Section: Pathology

Original Research Article

A STUDY OF CLINICAL AND HAEMATOLOGICAL PROFILE OF PATIENTS WITH PLASMODIUM VIVAX MONO-INFECTION

Sanju Daniel John[1], Renji Jacob[2], Mikhil Mundackal Manoj[3]

[1]Associate Professor, Azeezia Medical College, Diamond Hill, Kummalloor - Meeyannoor Rd, Kerala
[2]Consultant Pathologist, Neuberg Diagnostic Centre, Cochin
[3]Grade 11, Delhi Public school Doha Qatar

Received : 31/03/2023
Received in revised form : 28/04/2023
Accepted : 06/05/2023

Keywords:
P. Vivax Malaria, Mono-Infection, Haematology, Thrombocytopenia, Anaemia, Hrp-2.

Corresponding Author:
Dr. Renji Jacob
Email: renjijacob91@gmail.com

DOI: 10.47009/jamp.2023.5.3.140

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (3); 672-677

Abstract

Background: To study the clinical and haematological profile of patients admitted with P. vivax mono-infection at Azeezia Medical College, Kollam. **Materials and Methods:** This is a prospective cohort study was done from April 2022 to March 2023 on 200 patients admitted to Azeezia Medical College, Kollam. The subjects selected were positive for P. vivax by peripheral smear and negative for HRP-2 test. The patient selection was based on inclusion and exclusion criteria. **Result:** In this study group of 200 patients, 141 were males and 59 were females. Most subjects were in the second and third decades of life. The mean age of subjects was 37.32 years. Fever was seen in all patients. Other clinical symptoms were headache (68%), jaundice (28.5%), vomiting (27.5%), body pain (17.5%), pain abdomen (9%), diarrhoea (6.5%) and bleeding manifestations (2%) in the order of occurrence. Thrombocytopenia was observed in 187 (93.5%) patients. Thirty three patients (6.5%) had severe thrombocytopenia. Anaemia was seen in 59 (29.5%) patients. Leucocytosis and leucopenia were seen in 20 and 26 cases respectively. Complications observed were acute kidney injury (AKI), elevated transaminases, adult respiratory distress syndrome (ARDS) and cerebral malaria 2.5%, 2.5%, 1% and 1% respectively. **Conclusion:** The clinical spectrum of P. vivax mono infection varied from fever to bleeding manifestations. In this study, the most common symptoms were fever, headache, jaundice and vomiting. The commonest haematological variations observed were anaemia and thrombocytopenia.

INTRODUCTION

Malaria is a tropical protozoan infection affecting mankind since centuries. Despite of all the measures taken to control the disease, malaria still continues to be on the rise due to reasons like drug resistance and vector resistance to insecticides. There have been increasing reports of changing trends in the clinical presentation of the disease caused by Plasmodium vivax malaria in the last one decade.[1,2] WHO has declared malaria to be an endemic disease in India, especially in parts of Karnataka like Dakshina Kannada and Tumkur. Malarial fever is caused by P. vivax species, affecting approximately 100-300 million individuals world over annually.[3] The classical presentation of malaria consists of paroxysms of fever alternating with periods of fatigue, associated with chills, rigors, sweats, headache, myalgia and back pain.[4]

Infections due to P vivax were earlier thought to follow a benign course. Haematological abnormalities such as anemia, thrombocytopenia and changes in WBC counts have been seen in malarial infections. Recently life threatening complications like adult respiratory distress syndrome (ARDS), acute kidney injury (AKI) and severe anaemia have been reported in P. vivax malaria, which is of great concern. Malaria being endemic in Mangalore and lack of data from this geographic area on the clinical and haematological profile of malaria has prompted us to undertake this study.

MATERIALS AND METHODS

Source of Data

The data was collected from patients admitted to Azeezia Medical College, Kollam with peripheral smear tested positive for Plasmodium vivax and negative for Histidine rich protein-2 (HRP-2).

Study Design

This study was a prospective study done from April 2022 to March 2023.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

By purposive sampling a total of 200 patients were selected who were admitted to the hospital with peripheral smear positive for P. vivax and negative for HRP-2 test. They were followed from admission till recovery, discharge or death, whichever was earlier.

