HEMATOLOGICAL CHANGES IN MALARIA

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ABSTRACT: AIMS: This study examined the hematological effect of acute malaria. **METHODS AND MATERIAL:** This observational study was conducted in MLB medical college, Jhansi, U.P. over the period of two years. 200 patients were studied who were QBC or peripheral smear positive for malaria. Blood samples were examined by automatic counter and data was compared. **STATISTICAL ANALYSIS:** Paired and Unpaired t-test. **RESULTS:** In our study of 200 patients, anemia was found in 94% of patients, RBC counts and Hematocrit was reduced in about 90% (p value <0.0001), thrombocytopenia in 85%, leucopenia in 27%, RDW remains normal, MCV remains normal, MCH and MCHC was decreased in 15% and 25% respectively. MPV is increased in 25%, PDW was increased in 50% and PCT is decreased in 83% of our patients. **CONCLUSION:** Anemia, Thrombocytopenia is the major hallmark of malaria. Decrease in MCH, MCHC, PCT, WBC and raised MPV and PDW can be important predictors of malaria and can be used in diagnosis along with clinical manifestation. **KEYWORDS:** Hematological changes, Malaria, Anemia, Thrombocytopenia, Leucopenia, Mean platelet volume, Platelet distribution width.

INTRODUCTION: Malaria is one of the important parasitic diseases of human. In spite of intensive worldwide efforts to reduce its transmission, malaria remains the most serious and widespread protozoal infection of humans. Over 40% of the world's population is at risk of contracting malaria, which is endemic in 108 countries, mostly developing including India. It is estimated that malaria affects approximately 3 billion individuals per year accounting for 1-3 million deaths according to WHO. In India, total 1.49 million malaria cases had occur, out of which, 0.77 million (52.12%) cases were of *P. falciparum* in year 2010. Annual parasite infection (API) of India for the year 2010 was 1.3. Annual Blood Smear Examination Rate (ABER) of India for the year 2010 was 9.21.¹

Malaria usually presents with fever, chill with rigor, malaise, headache, myalgia, anorexia, vomiting, anaemia, enlarged spleen. However it can unusually present as coma, convulsion, bleeding manifestations, severe anaemia, jaundice, black water fever, shock, hypoglycaemia, metabolic acidosis, renal failure. It can rarely present as malarial hepatopathy, glomerulonephritis, nephrotic syndrome, GBS syndrome and peripheral neuropathy.

The haematological abnormalities that have been reported with malaria include anaemia, thrombocytopenia, splenomegaly, and rarely disseminated intravascular coagulation (DIC). There have also been reports of leucopenia and leucocytosis.

Haematological changes associated with malarial infection may vary with level of malaria endemicity, background hemoglobinopathy, nutritional status, demographic factors and malaria immunity. In this study, we analysed and statistically evaluated the haematological changes in cases of malaria and whether they could guide physicians to institute specific antimalarial treatment.

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MATERIAL AND METHOD: This observational study was conducted at department of medicine in MLB medical College, Jhansi over the period of two years (2012-2014). All the patients of fever with suspicion of malaria was examined and peripheral thick/thin smear and Quantitative Buffy Coat examination was done. Only peripheral smear/QBC positive patient were included in this study. 200 patients were enrolled in our study and were haematologically and clinically evaluated. All patients under study were examined for Hb, RBC, HCT, Platelet count, WBC, PDW, PCT, MPV, RDW, GBP and Vit. B12 levels (If required). A control of 100 patients was taken which were admitted in ophthalmology for cataract. Another CBC of the patients was done on 14th day after admission. All the data was analysed statistically with student t test. Comparison of cases and controls was done with unpaired t test and of cases on admission and on discharge was compared with paired t test. The p value < 0.05 was considered as significant.

OBSERVATION AND RESULTS: In our study of 200 patients, 140 were infected with *P. vivax*, and, 39 were infected with *P. falciparum*, and 21 were infected with mixed infection i.e. both *P. falciparum* and *Vivax*. 117 were male while 83 were female. 64 were of age 18-25yrs, 85 patients were of age 25-40, 35 patients are 40-55yrs of age and 16 patients are more than 55yrs of age i.e. around 75% of affected patients were in younger-middle age group i.e. between 18-40yrs of age. 175 patients had higher degree of parasitemia (4+ and 3+) and only 25 patients had lower degree of parasitemia (2+ and 1+).

