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Original Research Article

Deranged hematological profile in patients presenting with malarial parasitaemia

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ABSTRACT

Background: Alterations in the hematological parameters are thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria, thereby prompting a more meticulous search for malaria parasites.
Methods: 186 cases with malaria positive for immunochromatographic test (ICT) malaria presenting with fever ≥101 °F, confirmed on peripheral blood film, of 20-60 years were included. Patients with coagulopathy and bleeding disorders such as hemophilia, brain tumors, tuberculosis meningitis, viral or bacterial encephalitis and multiple sclerosis were excluded. Sample was taken to the laboratory, for routine investigations like ICT malaria and complete blood count (CBC) to diagnose anemia and low platelet count.
Results: Patients of 20 to 60 years of age with mean 41.80±8.51. Out of 186 patients, 101 (54.30%) were male and 85 (45.70%) were female with 1:2:1 ratio. Mean duration of disease was 4.91±1.32 days. Frequency of derangement in hematological parameters was anemia in 27 (14.52%) patients and 142 (76.34%) with thrombocytopenia. 127 cases were of *Plasmodium vivax* and 59 cases were of *Plasmodium falciparum*. Patients were more anemic as disease period prolonged. Patients infected by *Plasmodium vivax* showed more tendencies towards anemia and reduction in platelet count as compare to *Plasmodium falciparum*.
Conclusions: The frequency of derangement in hematological parameters i.e. anemia and low platelet count, among malarial patients is quite high and more cases were of *Plasmodium vivax* and it showed anemia and thrombocytopenia was more pronounced in *Plasmodium vivax*.

Keywords: *Plasmodium falciparum*, *Plasmodium vivax*, Malaria, Anemia, Platelet count

INTRODUCTION

Malaria, a disease mostly caused by Plasmodium falciparum, is a major public health problem. The global burden is 207 million malaria cases every year resulting into 627,000 deaths, sub-Saharan Africa being the most affected region. Four species of *Plasmodium*, namely *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*, can infect humans.[1,2] Malaria is present in endemic form in about 103 countries of the world and it is one of the most widespread human parasitic diseases ranking first in terms of its socioeconomic and public health importance in tropical and subtropical region of the world, especially in sub-Saharan African and Southeast Asian countries.[3-4] Pakistan is among top ten malarial endemic countries of the world with approximately 50,000 deaths annually due to plasmodium infection. Globally in year 2006 and 2010, 250 clinical cases of malaria with one million deaths and

219 million cases with 60,000 deaths respectively documented among young people and children under five years of age.[5] Malaria is also major public health problem and obstacle to socioeconomic development in Pakistan. *Plasmodium falciparum* and *vivax* malaria are major health problems in Pakistan.[6] Anaemia is frequent in developing countries and its aetiology is usually multifactorial. The most important factors that contribute to anaemia include parasitic infections, human immunodeficiency virus (HIV) infection, chronic inflammatory disorders, micronutrient deficiencies and genetic disorders. The main parasitic infections include malaria and helminth infections. Malaria related anaemia is associated with many factors which involve increased destruction and reduced production of red blood cells (RBCs). The relationship between malaria parasitaemia and haemoglobin has been well documented in previous studies in pregnant women. Fewer previous studies in developing countries have involved non-pregnant adults and a study from Cameron has documented anemia was 14.08% in patients with malaria.[7] Shaikh et al has reported 85.5% low platelet count in patients with malaria.[8] Platelets play a critical role in the pathogenesis of malarial infections by encouraging the sequestration of infected RBCs within the cerebral vasculature. Platelets also have well - established roles in innate protection against microbial infections. Inhibition of platelet function by aspirin and other platelet inhibitors inhibited the lethal effect of human platelets which they exert on *P. falciparum* parasites. Human platelets bind malarial-infected red cells and kill the parasite within; these indicate a protective function of platelets in the early stages of erythrocytic infection distinct from their role in cerebral malaria.[8]