The following investigations were done in all cases:

- Haemoglobin estimation by cyanmethemoglobin method.
- Total and differential leucocyte count.
- Platelet count- grading of platelet count as per National Cancer Institute Common Terminology Criteria for Adverse Events Version. 3.0.
- Peripheral smear for malarial parasite-both thick and thin smears stained with JSB stain and seen under oil immersion.
- Histidine rich protein-2 test to rule out P. falciparum.
- Liver function test – Total bilirubin, SGOT, SGPT.
- Renal function test – S.urea and S. creatinine.

Inclusion Criteria

1. Those admitted in Azeezia Medical College, Kollam positive for P. vivax by peripheral smear and negative for HRP-2 test
2. Age more than 18 years

Exclusion Criteria

1. Patients with P. falciparum infection.
2. Those with chronic kidney disease, chronic liver disease, haematological malignancies and those undergoing chemotherapy and radiotherapy.

RESULTS

A total of 200 patients admitted to Azeezia Medical College, Kollam having peripheral smear positive for P. vivax and negative for HRP-2 test were included in the study.

Among the 200 subjects who were studied, 149 (74.5 %) were males and 51 (22.5 %) were females. Ratio of male to female = 2.9:1.

Table 1: Age distribution of cases

Age (in years)	Number	Percent
15-20	29	14.5
21-30	78	39
31-40	32	16
41-50	27	13.5
51-60	20	10
>60	14	7

Patients included were aged between 17-82 years. The mean age in this study was 37.32 years.

Clinical Spectrum of the Disease

Fever was the presenting complaint in all the patients (100 %). Cyclical fevers, associated with chills and rigors were found to be the hallmark of malaria. Headache was observed in 136 (68.0%) subjects which was of diffuse type, not associated with photophobia Nausea was observed in 52 (26%) subjects and vomiting in 55 (27.5% %) subjects. Jaundice was observed in 59 (28.5%) subjects which was lemon yellow in colour, suggestive of haemolysis. Pain abdomen was observed in 18 (9.0%) subjects, body pain in 35 (17.5%) subjects and bleeding tendencies in 4 (2.0%) subjects. Cough and breathlessness were observed in 2(1.0%) subjects, not associated with chest pain, orthopnoea and paroxysmal nocturnal dyspnoea. Oliguria was observed in 1 subject (0.5%) who was not associated with facial puffiness and pedal edema.

Table 2: Symptoms of the disease

Symptoms	No. of patients	Percentage
Fever	200	100.0%
Headache	136	68.0%
Jaundice	59	28.5%
Vomiting	55	27.50%
Nausea	52	26%
Body pain	35	17.5%
Pain abdomen	18	9.0%
Diarrhoea	13	6.5%
Bleeding manifestations	4	2.0%
Cough and breathlessness	2	1.0%
Oliguria	1	0.5%

The graphical representation of the symptomatology of the malaria cases studied.

Table 3: Analysis of the signs

Sign	No. of patients	Percentage
Fever	200	100.0%
Icterus	59	28.5%
Hepatomegaly	37	18.5%

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Spleenomegaly	32	16.0%
Signs of dehydration	21	11.0%
Pallor	17	8.5%
CNS manifestations	15	7.5%
Bleeding	4	2.0%
Respiratory signs	2	1.0%

Respiratory manifestations in the form of cough and breathlessness along with clinical signs such as rhonchi and crepitations were observed in 2 (1%) subjects. CNS manifestations were observed in 15 (17.5%) subjects in the form of altered sensorium. Signs of dehydration (mild, moderate and severe) were observed in 21 (11.0%) patients. Bleeding manifestations were observed in 4 (2%) patients.

Vital Signs of 200 Patients Positive for Plasmodium Vivax Malaria

After the general physical examination of the 200 study subjects, the mean heart rate calculated was found to be 86.96 whereas the mean temperature was 100.1. The statistical analysis of the vital signs of the study subjects.

