

Malaria: Assessment on Haematological Basis

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ABSTRACT

Aim: To see effects of malaria on platelet count and haemoglobin in adults suffering from malaria.

Design: Descriptive study.

Setting: Arif Memorial Hospital Lahore.

Period: April 2011 to March 2013.

Methodology: Adults patients admitted with fever of less than seven days duration who had positive smear for malaria parasite were included in the study. After detailed history and thorough examination, patients were investigated to find out the cause of fever. All the patients with localizing cause for fever and history of drug (Anti malarials) intake were excluded. All patients were investigated with complete blood counts and serial peripheral smears for malarial parasite. Peripheral blood smear examination for malarial parasite was taken as gold standard for the diagnosis of malaria. Cut off value for low hemoglobin (anemia) was taken as 10gm/dl and platelet count of less than $150 \times 10^9/L$, was used to define thrombocytopenia. Patients with thrombocytopenia were divided in to three categories. Mild thrombocytopenia was defined as patients with platelet count of $<50 \times 10^9/L$ to $>150 \times 10^9/L$, moderate thrombocytopenia included patients with platelet counts of $<20 \times 10^9/L$ to $>50 \times 10^9/L$.

Results: A total of one hundred smear positive patients were analyzed, out of which 91% had low and 9% had normal platelet count. 95% had Vivax and only 5% had Falciparum malaria. Mean platelet count was $93 \times 10^9/L$. Mean platelet count in Falciparum was $54 \times 10^9/L$ whereas it was $98 \times 10^9/L$ in vivax malaria. Sixty eight (68%) patients had anaemia. Mean haemoglobin was 9.20gm/dl. Mean Hb in Falciparum malaria was 8.00 gm/dl in Vivax it was 9.40gm/dl.

Conclusions: Higher frequency of mild to moderate thrombocytopenia and anaemia was observed in hospitalized adult patient suffering from malaria.

Key words: Adults, Malaria, Thrombocytopenia, anemia.

INTRODUCTION

Malaria is a worldwide disease and an enormous public health burden. There are roughly 250 million cases and nearly one million deaths attributed to the disease annually⁴. Plasmodium Falciparum was among the leading cause of death. It is becoming increasingly apparent that high mortality and widespread impact of malaria are some of the major indicators of gradual evolution of malaria as a complicated health issue. Detailed analyses of haematological profiles provide some of the best-known clinical studies of strong positive selection in our population¹. Considerably enhanced information is deepening our concepts related to the fact that in patients with malaria, Plasmodium falciparum and vivax parasites multiply to enormous numbers in the bloodstream, initiating processes of erythrocyte destruction, endothelial activation and microvascular inflammation that cause devastating pathological

effects on host tissues and organs. Certain hints have emerged that shed light on the genotyping of species prevalent in Pakistan and better investigations using technological and informatics advancements are being leveraged to identify genetic loci under selection in the malaria parasite and to find variants that are associated with key clinical phenotypes, such as drug resistance^{2,3}. Rapidly accumulating statistical information provides substantial evidence that malaria has been a persistent problem in Pakistan. It had also been convincingly revealed that co-infection of P. vivax with P. falciparum was frequently noted in malaria endemic regions of Iran and Pakistan⁵.

METHODOLOGY

This study was conducted at Arif Memorial Hospital Lahore from April 2011 to March 2013. Admitted adult Patients having fever for less than seven days along with positive smear for malarial parasite was selected for the study. A comprehensive history and examination was carried out to rule out any other cause of fever. Patients having some local disease

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as a cause of fever and patients having signs and symptoms of chronic liver disease, history of bleeding disorder, thrombocytopenia or purpura were considered in exclusion criteria. Similarly patients who were taking sulpha drugs, chemotherapeutic agents and some forms of antimalarial drugs were also not included in this study.

Serial peripheral smear for malarial parasite on admission and at spike of fever and complete blood counts were performed on all the selected patients. Thick and thin smears were stained with Leishman stain and studied. X-Ray Chest, blood culture, serology for Salmonella and urine complete examination were done to rule out other causes of illness along with Serum chemistry (electrolytes, urea, creatinine and liver enzymes) was done on Microlab 200 Merck chemistry analyzer. Urine culture and abdominal imaging were done where indicated.

For the diagnosis of malaria, Peripheral blood smear examination for malarial parasite was taken as gold standard. The complete blood counts were done with an automated haematology analyzer Sysmex KX21 and peripheral smears were examined which was blinded to the automated hematology analyzer results. Two index tests i.e hemoglobin and platelet count were chosen. A Cut off value of 10gm/dl was taken for low hemoglobin (anemia) and platelet count less than $150 \times 10^9/L$, was used to define thrombocytopenia. The patients with reduced platelet count were re-evaluated by manual method.

