95±1.95	10.56±1.62	0.235

Table 3: Comparison of Studying PT and APTT Parameters in Case according to Age

Parameters	≤3 Years (Mean ± SD)	>3 Years (Mean ± SD)	*P-value*
PT	28.82±10.24	24.43±10.23	0.139
PTT	59.77±18.01	57.43±13.79	0.604

Table 4: Comparison of Study Parameters across Gender (n = 50 Cases)

Parameters	Male (Mean ± SD)	Female (Mean ± SD)	*P-value*
WBC	7.54±2.63	7.95±3.21	0.624

RBC	3.45±1.03	4.13±0.82	0.013
HGB	9.47±3.43	11.14±2.25	0.044
HCT	30.77±10.53	36.57±5.76	0.017
MCV	69.91±12.88	77.54±8.59	0.016
MCH	24.50±4.28	25.93±3.20	0.183
MCHC	32.00±4.00	31.25±3.04	0.455
PLT	104.77±33.56	112.29±25.34	0.371
LMY	45.27±21.25	38.81±13.71	0.199
MXD	9.91±3.80	9.38±3.31	0.598
NEUT	48.32±22.27	51.51±12.88	0.528
LMYY	2.81±2.22	1.98±1.25	0.101
MXDD	1.21±1.19	0.87±0.63	0.198
NEUTT	3.40±1.74	3.64±2.17	0.682
RDW.SD	40.20±4.03	40.93±3.53	0.499
RDW.C	13.95±2.85	12.38±1.76	0.020
PDW	12.38±2.94	12.01±2.19	0.608
MPV	9.95±2.18	10.56±1.37	0.235
PT	22.82±9.52	29.14±10.31	0.031
PTT	60.86±10.86	56.57±18.56	0.341

DISCUSSION

The study found that 56% of the cases were above three years of age. Commonly, based on the World Health Organization (WHO), about 86% of malaria deaths worldwide are children under 5 years of age. Because children are at the greatest risk of serious illness and death between six months and five years of age: during this age, children are more susceptible because they have lost maternal immunity and have not yet gained specific immunity to diseases [14].

In addition, our study recorded that more than half of the cases 56% were female, with a female ratio of 1:1.3. With this problem, many studies from African communities such as Kenya have argued that gender roles, particularly in urban and semi-rural (like in Gazira state-Sudan) communities, may play an important role in explaining the difference in the reported incidence of malaria [15] Similarly, Diiro et al. argued that the detection of environmental and socioeconomic factors of malaria is critical, and gender-based study can contribute positively to the creation of effective and sustainable malaria prevention programs[16] recognizing the role of gender in the prevention and management of malaria in families would be critical in enhancing the coverage and efficacy of malaria evaluation (both clinical and laboratory-based), managing and prevention strategies in the state.

Regarding the disparity in measurements between the two sample groups, there was a substantial difference in WBCs count, RBCs count, HB, HCT, MCV, MCH, MCHC, thrombocytes, lymphocytes, mixed cell proportion, neutrophils, MXDD, RDW.SD, PDW, prothrombin time, and partial thromboplastin with P-value < 0.05 in all. Likewise, in another Sudanese research by Mohieldin Elsayid et al., there was a significant disparity in mean hemoglobin and HCT measures between malaria patients and control, p. value of Hb = 0.005 and p. value of HCT=0.041, and malaria patients are linked with normocytic normochromic anemia [17]

In addition, another study in Sudan, by Sarah et al, 2018, observed that prothrombin time and APTT were substantially elevated in cases relative to the control group with (P. value.016) [18] Moreover, in Burkina Faso, Gansane et al. demonstrated that the infected children appeared to have considerably lower mean hemoglobin (p<0,001), mean lymphocyte count (p = 0.004), mean platelet count (p < 0.001) and

mean RBC count ($p < 0.001$) and a higher mean monocyte count ($p < 0.001$ compared to the control group [19]. In a Related sense, Inam Ullah, et al. in Pakistan, found that malaria-positive patients had correlated thrombocytopenia and peripheral blood anemia, accompanied in some cases by leukopenia in comparison with controls [20].

Similarly, in Iran, Fattahi Bafghi, et al. observed that the concentration of HGB (P=0.001), HCT (P=0.001), MCV (P=0.001), MCH (P=0.001), WBC (P=0.001), and Plt (P=0.002) had dramatically decreased in children with malaria compared to those without malaria [21]. Conversely, in India, Prasad et al., documented that coagulation profile disorders in the form of increased prothrombin time, APTT and/or TT could be seen in most malaria conditions, and thrombocytopenia was also observed and was statistically considerable [22] .

In Thailand, Manas Kotepui, et al. observed that the following measurements were considerably lower in malaria-infected patients: RBCs, Hb, platelet count, WBCs, neutrophil count, monocyte count, lymphocyte count and eosinophilic count, MCV, MCH, MCHC [23].

Dennis reported that soldiers with acute P. falciparum malaria increased intravascular coagulation with low platelet count, prolonged PT and APTT, reduced coagulation factors, and an indication of reduced plasminogen activation with an aggregation of FDPs in the blood [24]

There were some constraints to our analysis. The relatively small number of study participants (100 study participants with 50 cases from only one study area (Gezira state)) may negatively affect the likelihood of finding significant differences in blood parameters between children diagnosed with malaria in different Sudanese states.

CONCLUSION

This study found that P. falciparum has a possible impact on hematological parameters and the coagulation profile in children less than five years of age with malaria compared to normal healthy children.

Compliance with Ethical Standards

Disclosure of potential conflicts of interest

Author declares that they do not have conflict of interest

Research involving human participants and/or animals

Was approved by the ethical committee of National University

Funding Information

This study was not funded by any company or agency.