Table 4: Vital signs of patients

SIGN	MEAN	S.D.	C.I.
Heart Rate	86.96	9.669	85.61-88.32
Respiratory Rate	21.14	2.729	20.76-21.53
Diastolic Pressure	78.6757	5.284922	71.2336-86.1235
Systolic Pressure	119.6327	10.56301	118.1446-121.1207
Temperature	100.1	1.045	99.96-100.26

S.D-Standard deviation, C.I.-95% mean confidence interval.

Table 5: Grades of Thrombocytopenia Platelet counts in patients with vivax malaria

Grade	Platelet count	Number	Percentage
0	>1.5 lakh/cumm	5	2.5%
1	75k-1.5 lakh/cum	33	16.5%
2	50-75k/cumm	57	28.5%
3	25-50k/cumm	72	36%
4	<25k/cumm	33	33%

(Patients with PC=75000 are in Grade 1, PC=50000 in Grade 2 and PC=25000 in Grade 3)

The mean platelet count was 85277.8/cumm with a standard deviation of 49207.3 (ranging from 7000- 273000). Majority of the patients (36%) were found to have platelet counts within the range of 25000-50000/cumm.

Table 6: Leukocyte counts in patients with vivax malaria

	Mean± SD	Range
Total WBC(per cumm)	5777.5 ± 4452.6	1000 – 6200
Neutrophils (%)	72.8 ± 11.8	35 – 95
Lymphocytes (%)	21.9 ± 11.1	3 – 61
Eosinophils (%)	2.1 ±2.4	0 – 19
Monocytes (%)	2.7 ± 1.7	0 – 10

The range of total WBC count was between 1000- 6200 cells. Neutrophil count, lymphocyte count, eosinophil count and monocyte count ranged between 35%-95%, 3% - 61%, 0%-19% and 0% - 10 % respectively.

Table 7: Haemoglobin (in gram %)

Haemoglobin (in gram %)	No. of patients (%)
≤6	2 (1%)
6.1-11.9	57(28.5%)
≥12	141 (70.5%)

Only 2 (1 %) patients of the study population had a haemoglobin level less than 6 g/dl. Haemoglobin of less than 12 g/dl was seen in 55 (29.5%) patients. The mean Haemoglobin in the study population was 12.46 g/dl.

Table 8: Percentage of patients with acute kidney injury

Acute kidney injury	5 (2.5%)
Normal renal function	195 (97.5%)

Acute kidney injury was seen in 5 (2.5%) patients as seen in [Table].

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 9: Percentage of patients with elevated transaminases

Elevated transaminases	10 (5%)
Normal LFT	190 (95%)

Elevated transaminase was seen in 10 (5%) patients.

Table 10: Percentage of patients with ARDS

Present	2 (1%)
Absent	198 (99%)

Respiratory complication noted was ARDS, in 2 (1%) patients.

Table 11: Comparison of clinical symptoms

Symptoms	Echeverri(%),[6]	Shin(%),[3]	Gupta(%),[7]	Song(%),[8]	Present study (%)
Fever	99	100	100	100	100
Headache	22.1	83.2	-	-	68
Vomiting	36	16.8	86	34.1	27
Pain abdomen	25.6	8.9	-	29.5	9
Diarrhoea	13	23	5	15	6.5

Table 12: Comparison of clinical signs

Sign	Gupta (%),[5]	Shin(%),[3]	Present study (%)
Pallor	80	51	29.5
Icterus	2	11	13
Splenomegaly	20	42	16
Hepatomegaly	2	15.8	18.5

Table 13: Grades of thrombocytopenia

Grade	Gupta (%)	Present (%)
>1.5 lakh/cumm	13.04	2.5
75k-1.5 lakh/cumm	8.69	16.5
50-75k/cumm	10.86	28.5
25-50k/cumm	17.39	36
<25k/cumm	6.5	33

