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Hematological and biochemical alterations in malaria and their correlation with Parasitic Index.

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Abstract: *Malaria is a major health problem in India with 1.04 million cases reported in 2012 leading to 504 deaths. The clinical spectrum depends on the infecting species, level of parasitemia and the immune status of the host. Malaria pathogenesis is based on extensive changes in hematological and biochemical parameters. The objective of this study was to study the clinical features, hematological and biochemical parameters in malaria patients and correlate them with the parasitic index (PI).*

Material and methods: We conducted a study on 300 malaria patients. The frequency of various symptoms and signs of malaria caused by various plasmodium species were determined. The degree of anemia, WBC count, platelet count serum bilirubin, liver enzymes and serum creatinine levels were studied and their variation depending on the parasitic index was documented. Results: 197 patients had vivax malaria, 76 patients had falciparum malaria and 27 patients had mixed infection. 171 patients had a PI of less than 2%, 100 patients had PI between 2 to 5%, 23 patients had PI between 5 to 10% and only 6 patients had PI of more than 10%. 72.3% of patients had thrombocytopenia, 46.66% had anaemia, 25% had increased bilirubin 29.66% showed increased liver enzymes and 7.66% had increased creatinine levels.

Conclusion: There was a correlation between degree of parasitemia and severity of malaria in majority of cases. Derangements in hematological and biochemical parameters were more frequently seen in patients with higher PI. Hence PI can be used as an indicator by the clinician to know the severity of infection and plan appropriate treatment.

Keywords: *Malaria, Parasitic index, Anemia, thrombocytopenia, Hyperbilirubinemia, Severity*

I. Introduction

Malaria is a major health problem in India and many parts of the world.According to world malaria report 2013 there were 207 million cases of malaria in 2012 resulting in 627000 deaths.13% of these cases were reported from South East Asia,52% of which were reported from India.India contributed 1.04 million of malaria cases leading to 504 deaths.[1]Though in majority of cases, malaria presents as an uncomplicated fever with prompt recovery,it may present in severe form with systemic complications especially renal and hepatic failure, leading to high morbidity and mortality.[2]WHO recommends that all persons of all ages in all epidemiological settings with suspected malaria should have a confirmation of diagnosis in every case of malaria either by microscopy or rapid antigen detection test.Microscopy is the gold standard for diagnosis of malaria, identification of species and to assess the degree of parasitemia. There is a correlation between degree of parasitemia and severity of infection in a majority of cases.Parasitic index (PI) of >5% in non-immune individual is one of the criterion of severe malaria laid down by WHO in 2000.[3]Out of 181 million microscopy examination done for malaria in 2012 worldwide India was the global leader with 120 million microscopic smear examinations reported.[1]In all these cases PI can easily be done and used as an indicator to assess severity of infection.Moreover persistence of parasite density after treatment can indicate drug resistance.

The present study was done to reinforce the value of PI in the diagnosis of malaria.Clinical features, hematological and biochemical parameters of Plasmodium vivax,P falciparum and mixed infections were correlated with parasitic index. By this we could predicts the severity and prognosis of malaria patients and determine which of them needed hospitalization.

II. Material and methods

The present study was a prospective observational study done in the department of pathology at Dr. R.N. Cooper Municipal General Hospital Mumbai.The duration of the study was for a 2 year period between 1st June 2009 till 31st May 2011.Institutional ethics committee approval was obtained.The study population included all indoor and outpatients referred to pathology department for detection of malarial parasite.Study included patientsof all ages and both sexeswith blood film proven malaria.Patients of malaria with negative

smear were excluded from the study. A complete clinical history was taken and clinical examination was done with reference to the presence of fever, chills, headache, vomiting, diarrhea, oliguria, respiratory distress, altered mental status/convulsions, jaundice, bleeding spots, pallor and hepatosplenomegaly. Blood was tested by finger prick method using a lancet. Thick and thin smears were stained using field and JSB stain(Jaswant Singh and Bhattacharyastain).Smears were examined for presence of malarial parasite under oil immersion in at least 100 fields for not less than 5 minutes.PI was given by the counting the number of parasites per 1000 Red Blood Cellson thin smears.In cases of thick smear PI was counted by noting the number of parasites per 200 White Blood cells counted, multiplied by WBC count.[4]

A count of one lakh parasites/microliter corresponds to 2 % parasitemia and a count of 2.5 lakhsparasites/microliter is taken as 5% PI.[5,6]The degree of parasitemia, that is parasitic Index was graded as less than 2%, between 2 to 5%, between 5 to 10% and more than 10%.Venous blood sample was used to do the hematological and biochemistry parameters.CBC was done on automated cell counter (PCE210 ERMA INC) and biochemical profile was done on fully automated analyzer (ERBA XL 600).Hb, WBC count and platelet count were noted. Serum bilirubin,liver enzymes and serum creatinine levels were noted.Patients were divided into 2 groups those with parasitic Index >2% and those with PI <2%.Forstatistical evaluation the OpenEpi software was used.The Fischer's exact test and chi-square tests were used to analyze the association of hematological and biochemical alterations in patients with PI <2% and those with PI >2%.A p-value of <0.05 was considered as statistically significant.

