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Original Research Article

Variation of Hematological values in Malarial and Non-Malarial Acute Febrile Illness: Our Experience

Sheetal G. Gole[1], Gautam N. Gole[2]

[1]Professor & Head, Department of Pathology, Employee's State Insurance Corporation Medical College & Hospital, Faridabad, Haryana 121001, India. [2]Professor & HOD, Department of General Surgery, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Haryana 122107, India.

Corresponding Author:

Gautam N. Gole, Professor & Head, Department of General Surgery, Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Haryana 122107, India
E-mail: drgautamgole@rediffmail.com

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Abstract

Introduction: In tropics malaria is one of the cause of acute febrile illness. Hematological parameter changes involving major cell types such as erythrocytes, leucocytes and platelets are observed in malaria. Present study is done to evaluate hematological parameters in malaria.

Material and Methods: Present study was a two-year hospital-based study conducted at a tertiary health centre in rural Telangana. Total 368 cases diagnosed as acute febrile illness were studied. All the anticoagulated blood samples were submitted for complete blood count and peripheral blood smear for malarial parasite. Hemoglobin, Red cell distribution width, leukocyte count, and platelet counts were the parameters considered. Peripheral smear examination for malaria parasite was taken as gold standard for diagnosis of malaria. Diagnostic accuracy along with sensitivity, specificity, predictive values and likelihood ratios were statistically evaluated using 95% confidence intervals.

Results: Study included 368 patients and those with positive peripheral smear for malaria parasite were 140 (38.04%). Thrombocytopenia (platelet count < 150,000/cu mm) was a strong predictor for malaria (Sensitivity 60%, Specificity 88%, Likelihood ratio + 5.04) and in combination with anemia (Hb < 10 g/dl) it was next best parameter (Sensitivity 69%, Specificity 74%, Likelihood ratio + 2.77).

Conclusion: Thrombocytopenia along with combination of anemia and thrombocytopeniaproves to be of paramount importance in predicting malarial infection. These hematological parameters supported by clinical findings and gold standard microscopy methods help to improve malaria diagnosis and treatment.

Keywords: Plasmodium Falciparum; Plasmodium Vivax; Thrombocytopenia; Anemia.

Introduction

In tropics malaria is main differential diagnosis of acute febrile illness. It is a major communicable disease in developing countries. It forms 15% of clinical illnesses in tropical countries and is a foremost cause of morbidity and death [1,2,3]. Two hundred and nineteen million cases were reported worldwide in 2010 [4]. In some parts of tropical regions malaria accounts for 10% of death in

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children aged below three years. South-East Asian Region has about 40% of global population at risk of malaria [5].

Malaria is a mosquito-borne infectious disease caused by parasitic protozoa Plasmodium which infects and destroys red blood cells (RBCs). Four species of plasmodia (Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale and Plasmodium vivax) cause malaria in humans Plasmodium vivax being major malarial parasite in India [5]. Plasmodium falciparum constitutes severe forms of and deaths from malaria while the other species rarely produce serious complications [5]. Major complications include cerebral malaria, pulmonary edema, acute renal failure, severe anemia, and/or bleeding. Acidosis and hypoglycemia are the most common metabolic complications. Serious complications can develop rapidly and prove fatal within hours or days [6,7].

Malaria is transmitted to human being due to bite of anopheles mosquitoes and injection of invasive forms (sporozoites) of plasmodium. These invade liver and RBCs, and cause periodic fever, chills and rigors along with sweating and splenomegaly followed by severe anaemia. Parasitic invasion and development of parasite in the RBCs causes anemia and resultant RBCs destruction. Non-parasitized RBCs may undergo haemolysis in acute malaria and give positive Coomb's test.

In RBCs, parasite metabolizes globin from haemoglobin. Haem neutralizes to hemozoin, a gray-black malaria pigment. Haem-iron is unavailable for reuse in formation of haemoglobin and causes anemia.

Accurate diagnosis in malaria is required for effective disease management. Clinical diagnosis is unreliable due to diverse clinical presentation of malaria. In tropics poses difficulty in distinguishing from other causes of fever. Fever and other signs are sensitive yet they lack specificity and positive predictive values [8]. Peripheral blood smear (PBS) examination is gold standard for detecting malaria infection [9] It requires expertise and is time-consuming.