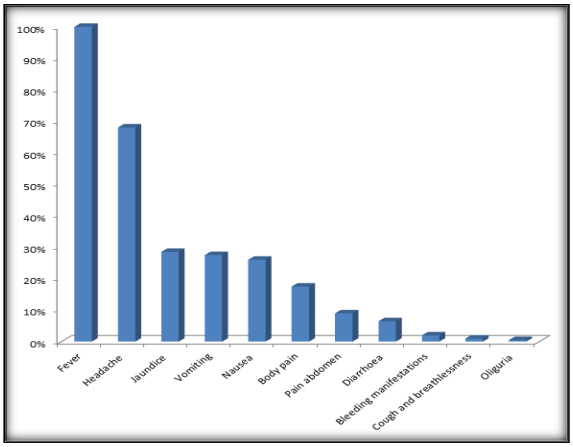

Figure 1: Symptoms of the disease

Analysis of Clinical Signs

Fever was present in 200 (100%) patients. Splenomegaly was detected in 32 (16.0%) subjects and 37 (18.5%) subjects had hepatomegaly. Pallor was present in 17 (8.5%) patients and 26 (13.0%) patients had jaundice.

DISCUSSION

Malaria, a zoonotic disease transmitted by the bite of female Anophelus mosquito, produces a spectrum of clinical illness and pathological changes in the body organs. Malaria has been endemic in many parts of India and there has been resurgence of malarial infections in the last few decades. The factors contributing to it are resistance of mosquitoes to insecticides and increased prevalence of chloroquine resistant malaria.

Sex Distribution

In the present study, the male to female ratio was 2.9:1. It correlated with the study done at Chuncheon, Korea[3] where the male to female ratio was 3:1. The incidence of malaria was more in men than in women due to their working pattern, i.e. men are exposed to outdoor mosquito bites than women. A study done by Gupta KN et al in Madhya Pradesh,[5] showed the ratio to be 1.9:1.

Age Distribution

In the present study, the maximum incidence was seen in the second decade (39 %) as they were exposed to fields and outdoors, followed by the third decade (16%). The mean age of presentation was 37.32 years. The results correlates with studies conducted at Columbia [6] and from Madhya Pradesh,[5] in India.

Socio-Economic Status

Malaria was more common among people belonging to low socioeconomic status. 60 percentages of the patients represented the low socioeconomic status and the cause for increased prevalence was due to lack of health education, personal protection and unsanitary condition.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Clinical Features

Symptoms:

The most common symptoms were fever, headache, and vomiting and pain abdomen. The percentage occurrences of the following symptoms in various studies are shown.

Headache was observed in 68% in the present study and was the second most common symptom. It was seen in 83.2% in study done by Shin et al,[3] and 22.1% in Echeverri et al,[6] Vomiting was seen in 27% in the present study. It was seen in 86% in a study done by Gupta et al, the percentage was high as patients with malaria were orally treated outside with antimalarial drugs which might have led to gastritis. The values almost correlated with the study done by Song et al and Shin et al. Pain abdomen was seen in 9% of our study population while in studies done by Song et al, Shin et al and Echeverri et al, it was 29.5%, 8.9% and 25.6% respectively. Diarrhoea was seen in only 6.5% of the study population, while in studies done by Gupta et al, Song et al, Shin et al and Echeverri et al, it was 5%, 15%, 23% and 13% respectively.

Neurological complication in the form of cerebral malaria was observed among 2 % of the patients in the present study compared to another study done at Mangalore,[9] where it was observed in 1.41 % cases. The results varied with the study done at Bikaner,[10] where the incidence of cerebral malaria as a presenting feature of P. vivax malaria was 12.5%, as the selected cases were severe malaria patients.

Cough and breathlessness were seen in 8.5% of the patients in our study. It correlated with the study conducted at Bikaner,[10] in which 10 % of the patients had these symptoms, as most patients had complicated vivax malaria.

Oliguria was a clinical manifestation in 0.5 % of the patients during the course of hospital stay in the present study group. This differed from the results of the study at Bikaner,[10] where the incidence was 45%. This difference can be credited to the fact that the latter study included only cases with severe P. vivax monoinfection. Bleeding manifestations such as conjunctival haemorrhage and epistaxis were seen in 2% of the patients. It correlates with the study done at Bikaner,[10] in which 5% cases had bleeding manifestations.

