ORIGINAL ARTICLE

Frequency of Bicytopenia in Malaria

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ABSTRACT

Background: We conducted this study to determine the frequency of thrombocytopenia and leukopenia in confirmed cases of malaria admitted in medical wards of CMH Lahore hospital between February 2013 to January 2014. It was found that good percentage of these patients showed thrombocytopenia and leukopenia.
Aim: To study the frequency of bicytopenia in malarial patients seen in CMH Lahore
Study design*:* Descriptive, cross sectional
Place and duration of study: CMH Lahore from February 2013 to January
Methods: The cross sectional observational study was conducted. All patients admitted with high grade fever with chills were followed. The diagnosis of malaria was established on thick and thin blood film microscopy positive tests. Patients having any co infection found in tests or with high clinical suspicion of any other disease like dengue were excluded .CBC of first day and 4th day of admission was seen and it showed decreased levels of thrombocytes(less than 150000) and leukocytes(less than 4000/mm3 .Hemoglobin was not found to be decreased in most of the patients
Results: 133 confirmed cases of malaria were included in the study .Out of these 131 were followed completely with CBC. All of them were males .All of them were admitted with fever having low grade fever in 43 patients and high grade fever in 90 patients. Out of these ,MP (malarial parasite) positive cases were112 in which sub strain could not be found, confirmed cases of vivax 13, and falciparum case were 2.CBC of day 1 and 4 was followed and entered. On day one CBC severe thrombocytopenia was seen in 30(22.6%), moderate in 67(50.4%) patients, mild in 26(19.5%) and normal platelet count in 8(6%) On day 4 severe in 14(10.5%), moderate in 45(33.8%) and mild 32(24.1%).Leucopenia on day 1 was seen in 39(29.3%) patients and leukocytes in 3(2.3%) patients, and normal in rest of patients. On Day 4 CBC leukopenia was seen in 27(20.3%).
Conclusion: Patients of malaria in our study were found to show bicytopenia with decreased platelets and leucocytes. Hemoglobin on the other hand was not that much decreased.
Keywords: MP; malarial parasite, Bicytopenia; Decreased platelets and leucocytes, CBC; complete blood count, Thrombocytopenia; platelet count less than 150,000, Leukopenia; White blood cell count less than 4000

INTRODUCTION

Malaria is very common disease all over the world .It is endemic throughout most the tropics. Of the 3 billion people living in 108 countries, approximately 243 million develop symptomatic malaria with 1 million deaths per year [1] and about 2000 patients are dying of malaria especially African children.[2] Malaria is a protozoan disease transmitted by the bite of infected *Anopheles* mosquitoes. It is the most important of the parasitic diseases of humans. Malaria has been eliminated from the United States, Canada, Europe, and Russia; in the late twentieth and early twenty-first centuries, however, its prevalence rose in many parts of the tropics[3,4]. Despite enormous control efforts, increases in the drug resistance of the parasite, the insecticide resistance of its vectors, and human travel and migration have contributed to this resurgence. Occasional local transmission after importation of malaria has occurred in several southern and eastern areas of the United States and in Europe, indicating the continual danger to nonmalarious countries. Although there are many promising new control and research initiatives, malaria remains today, as it has been for centuries, a heavy burden on tropical communities, a threat to non-endemic countries, and a danger to travelers[5,6,7].

Quite a lot burden of fever in Pakistan is being carried by malarial cases. Malaria is the second most common and devastating disease in Pakistan and accounting for quite a number of outpatient burden and admissions.[8] Commonest species causing malaria are plasmodium vivax and falciparum[9], former being most common and later being most fatal. The disease presents with high grade fever with

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chills and clinical important sign being splenomegaly. it can present with cerebral malaria presenting with altered mental status and seizures, patient can develop renal impairment with black water fever and nephrotic syndrome. Metabolic acidosis and hypoglycemia can be the complications of severe malaria. Malarial patient develop anemia because of frequent association with hemolysis. The hemolytic anemia of malaria is a well-known and well-studied feature. Patients may develop jaundice and anemia with acute febrile illness. Splenomegaly is found to be a common finding.