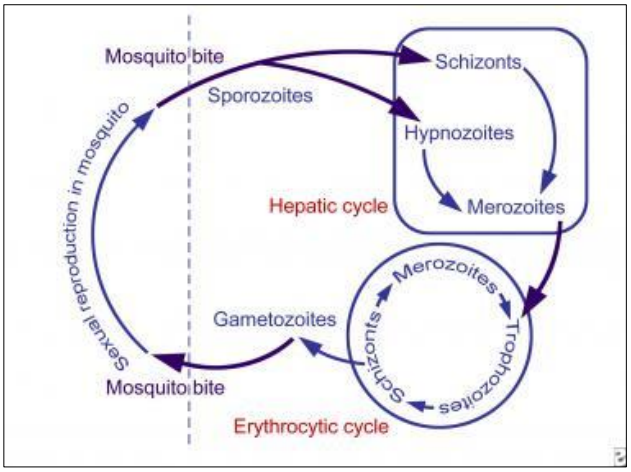

Figure 1: The various stages of *Plasmodium* life cycle are shown. Knowledge of the life cycle of the malarial parasite is essential to understanding the chemotherapy of malaria.

This proposed study has been designed to document derangement in hematological parameters in patients with malaria. The results of this proposed study will generate baseline database of our local population as there is no such study done in our local population and we have different environmental conditions and genetic diversity in our population as compared to different parts of the world. So there is a dire need to conduct such study in our population to report current magnitude of the problem and help clinicians to anticipate such derangements leading to early diagnosis and proper management. This will help to decrease disease related morbidity and mortality among such patients and improve quality of life of these patients.

Objectives

Objectives of the study were to determine the frequency of derangement in hematological parameters among patients with malaria.

METHODS

Sample size

Sample size is 186 cases, calculated by using following formula.

$$n = z^2pq/d^2$$

where z=1.96, p=14.08% (frequency of anemia in malaria), q=100-p, d=5% at 95% confidence level).[8]

Sample technique

It was non-probability, consecutive sampling technique. This study was conducted in department of hematology, Combined Military Hospital, Multan from 29 April 2019 to 28 October 2019.

Data collection procedure

A specialized performa has been developed to record the findings of this study. All the cases of malaria, fulfilling inclusion criteria were recruited from outpatient department (OPD) of department of medicine, Combined Military Hospital, Multan. Prior permission was taken from institutional ethical committee of Combined Military Hospital, Multan with reference number HEM-2014-097-489 to conduct this study. Informed consent was taken from parents of each patient; they were briefed about objectives of this study, ensuring them confidentiality of the information provided and fact that there is no risk involved to the patient while taking part in this study. Specimens were collected with the suspicion of malaria. Venous blood (5 ml) sample was drawn into ethylenediaminetetraacetic acid (EDTA) tube and taken to the laboratory of Hospital, for routine investigations like immunochromatographic test (ICT) malaria and CBC to diagnose parasitic presence, anaemia and low platelet count. The inclusive criteria were selecting patient either male or female with age range from 20–60 years, patients with malaria having fever ≥101 ºF assessed on thermometer plus positive test with ICT malaria and

disease duration should be less than 7 days were included in this study. Known patients with coagulopathy and bleeding disorders such as hemophilia (confirmed from patient record file), with history of intake of anti-malarial drugs within 48 hours, previously diagnosed cases of brain tumors, tuberculosis meningitis, viral or bacterial encephalitis and multiple sclerosis and who are not taking iron supplementation during last 30 days were excluded.

Statistical analysis

Obtained data was entered in excel spread sheet and analyzed by statistical package for the social sciences (SPSS)-20.

Descriptive statistics were applied to calculate mean and standard deviation for the age of patients, platelet count and hemoglobin levels. Frequencies and percentages were calculated for categorical variables like gender, age groups, type of malaria, and intake of anti-malarial drugs, residential status, family income, anemia and low platelet count. Effect modifiers like age, type of malaria, residential status, family income, gender, disease duration, intake of anti-malarial drugs (before 48 hours) were controlled by stratification. Post stratification chi-square test was applied to see their effect on outcomes (anemia and low platelet count), p value equal or less than 0.05 was considered as significant.

RESULTS

Age range in this study was from 20 to 60 years with mean age of 41.80±8.51 years as shown in Table 1.

Table 1: Derangement hematological parameters among patients with relevant to their demographic characteristics.

