Original Research Article

To study hematological profile in malaria patients

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Received: 05 May 2017
Accepted: 10 May 2017

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ABSTRACT

Background: Malaria has been a problem in India for centuries and it is responsible for many deaths in rural areas. This study was done to observe hematological profile in malaria patients and to study the incidence of complications in different species of malaria patients and to find any relation with hematological changes.
Methods: The study was conducted at MLN Medical College, Allahabad in the Department of Medicine between January 2016 to December 2016. One hundred consecutive patients aged 18 years or more with malaria fever were interviewed and examined.
Results: Out of 100 patients 26 patients had *Plasmodium vivax* malaria and 59 patients had *Plasmodium falciparum* infection while 15 patients had mixed PV and PF infection. In present study thrombocytopenia was most common hematological abnormality. Thrombocytopenia was present in 87 patients, out of them 18 had very severe thrombocytopenia while 69 had mild to moderate thrombocytopenia. Frank bleeding was present in 14 of total studied population and had both PV and PF infection. Petechial rashes were present in 10 patients. Anemia was present in 80 patients.
Conclusions: Thrombocytopenia is very frequent finding in patients suffering from malaria, and even in presence of thrombocytopenia bleeding manifestations are uncommon. So, platelet transfusion should not be performed routinely in all thrombocytopenia patients, rather it should be indicated only if bleeding manifestations are present. Anemia, pancytopenia and leucopenia are other frequent laboratory findings of malaria infection.

Keywords: Malaria, Hematological profile, Thrombocytopenia

INTRODUCTION

Malaria has been a problem in India for centuries. Details of this disease can be found even in the ancient Indian medical literature like the Atharva Veda and Charaka Samhita. During the latter parts of nineteenth and early twentieth centuries, nearly one-fourth of India's population suffered from malaria, particularly in the states like Punjab and Bengal. According to the World Malaria Report 2014, 22% (275.5 million) of India's population live in high transmission (> 1 case per 1000 population) areas, 67% (838.9 million) live in low transmission (0-1 cases per 1000 population) areas and 11% (137.7 million) live in malaria-free (0 cases) areas.[1] From the beginning of the 21st century, India has demonstrated significant achievements in malaria control with a progressive decline in total cases and deaths. Overall, malaria cases have consistently declined from 2 million in 2001 to 0.88 million in 2013, although an increase to 1.13 million cases occurred in 2014 due to focal outbreaks. The incidence of malaria in the country therefore was 0.08% in a population of nearly 1.25 billion. In 2015, 1.13 million cases (provisional) were also reported. It is worthwhile to note that confirmed deaths due to malaria have also declined from 1005 in 2001 to 562 in 2014. In 2015, the reported number of

deaths has further declined to 287 (provisional). Overall, in the last 10 years, total malaria cases declined by 42%, from 1.92 million in 2004 to 1.1 million in 2014, combined with a 40.8% decline in malaria-related deaths from 949 to 562. India contributes 70% of malaria cases and 69% of malaria deaths in the South-East Asia Region. However, a WHO projection showed an impact in terms of a decrease of 50-75% in the number of malaria cases by 2015 in India (relative to 2000 baseline), which showed that the country has been on track to decrease case incidence 2000-2015.[2-4]

However, data from some foreign studies suggest entirely different scenario. A study conducted by teams from the office of the Registrar General of India, Centre for Global Health Research at St Michael's Hospital and University of Toronto, Canada, published in The Lancet on 20 November 2010 has reported that malaria causes 205 000 malaria deaths per year in India before age 70 years (55 000 in early childhood, 30 000 at ages 5-14 years, 120 000 at ages 15-69 years) with a 1.8% cumulative probability of death from malaria before age 70 years.[5] The report says that 90 per cent of the deaths were recorded in rural areas, of which 86 per cent occurred at home without any medical attention. It also found that Orissa reported the highest number of deaths - 50,000, followed by Chhattisgarh, Jharkhand and Assam. The study, which began in 2002, covered 6,671 areas, each with about 200 households. However, WHO has rebutted these estimates. Yet other study on the global malaria mortality between 1980 and 2010 by Murray at al published in The Lancet in February 2012, estimated the malaria mortality in India was around 46,800 in 2010.[6]