Other than anemia other hematological abnormalities are also found to in malaria patients. They may show thrombocytopenia, leucopenia and sometimes even leukocytosis[10]. It was found to be associated with lymphopenia and few no of cases being worked up for pancytopenia showed malaria the etiological factor. Similarly cases of thrombocytopenia showed malaria as cause. Malaria was found to be associated with decreased platelet counts. Amongst the leukocytes f counts as well as decreased leukocytes especially neutropenia was found to be more associated with vivax and lymphopenia was found to be associated with plasmodium falciparum.

Leukocyte depression is associated with cytokine based inflammatory response which needs to be further studies and confirmed in further studies[11]. While working up a case of acute febrile illness leukopenia and thrombocytopenia are associated with other diseases like typhoid and dengue fever misdiagnosed so it can be clinically misdiagnosed as non-malarial illness. Once we know that it is well associated with bicytopenias or pancytopenia then malarial cases can be diagnosed and treated early[12].

Pakistan every year deals with quite a lot no of cases of malaria as the acute febrile illness. it has been also found as coinfection with dengue fever in previous academics. World malaria report 2013 for Pakistan showed the cases of malaria, admissions and mortality increased from 2010 to 2012. High transmission case i.e. more than 1 case per 1000 population was seen in 29 percent population and low transmission case i.e., 0-1 case per 1000 was seen in 69 percent population. Only 2 percent of the population was found to be malaria free i.e. 0 cases per 1000[13].

For such a common disease need is to have more studies for the pathogenesis, presentation treatment and resistance.

Malaria elimination programs are being carried out in some countries aiming at prevention and early detection even by screening the normal population and treating them if needed.

METHODS

All workup of acute febrile illness including baseline investigations, NS1 and anti-dengue IgM antibody, malarial parasite testing with thick and thin smears, typhidot IgM, and urinalysis was done. All cases in which clinical or investigational evidence was found of any infection other than malaria or co infection were excluded .Fever grade and splenomegaly was recorded and entered in the study. Any other clinical manifestations were recorded and entered. Only confirmed cases of malaria were the study cases. Complete blood count was done daily and trend was seen .CBC of day one and day 4 was entered in the study. TLC below 4000 was considered to be low and above 12000 was considered high. Platelet count below 150,000 was considered low with sub grouping of mild thrombocytopenia100, 000-150,000, moderate thrombocytopenia 50,000-100,000 and severe thrombocytopenia less than 50,000.hemoglobin below 12g/dl was considered as low.

Data Analysis: Data was entered and analyzed using SPSS 22. Frequency tables were generated for the age, sex, Fever, bilirubin and splenomegaly. Quantitative variables of the study like age, bilirubin, hemoglobin, platelet and leukocyte count were expressed as Mean ± SD. The splenomegaly malarial parasite types found were presented as percentage .Averages, means and analysis of variance was done where applied. T test was used to compare the means.

RESULTS

A total of 133 patients, confirmed cases of malaria were entered of which 99(74.4%) were of age <30. 32 patients (24.1%) were between age range of 30-60 years. Only 2 (1.5%) were of >80yrs. All patients were males. All the patients included in the study were the ones presenting in outdoor or emergency with acute febrile illness later on confirmed as cases of malaria by thick and thin smear testing. High grade fever (>101 F) was recorded in 90 patients (67.7%) and low grade (99-101F) was seen in 43(32.3%) patients. Splenomegaly was seen in 31(23.3%) patients while it was not enlarged in rest of patients. All workup of acute febrile illness including baseline investigations, NS1 and anti-dengue IgM antibody, malarial parasite testing with thick and thin smears, typhidot IgM, and urinalysis was done. All cases in which clinical or investigational evidence was found of any infection other than malaria or co infection were excluded. Only confirmed cases of malaria were the study cases. Complete blood count was done daily and trend was seen. CBC of day one and day 4

was entered in the study. Out of 133 patients 112(84.2%) patients had malarial parasite positive in blood (strain could not be identified), 13(9.8%) showed BT vivax, 3(2.3%)were plasmodium ovale, 2(1.5%) falciparum and 3(2.3%) patients were co infected with vivax and falciparum. Bilirubin was increased (≥17 micromole/l) in 38(28.6%) patients and normal in rest of the patients.