Demographic characters	Total followed (%)	Low platelet count (%)	Normal platelet count (%)	Anemia (%)	Normochromic (%)	Total (%)
Age (years)						
20-40	93 (50.00)	77 (82.79)	16 (17.21)	18 (19.35)	75 (80.65)	93 (100)
41-60	93 (50.00)	65 (69.89)	28 (30.11)	09 (9.68)	84 (90.32)	93 (100)
Total	186 (100)	142 (76.34)	44 (23.66)	27 (14.52)	159 (85.48)	186 (100)
Gender						
Male	101 (54.30)	81 (80.20)	20 (19.80)	14 (13.86)	87 (86.14)	101 (100)
Female	85 (45.70)	61 (71.76)	24 (28.24)	13 (15.29)	72 (84.71)	85 (100)
Total	186 (100)	142 (76.34)	44 (23.66)	27 (14.52)	159 (85.48)	186 (100)
Duration of disease (in days)						
≤3	131 (70.43)	98 (74.80)	33 (25.20)	20 (15.27)	111 (84.73)	131 (100)
>3	55 (29.57)	44 (80.00)	11 (20.00)	10 (18.18)	45 (81.82)	55 (100)
Total	186 (100)	142 (76.34)	44 (23.66)	27 (14.52)	159 (85.48)	186 (100)
Malarial species						
Falciparum	59 (31.72)	41 (69.49)	18 (30.51)	07 (11.86)	52 (88.14)	59 (100)
Vivax	127 (68.28)	101 (79.52)	26 (20.48)	20 (15.74)	107 (84.26)	127 (100)
Total	186 (100)	142 (76.34)	44 (23.66)	27 (14.52)	159 (85.48)	186 (100)

Table 2: Frequency of derangement in hematological parameters among patients with malaria.

Derangement in hematological parameters	Frequency (%)	
	Yes	No
Anemia	27 (14.52)	159 (85.48)
Low platelet count	142 (76.34)	44 (23.66)

We divided patients between two age sub-groups, 20-40 and 41-60 with 93 (50%) patients each. Out of 186 patients, 101 (54.30%) were male while 85 (45.70%) were female which showed there was no significant difference relevant to malarial infection between both genders. Mean duration of the disease was 4.91±1.32 days. Frequency of derangement in hematological parameters among patients with malaria was observed, 27 (14.52%) patients were found with anemia and 142 (76.34%) patients with low platelet count as stated in Table 2.

Table 3: Stratification of the derangement in hematological parameters with respect to gender.

Hematological parameters	Male (n=101)	Female (n=85)	P value
Anemia			
Yes	14	13	0.782
No	87	72	
Low platelet count			
Yes	81	61	0.757
No	23	21	

Out of 186 cases, total *Plasmodium vivax* cases were 127 (68.28%) and the remaining 59 (31.72%) cases were of Plasmodium falciparum. Low platelet and anemia was

more observed in patients between the ages of 20-40 years. There is no significant difference observed among genders relevant to low platelet count and anemia. Platelet count decreased as number of days of infection increases same findings were observed in case of anemia. Patients were more anemic as disease period prolonged. Patients infected by *Plasmodium vivax* showed more tendencies towards anemia and reduction in platelet count as compare to *Plasmodium falciparum.*