Pallor was present in 29.5 % of cases in the present study as compared to the study done in Madhya Pradesh where it was observed in 80%.[7] The increase in incidence of pallor was more in the latter study since it had both falciparum and mixed malaria cases. Icterus was noted in 13 % of the patients in the present study as compared to the studies done by Gupta et al,[7] and Shin et al,[3] where it was observed in 2% and 11% as seen in table.

Splenomegaly was observed in 16% of cases in the present study. Similar rates were demonstrated in a study done by Gupta et al.[7] Hepatomegaly was observed in 18.5% of cases in the present study as compared to the study done in the Republic of Korea, it was observed in 15.8%.[3]

ARDS was seen in only 1 % of the cases in the present study. The incidence of ARDS in a study done at Buritus,[11] was 21.05 % as they had included only severe P.vivax cases. Acute renal failure was observed in 2.5 % cases in the present study. In the study conducted in Mumbai, its incidence was 5.9%. The incidence of ARF in India has been reported to be between 13% and 17.8%.[12]

Cerebral malaria was observed in 2% of cases in the present study population, while it was seen in 1.41 % cases in the study done at Mangalore.[9]

Anaemia (Hb <12g/dL)

In the present study, 29.5% patients had anaemia and the study done by Gupta,[5] et al showed that 80% of cases had anaemia (Hb<12 g%) and 49% of cases in a study done in Korea.[3] The reason could be because male population was predominant (75%) in the present study.

Leucocyte Abnormalities

Leucocytosis was seen in 10% of the patients in this study. Similar observations were made in a study conducted by Sharma SK et al,[13] and Shin et al,[3] where the incidence of leucocytosis were 13.3% and 12% respectively. All the patients who had leucocytosis, presented with neutrophilia. In the present study, the mean leucocyte count was 5777.50 cells/cumm. It indicated that the majority of patients had normal leucocyte count.

Neutrophil

In this study, there was a significant increase in neutrophil percentage. This finding is comparable with that of Bashawari et al .The latter study documented an increase in the neutrophil percentage in falciparum and the mixed malarias but not in vivax malaria. Neutrophilia in this series represents the initial response of the body to acute infection.[15]

Lymphocyte

In the present study, lymphopenia was observed in 23.9% of the cases. In another study conducted by Bashwari et al, it was 35%, as their study included severe malaria cases. It may be because of immune response.[15]

Monocyte

Monocytosis was observed in 3% of the study population. In a study done by Hakim et al, it was observed in 15% of their study population. It may be a result of increased chemotaxis, as monocytes tend to become phagocytic.

Eosinophil

Eosinophilia was observed in 5% of the study population. It was noted in few patients in a study conducted by Ladhani et al.[14] Eosinophils might be stimulated by the parasites itself or by release of granule proteins like eosinophilic cationic protein(ECP) and eosinophil protein X(EPX).[12]

Thrombocytopenia

Thrombocytopenia (<1.5 lakh/µL) was seen in 93.5 % of the subjects in the study.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table below shows a comparison of the grades of thrombocytopenia with our study and study done by Gupta et al,[5] in Madhya Pradesh.

Exact mechanism of thrombocytopenia in malaria is unknown. The proposed mechanisms include splenic sequestration; decrease in the platelet life span, circulating iimmune complexes, platelet phagocytosis by hyperactive macrophages, activation of platelets by ADP released from haemolysed RBCs, oxidative stress and disseminated intravascular coagulation.

Elevated Transaminases

Elevated transaminases were seen in 5 % cases in the present study. In the study conducted in Bikaner, 58 % of the patients presented with elevated transaminases as it included severe malarial cases.[10]

Renal Dysfunction

Acute kidney injury was seen in 3 % cases in our study and 5% patients in Mumbai. Our results varied with the study done at Bikaner in which a high incidence of renal dysfunction of about 45% was noted as patients included in their study had severe malaria. The various nonspecific effect of infection like hemolysis, DIC, jaundice contributes to acute renal failure. The associated endothelial activation leads to release of several vasoactive cytokines and mediators which lead to decreased systemic vascular resistance and eventually decreased renal blood flow and renal ischaemia.[12]

CONCLUSION

Malaria is a common cause for fever in the tropical countries. The common clinical symptoms of P. vivax malaria in this study were fever, headache, jaundice, vomiting and abdominal pain. The predominant signs observed were pallor, icterus and hepato-splenomegaly. Haematological variations noticed in this study were anaemia, thrombocytopenia, leucocytosis, leucopenia and monocytosis. In this study, it was observed that 33 patients (6.5%) had severe thrombocytopenia.