In complete blood picture hemoglobin (normal 14-18 G/dl for males) WBC (4-11 normal) and platelet count (normal 150,000-450,000a). Platelet count was labeled as severe thrombocytopenia if less than 50,000, moderate deficiency was considered for the levels 50,000–100,000 and mild thrombocytopenia (100,000-150,000).

On day one CBC severe thrombocytopenia was seen in 30(22.6%), moderate in 67(50.4%) patients, mild in 26(19.5%) and normal platelet count in 8(6%) On day 4 severe in 14(10.5%), moderate in 45(33.8%) and mild 32(24.1%).

Leucopenia on day 1 was seen in 39(29.3%) patients and leukocytes in 3(2.3%) patients, and normal in rest of patients. On Day 4 CBC leukopenia was seen in 27(20.3%), leukocytosis in 2(1.5%) and normal count in rest of patients.

Mean platelet count was 77.7and 105.5 with SD ± 40 and 62.7 for day 1 and 4 respectively. Mean TLC was 5.15 and 5.23 with SD of ±2.3 and 1.6 for day 1 and 4.Hemoglobin levels were between 12-14g/dl with mean of 12.95, standard deviation of ±1.2 and day 4 mean 13.54 with standard deviation of ±1.2.CBC counts were compared with malarial parasite positivity. It was found that lowest platelet count was seen in vivax and lowest TLC was seen in ovale group. P value 0.05 confidence interval 95

DISCUSSION

Malaria is a very common disease .It has been eradicated from many countries but still a major problem of many tropical countries like Pakistan with about I million cases mortality reported every year. In every hospital outpatient cases especially in mosquito months acquire quite a no of patients presenting with fever. A good number is coming to emergencies and is being admitted because of complications. Most common emergency admissions are with cerebral malaria. Diagnosis of malaria is mainly clinical with help of CBC and ruling out other diseases. Diagnosis of malaria in laboratory is done mainly by thick and thin smear microscopy and visualization of the protozoan[14]. This test is operator dependent and usually does not give a good yield because of burden, reagent problems, sampling and slide preparation issues. Other tests which can be done are antigen detection, molecular analysis by PCR and quantitative parasite level estimation etc[15].[16]. In developing countries like us we are more depending on clinical assessment because of the availability and yield of these tests. That way we are sometimes under diagnosing or over diagnosing the patients. Help is taken by complete blood picture as malaria is found to be associated with cytopenias. so a clinical assessment with jaundice, spleen and CBC can help us make the complete diagnosis and ruling out other diseases as well. Leukopenia is frequently associated with disease like typhoid fever so while making clinical assessment of malaria some time getting leukopenia misdirects the clinician against the diagnosis of malaria and towards other delay in management and recovery of the patient.by knowing that pancytopenia is seen in quite a number of confirmed cases of malaria helps in early diagnosis, confident management and earlier discharge of the patient.

We, for this reason included in our study confirmed cases of malaria, diagnosis confirmed by microscopy and followed these patients for complete blood picture and found that a good number of confirmed cases of malaria was having leukopenia and thrombocytopenia. This bicytopenia was more frequently seen as compared to anemia and other clinical findings like splenomegaly. In previous studies also cytopenias were reported and almost leukocyte changes and thrombocytopenias was seen. More supporting evidence we see was made for thrombocytopenia whereas we observed that patients are having bicytopenias. Moreover we saw more bicytopenias in vivax strain and unlabeled strain which is most likely to be believed by containing cases of vivax and ovale.

My study has certain limitations. Prediction models may vary with the nature of the patient population. My study group represented a select group of patients with male patients mostly young soldiers admitted in medical wards so lacking randomization.

Mechanisms involving in suppression of blood counts need to be seen in further studies.

CONCLUSION

Significant number of confirmed cases of malaria was found to be associated with thrombocytopenia and leukopenia.

Bicytopenia were more commonly seen than the routine clinical findings like splenomegaly. Maximum cases of malaria are caused by plasmodium vivax and ovale subtypes in our study equating the common subtypes seen in Pakistan. Co infection with two malarial serotypes was seen in few cases.

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