DISCUSSION

The World Health Organization recommends that all persons of all ages in all epidemiological settings with suspected malaria should receive a parasitological confirmation of diagnosis.[9] Microscopic detection and identification of plasmodium species in Giemsa stained thick blood films (for screening) and thin blood films (for species confirmation) is the accepted worldwide "gold standard" used for the routine diagnosis of malaria.[9,10] Age range in this study was from 20 to 60 years with mean age of 41.80±8.51 years. Out of 186 patients, 101 (54.30%) were male and 85 (45.70%). In our study, frequency of derangement in hematological parameters among patients with malaria was found to be anemia in 27 (14.52%) patients and low platelet count in 142 (76.34%) patients. Fewer previous studies in developing countries have involved non-pregnant adults and a study from Cameron has documented anemia was 14.08% in patients with malaria.[7] Shaikh et al has reported 85.5% low platelet count in patients with malaria.[8] Platelets and coagulation factors are vital components of the extraordinary complex environment that surrounds flowing or sequestered parasitized RBCs and the enclosing tubular vascular endothelium.[11] Because of that, a lot of research work has been dedicated to determining the effects of malaria on platelet homeostasis. What is now apparent from those studies is the fact that thrombocytopenia is a major complication of malaria, the magnitude of which is dependent on the parasite species or disease severity.[12-14] In light of the above, *P. vivax* malaria infection and severe malaria have been associated with a more heightened and severe thrombocytopenia than *P. falciparum* infection and uncomplicated malaria. In this study, although the mean platelet count in parasitemic patients (172.43 (±80.41) × 103/µl) was normal, it was significantly (p=0.00) lower than that of the non-parasitemic group (217.82 (±95.96) × 103/µl). This only reiterates the fact that acute uncomplicated malaria is not associated with a marked reduction in platelets, as compared to severe malaria. Thrombocytopenia was the most common hematological abnormality in malaria patients. The result of this study is higher when compared with the findings from the studies by Bashawri et al and Khan et al.[15,16] This difference may be attributed to the difference in *Plasmodium* parasite strain, which can have different virulence and disease patterns, or the difference in the level of malaria endemicity in different geographical areas.[17] The cause of thrombocytopenia in malaria is poorly understood; however, increased platelet destruction and reduced platelet lifespan are suggested to occur during malaria, which is often associated with palpable splenomegaly and circulating immune complexes.[18] Anemia was the second most frequently noticed hematological abnormality in malaria infections. Anemia was predominantly presented in *P. falciparum* cases compared to *P. vivax* in this study. This indicates that anemia has shown more association with *P. falciparum* infection. This study is consistent with studies conducted by Jain and Kaur and Shah et al, but differs from studies conducted in Dubai which indicated that there was no significant difference in the incidence of anemia between *P. falciparum (*67%) and *P. vivax* (63%) infections, 76 and there was also a nearly equal frequency of anemia in the two malaria groups, 56% in *P. falciparum* and 61.9% in *P. vivax*.[19-21] Tumor necrosis factor and IL-10 have also been implicated in the development of *P. falciparum* malarial anemia. [17] Our results predicted that patients who were infected by *P. vivax* had more tendency to be anemic and reduction in platelet count and almost similar findings were presented by different researchers in their research works. The primary target of human *Plasmodium* species is the red blood cell. *P. vivax* has a very strong predilection for red blood cells that have emerged from the bone marrow within the last 14 days, in particular reticulocytes, whereas *P. falciparum* has only a moderate predilection for young red blood cells and significant ability to infect older cells.[22-24] The natural history of erythrocytes infected by either species is to host the replicating parasite for approximately 48 hours before bursting and releasing daughter merozoites. The range of peripheral parasitaemia in *P. vivax* infections is lower than in symptomatic *P. falciparum* malaria and parasitaemia >2% is rare.[8] Despite this, mathematical models suggest that premature death of infected reticulocytes due to *P. vivax* infection should be sufficient to lead to extreme anaemia over a period of several months by choking the supply of mature red blood cells.[25-27] The pathogenesis of anemia in malaria is multifactorial and incompletely understood; factors such as mechanical destruction of the parasitized red blood cells, reduced RBC production in the bone marrow, and phagocytosis of parasite infected RBC are among the mechanisms suggested to be involved.[12]

CONCLUSION

This study concluded that the frequency of derangement in hematological parameters i.e. anemia and low platelet count, among patients with malaria is quite high. Blood CP with low platelet count has more chances of malaria. So, we recommend that clinicians should screen these derangements in hematological parameters among patients with malaria, so that early and proper management can be taken in order to decrease the complications as well as the morbidity of these particular patients.