At admission, 63 patients were severely anaemic with Hb <8gm% while, 87 patients were moderately anaemic, 38 patients had mild anaemia and 12 patients were not anaemic. Among controls none of the patients were severely anaemic, 37 patients were moderately anaemic, 34 patients were mildly anaemic and 29 were non-anaemic. The mean haemoglobin concentration at admission of patients with malaria was 8.96gm% with standard deviation±2.87 and the mean Haemoglobin of controls was 11.84gm% with standard deviation±1.49. According to the unpaired t-test, the difference in values were significant (p value <0.0001). Hence there was fall haemoglobin concentration in patients admitted to us with malaria.

Hb (At Admission) in gm/dl	<8	8-10.9	11-12.9	>13
Cases	63	87	38	12
Controls	0	37	34	29
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
Hb(gm/dl)	8.96±2.87	11.84±1.49	9.41	<0.0001
Table 1				

There was significant fall in RBC counts in about 85% of patients and fall in PCV/HCT in 92% of patients.

MCV of most of the patients remained normal while in some patients it increases. The increase is not due to Vit. B12 deficiency as it comes out to normal in all subjects.

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MCV(At Admission) in Fl	<76	76-96	>96	
Cases	16	103	81	
Controls	0	82	18	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
MCV (Fl)	94.3±14.91	94.88±7.54	0.34	0.73

Table 3

MCH and MCHC were s decreased in malaria which is statistically significant as compared to controls.

MCH (At Admission) (in Pg/Cell)	<27	27-32	>32	
Cases	51	93	56	
Controls	6	44	50	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
MCH (in Pg/Cell)	30.25±5.46	32.22±3.48	3.28	0.001
MCHC (AT ADMISSION) (in g/dl)	<30	30-35	>35	
Cases	29	151	20	
Controls	0	71	29	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
MCHC (in g/dl)	31.96±2.65	33.65±1.72	5.76	<0.0001

Table 4

RDW in our patients shows no significant change between case and controls.

At admission 171 patients had platelet counts less than 1.5 lacks, 29 patients had platelet counts in normal range i.e. 1.5-4.5 lacks. Among controls, out of 100 patients, 10 patients had PLT counts less than 150, 90 patients had PLT counts between 150-450, and none more than 450. The mean PLT count at admission of patients with malaria was 106.07 with standard deviation±71.51 and the mean PLT counts of controls were 210.97 with standard deviation±54.33. According to the unpaired t-test, the difference in values were significant (p value <0.0001). Hence there was significant fall in PLT counts in patients admitted to us with malaria.

PLT (At Admission) (1000cells/dl)	<150	150-450	>450	
Cases	171	29	0	
Controls	10	90	0	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
PLT (1000cells/dl)	106.07±71.51	210.97±54.33	12.9	<0.0001

Table 5

There was rise in PDW in patients with malaria which was statistically significant as compared to controls.

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PDW (At Admission) (in %)	<9	9-17	>17	
Cases	0	105	95	
Controls	0	69	31	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
PDW (in %)	16.92 ± 2.81	15.33 ± 2.43	4.81	<0.0001

Table 6

There was significant rise in mean platelet volume (MPV).

MPV (At Admission) (in FL)	<9	9-13	>13	
Cases	14	137	49	
Controls	10	81	9	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
MPV (in FL)	11.96 ± 2.25	10.83 ± 1.47	4.56	<0.0001

Table 7

Plateletcrit decreases in acute malaria significantly.

PCT (At Admission) (in %)	<0.19	0.19-0.4	>0.4	
Cases	167	30	3	
Controls	27	64	9	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
PCT (in %)	0.12 ± 0.07	0.25 ± 0.11	11.45	<0.0001

Table 8

A WBC count varies largely in malarial infection. In our study most of the patients have normal WBC counts while 26% patients had decreased WBC counts.

WBC (At Admission) (Cells/dl)	<4000	4000-11000	>11000	
Cases	53	129	18	
Controls	4	89	7	
Variables	Mean±SD (Cases)	Mean±SD (Controls)	t value	p value
WBC (cells/dl)	6305.65±3657.76	7520±2383.53	3.01	0.0028

Table 9

DISCUSSION: Malaria is a major health problem in the tropical regions of the world including India and poses a significant burden on health expenditure. We studied 200 patients which are QBC or peripheral smear positive for malaria and 100 non malarial patients were taken as control. This study was conducted in medicine department MLB medical college hospital, Jhansi during July 2012 to September 2014.

