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Original Research Article

Study of Complications and Outcome of *Plasmodium Vivax* Malaria Mono Infections in an Indian Tertiary Care Hospital: A Cohort Study

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Conflict of interest: Nil

Abstract

Background: One of the most serious parasite infections that affects humans, *Plasmodium vivax (P. vivax)* malaria affects over 243 million people globally, with up to 2.5 billion individuals at risk and an estimated 70–80 million cases per year.

Objectives: To study the complications and outcome of *Plasmodium Vivax* malaria mono infections in Father Muller Medical College Hospital, Mangalore.

Methods: During the course of two years, a prospective cohort study was carried out at Father Muller Medical College Hospital. 200 individuals with a fever of ≥38.5°C and a peripheral smear or a malarial parasite fluorescence test that was positive for *P. vivax* made up the research cohort.

Results: A total of 200 participants were included in the trial, 64 women and 136 men. Patients in their second decade made up the majority. Thirty-six percent of patients had vomiting, and forty-five percent of patients had jaundice. 53% of patients had hepatomegaly, while 47% had splenomegaly. 8.5% of patients exhibited ARDS. 3.5% of individuals had cerebral malaria, whereas 3% had acute renal damage. In 3% of instances, multiple organ dysfunction was seen. 4 people died in the trial as a result of multiple organ dysfunction.

Conclusion: *P. vivax* mono infections can result in life-threatening consequences include acute respiratory distress syndrome, acute renal damage, cerebral malaria, and multi-organ dysfunction syndrome.

Keywords: *Plasmodium Vivax* Malaria, mono infections, acute respiratory distress syndrome, acute kidney injury, multi organ dysfunction syndrome

Introduction

Mankind has been impacted by malaria for a long time. Malaria has an intriguing history. Although it is typically dismissed as a minor febrile sickness, it can sometimes have fatal consequences. It stopped the economic growth of broad areas of the planet for millennia. In many places of the world, it is still a major social, economic, and health issue. According to estimates, there are 300–500 million clinical cases of malaria globally each year, which result in one–3 million fatalities [1]. In India and the tropical nations of Africa, it is endemic. The most recent WHO figures indicate that there were around 207 million cases of malaria in 2012 and 627 000 fatalities. Sub-Saharan

Africa accounts for 90% of all malaria fatalities [2]. One of the main issues with public health in India is still malaria. A total of 1.31 million and 1.06 million cases of malaria were recorded in India in 2011 and 2012, respectively, according to the National Vector Borne Disease Control Program report. In India, there were 754 and 519 fatalities overall in 2011 and 2012, respectively [3]. With up to 2.5 billion individuals potentially at risk and an estimated 70–80 million cases annually [4], *P. vivax* is extensively dispersed. Research on *P. vivax* malaria has been neglected and overshadowed by *P. falciparum,* despite the fact that it poses a significant health burden and negatively affects human longevity and overall prosperity [4].

Current research has revealed that *P. Vivax* problems are increasing, and their results are comparable to those of *P. falciparum* malaria [4, 5]. The objective of the study was the complications and outcome of *Plasmodium vivax* malaria mono infections in Father Muller Medical College Hospital, Mangalore.

Methods

Source of data

The data was collected from patients admitted to Father Muller medical college hospital with fever (≥38.5˚C) and peripheral smear or malarial parasite flourescent test (MPFT) positive for *Plasmodium vivax.*

Study design

This study was a prospective study done over a period of two years from May 2010 to April 2012. A total of 200 patients admitted to the hospital with fever of ≥38.5˚ C and peripheral smear or MPFT positive for *P. vivax* were selected using purposive sampling techniques. 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,
- ESR estimation by Westergren method,
- Peripheral smear for malarial parasite-both thick and thin smears stained with JSB stain and seen under oil immersion and MPFT (QBC),
- Histidine rich protein-2 test to rule out *P. falciparum,*
- Random blood sugar,
- Urine analysis,
- Liver function test – Total and Direct Bilirubin, SGOT, SGPT, S.protein and S.albumin
- Renal function test – S.urea and S. creatinine,
- Coagulation profile – Bleeding time, Clotting time, activated partial thromoplastin time, Prothrombin time.

In selected cases, chest x ray, blood culture, cerebrospinal fluid analysis, and arterial blood gas analysis were done.

Inclusion criteria

1. Those admitted in Father Muller medical college hospital having fever (≥38.5˚C) and peripheral smear or MPFT positive for *P. vivax.*
2. Age more than 15 years.