III. Results

Three hundred patients were enrolled in this study during this period.Out of the 300 cases 197 patients had vivax malaria, 76 patients had falciparum malaria and 27 patients had mixed infection.[Table 1]

Age and sex distributions are shownin table 2.Out of the 300 cases,200 were males and 100 were females.Male to Female ratio was 3:2.Malaria was most prevalent among the age groups of 26-50 years.PI was calculated. One seventy one patients had PI less than 2%,100 patients had a PI between 2-5%,23 patients had PI of 5-10% and only 6 patients had PI >10%.

A correlation was done between the clinical features, species involved and PI.[Table 3] Fever (95%),headache (97%) and chills (92%) were the common symptoms present irrespective of species involved and PI.Vomiting (20%),diarrhea (20.3%),jaundice(13%) and pallor(11%) were the other significant symptoms.These were more common in P. falciparum and mixed infection than in P. vivax.2 patients had oliguria and 2 patients had convulsions.They were cases of Falciparum malaria with PI of greater than 5%.One case of Pvivax had respiratory distress with PI greater than 5%.Hepatomegaly was seen in 12.6% patients and 17% patients hadsplenomegaly. They were more common in mixed and P falciparum infections than P vivax infections and were associated with higher parasitic load.

Hematological and biochemical parameters inP. vivax, P.falciparum and mixed infections were studied and correlated with PI.[Table4,5,6] Both the above parameters were also studied in group of patients with PI <2% and those with PI >2%.[Table 7]

72.3% patients had thrombocytopenia. It was more common in mixed (100%) and P. vivax (73.6%) infections than in P. falciparum (59.21%)infections.Anemia was seen in 46.66%of cases and was more common in mixed(70.37%) andP. falciparum(50%)than in P. vivax infection(42.13%).Incidence of anemia and thrombocytopenia was significantly higher (p-value<0.001) in patients with PI>2% than in patients with PI value <2%.Leucopenia was seen in 13% and leukocytosis was seen in 2.6% patients.

In our study, 25% patients had hyperbilirubinemia which was seen in 19.8% cases ofvivax,27.63% cases of falciparum and 55.5% cases of mixed infection.Increase in liver enzymes were seen in 29.66% of total cases,21.83% cases of P vivax, 28.94% cases of P. falciparum and 88.88% of mixed infection had raised liver enzymes.

Only 7.66% cases showed increase creatinine levels.3.04%cases of vivax, 15.79% cases of falciparum and 14.81% of mixed infection showed increased creatinine levels.High creatinine levels were seen more commonly in falciparum infections with PI >2% and in mixed and P. vivax infection with PI>5%. Incidence of hyperbilirubinemia, raised liver enzymes and increased creatinine levels was significantly higher (p-value <0.001)in patients with PI >2% than in patients with PI value < 2%.

IV. Discussion

Human malaria is caused by protozoan of the genus plasmodium with four species pathogenic to man, namely vivax, falciparum, ovale and malariae. In India, the prevalence of vivax and falciparum infection is 50% each but proportion of cases in different regions is variable.[7] In our study 65.66% of cases were of vivax,25.33% of falciparum and 9% were of mixed infections.This is similar to study done by Jadhav et al[8] in Navi Mumbai while Kochar et al have reported a higher incidence of falciparum infection in Bikaner.[9]

Hyperparasitemia is one of the criterion of severe malaria laid down by WHO for more than 2 decades.[10]In 2010 WHO has defined hyperparasitemia as >2lakh parasites per microliter or .>2% PI in low intensity transmission areas or >5% PI i.e.2.5lakh parasites per microliter in areas of high stable malaria transmission intensity.[11]

Majority of our patients (57%)had a PI of <2%.We attribute this finding because every case of fever is subjected to malaria testing at time of presentation.Howeverin mixed infections, most of the patients had a PI >2% at the time of diagnosis. In our study 95.41% cases of P vivax had a PI <5% while 81.57% patients of P falciparum had PI<5% and 85.19% of mixed infection had PI <5%.A study by Ganguly and Dutta found >5% PI in 29.8% of cases of severe malaria in children while Tripathi et al reported >5% PI in 31.8% cases of severe malaria.[12,13]