Out of 200 patients with malaria, 140 patients were infected with *Plasmodium vivax* (i.e. 70% of all cases), 39 patients were infected with *plasmodium falciparum* (i.e. 19.5% of all cases) and 21

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patients were infected with both vivax and falciparum. However, Zeeba Shamim Jairajpuri (2014) had reported the incidence of 51.6% for Plasmodium vivax, 47.1% mixed and only 1.1% of P. falciparum.² According to A. K. Agarwal and Sarit Chatarjee (2012), India harbors both P. vivax (55% to 60%) and P. falciparum (35% to 40%) and contributes 70% of malarial cases in the South East Asian region.³ Our study is in concordance with these studies that vivax is more common in this region.

Out of 200 cases, 117 patients were male (i.e. 58.5% of all cases) and 83 were female (i.e. 41.5% of all). This shows that malaria more frequently occur in males. The male preponderance may be due to the fact that male are more involved in outdoor activities.

In our study of 200 patients, 64 (32%) were of age 18-25yrs, maximum number of patients were of middle age group i.e. 85 (42.5%) patients were of age 25-40, 18% patients are 40-55yrs of age and 8% patients are more than 55yrs of age. This indicates that almost 75% of all patients in our study were in younger to middle age group i.e. between 18-40yrs of age. According to Zeeba Shamim Jairajpuri in 2014, the mean age of patients affected with malaria was 29.2 years and the highest proportion of cases (46%; 76 cases) was seen in the 20-30years age group. Almost 81% of the malaria positive cases were seen among the adults.² This is in concordance with our study. This may be due to the fact that these groups of people are mainly involved in outdoor activities.

Anemia was present in 94% of cases in our study and in majority of these cases, anaemia was normocytic normochromic type. According to Tanomsri Srichaikul in 1999, Anemia is one of the most common complications in malaria. The incidence of anaemia in malaria was reported to be as high as 80%.⁴ C. Igbeneghu and A.B. Odaibo in 2013 studied 671 patients with malaria. Anemia was present in 426 patients (63.5%).⁵ These studies are in concordance with our study.

The pathogenesis of anaemia in malaria is particularly complex, multi factorial and incompletely understood. It is thought to result from a combination of hemolysis of parasitized red blood cells; accelerated removal of both parasitized and innocently un-parasitized red blood cell, depressed as well as ineffective erythropoiesis with dyserythropoietic changes and anaemia of chronic disease. Other factors causative to anaemia in malaria include decreased red blood cell deformability, splenic phagocytosis and/or pooling, so they have an increased rate of clearance from the circulation.

RBC counts and Hematocrit runs in parallel to haemoglobin values. These parameters, similar to haemoglobin, also changes in acute malaria. In our study of 200 patients infected with malaria, RBC counts were reduced in around 85% and hematocrit was reduced in 96% of patients. Agravat, A. H. and Dhruva, G. A (2009) studied 287 patients, in which decreased RBC count was seen in 83.5% P. falciparum and 50.8% in P. vivax cases respectively.⁶ Thus RBC count reduction was strongly associated with P. falciparum infection which was subsequently responsible for severe anaemia in patients. This is in concordance with our study. In our study 96% of patients had reduced hematocrit. According to Agravat, A. H. and Dhruva, G. A (2009), 91% had low hematocrit and only 9% had normal haematocrit.⁶ P.Senthilkumar and S.Sarojini studied 20 patients (2013), they confirmed the significant difference in platelet count and hematocrit among patients of malaria.⁷ These result are similar to our study.

There is no change in RDW in malaria in our study. According to a study by Robert N Maina et. al, in year 2010, there was no significant difference in RDW between the parasitemic and the non-parasitemic groups.⁸ These results are in concordance with our study.

The reduction in circulating platelet count is consistently reported in the different types of malaria. In our study 85.5% of patients with malaria developed thrombocytopenia. According to Manmeet K Gill et al., a total of 120 patients with malaria were studied in 2013 by conventional

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microscopy. Platelet count was done on a fully automated, quantitative, hematology analyzer. They concluded that thrombocytopenia was noted in 63.33% cases.⁹ Bhawna Sethi et al (2013) studied 200 patients of malaria. The platelet count was low in 62% cases and ranged from 10.1 to $530 \times 10^9/l$ with mean of $90.3 \times 10^9/l$. Eleven (5.5%) cases revealed severe thrombocytopenia out of which one had bleeding manifestation.¹⁰ Results of all these studies are in concordance with our study.

