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Original Article

Pathology Section

Comparison of Hematological Parameters in Various Acute Febrile Illnesses

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ABSTRACT

Introduction: The common causes of acute febrile illnesses (AFI) are malaria, dengue, typhoid, Chikungunya fever, meningitis, Urinary Tract Infection (UTI) and other miscellaneous diseases.

Aim: To detect if certain hematological parameters would increase the probability to reach a provisional diagnosis of various acute febrile illnesses and prompt institution of specific therapy.

Materials and Methods: This prospective study was conducted in Department of Pathology, Subharti Medical College, Meerut, from September 2013 to June 2015 and included total 300 cases of acute febrile illnesses in age group 18 to 58 years. Complete blood count and malarial parasite microscopy were performed for each patient. Other relevant tests wherever required, were done for confirmation of diagnosis.

Results: Among 300 cases of AFI, malaria was detected in 17%, dengue in 28%, typhoid in 16.3%, UTI in 14.7%, meningitis in 7% and non-specific fever in 17%. There were 159/300 males and 141/300 females. Maximum number of cases (43%) were seen in age group 18 to 28 years. Thrombocytopenia, anemia, increased Red Cell Distribution Width (RDW) and Platelet Distribution Width (PDW) while reduced Packed cell volume (PCV) showed a statistically significant correlation in malaria. A relatively more thrombocytopenia, anemia and reduced RBC and PCV were noted in *P. falciparum* in comparison to *P.vivax*. In dengue, a more reduction in platelet count, leucopenia with lymphocytosis and 56% cases with reduced PCV were noted. Increase in TLC and neutrophil count was consistent features seen in UTI and meningitis. In typhoid patients normal platelet count, mild anemia and mildly reduced PCV was observed while comparing with malaria.

Conclusion: We conclude that routinely used laboratory tests such as hemoglobin, PCV, leukocyte count, platelet count and even red cell indices can act as diagnostic indicators in patients with acute febrile illness.

Keywords: Dengue, Malaria, Thrombocytopenia, Typhoid

INTRODUCTION

Acute febrile illness (AFI) is fever of atleast two consecutive days with body temperature >38°C. The common causes of acute febrile illnesses are malaria, dengue, typhoid, chikungunya fever, meningitis, urinary tract infection and other miscellaneous diseases [1]. Studies have observed that among malaria patients hematological changes do take place resulting in anemia and thrombocytopenia, as the disease progresses. Likewise in case of dengue patients decrease in platelet counts takes place which can also be determined by blood test [2]. Hematological parameters in typhoid include leucopenia with relative lymphocytosis [3]. In the same way leukocytosis is common finding in UTI [4] and bacterial meningitis [5]. Based on these hematological changes which are the measurable parameters of blood and can be easily ascertained by blood examination, the present study aims to detect if certain hematological changes do increase the probability to reach a provisional diagnosis of various acute febrile illnesses and initiate specific therapy without much delay [6].

MATERIALS AND METHODS

Present prospective study was conducted from September 2013 to June 2015 in the Department of Pathology, Subharti Medical College, Meerut. Ethical committee approval was obtained for conducting the study. Total 300 cases of acute febrile illnesses in age group 18 to 58 years admitted in In-Patient-Department (IPD) of Chhatrapati Shivaji Subharti Hospital were included in the study. Because all these cases were of admitted patients, where by default permission for routine examination, blood and other tests is taken, and also as identity of patient is not revealed only their test result data are used, therefore separate consent was not required.

Patient with fever for atleast 2 consecutive days with temperature ≥38°C (100.4°F) were included in the study, whereas patients with septicemia, transfusion reaction and

allergic / drug reactions were excluded. Detailed history was taken of patients fulfilling the selection criteria. Complete clinical examination was done and clinical findings were noted. Venous blood sample for CBC and General blood picture (GBP) were collected in EDTA vacuum tubes (2mg/ml of blood). CBC was done by automatic 5- parts full digital hematology analyzer ABX pentra DF 120 and HORIBA ABX pentra 80. Thin blood smears were prepared, stained with Leishman's stain and studied for GBP and malarial parasite identification. Other test- Quantitative buffy coat (QBC) and Rapid diagnostic test were also done for malaria confirmation whenever needed. Dengue was confirmed by IgM/ IgG antibody test and commercial antibody-capture NS1 antigen test. Typhoid was confirmed using Widal tube test and Typhoid IgG/IgM test. Pus cells >5/hpf with and without bacilli in a clean catch midstream urine sample was considered positive for UTI [7]. TLC >5 cell/mm^3 in CSF was considered positive for meningitis [8]. Normal reference ranges of hematological parameters were taken from Dacie and Lewis practical hematology 9th edition [9].