Hemoparasites induce hematological changes and which may lead to clinical suspicion [1,8,10,11]. These changes are anemia, thrombocytopenia, splenomegaly, leucocytosis or leucopenia, mild-to-moderate atypical lymphocytosis and rarely disseminated intravascular coagulation (DIC) [12,13]. Some hematological changes are species specific. Thrombocytopenia is a common and early sign of malarial infection. Most of these findings are more pronounced in Plasmodium falciparum [5,14].

Present study statistically evaluates hematological parameters such as haemoglobin (Hb), total leucocyte count (TLC), red cell distribution width (RDW), and platelet count in malaria infected cases and compared with uninfected people.

Material & Methods

Present study was a two-year hospital-based study conducted at a tertiary health centre in rural Telangana. The inclusion and exclusion criteria were as follow:

Inclusion criteria: Patients with fever of < 7 days duration were included.

Exclusion criteria: Patients where localizing cause for fever could be determined were excluded.

A total of 368 patients presenting with acute febrile illness at our hospital were evaluated. A complete blood count and malarial parasite microscopy were performed for each patient.

Hemoglobin, Red cell distribution width (RDW), Total leucocyte count (TLC), and platelet counts estimation was done by automated cell counter (Mindray BC-5000). PBS examination for malarial parasite was considered gold standard for diagnosis of malaria. Slides for PBS were stained with the Romanowsky (Leishman) stain.

Diagnostic accuracy was measured by computing sensitivity, specificity, predictive values and likelihood ratios. Precision of findings was evaluated using 95% confidence intervals.

Statistical Analysis: The t test for continuous variables and the $\chi 2$ test for categorical variables to determine the univariate association of age, gender and hematological indices predictive of malaria. Diagnostic accuracy was measured by computing sensitivity, specificity, predictive values and likelihood ratios. The precision of these estimates was evaluated using 95% confidence intervals. We also used hematological parameters in combination. Data analysis was done using SPSS (Statistical Package for Social Sciences) 20.0 software package.

Results

Present study included 368 patients of acute

febrile illness without localizing signs. Of these 368 cases, 218 (59.23%) were males and 150 (40.76%) were females. Positive PBS for malaria parasite was seen in 140 (38.04%) cases and remaining 228 (61.95%) cases were negative. Of these 140 cases of PBS for malaria positive 86 (61.42%) were males and 54 (38.57%) were females. Plasmodium falciparum positive cases were 128 (91.42%), and Plasmodium vivax positive cases were 12 (8.57%). Base line characteristics of each patient such as age, sex, Hb concentration, RDW, TLC, platelet count of the study population was documented and it was noted that there was no difference in age, and sex profile in those who were slide positive for malaria and those who were not. Hemoglobin level and platelet counts were significantly lower in PBS positive malaria when compared with other fevers. (Table 1).

Sensitivity, specificity, predictive values (positive: PPV; negative: NPV) and likelihood ratio (LR+; LR-) for various hematological parameters in diagnosis of malaria were calculated. (Table 2) Sensitivity (95% confidence interval) for Hb<10 g/dl, RDW>15%, and platelets<150000/cumm was 52%, 41%, 60% respectively. Specificity (95% confidence interval) for Hb<10 g/dl, RDW>15%, and platelets<150000/cumm was 73%, 66%, 88% respectively. Anemia, TLC, or high RDW had poor sensitivity and specificity in malaria diagnosis. However, thrombocytopenia alone (platelet count <150,000/cu mm) specifically predicted malaria with sensitivity 60%, specificity 88%, likelihood ratio + 5.04. Thrombocytopenia was found to be the only differentiating parameter, with positive & negative likelihood ratio of 5.04, & 0.45 respectively. (Table 2).

The combination of hematological parameters in diagnosis of malaria were used to see if it increased the diagnostic yield. (Table 3) Hematological parameters such as anemia (Hb< 10 g/dl) & thrombocytopenia in combination had higher sensitivity 69%, specificity 74%, & positive likelihood ratio of 2.77 and was next best parameter.