Patients with thrombocytopenia were divided in to three categories. Mild thrombocytopenia was defined as patients with platelet count of $<150 \times 10^9/L$ to $>50 \times 10^9/L$. moderate thrombocytopenia as patients with platelet counts of $<50 \times 10^9/L$ to $>20 \times 10^9/L$ and severe thrombocytopenia as patients with platelet counts of $<20 \times 10^9/L$.

RESULTS

A total of hundred (100) patients with positive Malarial Parasite (MP) smear were chosen and studied in detail. Among them 91(91%) had decreased platelet count and only 09(9%) had normal count. Those with low counts, seventy two patients 72(72%) had mild and 19(19%) had moderate thrombocytopenia. None of them was reported to have severe form of the disorder (Table 1). Regarding the species of the malarial parasite, ninety five patients (95%) had Vivax and only five patients (5%) had Falciparum malaria. The patient's positive for falciparum malaria (i.e.05) and those positive for Vivax i.e. 14 patients had moderate thrombocytopenia (Table 2). Mean platelet count was $93 \times 10^9/L$ (Normal $150-400 \times 10^9/L$ Maximum platelet count was $193 \times 10^9/L$ and minimum count was

$30 \times 10^9/L$. Mean platelet count in Falciparum was $54 \times 10^9/L$ whereas it was $98 \times 10^9/L$ in Vivax malaria. Sixty Eight (68%) patients had anaemia. Mean haemoglobin (Hb) was 9.20 gm/dl whereas maximum Hb was 13.8gm/dl and minimum Hb was 6.5gm/dl. Mean Hb in Falciparum malaria was 8.0 gm/dl and in vivax it was 9.40gm/dl

Table 1: Platelet counts in patients with malaria (n = 100)

Platelet count X $10^9/L$	=n	%age
<20	-	-
20-50	19	19
50-150	72	72
>150	9	9

Table 2: Platelet Counts in P.Vivax and P. Falciparum malaria

	Plasmodium Falciparum	Plasmodium Vivax
No patient	5	95
< $20 \times 10^9/L$	-	-
$20-50 \times 10^9/L$	5	14
$50-150 \times 10^9/L$	-	72
$>150 \times 10^9/L$	-	9

DISCUSSION

Malaria is known as commonest cause of acute febrile illness in all the developing countries including Pakistan. Clinical signs and symptoms overlap with other diseases thus making its diagnosis considerably complicated. As far as Hematological findings like thrombocytopenia and anemia are concerned, these are common in other disorders as well. Thrombocytopenia occurs in 60-80%⁶ and anemia in 25%⁷. Co-existence of thrombocytopenia with anemia is an important clue to the diagnosis of malaria in patients suffering from acute febrile illness⁸. The cause of thrombocytopenia is poorly understood, although increased platelet destruction is significant and platelet lifespan is reduced during malaria. The suggested mechanisms for thrombocytopenia include disseminated intravascular coagulation or excessive removal of platelets by reticulo-endothelial system⁹. Anti-Platelet IgG antibodies have also been implicated in the pathogenesis of thrombocytopenia¹⁰. Thrombocytopenic malaria, in contrast to the non-Thrombocytopenic variety correlates with a higher degree of parasitemia and increased cytokine production¹¹. In this study 91% of patients suffering from malaria showed some degree of thrombocytopenia. This figure is consistent with the results of the studies done by other investigators as 71% by Robinson¹², 69% by Shuaib Ansari et al¹³ and 58.97% by Rodriguez et al¹⁴. Similar results were found in another study from Pakistan, 93% by Malik

NA et al¹⁵. However some studies have shown relatively low percentage, 35% by Climent et al¹⁶. Thrombocytopenia is considered to be an important predictor of severity in childhood *Falciparum malaria*¹⁷. It was observed that mean platelet count was lower ($54 \times 10^9/L$) in *Falciparum* as compared to *Vivax malaria* ($98 \times 10^9/L$). Mean haemoglobin was also less in *Falciparum* as compared to *Vivax malaria*. However severe thrombocytopenia was not observed in this study as compared to Shuaib et al¹³ who found severe thrombocytopenia in 10% of their patients. Thrombocytopenia 91 % together with anemia 68% was found in cases of this study. Similar results were also found by Malik NA et al¹⁵ and Alfonso J et al¹⁸ who reported anemia in 54% and thrombocytopenia in 93% in their study. Virus induced thrombocytopenia is seen in patients with acute febrile illness but its presence is considered as a potential diagnostic marker for malaria in endemic areas as suggested by other investigators¹⁹ and particularly so when associated with anemia²⁰. Hence patients with acute febrile illness without localizing signs and having combination of anemia and thrombocytopenia should alert the treating physician about the possibility of malaria infection which can be confirmed with specific tests like smears for malarial parasite and immuno chromatographic technique (ICT). It is therefore relevant to mention that a better understanding of the biology of malaria will be helpful in elimination of malaria and data obtained through an expanded repertoire of antimalarials, will enable us to select new drugs with minimal off target effects that kill circulating *P. falciparum* gametocytes, thereby preventing transmission.