Data analysis was done by Statistical Package for the Social Sciences (SPSS) version 10. The Statistical analysis was done by using Independent't' Test and chi- square test. The p value < 0.05 was considered as statistically significant and p value < 0.01 was taken as highly significant while p value >0.05 was regarded as non significant.

RESULT

Out of total 300 cases of AFI, dengue was detected in 84(28%), malaria in 51(17%), typhoid in 49(16.3%), UTI in 44(14.7%), meningitis in 21(7%) and 51(17%) patients were of non-specific fever. Number of male patients (53%) predominated the number of female patients (47%). Maximum number of patients (43%) was in age group 18-28yrs, followed by 23.6% in the age group of 29-38yrs [Table/Fig-1].

Among all febrile illnesses, malaria showed maximum (74.5%) number of cases with hemoglobin below 11gm/dl. Out of 48 patients showing leucopenia, maximum (27) were suffering from dengue. Patients of meningitis (81%) showed maximum neutrophilia followed by UTI (63.6%). Lymphocytosis was seen maximum in dengue patients (37%) [Table/Fig-2]. It was noted that majority (56%) of cases of dengue had platelet count less than 50000/mm^3, while malaria showed maximum (39.3%) cases with platelet count between 50000-100000/mm^3 [Table/Fig-3]. Maximum cases of reduced PCV were of malaria (78.4%), followed by UTI (72.7%) [Table/Fig-4]. Normocytic normochromic blood picture (67.7%) predominated among all AFI.

In present study while comparing hematological parameters among malaria and dengue, mean platelet count, mean RDW and mean neutrophil count was much less in dengue patients as compared to malaria. Whereas, the values of mean Hb, mean PCV, mean MCV, mean MCH and mean MCHC were higher in dengue patients. The values of mean WBC and mean neutrophil were significantly higher in meningitis patients as compared to malaria. Thrombocytopenia with increased PDW was noted in malaria while normal platelet count and relative

Age groups (yrs)	Malaria	Typhoid	Dengue	UTI	Meningitis	Non-specific	Total No. of cases
Group I (18-28)	28	13	38	17	9	24	129 (43%)
Group II (29-38)	15	15	16	6	6	13	71 (23.6%)
Group III (39-48)	4	13	14	10	2	7	50 (16.7%)
Group IV (49-58)	4	8	16	11	4	7	50 (16.7%)
Total No. of cases	51	49	84	44	21	51	300

[Table/Fig-1]: Etiology based distribution of patients in different age (n=300).
P value= 0.112 (>0.05) Non-significant –chi square test.

Parameters	Malaria (n=51)	Typhoid (n=49)	Dengue (n=84)	UTI (n=44)	Meningitis (n=21)	Non specific fever (n=51)	Total	
Hemoglobin (<11 gm/dl)	38 (74.5%)	25 (51%)	34 (40.5%)	28 (63.6%)	11 (52.3%)	14 (27.4%)	150 (50%)	300
Hemoglobin (>11 gm/dl)	13 (25.5%)	24 (49%)	50 (59.5%)	16 (36.4%)	10 (47.7%)	37 (72.5%)	150 (50%)	
Low WBC (<4x10^3/mm^3)	8 (15.6%)	9 (18.4%)	27 (32.1%)	1 (2.3%)	2 (9.5%)	1 (2%)	48 (16%)	300
Normal WBC (4x10^3/mm^3-11x10^3/mm^3)	37 (72.5%)	30 (61.2%)	44 (52.4%)	28 (63.6%)	11 (52.4%)	46 (90.1%)	196 (65.3%)	
High WBC (>11x10^3/mm^3)	6 (11.7%)	10 (20.4%)	13 (15.5%)	15 (34.1%)	8 (38.1%)	4 (7.9%)	56 (18.7%)	
Neutrophil Count (>70%)	24 (47%)	24 (49%)	23 (27.4%)	28 (63.6%)	17 (81%)	11 (21.6%)	127 (42.3%)	300
Neutrophil Count (<70%)	27 (53%)	25 (51%)	61 (72.6%)	16 (36.4%)	4 (19%)	40 (78.4%)	173 (57.7%)	
Lymphocyte Count (>40%)	8 (15.6%)	9 (18.4%)	31 (37%)	1 (2.3%)	1 (4.8%)	12 (23.5%)	62 (20.7%)	300
Lymphocyte Count (<40%)	43 (84.4%)	40 (81.6%)	53 (63%)	43 (97.7%)	20 (95.2%)	39 (76.5%)	238 (79.3%)	