Clinical presentation of fever, headache and chills was seen in all species and with mixed infection irrespective of level of parasitemia as has been reported in many studies.[14,15,16] Only patients with PI of >2% had jaundice and hepatosplenomegaly. It was seen more frequently in mixed and P falciparum infections than in vivax infections.Proportion of cases with splenomegaly is less in our study compared to others.[17] Patients with clinical features of respiratory distress,convulsions and oliguria all had a PI >10%.Studies by Aarthi et al[18] and Trang TT et al[19] have reported that development of renal failure is influenced by parasite load as most of their cases with renal involvement had PI >10%.Hence we should note that the clinical presentation in malaria is diverse and it is vital to keep a differential of malaria in febrile illness even presenting with jaundice or renal failure.In these cases a high level of parasitemia is detected.Hyperparasitemiais an indicator of severe malaria with systemic involvement.It is believed to be an important cause of multiorgan failure and death in malaria.[20,21,22]

Alterations in hematological parameters are also thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria prompting more meticulous search for malarial parasites.[23]

Anemia and thrombocytopenia are the most frequently found abnormality in patients suffering from malaria.[24]If platelet count is <1.5lakh it raises the possibility of malaria 12 to 15 times. In our study 72.3% patients presented with thrombocytopenia.Faseela et al[25] found 82.77% of patients with thrombocytopenia and Colonelet al[26] found 72% of patients with thrombocytopenia. Thrombocytopenia was more frequently seen in mixed and vivax infections than in falciparum infections as has been reported by Gupta et al[27] and other studies.

Anemia was seen in 46.66% of patientswhile Rao et al[28] have reported 60.17%of patients with anemia(29)and Faseela et al[25] reported 18% cases of malaria with anemia.Degree of anemia correlated with higher PI and was seen more in Pfalciparum and mixed infections. Leucopenia was seen in 13% and leukocytosis was seen in 2.6% patients.Jhadhav et al[8] found 14% leucopenia and 4.9% cases of leukocytosis in malaria.Hence alteration in WBC parameters is not significant in large proportion of cases.

The incidence of jaundice in malaria ranges from 20-31% and it is predominantly of hemolytic type and is associated with a high parasite load.[20]Instudy by AarthiRajkumar et al[18] 5 casesof jaundice had a high PI.In our study incidence of high bilirubin was seen in 25% of patients and 29.66% had increased liver enzymes.More than half cases of mixed infection had increased bilirubin and 88.88% had increased liver enzymes, while about one fourth cases of falciparum had increased bilirubin and liver enzymes and only 20% cases of vivax had increased bilirubin and enzyme levels. Similar findings have been reported by Charulata a et al[29] with increased bilirubin and liver enzymes seen more in mixed and falciparum than in vivax infection and more in patients with high PI.In our study 7.66% patients had increased serum creatinine and 2 had acute renal failure.Most cases of renal dysfunction were due to falciparum infection with concomitant hyperparesetemia.Sharma et al[30]have reported 7.6%cases with increased creatinine levelswhile Mishra et al[31]have reported increased creatinine levels in 11.8% cases of malaria.However rarely patients with high PIhad no hematological and biochemical abnormality, while patients with low PI had severe derangement in hematological and biochemical parameters.This is attributed to differences in immunity between different patients.

Hence this study has shown that hyperparesetemia is associated with clinical features of severe malaria with hematological and biochemical alterations in majority of the patients and can be used as an indicator for severe infection. These patients need to get prompt and hospital based treatment to decrease morbidity and mortality associated with malaria.

The study findings demonstrate that parasitic index should be reported while evaluating a case of malaria.Parasite density helps the clinician to know the severity of infection and if the patient is responding to treatment when done as a follow up after treatment. It is even more important in P. falciparum infection which is often considered potentially dangerous. In this study PI correlated well with the severity of the disease and derangement in biochemical and hematological parameters. Complication and mortality will be more often seen in patients with higher degree of parasitemia. Hence knowledge of PI can be used as a valuable tool for predicting clinical outcome and planning appropriate therapy.The presence of the thrombocytopenia and anemia raises the probability of malaria.Increased liver enzymes, bilirubin and creatinine should alert the clinician to the possibility of severe malaria and prompt admission is crucial. Today the most important problem in management of malaria is not only its drug resistance but also the occurrence of multisystem complications. Most of these systemiccomplications are due to hyperparesetemia. The study findings demonstrate that when evaluating a febrile illness in malaria endemic zones clinical presentation may be varied and immune patients with high PI may be nearly asymptomatic while nonimmune patients may have severe manifestation even with low PI.

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