CONCLUSIONS

The frequency of mild to moderate thrombocytopenia and anaemia noted was significantly higher in our studied population but these findings can be used as a tool in diagnosing and treating patients at outdoor level thus decreasing load on indoor services with financial benefits to patients simultaneously.

REFERANCES

1. Haroon H, Fazel PA, Naeem M, Mobin A, Naqvi AH, Makki K. Hide and seek: hematological aspects of malaria - a developing country perspective. *J Infect Dev Ctries*. 2013 Mar 14; 7(3):273-9.
2. Raza A, Ghanchi NK, Thaver AM, Jafri S, Beg MA. Genetic diversity of *Plasmodium vivax* clinical isolates from southern Pakistan using *pvcsp* and *pvmSP1* genetic markers. *Malar J*. 2013 Jan 11; 12:16. doi: 10.1186/1475-2875-12-16.
3. Zakeri S, Afsharpad M, Ghasemi F, Raeisi A, Kakar Q, Atta H, Djadid ND. *Plasmodium vivax*: prevalence of mutations associated with sulfadoxine-pyrimethamine resistance in *Plasmodium vivax* clinical isolates from Pakistan. *Exp Parasitol*. 2011 Jan; 127(1):167-72
4. "WHO World Malaria Report 2008." Centers for Disease Control. 10 Dec. 2008.
5. Zakeri S, Kakar Q, Ghasemi F, Raeisi A, Butt W, Safi N et al. Detection of mixed *Plasmodium falciparum* & *P. vivax* infections by nested-PCR in Pakistan, Iran & Afghanistan. *Indian J Med Res*. 2010 Jul; 132:31-5.
6. Kreil A, Wenisch C, Brittenham G. Thrombocytopenia *P Falciparum malaria*. *Br J Hematol* 2000; 109 534-36.
7. Kathryn NS, Kevin C, Jay SK. *Malaria CMAJ* 2004; 170 (11): 1503-18.
8. Patel U, Gandhi G, Friedman S, Niranjana S. Thrombocytopenia in malaria. *J Natl Med Assoc* 2004; 95(9): 1212-4.
9. Beale PJ, Cormack JD, Oldrey TB. Thrombocytopenia in malaria with IgM changes. *BMJ* 1972;1:345-9.
10. Yamaguchi S, Kubota T, Yamagishi T, Okamoto K. T. Takada M et al. Severe thrombocytopenia suggesting immunological mechanisms in two *casA4* of *vivax malaria*. *Am J Hemato* 1997;56:183-6.
11. Park JW, Park SH, Yeom JS. et al. Serum cytokin profiles in patients with *Plasmodium vivax malaria*: A comparison between those who presented with and without thrombocytopenia. *Ann Trop Med Parasol* 2003;97:339-44.
12. Robinson P, Jenney AW, Tachado M, Yung A, Man. Taylor K et, al. Biggs BA. Imported malaria treated in Melbourne, Australia. *J Travel Med* 2001; 8(2): 76-8-
13. Shuaib Ansari, Hail Khan Khoharo. Allauddin Abro 1.5-r Ahmd Akhundt. Fatima Qureshi. Thrombocytopenia *Plasmodium Falciparum malaria* J. Ayub Med college Abbottabad, 2009;21(2), 145-47.
14. Rodriguez-Morales AJ, Sanchez E, Vargas M, Piccolo C, Colina R, Arria M. Anemia and Thrombocytopenia in children with *Plasmodium vivax malaria*. *J Trop Pediatr*. 2005; 10: 1093.
15. Malik NA, Ahmad TM, Khan A, Jaffery S. Malaria; Assesment of haematological changes. *Professional Med J* 2013;20(2): 227-231.
16. Climent Casals-Pascual, Oscar Kai, Charles R. _ Newton, Norbert Peshu, and David J. Roberts. Report: Thrombocytopenia In *Falciparum Malaria* s associated with high concentrations of IL-10. *Arr, Trop. Med. Hyg.*, 75(3), 2006, pp. 434-436.
17. Imbert P Criteria of severity in childhood *Falciparum malaria*. *Arch Pediatr*. 2003; 10 suppl 5:532s-38s.
18. Alfonso J, Rodriguez-Morales, Ella Sanchez , Miguel Vargas, Carmelina Piccolo, Rosa Colina and Melissa Arria. Anemia and Thrombocytopenia in Children with *Plasmodium Vivax malaria*. *Journal of Tropical Pediatrics Volume52, Issue 1, Feb 2006, Pp. 49-51.*
19. Patel U, Gandhi G, Friedman S, Niranjana S. Thrombocytopenia in malaria. *J Natl Med Assoc* 2004; 96(9):1212-4.
20. Lathia TB, Joshi R. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? *Indian J Med Sci* 2004; 58(6): 239-44.