[Table/Fig-2]: Comparison of hemoglobin, WBC, neutrophil and lymphocyte count in various acute febrile illnesses (n=300). In all parameters p value <0.01 highly significant -chi square test.

Platelet Count	Malaria	Typhoid	Dengue	UTI	Meningitis	Non-specific	Total
(<50000/mm^3)	17 (33.3%)	2 (4.1%)	47 (56%)	1 (2.3%)	1 (4.8%)	1 (2%)	69 (23%)
(50000/mm^3-100000 /mm^3)	20 (39.3%)	2 (4.1%)	27 (32.1%)	0	2 (9.5%)	1 (2%)	52 (17.3%)
(100001/mm^3-150000/mm^3)	7 (13.7%)	6 (12.2%)	2 (2.4%)	4 (9.1%)	2 (9.5%)	1 (2%)	22 (7.4%)
(150001/mm^3-450000/mm^3)	7 (13.7%)	39 (79.6%)	8 (9.5%)	39 (88.6%)	16 (76.2%)	48 (94%)	157 (52.3%)
Total	51	49	84	44	21	51	300

[Table/Fig-3]: Comparison of platelet count in various febrile illnesses (n=300).

PCV (%)	Malaria	Typhoid	Dengue	UTI	Meningitis	Non-specific	Total
Low (F<36) (M<40)	40 (78.4%)	34 (69.4%)	47 (56.0%)	32 (72.7%)	14 (66.7%)	12 (23.5%)	158 (52.7%)
Normal (F=36-46) (M=40-50)	11 (21.6%)	14 (28.6%)	32 (38.1%)	12 (27.3%)	7 (33.3%)	38 (74.5%)	135 (45%)
Raised (M>50) (F>46)	0	1 (2.0 %)	5 (5.9%)	0	0	1 (2%)	7 (2.3%)
Total	51	49	84	44	21	51	300

[Table/Fig-4]: Comparison of PCV in various febrile illnesses (n=300).

lymphopenia was observed in meningitis. Thrombocytopenia, anemia and increased PDW were statistically significant features noted in malaria as compared to typhoid. Mean platelet count was within normal limit in typhoid cases. Mean PCV values were higher in typhoid in comparison to malaria positive cases. The values of mean WBC and mean neutrophil count were higher in UTI patients as compared to Malaria patients. Thrombocytopenia with increased PDW was noted in malaria while normal platelet count and relative lymphopenia was observed in UTI. In non-specific fever, the hematological parameters were within normal range in majority of cases [Table/Fig-5].

DISCUSSION

In our study, out of all febrile illnesses, malaria showed maximum number of cases of anemia. Anemia in malaria can be due to hemolysis of parasitized RBC's, ineffective erythropoiesis, decreased RBC deformability which causes splenic pooling and phagocytosis [10]. Increased RDW was also observed in malaria, which could be due to macrocytosis and red cell response to malarial parasite [11].