Malaria is an acute, recurrent and sometimes chronic vector borne protozoan disease which has worldwide distribution in tropical and subtropical regions. Infection is caused by a parasite of genus Plasmodia which is transmitted to human beings by a pre-infected female Anopheles mosquito. Genus Plasmodium has 4 species- *P. vivax* (PV), *P. falciparum* (PF), *P. malariae* and *P. ovale*. In India, *P. vivax* and *P. falciparum* are the species commonly found.[7] In spite of worldwide efforts to reduce malaria transmission, it is still the major cause of morbidity and mortality, with overall fatality rate of 10-30% was seen.[8] The main areas where disease predominates are the rural and remote areas, where prompt treatment is not available or not detected in time. As the target of malarial parasite is RBC, peripheral blood smear examination is the major diagnostic tool of the disease. Some hematological changes are species specific. The majority of complications in malaria are due to hyperparasiteamia. Mortality is very high (10-30%) in complicated *P. falciparum* infection. Hematological changes play a significant role in these serious complications. The hematological abnormalities comprise anemia, leucopenia or leucocytosis, thrombocytopenia, and infrequently disseminated intravascular coagulation. Malaria can cause hemostatic abnormalities leading to bleeding manifestations that range from asymptomatic

thrombocytopenia to fulminant disseminated intravascular coagulation (DIC). In recent years clinicians have recognized thrombocytopenia as a common and early sign of *P. vivax* or *P. falciparum* malaria infection, whereas DIC is rare. The mechanism of thrombocytopenia in malaria is uncertain. Coagulation disturbances, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production, antibody mediated destruction, oxidative stress, platelet destruction have all been postulated Lacerda et al.[9]

Thus, if hematological changes are noticed in time, the course of the disease and the outcome can surely be modified is the purpose of the present study. The present study evaluates the hematological disturbances in relation to thrombocytopenia, anemia, leucopenia, pancytopenia in *P. vivax* malaria.

The objective of this study was to observe hematological profile in malaria patients and to study the incidence of complications in different species of malaria patients and to find any relation with hematological changes.

METHODS

This was a cross section observational study. All consecutive patients of malaria fever admitted to the Department of Medicine, MLN Medical College, Allahabad between January 2016 to December 2016 were included in the study.

146 patients admitted with suspected malaria fever were selected for the study. Out of them, 118 patients had malaria confirmed by peripheral blood film examination or rapid diagnostic test detecting malarial antigen. Out of this 100 were selected after exclusion.

Inclusion criteria

- Age group of ≥ 18 years
- Confirmed malaria cases by peripheral blood film examination or rapid diagnostic test detecting malarial antigen.

Exclusion criteria

- Patients on medications affecting hematological parameters
- Patients with chronic liver disease
- Patients with chronic kidney disease.

The local ethical committee approved the research.

A written informed consent was taken. Baseline clinical characteristics including age, sex, socio- demographic data, diabetes mellitus, hypertension, history of chronic kidney disease, history of chronic liver disease, any other chronic illness and smoking history were obtained. The diagnosis of malaria fever was confirmed by peripheral

blood film examination or rapid diagnostic test detecting malarial antigen. Thin and thick films were stained with Leishman's stain and Giemsa stain for identification of species and grading of parasitemia respectively as described by Dacie and Lewis. Grading is as follows: 1-10 parasites per 100 thick film high power field (HPF): +; 11-100 parasites per 100 thick film HPF: ++; 1-10 parasites per one thick film HPF: +++; >10 parasites per one thick film HPF: ++++. Blood samples were collected for admission plasma glucose, complete blood count including hematocrit, liver and renal function tests, serum electrolytes including calcium and magnesium. Occurrence of symptoms like fever, bleeding, and abdominal pain were noted. Cardiac symptoms like chest pain, dyspnea and palpitations were identified. All the enrolled subjects were evaluated for hematological profile. Anemia was defined as hemoglobin (Hb) level <12g/dl in female and <13g/dl in male according to WHO criteria. Thrombocytopenia was defined as platelet count <150000/µl and leucopenia as total leukocyte count <4,000/µl.

All patients received standard medical treatment on the basis of the current standards of care recommended by published guidelines. Patients were followed during admission by daily vitals monitoring, pulse pressure measurement, bleeding manifestations like petechial rashes, evidence of fluid leak in form of pleural effusion or ascites and intake output monitoring.

Statistical analysis

In this study, the chi square test (χ2 test) for independent samples was used for data analysis, with data presented as mean±SD unless otherwise specified. Pearson's correlation was applied and P value <0.05 considered significant.

RESULTS

Patient characteristics

Table 1: Baseline clinical characteristics of malaria patients (n= 100).