Table 1: Variables of study group (*values in percent)

Variable Malaria (n=140)	Malaria (n=140)	No Malaria (n=228)	P value
Age (years)	38.4 (17.2)	37.3 (14.3)	0.64§
Male sex*	86 (61.42)	132 (57.89)	0.22†
Hb (g/dl)	8.9 (2.7)	10.9 (2.7)	<0.01§
RDW (%)	16.2 (2.4)	16.5 (3.6)	0.7§
TLC (per cu mm)	6675 (2695)	7849 (5168)	0.08§
Platelet count (per cu mm)	0.83 (0.6)	2.1 (1.2)	<0.01§

All values indicate mean (Standard deviation), unless indicated

* Number (%), § student's t test, † chi square test

Table 2: Sensitivity, specificity, predictive value and likelihood ratio for hematologicalchanges in malaria (*values in percent)

Variable	Sensitivity* (95% CI)	Specificity* (95% CI)	PPV* (95% CI)	NPV* (95% CI)	LR+ (95% CI)	LR- (95% CI)
Hb<10 g/dl	52 (41, 63)	73 (63, 80)	54 (45, 63)	28 (23, 34)	1.95 (1.33, 2.85)	0.65 (0.5, 0.88)
RDW>15%	41 (32, 51)	66 (55, 76)	43 (34, 52)	34 (30, 40)	1.25 (0.85, 1.83)	0.88 (0.7, 1.1)
Platelets <150000/cu mm	60 (50, 69)	88 (79, 93)	75 (62, 84)	21 (17, 26)	5.04 (2.7, 9.2)	0.45 (0.3, 0.5)

Table 3: Combination of hematologicalchanges for malaria diagnosis (*values in percent)

Variable	Sensitivity* (95% CI)	Specificity* (95% CI)	PPV* (95% CI)	NPV* (95% CI)	LR+ (95% CI)	LR- (95% CI)
Hb<10 g/dl & Platelets <150000/cu mm	69 (56, 81)	74 (66, 81)	62 (54,70)	19 (13,27)	2.77 (1.96,3.91)	0.40 (0.26,0.61)
RDW > 15 & Platelets <150000/cu mm	67 (54, 79)	75 (66, 81)	62 (53,70)	20 (15,28)	2.71 (1.9,3.85)	0.43 (0.29,0.64)
Hb<10g/dl, TLC<4000/cu mm & Platelets <150000/cu mm	61 (40, 80)	65 (57, 72)	52 (42,61)	26 (17,38)	1.77 (1.19,2.63)	0.59 (0.34,1.02)

The NPV and LR of this combination (19% & 0.40 respectively) suggested that malaria may be ruled out if this combination is absent. Various other combinations (High RDW & low platelets, & low Hb, low WBC count, & low platelets) were not of much diagnostic aid.

Discussion

Malaria is a major health problem in tropical and temperate regions of the world. In India, it is seen on both rural and urban areas.

Present study included 368 patients. Of these 368 cases, 218 (59.23%) were males and 150 (40.76%) were females. Positive PBS for malaria parasite was seen in 140 (38.04%) cases and remaining 228 (61.95%) cases were negative. Of these 140 cases of PBS for malaria positive 86 (61.42%) were males and 54 (38.57%) were females. Plasmodium falciparum positive cases were 128 (91.42%), and Plasmodium vivax positive cases were 12 (8.57%).

Joshi HJ *et al.* [5] study had 51 cases, 41 (80.3%) were of Plasmodium vivax and 10 (19.6%) cases of Plasmodium falciparum. Their study included 37 (72.54%) males and 14 (27.45%) females. Ranjini CY *et al.* [15] study had male (80.24%) and female (19.75%) Faseela TS *et al.* [16] and Jairajpuri ZS *et al.* [17] study had large number of male cases as compared with females. Present study also showed more male incidence.