We observed normal WBC count in 64.5% of the patients and leucopenia in 26% patients, leucocytosis (9%) was seen rarely in some cases with the highest TLC value of 20×10^9 the mean remained at $6.3 \times 10^9/L$. Leucopenia was present more frequently in *P. falciparum*-infected patients (25.6%) than in *P. vivax*-infected patients (22.1%) in our study. According Jadhav UM, Singhvi R, Shah R, who studied 264 patients in tropical endemic areas of India (2003); WBC counts in *P. falciparum*- and *P. vivax*-infected patients, found no difference between mean WBC counts among the two groups. This study reported WBC counts of <4000 cells/mm³ (its definition of leucopenia) in 10.7% of 112 *P. falciparum*-infected patients and in 15.2% of 118 *P. vivax*-infected patients.¹¹

Leucopenia is thought to be due to the localization of leucocytes away from the peripheral circulation, splenic sequestration and other marginal pools rather than actual depletion or stasis.

Changes in blood indices i.e. MCV, MCH, MCHC, varies significantly among various studies on malaria. In our study around 52% patients have MCV in normal range and around 40% of patients had MCV more than 96. The raised MCV is not due to Vit. B12 deficiency as S. Vit. B12 levels were in normal range in these patients. But the change in MCV is not statistically significant as compared to the control population. MCH and MCHC were lower in our patients of malaria. MCH was lower in around 26% of our patients and MCHC was lower in around 15% of patients. These values were statistically significant as compared to control group. These findings are consistent with various other studies. According to a study by Bharti Arora on malaria (2013), blood indices including mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) were reduced in 29, 30.5 and 20.5% ranging 59.0-101.5 fl, 15.5-33 pg and 29.5-35.0 g/dl with mean of 77.8, 28.4 and 31.2 respectively.¹⁰

In another study conducted by Agravat, A. H. and Dhruva, G. A, in 2010 on haematological changes in malaria, variation in MCV, MCH and MCHC was described. There was equal number of patients with normal and low MCV 47.2% and 50.6% respectively. Amongst the two species, *P. Vivax* had more number of patients with low MCV 57.1%. MCH was predominantly normal in 56.7% cases. 32.2% had low MCH whereas 11.2% had high levels. No species specific difference was noted in values of MCH. MCHC was normal in 61.8%, high in 35.6% and low in 2.6%. High MCHC values were observed in both the species (38.2% and 28.6% respectively).⁶ The result of our study is in concordance with these studies. There are only few studies describing changes in these blood indices and most of the studies among them have different results.

The variation of plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW) were also described only in few studies. In our study, we found that around 88% of patients have plateletcrit less than normal with mean PCT was 0.12%, on comparing it with controls which were having mean PCT 0.25%. According to AGRAVAT, A. H. AND DHARUVA, G. A., Plateletcrit value was found low in both the species. Only 11.7% patients had normal plateletcrit⁶. This is in concordance with our study.

In our study the 47.5% patients with malaria showed increase in PDW. According to a study conducted by Fabio A Leal-Santos, Soraya BR Silva, Natasha P Crepaldi et al, (2013), PDW was increased in most of the patients with malaria but it does not rise with severity of malaria¹². Gauri S.

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Metkar (2013) showed that PDW rises significantly with increase in grade of malaria¹³. This is in concordance with our study.

In our study Mean platelet volume was normal in 67.5% cases; low mean platelet volume was noted in 7% and high MPV in 24.5% of cases. The mean MPV at admission of patients with malaria was 11.96 ± 2.95 fl and the mean MPV controls was 10.83 ± 1.47 fl. The difference in values were statistically significant (p value <0.0001, unpaired t-test). In a study conducted by Fabio A Leal-Santos, Soraya BR Silva, Natasha P Crepaldi et al, (2013), MPV was higher than the median value in 46.2% of the patients¹². These finding are also similar to our study which depict the significant fall in PCT, rise in PDW and rise in MPV in patients with acute malaria.

Hence in our study of 200 patients, major haematological changes seen were anaemia, thrombocytopenia, decrease in RBC counts, hematocrit, plateletcrit, while there was increase in mean platelet volume and platelet distribution width. These finding are in concordance with other studies as mentioned above.

CONCLUSION: There were statistically significant changes in haematological profile a patient with acute malaria. Haemoglobin, RBC counts, Hematocrit, platelet count and plateletcrit decreases statistically significantly in malaria which tends to increase after treatment. Mean platelet volume and platelet distribution width increases in malaria which tends to normalize after treatment. Most of the patient had normal WBC, only few had leucopenia and rare patients had leucocytosis.

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