Majority of cases of dengue had platelet count less than 50000/mm^3, while malaria showed maximum cases with platelet count between 50000-100000/mm^3. In similar studies done by Chrispal A et al., [12] in 398 patients of AFI

Hematological Parameters (Mean values)	Malaria (n=51)	Dengue (n=84)	Meningitis (n=21)	Typhoid (n=49)	UTI (n=44)	Non specific fever (n=51)
Mean Hb (gm/dl)	9.71	11.98 §	10.60	11.20*	10.62	12.71 §
Mean PCV (%)	30.05	35.38*	32.84	34.36*	33.21	40.71 §
Mean WBC (x 10^3/mm^3)	6.74	6.51	9.48 §	7.67	11.64 §	7.48
Mean Neutrophil count (%)	67.14	61.56*	80.05 §	67.90	72.20*	63.00*
Mean Lymphocyte count (%)	31.49	35.57	18.38 §	28.27	21.11 §	32.27
Mean Monocyte count (%)	0.27	0.42	0.10	0.51	0.09	0.16
Mean Eosinophil count (%)	1.28	2.50 §	1.48	3.33 §	3.67 §	4.57 §
Mean Basophil count (%)	0	0	0	0	0	0
Mean RBC (x 10^6/mm^3)	3.62	3.91	3.97	3.96	3.98	4.62 §
Mean RDW (%)	15.35	12.94 §	15.77	14.65	14.24 §	15.92
Mean MCV (µm^3)	86.06	92.13 §	83.19	87.96	84.20	87.71
Mean MCH (pg)	27.84	31.32 §	26.85	28.75	26.96	27.66
Mean MCHC (gm/dl)	32.17	33.81 §	31.99	32.49	31.93	31.33 §
Mean Platelet count (/mm^3)	88058.82	62916.67*	303142.86 §	250693.88 §	268915.91 §	264764.71 §
Mean MPV (µm^3)	10.25	9.82	9.54	9.83 §	10.00	9.88
Mean PDW (%)	22.98	23.02	18.28 §	18.81	18.31 §	18.05 §

[Table/Fig-5]: Comparison of hematological parameters in various acute febrile illnesses.
(*p value <0.05, § p value <0.01 - Independent 't' Test).

and Bottieau E et al., [13] in 1962 patients of AFI, dengue and malaria showed moderate to severe thrombocytopenia. The bone marrow depression observed in dengue fever in the acute stage may account for thrombocytopenia. In addition, direct infection of megakaryocyte by dengue virus could lead to an increased destruction of platelet cells [14]. In patients of malaria thrombocytopenia seems to occur due to peripheral as well as splenic destruction of platelets, immune mediated destruction of circulating platelets and platelet consumption by process of DIC [15].

While comparing hematological parameters among malaria and dengue, mean platelet count, mean RDW and mean neutrophil count was much less in dengue patients as compared to malaria. Whereas the values of mean Hb, mean PCV, mean MCV, mean MCH and mean MCHC were higher in dengue patients as compared to malaria. Similar results were seen in study done by Sethi B et al., [10]. The values of mean WBC and mean neutrophil count were higher in meningitis and UTI patients as compared to Malaria. When malaria was compared with typhoid, the values of mean Hb, mean PCV, mean platelet count were higher in typhoid infected patients as compared to malaria. But values of mean PDW were higher in malaria patients as compared to typhoid. Emenuga VN et al., [16] in their study among 200 typhoid patients also reported a decrease in mean hemoglobin count. Similar to our study, Dangana A et al., [17] noted mean PCV 34.14% in a study conducted among 200 cases of enteric fever. Abro AH et al., [18] and Chrispal A et al., [12] in their studies on typhoid patients reported platelet count to be in normal range.

LIMITATIONS

As only IPD patients were included in the present study, no Out Patient Department (OPD) patients were included due to lack of patients follow-up, hence we could not assess the effect of different strains of disease causing organisms on various hematological parameters in a specified period of time.

CONCLUSION

We observed that hematological changes such as thrombocytopenia, anemia, increased RDW and PDW, while reduced PCV showed a statistically significant correlation with malaria. When malaria was compared to dengue, a more reduction in platelet count, leucopenia and a relative increase in lymphocyte count, mean MCV, mean MCH and mean MCHC in dengue patients as compared to malaria increases the probability of dengue infection. While comparing malaria with UTI and meningitis, it was observed that an increase in TLC and neutrophil count could discriminate malaria from UTI and meningitis. When typhoid was compared to malaria, a normal platelet count, mild anemia and mildly reduced PCV provided diagnostic clues towards typhoid. We conclude that routinely used laboratory findings such as hemoglobin, leukocyte and platelet count and even red cell indices can act as diagnostic indicators in patients with acute febrile illness, thus increasing the probability of correct diagnosis of disease and enhancing prompt initiation of treatment.