Jairajpuri ZS *et al.* [17] study, had 84.8% cases of Plasmodium vivax followed by 10.5% mixed infection (both Plasmodium vivax and Plasmodium falciparum) and 4.5% Plasmodium falciparum. Faseela TS *et al.* [16] study reported an incidence of 51.6% for Plasmodium vivax, 47.1% mixed and only 1.1% of P. falciparum. Malik AM *et al.* [18] reported frequency of Plasmodium vivax (52%).

In the present study the mean age of malaria positive patients was 38.4 years and non-malaria cases 37.3 years. Mean age of patients in Jairajpuri ZS *et al.* [17] study, was 29.2 years.

Hemoglobin

In the present study hemoglobin concentration showed mean values of 8.9 g/dL for smear positive cases and 10.9 g/dL for smear negative. In Bakhubaira S *et al.* [1] study hemoglobin levels showed 3.5 g/dL as least mean values. In malaria anemia occurs mainly due to Plasmodium falciparum malaria rather than other species. Plasmodium vivax and Plasmodium ovale infect reticulocytes and Plasmodium malariae infect senescent RBCs hence these rarely cause anemia. Joshi HJ *et al.* [5] study observed anemia in 25 (49.01%) patients, with statistically significant species variation in causing anemia (p value<0.05).

Anemia in malaria has complex and multifactorial pathogenesis. Causes for anemia in malaria are: Hemolysis and splenic sequestration of both parasitized and non-parasitized RBCs, bone marrow suppression, ineffective erythropoiesis with dyserythropoietic changes, level of parasitemia, and anemia of chronic disease [19,20].

Mechanical destruction of RBCs and splenic clearance of parasitized and defective RBCs is the cause of microcytic anemia in Plasmodium falciparium malaria infection. Immune destruction of RBCs may also occur. Mechanisms of RBCs destruction also include reticuloendothelial hyperplasia, reduced deformability of infected RBCs, membrane changes and accelerated immune destruction [5,14].

Malarial parasites show differential preference in infecting RBCs of different ages. Plasmodium vivax infects reticulocytes or young RBCs. Plasmodium vivax malaria infection has milder pathology due to less parasitemia, increased activation of host inflammatory immune response and increased deformability of infected RBCs causing reduced cytoadherence in microvasculature [5]. Plasmodium falciparum attacks RBCs of all ages and destruction of both parasitized and non-parasitized RBCs occur hence, increased frequency of anemia is observed in falciparum malaria.

Present study revealed low sensitivity and specificity (95% confidence interval) for Hb<10 g/dl, was 52% and 73% respectively and LR+ 1.95 for Hb (<10gm/dl). (Table 2) This was in concordance with Jairajpuri ZS *et al.* [17] study that showed the probability of malaria (LR+ 1.61) increased with low Hb (<10gm/dl) which is a statistically significant variable (p<0.005). However their study also had low sensitivity and specificity. Manas K *et al.* [21] study, reported reduction of Hb and RBC count. But RBC indices level in malaria infected patients were higher as compared to non-malaria infected.

Platelets

Present study revealed thrombocytopenia the strongest predictor of malaria. Bakhubaira S *et al.* [1] study showed thrombocytopenia in 42.9% of patients having severe malaria and 18.2% patients

had a count of <50.0x109/L. Banzal S *et al.* [22] study showed thrombocytopenia in 50.4% of patients. Study by Khan SJ *et al.* [23] revealed 26.8% Plasmodium falciparum malaria cases having grade 3 thrombocytopenia (<50.0x109/L platelet count). Francis *et al.* study showed significantly lower platelet count (p<0.05). Senthilkumaar P [24] study showed platelet counts and serum potassium levels in malaria infected were lower than in non-infected cases.