Character	Number of patients
Age range (years)	
18-35	49
35-50	30
50-65	21
Sex	
Males	57
Females	43

A total of 100 Malaria fever patients were studied. Table 1 shows baseline clinical characteristics of malaria patients. Mean age was 34.3±12 years, a youngest patient was 18 years and oldest was 62 years old. There were 57 males and 43 females. Mean value of Hb was 10.03±2.73 g/dl, (male 10.53±3.24 g/dl and female 9.10±2.64 g/dl). Mean platelet count was 2,30000/ µl. Mean leucocyte count was 7325/µl.

Table 2: Hematological profile in malaria patients.

	Plasmodium vivax (n=26)	*Plasmodium falciparum* (n=59)	Mixed infection (n=15)	Total
Anemia	21	48	11	80
Thrombocytopenia	18	57	12	87
Leukopenia	8	22	5	35
Pancytopenia	5	27	8	40

Table 3: Relation of bleeding manifestation with platelet count.

Platelet count	Number of patients (n=100)	Patients with bleeding manifestations (n=18)	Patients without bleeding manifestations (n=82)
Less than 20,000/µl	18	8	10
20,000 to 50,000/µl	27	6	21
50,000 to 150,000/µl	42	4	38
More than 150,000/µl	13	0	13

Out of 100 patients 26 patients had *Plasmodium vivax* malaria and 59 patients had plasmodium falciparum infection while 15 patients had mixed PV and PF infection. Table 2 shows that in vivax malaria, anemia was observed in 21 (80%) patients, more in female (88%) than in males (71%). Thrombocytopenia was present in

18 (69%) and leucopenia in 8 (30%) patients. Pancytopenia was present in 5 (19%) patients. In falciparum malaria, anemia was observed in 48 (81%) patients, more in female (82%) than in males (76%). Thrombocytopenia was present in 57 (96%) and leucopenia in 22 (37%) patients. Pancytopenia was

present in 27 (45%) patients. While in mixed infection malaria, anemia was observed in 11 (73%) patients, more in female (72%) than in males (76%). Thrombocytopenia was present in 12 (80%) and leucopenia in 5 (33%) patients. Pancytopenia was present in 8 (53%) patients. Majority of patients (80%) had anemia of mild to moderate grade (>8 g/dl), but 20% had anemia of severe grade (<8 g/dl). Of total anemic male patients 7% had severe anemia while of total anemic female patients 38% had severe anemia.

Table 3 shows that 87 patients had thrombocytopenia and out of them 69 patients having mild to moderate

thrombocytopenia while 18 patients had severe thrombocytopenia (platelet count <20000/ µl).

Bleeding manifestations were present in 18 patients. Out of these patients 11 showed frank bleeding and 7 had petechial rashes. Out of 18 only 8 patients with platelet count <20,000/µl showed bleeding manifestation. 10 patients with platelet count >20,000/µl showed bleeding manifestation and 82 did not show bleeding manifestation. Table 4 shows severe complications in malaria patients. Jaundice was the most common complication while convulsions were least common.

Table 4: Incidence of severe complications in malaria.

Complications	*Plasmodium vivax* (n=26)	*Plasmodium falciparum* (n=59)	Mixed infection (n=15)
Hypoglycemia	2	10	4
Jaundice	6	18	9
convulsions	0	3	1
Renal failure	3	17	5
Pulmonary edema or ARDS	0	4	2

DISCUSSION

Most of the patients in this study were between age of 18 to 35 years, which comprises about 49% of whole studied population, 30% between age of 36 to 50 years, 21% were above age of 50 years, and we have not included pediatric population in this study. This can be due to high endemicity of malaria in this region. Male predominate the study population and comprises about 57% of population. This may be because of male dominated society where male seeks more medical treatment than females. Shah et al reported 87.4 adults between 12 to 60 years of age, and 10% pediatric, and 2.6% geriatric, above 60 years of age.[10]

In this study 26 patients had PV infection and 15 had both PF and PV infection, rest 59 were suffering from PF infection. Which is comparable to study done by Shah et al at Ahmadabad in 2011 which showed 80% of cases were infected with PF and 18.67% cases were infected with PV, and is also comparable to Agravat et al Rajkot Gujarat 2010, which showed 70.6% of cases were infected with PF, and 28.7% of cases with PV.[10,11]