Exclusion criteria

1. Patients with *P. falciparum, P. ovale, P. malariae* co-infection.
2. Age less than 15 years.

Statistical Analysis

Data collected was analyzed by frequency, percentage, mean, standard deviation and chi-square test. Once the patient was diagnosed to have malaria, they were started on anti-malarial drugs according to the new WHO guidelines for treatment of malaria. Other supportive treatment was given according to the patient's conditions.

Results

A total of 200 patients admitted to Father Muller medical college hospital having fever (≥38.5˚C) and peripheral smear or MPFT positive for *P. vivax* were included in the study.

Table 1: Sex and age distribution

Sex	Number	Percent
Male	64	68
Female	136	32
Age (in years)	**Number**	**Percent**
15-20	29	14.5
21-30	68	34
31-40	41	20.5
41-50	14	7
51-60	17	8.5
61-70	15	7.5
< 70	16	8

Table 1 showing the 200 cases studied, 64(68%) were males and 136(32%) were females. Ratio of male to female = 2.125:1. The age of the study subjects ranged from 17-96 years. The predominant age group affected was that between 21-30 years. The mean age in this study was 37.32 years.

Table 2: Symptom analysis

Clinical features	No. of patients	Percentage
Fever	200	100.0%
Jaundice	81	40.5%
Vomiting	72	36.0%
Headache	45	22.5%
Pain abdomen	52	26%
Cough	25	12.5%
Breathlessness	12	6.0%
Bleeding	12	6.0%
Altered sensorium	6	3.0%
Oliguria	5	2.5%
Petechiae	4	2%
Convulsions	1	0.5%

Table 2 fever was the presenting complaint in all the patients (100%). Jaundice was seen in 81(40.5 %) cases and vomiting in 72(36%) cases. Headache was seen in 45(22.5%) patients and pain abdomen in 52(26%) patients.

Table 3: Analysis of the signs

Sign	No. of patients	Percentage
Pallor	41	20.5%
Icterus	82	41.0%

Pedal oedema	2	1.0%
Splenomegaly	94	47.0%
Hepatomegaly	106	53.0%
Respiratory signs	37	18.5%
CNS manifestations	7	3.5%

Table 3 showing, Pallor was seen in 41(20.5%) patients and 82(41%) patients had icterus. Splenomegaly was present in 94(47%) patients and 106(53%) patients had hepatomegaly. Respiratory involvement in the form of bronchitis (n=25, 12.5%) and ARDS (n=17, 8.5%) was seen. CNS manifestations was seen in 3.5 % cases in the form of altered sensorium (n=6,3%) and seizures (n=1,0.5%).

Table 4: Laboratory findings of Haemoglobin, platelet, leucocyte and S. Bilirubin counts

Haemoglobin (in gram %)	**No. of patients (%)**	
≤6	2 (1%)	
6.1-11.9	72 (36%)	
≥12	126 (63%)	
Platelets (per µL)	**No. of patients**	
≤50 K	74	
50,001-1L	74	
1,00,001-1,50 K	35	
≥1.5 L	17	
Leucocyte	**Mean± SD**	**Range**
Total WBC	6148 ± 4076	2600 – 42000
Polymorphs (%)	75.2 ± 11.12	40 – 96
Lymphocytes (%)	20.37 ± 10.58	1 – 52
Eosinophils (%)	1.71 ± 1.93	0 – 22
Monocytes (%)	2.78 ± 1.86	0 – 13
S.Bilirubin (mg/dL)	**No. of patients**	
≤2.9	147	
3-5.9	46	
≥6.1	7	

As seen in the Table 4 only 2(1%) patients of the study population had an Hb less than 6 g/dl. Haemoglobin of less than 12 g/dl was seen in 72 (36%) patients. The mean Haemoglobin in the study population was 12.46 g/dl. Thrombocytopenia of <1.5 lakh /µL was seen in 182 (91%) patients in our study and severe thrombocytopenia (<50,000/µL) was seen in 74 (37 %) cases. The above Table 4 shows that the range of total WBC count was between 2600 42000 cells. Polymorph count was between 40%-96%. Lymphocyte count was 1% - 52%. Eosinophil count was 0%-22% and Monocytes were in the range of 0% - 13%. Leucocytosis (>12,000/cumm) was seen in 11 (5.5%) cases and leucopenia was seen in 49 (24.5 %) cases. S.Bilirubin of more than 3 mg/dl was seen in 53 (26.5%) cases of which 79.24% had predominantly unconjugated type of hyperbilirubinaemia.