Severe thrombocytopenia is usually seen in Plasmodium falciparum infection and also in those patients who are coinfected with Plasmodium vivax. It rarely occurs in Plasmodium vivax malaria patients [25]. Various mechanisms postulated are splenic pooling, immune mediated lysis by generation of anti-platelet antibodies, oxidative stress, causing premature peripheral platelet death, disseminated intravascular coagulation (DIC) and bone marrow dyspoeisis. Various studies have revealed that immune complexes produced by malarial antigens cause sequestration of injured platelets by splenic macrophages and a shortened life span of platelets [1,8,13,18,25,26]. Bone marrow thrombopoiesis is normal as the megakaryocytes are normal or increased, hence it is not a cause for thrombocytopenia. Thrombocytopenic malaria, in contrast to non-thrombocytopenic correlates with a higher degree of parasitemia and increased cytokine production [27]. In malaria there is endothelial activation and it is responsible for loss of barrier function of endothelium. Due to this endothelial activation to regulate permeability, platelets and its proteins are utilised and hence the thrombocytopaenia [28]. Dhungat MP *et al.*[29] states that thrombocytopaenia is reliable diagnostic marker, yet it has no prognostic significance in malaria.

In present study for platelets<150000/cumm, sensitivity and specificity (95% confidence interval) was 60% and 88% respectively. It was the only discriminator parameter, with positive & negative likelihood ratio of 5.04, & 0.45 respectively. (Table 2)

Thrombocytopenia (platelet<100,000/cumm) is a strong predictor of malaria as per many other studies [16,17,18,20]. Jairajpuri ZS *et al.*[17] has found significant (p<0.001) association of low platelets in malaria as compared to non-malaria. Their study revealed sensitivity (81%) and specificity (87%) with an increased probability of malaria by factor 6.2, similar observations were seen in the present study. Sensitivity and negative predictive value is high at low platelet counts was concluded by Khan SJ *et al.* [23] and Jairajpuri ZS *et al.*[17] studies. Platelet counts were significantly reduced in 84.9% malaria-infected cases was observed by Manas K *et al.* [21] Thrombocytopenia (platelet counts <150,000/µl) with sensitivity (85%), specificity (85%) and negative predictive value (97%) and positive predictive value (48%) was observed in Manas K *et al.* [21] study.

Study done by Erhart LM *et al.* [30] reported platelet count of less than 150,000/µL increased the likelihood of malaria by 12-15 times in febrile patients.

Study done by Joshi HJ *et al.* [5] observed, out of 51 cases of malaria 48 had thrombocytopenia. Their study showed statistically significant species variation in causing thrombocytopenia (P value >0.05) and thrombocytopenia was observed in 90% of Plasmodium falciparum and 95.11% of Plasmodium vivax infections. Their study had mild (33.33%), moderate (35.23%) and severe (25.49%) thrombocytopenia cases.

Red cell distribution width (RDW)

RDW along with mean corpuscle volume (MCV) of RBCs are the new parameters in malaria. Increased RDW in malaria has been attributed to RBC response to malarial parasite and correlated with degree of macrocytosis [31]. RDW describes RBC population dispersion of volume or range of changes in RBC size which is enlarged (especially Plasmodium vivax) after malarial invasion [32]. Initial increase in size is followed by rupture of infected RBCs. RBCs of different sizes are identified because malarial life cycle is never synchronous and parasites at more than one stage of development can be seen in the PBS. This is not similar in Plasmodium falciparum malaria where RBCs maintain their original size [32]. In present study sensitivity and specificity (95% confidence interval) for RDW>15% was 41% and 66% respectively. (Table 2) The 95% confidence interval for RDW crosses one, which implies measurement of this parameter to be less precise.

Studies of Jairajpuri ZS *et al.* [17] and Koltas IS *et al.* [32] noted high RDW values in malaria cases than non-malaria cases. However, it is in contrast with our findings. Jairajpuri ZS *et al.* [17] study had majority of cases of Plasmodium vivax, and hence this explains increased RDW. In our study maximum cases were of Plasmodium falciparum, so RDW changes were not observed.

Total leucocyte count (TLC)

Leucopenia is a common observation in malaria although leukocytosis is also seen. Causes of leucopenia are: WBCs are located away from peripheral circulation, splenic sequestration of WBCs and other marginal pools rather than actual depletion or stasis. [33] Few cases of malaria are accompanied by neutropenia. Manas K *et al.* [21] study observed leucopenia (WBCs <4,000/µL). They found association of malaria with leucopenia (2.7 times) than with normal WBC count; leucopenia had sensitivity (17%), and specificity (94%) to predict malaria.