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REFERENCES

1. Mohammed H, Mindaye T, Belayneh M, Kassa M, Assefa A, Tadesse M, et al. Genetic diversity of Plasmodium falciparum isolates based on MSP-1 and MSP-2 genes from Kolla-Shele area, ArbaminchZuria District, southwest Ethiopia. Malar J. 2015;14:73.
2. Hamid MM, Mohammed SB, El Hassan IM. Genetic Diversity of Plasmodium falciparum Field Isolates in Central Sudan Inferred by PCR Genotyping of Merozoite Surface Protein 1 and 2. N Am J Med Sci. 2013;5(2):95-101.
3. Worku L, Damtie D, Endris M, Getie S, Aemero M. Asymptomatic malaria and associated risk factors among school children in Sanja town, Northwest Ethiopia. Int Scholarly Res Notices. 2014;303269.
4. Maltha J, Guiraud I, Kaboré B, Lompo P, Ley B, Bottieau E, et al. Frequency of severe malaria and invasive bacterial infections among children admitted to a rural hospital in Burkina Faso. PLoS One. 2014;9(2):e89103.
5. Yaseen M, Ali NH. Frequency and Seasonal Distribution of Plasmodium falciparum and Plasmodium vivax in Children in Tertiary hospital Karachi – Pakistan. Int J Endorsing Health Sci Res. 2015;3(1):23-5.
6. Fazil M. The frequency of various human malaria parasite infections at private clinic in Mardan district of Khyber Pakhtunkhwa: a study of 230 cases of Malaria. Pak Paed J. 2013;37(3):173-6.
7. Takem EN1, Achidi EA, Ndumbe PM. An update of malaria infection and anaemia in adults in Buea, Cameroon. BMC Res Notes. 2010;3:121.
8. Shaikh MA, Ahmed S, Diju IU, Dur-E-Yakta. Platelet count in malaria patients. J Ayub Med Coll Abbottabad. 2011;23(1):143-5.
9. World Health Organization. Universal Access to Malaria Diagnostic Testing: an Operational Manual. WHO; Geneva, Switzerland. 2011. Available at: https://apps.who.int/iris/handle/10665/44657. Accessed on 14 May 2021.
10. Jain M, Gupta S, Jain J, Grover RK. Usefulness of automated cell counter in detection of malaria in a cancer set up-Our experience. Indian J Pathol Microbiol. 2012;55(4):467-73.
11. Abdalla SH, Pasvol G. Malaria: A Hematological Perspective. Imperial College Press; London, UK. 2004.
12. Maina RN, Walsh D, Gaddy C. Impact of Plasmodium falciparum infection on haematological parameters in children living in Western Kenya. Malaria J. 2010;9(3):S4.
13. Taylor WRJ, Widjaja H, Basri H. Changes in the total leukocyte and platelet counts in Papuan and non Papuan adults from northeast Papua infected with acute Plasmodium vivax or uncomplicated Plasmodium falciparum malaria. Malaria J. 2008;7:259.
14. Khan SJ, Abbass Y, Marwat MA. Thrombocytopenia as an indicator of malaria in adult population. Malaria Res Treatment. 2012;405981.
15. Bashawri L, Mandil A, Bahnassy A, Ahmed M. Malaria: Hematological aspects. Ann Saud Med. 2002;22:5-6.
16. Khan S, Khan F, Usman M, Zahid S. Malaria can lead to thrombocytopenia. Rawal Med J. 2008;33:183-5.
17. Kassa D, Petros B, Mesele T, Hailu E, Wolday D. Characterization of peripheral blood lymphocyte subsets in patients with acute Plasmodium falciparum and P. vivax malaria infections at Wonji Sugar Estate, Ethiopia. Clin Vaccine Immunol. 2006;13(3):376-9.
18. Jain MA, Kaur MB. Comparative study of microscopic detection methods with hematological changes in malaria. Ind J PatholMicrobiol. 2005;48(4):464-7.
19. Shah AM, Dave KK, Sakera BL, Gonsai RN. Comparative study of microscopic detection methods with hematological changes and coagulation profile in malaria. News Bulletin. 2007;2(7):37-40.
20. Abro AH, Ustadi AM, Younis NJ, Abdou AS, Hamed DA, Saleh AA. Malaria and hematological changes. Pak J Med Sci. 2008;24(2):287-91.
21. Win S. Hematological changes in malaria. J Evol Med Dent Sci. 2006;4(65):11367-74.
22. Jain M, Gupta S, Jain J, Grover RK. Usefulness of automated cell counter in detection of malaria in a cancer set up-Our experience. Indian J Pathol Microbiol. 2012;55(4):467-73.
23. George IO, Ewelike-Ezeani CS. Haematological changes in children with malaria infection in Nigeria. J Med Medical Sci. 2011;2(4):768-71.
24. Abdalla SH, Pasvol G. Malaria: A Hematological Perspective. Imperial College Press; London, UK. 2004.
25. Akhtar S, Gumashta R, Mahore S, Maimoon S. Hematological changes in malaria: a comparative study. J Pharm Biol Sci. 2012;2(4):15-9.
26. Chandra S, Chandra H. Role of haematological parameters as an indicator of acute malarial infection in uttarakhand state of India. Mediterranean J Hematol Infect Dis. 2013;5(1):e2013009.
27. Maina RN, Walsh D, Gaddy C. Impact of Plasmodium falciparum infection on haematological parameters in children living in Western Kenya. Malaria J. 2010;9(3):4.

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