Anemia was pre-dominant feature of this study. Mean hemoglobin of studied population was 10.03 gm/dl and mean hemoglobin for male was 10.58 gm/dl, and female mean hemoglobin was 8.63 gm/dl. About 80% of studied population was anemic out of them 25% were mild anemic, 55% had moderate anemia and 20% of studied population had severe anemia. In this study 60% of anemic patients had plasmodium falciparum infection, 26% patients infected with *P. vivax* and 14% had mixed both PV and PF infection. Anemia was more common in

females than males. In a study conducted by Shah et al at Ahmadabad found 87.5% and 12.5% patients during PF and PV infections were anemic, respectively, while in this study 78. 57% plasmodium falciparum infection had anemia, and 40% plasmodium vivax infected patients had anemia.[10] And other study done by Gupta et al, Indore showed 56.06% suffering from PF and 31.80% suffering from PV infection had anemia respectively.[12]

Leucopenia was present in 35% of studied population. Average leucocyte count was 7325/micol in this study. Among leukopenic patients 62% patients were suffering from PF and 22% had PV infection and rest 16% patients had mixed PF and PV infection Pancytopenia was present in 40% of studied population, out of them 67% were suffering from PF, and only 26% had mixed PF and PV infection while 7% patients had *P. vivax* infection. Study done by Chetiwal R et al had showed in study that leukopenia was present in 27.66% of cases, and with mean leukocyte count of 6000/microl, similar in female and male.[13] They also showed that pancytopenia was present in 13.68% of patients.

In present study thrombocytopenia was present in 87% of studied population and out of them 18 had very severe thrombocytopenia while 69 patients had mild to moderate thrombocytopenia. Mean platelet count was 2.30 lcs/microl, lowest platelet that was observed was 2000/microl, and maximum platelet count was 3.80 lac/microl. In study done by Agravat et al Rajkot Gujarat, showed 81.5% patients had thrombocytopenia, which was mild in 26.1%, moderate in 31% and severe in 21.3%, and profoundly low in 3.1% of cases.[11] In PV mild and moderate degree of thrombocytopenia was more

common, whereas in PF malaria severe thrombocytopenia was more common. Cause of thrombocytopenia in malaria is uncertain however coagulation disturbances, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production, antibody mediated destruction, oxidative stress, platelet destruction have all been postulated Lacerda et al.[9] The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypo activity is seen following this phase and returns to normal in 1 to 2 weeks. Study done by Gill MK et al observed 82% of patients had thrombocytopenia which is comparable to our study.[14] Another study done by Kochar DK et al showed only 31% patients had thrombocytopenia, this difference is because they had included both inpatients as well as outpatients suffering from malaria.[15] One other study on outpatients only by Goyal et al, showed 77% patients had thrombocytopenia.[16]

Frank bleeding was present in 14 of total studied population and had both PV and PF infection, and all were pancypenic. Petechial rashes were present in 10 all were suffering from PF, none PV infected patients had petechial rashes. Mean platelet count with bleeding manifestations had platelet count was 24000/µl.

In this study only 18 patients had platelet count less than 20000/microl, and out of them only 8 patients had bleeding manifestations, while rest 10 patients had no bleeding manifestation. This must be considered in the context that very low platelet counts can be transient in the course of malaria illness and may not necessarily have bleeding manifestation or require platelet transfusion. Study done by Kochar DK et al showed 18.18% patients had platelet count less than 20000/microlitre, and only 0.6% patients had bleeding manifestations.[15] Study done by Chetiwal R et al showed 88% patients had thrombocytopenia, and mean platelet count was 79442/ microlitre, 6.9% patient had platelet count less than 20000/microlitre, and only 2.3% patients had bleeding manifestations.[13]

In this study life, threatening complications were present in 46 patients. Out of them 17 patients had one complication while 29 patients had two or more complications. Sever complications were observed more commonly in falciparum malaria and in mixed infection as compared to vivax malaria. Hematological abnormalities were present in all 46 patients with severe complications. So, the presence of hematological abnormalities might be useful in early detection of complications related to malaria. If hematological changes are noticed in time, management, course of the disease and the outcome can be modified. In developing countries like India where malaria is endemic, these simple hematological tests can play vital role in preventing mortality related to malaria.

Limitations of this study was first, study included a population admitted to a single center. Second, the study population was possibly underpowered to detect a significant difference in in-hospital mortality. Third, our data are only hypothesis generating, because they do not provide evidence to support a causal relationship, and they require confirmation in suitably designed clinical trials.

CONCLUSION

Thrombocytopenia is very frequent finding in patients suffering from malaria, and even in presence of thrombocytopenia bleeding manifestations are uncommon. So, platelet transfusion should not be performed routinely in all thrombocytopenia patients, rather it should be indicated only if bleeding manifestations are present. Anemia, pancytopenia and leucopenia are other frequent laboratory findings of malaria infection.

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