Ladhani S *et al.* [13] study showed patients with leucocytosis in malaria compared with controls. Francis U *et al.* [3] study, suggests significant increase in WBC count of malaria infected patients ($p<0.05$) compared with control. This is due to an increase in release of WBCs at early stage of infection to fight the infection.

Malaria infected cases showed predominantly reduced WBCs, lymphocytes, eosinophils. But the monocyte and neutrophil counts were significantly higher in comparison to non-malaria infected patients [1,8,10,21,23,30].

Present study showed no deviation of mean WBC count from normal reference range and TLC was found to have poor sensitivity and specificity in diagnosis of malaria. Our study noted findings similar to studies of Bakhubaira S *et al.* [1] and Bashawri LA *et al.* [20]

Combination of hematological parameters

Present study demonstrates low hemoglobin and platelet counts are the two hematological variables that increase the probability of malaria, by factor of 1.95 and 5.04 respectively. These two variables also emerge useful when used in combination (Likelihood ratio 2.77). Hematological parameters such as anemia (Hb< 10 g/dl) & thrombocytopenia in combination had higher sensitivity 69%, specificity 74%, & positive likelihood ratio of 2.77 and was next best parameter. The NPV and LR of this combination (19% & 0.40 respectively) suggested that malaria may be ruled out if this combination is absent. (Table 3) The various other combinations (High RDW & low platelets, & low Hb, low WBC count, & low platelets) did not increase the diagnostic yield. Similar observation of combination of variables showed increased probability of malaria diagnosis in Jairajpuri ZS *et al.* [17] study.

Conclusion

This study concluded that there is variation in hematological parameters of malaria infected patients and healthy uninfected individuals. Thrombocytopenia is an important predictor of malaria infection. Combination of anemia & thrombocytopenia was the next best parameter. Hematological investigation is inexpensive and technically easier for detecting malarial parasite. These hematological parameter changes help clinicians to start an effective and early therapeutic intervention and thus prevent from developing major complications. These hematological parameters along with clinical diagnosis & gold standard microscopy methods, are reliable and competent measures for diagnosis of malaria diagnosis.

References

1. Bakhubaira S. Hematological parameters in severe complicated *Plasmodium falciparum* malaria among adults in Aden. Turk J Haematol 2013;30:394–99.
2. Igbeneghu C, Odaibo AB. Impact of Acute Malaria on Some Haematological Parameters in a Semi-Urban Community in Southwestern Nigeria. ActaParasitologicaGlobalis 2013;4:1-05.
3. Francis U, Isaac Z, Yakubu A, Enosakhare A, Felix E. Haematological Parameters of Malaria Infected Patients in the University of Calabar Teaching Hospital, Calabar, Nigeria. J Hematol Thrombo Dis 2014;2(6):171.
4. WHO. World malaria report 2012. Geneva: World Health Organization; 2012.
5. Joshi HJ and Sapre JP. A Study of Different Hematological Parameters in Malaria. Journal of Medical Science and Clinical Research 2017;5(5):21503-08.
6. Severe falciparum malaria. World Health Organization, Communicable Diseases Cluster. Trans R Soc Trop Med Hyg 2000;94(Suppl. 1):1-90
7. Severe and complicated malaria. World Health Organization, Division of Control of Tropical Diseases. Trans R Soc Trop Med Hyg 1990;84 (Suppl. 2):1-65.
8. Maina RN, Walsh D, Gaddy C, Hongo G, Waitumbi J, Otieno L, Jones D, Ogutu BR. Impact of *Plasmodium falciparum* infection on haematological parameters in children living in Western Kenya. Malar J 2010;9(Suppl 3):S4.
9. WHO. World Malaria Report 2010. Geneva: World Health Organization; 2011.
10. van Wolfswinkel ME, Vliegenthart-Jongbloed K, De Mendonca Melo M, Wever PC, McCall MB,

Koelewijn R, Van Hellemond JJ, Van Genderen PJ. Predictive value of lymphocytopenia and the neutrophil-lymphocyte count ratio for severe imported malaria. Malar J 2013;12:101.