REFERENCES

[1] Capending MR, Chua MN, Hadinegoro SR, Hussain II, Nallusamy R, Pitisuttithum P, et al. Dengue and other common causes of acute febrile illness in Asia: An active surveillance study in children. *PLoS Negl Trop*. 2013; 7(7):52-53.

[2] 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):12-17.

[3] Ananthanarayan R, Paniker CK, Kapil A. Enterobacteriaceae III: Salmonella. Ananthanarayan and Paniker's Textbook of Microbiology. 9th ed. Hyderabad: Universities press; 2013:299.

[4] Aminzadeh Z and Parsa E. Relationship between age and peripheral white blood cell count in patients with sepsis. *Int J Prev Med.* 2011; 2(4):238–42.

[5] Hoffman O and Weber JR. Pathophysiology and treatment of bacterial meningitis. *Ther Adv Neurol Disord*. 2009; 2(6):401-12.

[6] Jivani P, Panchal B, Parmar S, Mehta N, Savaliya C, Sorani A. Comparative study of effect of P. falciparum and P. vivax malaria on platelet count. *IJBAP*. 2014; 3(1):303-07.

[7] Pherson MC, Pincus MR. Basic examination of urine. In: McPherson RA, Ben-Ezra J, editors. Henry's clinical diagnosis and management by laboratory methods, 22nd edition. Elsevier; 2011:465.

[8] Pherson MC, Pincus MR. Medical Parasitology. In: Karcher DS, McPherson RA, editors. Henry's clinical diagnosis and management by laboratory methods, 22nd edition. Elsevier; 2011:482.

[9] Lewis SM, Bain BJ, Bates I. Reference ranges and normal values. In: Lewis SM. Dacie and Lewis practicle hematology, 9th edition. London: Harcourt Publishers; 2001:9-18.

[10] Sethi B, Arora B, Kumar Y, Aggarwal R. Parasitemia and hematological alterations in malaria: a study from the highly affected zones. *I J P*. 2013; 8(1):01-08.

[11] Lathia TB, Joshi R. Can hematological parameters discriminate malaria from non malarious acute febrile illness in the tropics? *Indian J Med Sci*. 2004; 58(6):239-44.

[12] Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JA, Thomas EM, et al. Acute undifferentiated febrile illness in adult hospitalized patients: the disease spectrum and diagnostic predictors - an experience from a tertiary care hospital in South India. *Trop Doct*. 2010; 40(4):230-34.

[13] Bottieau E, Clerinx J, Vanden EE, Esbroeck MV, Colebunders R, Gompel AV et al. Fever after a stay in the tropics: diagnostic predictors of the leading tropical conditions. *J Med Baltimore*. 2007; 86(1):18-25.

[14] Bashir AB, Mohammed BA, Saeed OK, Ageep AK. Thrombocytopenia and bleeding manifestations among patients with dengue virus infection in Port Sudan, Red Sea State of Sudan. *J Infect Dis Immun*. 2015; 7(2):7-13.

[15] Kotepui M, Phunphuech B, Phiwklam N, Chupeerach C, Duangmano S. Effect of malarial infection on haematological parameters in population near Thailand-Myanmar border. *Malaria Journal*. 2014; 13:218.

[16] Emenuga VN, Ureme SO, Ohanu ME, Ejezie FE, Nnabuchi CI. Some haematological and biochemical profiles of typhoid fever in IGBOS of Nigeria. *I J App Res*. 2014; 4(3):330-32.

[17] Dangana A, Ajobiewe J, Nuhu. Haematological changes associated with Salmonella typhi and Salmonella paratyphi in humans. *Int J Biomed Hlth Sci*. 2010; 6(4):219-22.

[18] Abro AH, Abdou AM, Gangwani JL, Ustadi AM, Younis NJ, Hussaini HS. Hematological and biochemical changes in typhoid fever. *Pak J Med Sci*. 2009; 25(2):166-71.

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