ACKNOWLEDGMENTS

This Publication was supported by the Deanship of Scientific Research at Prince Sattam bin Abdulaziz University.

Conflict of interest

Author declared that there is no conflict of interest in this research.

REFERENCES

1. Bartoloni A, Zammarchi L. (Clinical aspects of uncomplicated and severe malaria. Mediterr J Hematol Infect Dis. 2012; 4(1): e2012026.
2. Autino B, Corbett Y, Castelli F, Taramelli D. (Pathogenesis of malaria in tissues and blood. Mediterr J Hematol Infect Dis. 2012; 4(1): e2012061
3. Elsheikh, SH, Khalifa NM, Babiker NB, Abdo E, Alfadil R, Madani M, Waggiallah HA and Eltayeb LB. a comparative study of blood film, immunochromatographic test and polymerase chain reaction in the diagnosis of plasmodium vivax infected patients in Khartoum state- sudan.. WJPR. 2019; 8(3): 176-189
4. Eltayeb LB, Abdelghani S, Madani M, Waggiallah HA. Molecular Characterization of msp-1 and msp-2 among Plasmodium falciparum-infected Children: A Gene Polymorphisms analysis. J Biochem Tech. 2020;11(2): 102-107
5. Hijazi H, Waggiallah H, Alagib A. Oxidative Low Density Lipoprotien Prohibited Plasmodium Falciparum Clearance in type 2 Diabetes Mellitus Via Cluster Differentiation 36. NAJMS. 2013; 5(12): 703-706
6. Moore LR, Fujioka H. Williams PS. Hemoglobin degradation in malaria-infected

erythrocytes determined from live-cell magnetophoresis. FASEB J.; 2006; 20(6):747-9.
7. Mohandas N, An X. Malaria and human red blood cells. Med MicrobiolImmunol. Nov;2012(4):593-8.
8. Mohamed W A I, Badr N M, Fouad B E, Abd Alaal M E M. Efficacy of Intermittent Pneumatic Compression on Blood Flow in Patient with Varicose Veins. Arch. Pharm. Pract. 2020;11(2):149-53
9. Van Ta T, Nguyen HB, Tran HT. Evaluating the Association of Red Blood Cell Parameters and Glycemic Control in Type 2 Diabetic Patients at Tien Giang General Hospital. Arch. Pharm. Pract. 2019;10(4):153-60.
10. Nobandegani AS, Motamedifar M. Antibiotic Sensitivity Profile of the Bacterial Isolates from The Blood Samples of the Patients in Different Wards of A Major Referral Hospital, SHIRAZ, Iran 2015-2016. Pharmacophores. 2019;10(2):30-36
11. Andrusenko S F, Denisova E V, Anfinogenova O I, Melchenko E A, Kadanova A A, Brycina I E. Changes in the Concentration of Ethyl Alcohol in the Blood When It Is Stored In Different Temperature Conditions. Pharmacophores. 2020; 11(3): 75-7.
12. National Guideline Centre (UK). Preoperative Tests (Update): Routine Preoperative Tests for Elective Surgery. London: National Institute for Health and Care Excellence (UK); Apr. (NICE Guideline, No. 45.) 11, Full blood count test. 2016
13. Raber MN. Coagulation Tests. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; Chapter 157. 1990
14. World Health Organization. World Malaria Report. WMR. 2011- noprgilse – lowres.
15. Woldu DO, Haile ZT. Gender roles and perceptions of malaria risk in agricultural communities of Mwea Division in Central Kenya. Women Health. 2015;55(2):227-43.
16. Diiro GM, Affognon HD, Muriithi BW, Wanja SK, Mbogo C, Mutero C. The role of gender on malaria preventive behavior among rural households in Kenya. Malar J. 2016; 15:14.
17. Elsayid M, Elbasheer MA, Othman AA, Belal RH, Elfaki TE. Estimation of complete blood count and platelets indices in Sudanese patients with malaria. American Journal of ResearchCommunication, 2017; 5(1) :1-10.
18. Abdabagi S, Altayeb FM, AbdAlla AB, Osman RA, and Elaminnasir A. evaluation the effect of the malaria parasite on prothrombin time and activated partial thromboplastin time levels among sudanese patient in Khartoum state- Sudan. int. j. of adv. Res. 2018; 6 (9). 1045-1049
19. Gansane A, Ouedraogo IN, Henry NB. Variation in haematological parameters in children less than five years of age with asymptomatic Plasmodium infection: implication for malaria field studies. Mem Inst Oswaldo Cruz.2013;108(5):644-50.
20. Inam Ullah I, Ali MU, Ali S, Rafiq A, Sattar Z, Hussain S. Hematological Profile of Patients Having Malaria-positive Peripheral Blood Smears: A Cross-sectional Study at a Diagnostic Research Center in Khyber Pakhtunkhwa, Pakistan. Cureus.2018;10(9): e3376.
21. Fattahi Bafghi A, Hashemi A, Abolhasanizadeh S. Comparison of hematological aspects among children with Malaria and healthy children. Iran J PedHematolOncol.2015;5(2):89-92.
22. Prasad R, Das BK, Pengoria R, Mishra OP, Shukla J, Singh TB. (Coagulation status and platelet functions in children with severe falciparum malaria and their correlation of outcome. J Trop Pediatr. 2009; 55(6):374-8.
23. Kotepui M, Phunphuech B, Phiwklam N, Chupeerach C, Duangmano S. Effect of malarial infection on haematological parameters in population near Thailand-Myanmar border. Malar J. 2014; 13:218.
24. Dennis LH, Eichelberger JW, Inman MM, Conrad ME. Depletion of coagulation factors in drug-resistant Plasmodium falciparum malaria. Blood. 2007; 29(5):713-21.