The complications detected were acute kidney injury (2.5%), elevated transaminases (2.5%), ARDS (1.0 %) and cerebral malaria (1.0%). Statistics imply that the developments of these complications which are often encountered in P. falciparum monoinfection and mixed malaria are also present with P. vivax mono-infection. These complications have been grossly undermined.

In conclusion, patients presenting with fever and thrombocytopenia in an endemic area should undergo relevant investigations for the detection of malaria. This will help in early diagnosis of the disease, prompt initiation of treatment and prevent further complications.

REFERENCES

1. Sachs J, Malaney P. The economic and social burden of malaria. Nature 2002; 415**:** 680-5.
2. World Health Organization. The guidelines for the treatment of malaria. 2nd ed. Geneva: WHO 2010.
3. Oh MD, Shin H, Shin D, Kim U, Lee S, Kim N et al. Clinical features of vivax malaria. Am J Trop Med Hyg 2001; 65:143-6.
4. Mohapatra MK, Padhiary KN, Mishra DP, Sethy G.. Atypical manifestations of Plasmodium vivax malaria. Indian J Malariol 2002; 39:18-25.
5. Gupta NK, Bansal SB, Jain UC, Sahare K: Study of thrombocytopenia in patients of malaria. Trop Parasit 2013; 3:58-61.
6. Echeverri M, Tobón A, Alvarez G, Carmona J, Blair S. Clinical and laboratory findings of Plasmodium vivax malaria in Colombia, 2001. Rev Inst Med Trop Sao Paulo 2003; 45:29-34.
7. Adeoye GO, Nga IC. Comparison of Quantitative Buffy Coat technique (QBC) with Giemsa-stained Thick Film (GTF) for diagnosis of malaria. Parasitol Int 2007; 56:308-12.
8. Song HH, O SO, Kim SH, Moon SH, Kim JB, Yoon JW et al. Clinical features of Plasmodium vivax malaria. Korean J Intern Med 2003; 18:220-4.
9. Naha K, Dasari S, Prabhu M. Spectrum of complications associated with Plasmodium vivax infection in a tertiary hospital in South-Western India. Asian Pac J Trop Med 2012; 5:79-82.
10. Kochar DK, Shubhakaran, Kumawat BL, Kochar SK, Halwai M, Makkar RK et al. Cerebral malaria in Indian adults: a prospective study of 441 patients from Bikaner, north-west India. J Assoc Physicians India 2002; 50:234-41.
11. Andrade BB, Reis-Filho A, Souza-Neto SM, Clarencio J, Camargo LM, Barral A et al. Severe Plasmodium vivax malaria exhibits marked inflammatory imbalance. Malaria Journal 2010, 9:13.
12. Mehta KS, Halankar AR, Makwana PD, Torane PP, Satija PS, Shah VB. Severe acute renal failure in malaria: J Postgrad Med 2001; 47:24-6.
13. Sharma SK, Das RK, Das BK, Das PK. Haematological and coagulation profile in falciparum malaria. J Assoc Physicians India1992; 40:581-3.
14. Ladhani S, Lowe B, Cole AO, Kouwuondo K, Newton CR. Changes in white blood cells and platelets in children with falciparum malaria: relationship to disease outcome. Br J Hematol 2002; 119:839-47.
15. Bashawri LAM, Mandil AA, Bahnassy AA, Ahmed MA. Malaria: Haematological aspects. Annals of Saudi medicine 2002; 22:372-7.

ISSN (O): 2687-5365; ISSN (P): 2753-6556