11. Warimwe GM, Murungi LM, Kamuyu G, Nyangweso GM, Wambua J, Naranbhai V, Fletcher HA, Hill AV, Bejon P, Osier FH, Marsh K. The ratio of monocytes to lymphocytes in peripheral blood correlates with increased susceptibility to clinical malaria in Kenyan children. PLoS One. 2013;8:e57320.
12. Facer CA. Hematological aspects of malaria, In: Infection and Hematology. Oxford: Butterworth Heinmann Ltd., 1994.pp.259-94.
13. Ladhani S, Lowe B, Cole AO, Kowuondo K, Newton CR. Changes in white blood cells and platelets in children with falciparum malaria: relationship to disease outcome. Br J Haematol 2002;119(3):839-47.
14. Sen R, Tewari AD, Sehgal PK, Singh U, Sikka R, Sen J. Clinico-haematological profile in acute and chronic P.falciparum malaria in children. J Com Dis 1994;26:31-8.
15. Ranjini CY, Roopa Murgod et al. comparison of hematological parameters between Vivax and Falciparum malaria. Int J Pharm Bio Sci 2012;3(4):(B)1120–8.
16. Faseela TS, Ronald AR, Anita KB, Chaithra SM, Yashwanth R. Diagnostic Value of Platelet Count in Malaria. Journal of Clinical and Diagnostic Research 2011;5:464-6.
17. Jairajpuri ZS, Rana S, Hassan MJ, Nabi F, Jetley S. An Analysis of Hematological Parameters as a Diagnostic test for Malaria in Patients with Acute Febrile Illness: An Institutional Experience. Oman Medical Journal 2014;29(1):12-7.
18. Malik AM, Zaffar N, Ali Nadir, Malik AM, Khan R. Hematological Findings And Endemicity of Malaria In Gadap Region. Journal of the college of Physians and Surgeons 2010;20:112-6.
19. Perkins DJ, Were T, Davenport GC, Kempaiah P, Hittner JB, Ong'echa JM. Severe malarial anemia: innate immunity and pathogenesis. Int J Biol Sci 2011;7:1427-42.
20. Bashawri LA, Mandil AA, Bahnassy AA, Ahmed MA. Malaria: hematological aspects. Ann Saudi Med 2002;22:372-7.
21. Manas K, 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.
22. Banzal S, Ayoola EA, El-Sammani EE. The clinical pattern and complications of severe malaria in the Gizan Region of Saudi Arabia. Ann Saudi Med 1999;19:378-80.
23. Khan SJ, Abbass Y, Marwat MA. Thrombocytopenia as an Indicator of Malaria in Adult Population. Malaria Research and Treatment 2012;405981:1–4.
24. Senthilkumaar P, Sarojini S. Haematological studies in malaria affected patients in North Chennai, Tamil Nadu. Euro J Exp Bio 2013;3:199-205.
25. Makkar RP, Mukhopadhyay S, Monga A, Gupta AK. Plasmodium vivax malaria presenting with severe thrombocytopenia. Braz J Infect Dis 2002; 6:263-65.
26. Looareesuwan S, Davis JG, Allen DL, Lee SH, Bunnag D, White NJ. Thrombocytopenia in malaria. Southeast Asian J Trop Med Public Health 1992;23:44-50.
27. Park JW, Park SH, Yeom JS, et al. Serum cytokine profiles in patients with Plasmodium vivax malaria: A comparison between those who presented with and without thrombocytopenia. Ann Trop Med Parasitol 2003;97:339-44.
28. Brouwers J, Noviyanti R, Fijnheer R, de Groot PG, Trianty L, Mudaliana S, Roest M, Syafruddin D, van der Ven A, de Mast Q. Platelet activation determines angiopoietin-1 and VEGF levels in malaria: implications for their use as biomarkers. PLoS One. 2013;8:e64850. doi: 10.1371/journal. pone.0064850.
29. Dhungat MP, Dhungat PP. Thrombocytopenia in Patients of Malaria – Correlation with type of Malaria and its Clinical Significance. Online International Interdisciplinary Research Journal 2013;3:21-6.
30. Erhart LM, Yingyuen K, Chuanak N, Buathong N, Laoboonchai A, Miller RS, Meshnick SR, Gasser RA Jr, Wongsrichanalai C. Hematologic and clinical indices of malaria in a semi-immune population of western Thailand. Am J Trop Med Hyg 2004; 70:8–14.
31. Bunyaratvej A, Butthep P, Bunyaratvej P. Cytometric analysis of blood cells from malaria-infected patients and in vitro infected blood. Cytometry 1993;14(1):81-5.
32. Koltas IS, Demirhindi H, Hazar S, Ozcan K. Supportive presumptive diagnosis of Plasmodium vivax malaria. Thrombocytopenia and red cell distribution width. Saudi Med J 2007;28(4):535-9.
33. McKenzie FE, Prudhomme WA, Magill AJ, Forney JR, Permpanich B, Lucas C, et al. White blood cell counts and malaria. J Infect Dis 2005;192(2):323-30.

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Indian Journal of Hospital Infection	Semiannual	12500	12000	938	901
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Indian Journal of Legal Medicine	Semiannual	8500	8000	607	550
Indian Journal of Library and Information Science	Triannual	9500	9000	742	703
Indian Journal of Maternal-Fetal & Neonatal Medicine	Semiannual	9500	9000	742	703
Indian Journal of Medical & Health Sciences	Semiannual	7000	6500	547	508
Indian Journal of Obstetrics and Gynecology	Bi-monthly	9500	9000	742	703
Indian Journal of Pathology: Research and Practice	Monthly	12000	11500	938	898
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Indian Journal of Preventive Medicine	Semiannual	7000	6500	547	508
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Indian Journal of Surgical Nursing	Triannual	5500	5000	430	391
Indian Journal of Trauma and Emergency Pediatrics	Quarterly	9500	9000	742	703
Indian Journal of Waste Management	Semiannual	9500	8500	742	664
International Journal of Food, Nutrition & Dietetics	Triannual	5500	5000	430	391
International Journal of Neurology and Neurosurgery	Quarterly	10500	10000	820	781
International Journal of Pediatric Nursing	Triannual	5500	5000	430	391
International Journal of Political Science	Semiannual	6000	5500	450	413
International Journal of Practical Nursing	Triannual	5500	5000	430	391
International Physiology	Triannual	7500	7000	586	547
Journal of Animal Feed Science and Technology	Semiannual	7800	7300	609	570
Journal of Cardiovascular Medicine and Surgery	Quarterly	10000	9500	781	742
Journal of Forensic Chemistry and Toxicology	Semiannual	9500	9000	742	703
Journal of Global Medical Education and Research	Semiannual	5900	5500	440	410
Journal of Global Public Health	Semiannual	12000	11500	896	858
Journal of Microbiology and Related Research	Semiannual	8500	8000	664	625
Journal of Nurse Midwifery and Maternal Health	Triannual	5500	5000	430	391
Journal of Orthopedic Education	Triannual	5500	5000	430	391
Journal of Pharmaceutical and Medicinal Chemistry	Semiannual	16500	16000	1289	1250
Journal of Plastic Surgery and Transplantation	Semiannual	26400	25900	2063	2023
Journal of Practical Biochemistry and Biophysics	Semiannual	7000	6500	547	508
Journal of Psychiatric Nursing	Triannual	5500	5000	430	391
Journal of Social Welfare and Management	Triannual	7500	7000	586	547
Medical Drugs and Devices Research	Semiannual	2000	1800	156.25	140.63
New Indian Journal of Surgery	Bi-monthly	8000	7500	625	586
Ophthalmology and Allied Sciences	Triannual	6000	5500	469	430
Otolaryngology International	Semiannual	5500	5000	430	391
Pediatric Education and Research	Triannual	7500	7000	586	547
Physiotherapy and Occupational Therapy Journal	Quarterly	9000	8500	703	664
RFP Indian Journal of Medical Psychiatry	Semiannual	8000	7500	625	586
RFP Journal of Gerontology and Geriatric Nursing	Semiannual	5500	5000	430	391
Urology, Nephrology and Andrology International	Semiannual	7500	7000	586	547

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