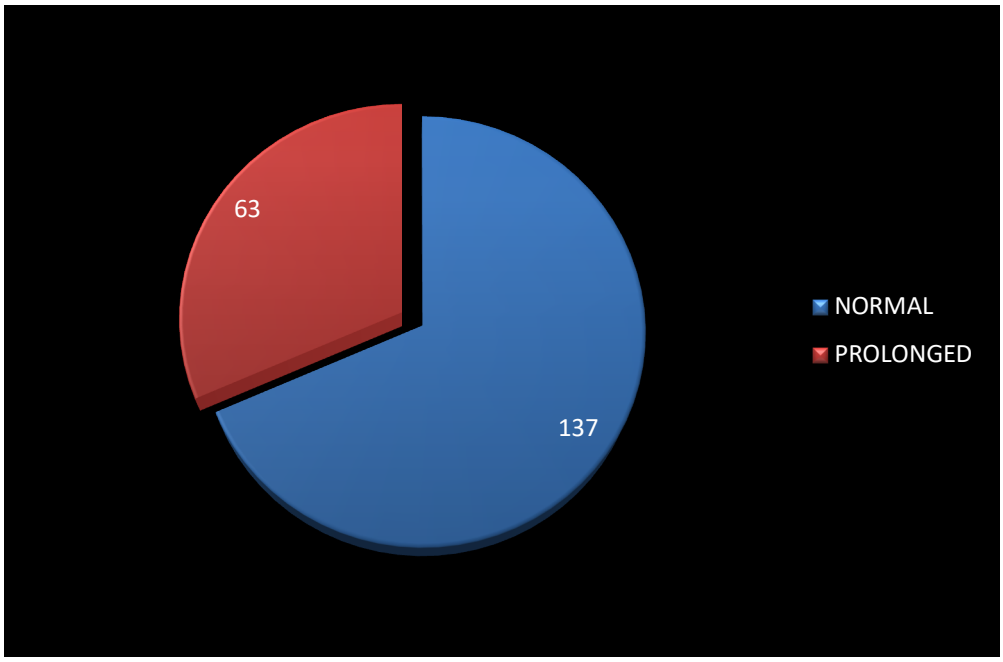

Figure 1: Prolonged prothrombin time

Figure 1: Prothrombin time was prolonged (≥ 3 sec) in 63 (31.3%) patients.

Cerebral malaria

Cerebral malaria was seen in 7(3.5%) cases of the study population of which 6(3%) patients presented with altered sensorium and 1(0.5%) patient had seizures, **Figure 2.**

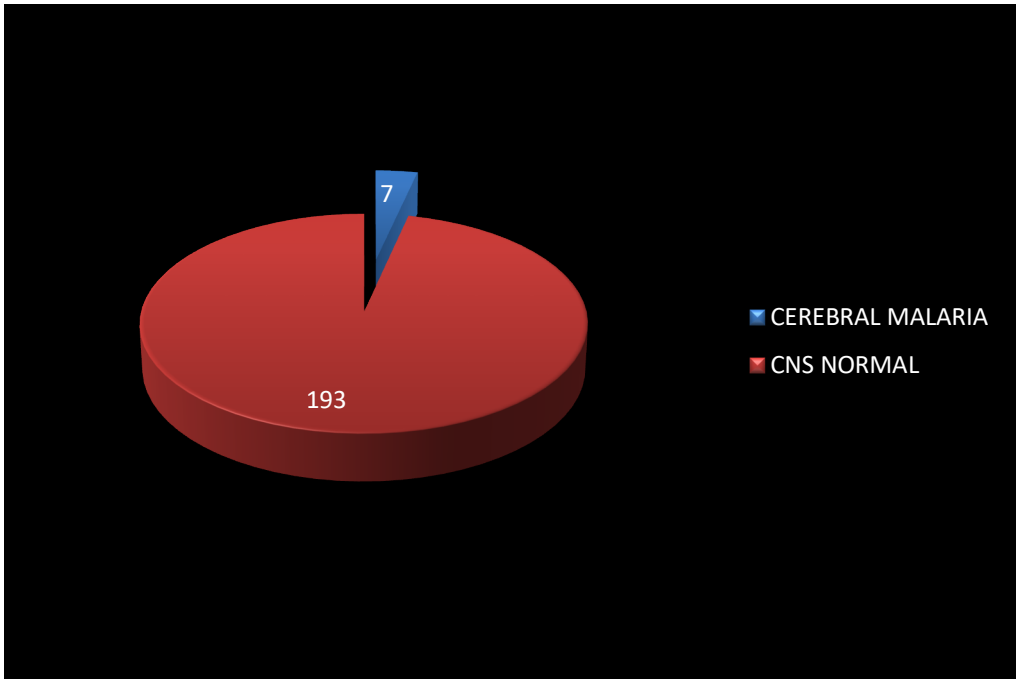

Figure 2: Cerebral malaria

Respiratory manifestations

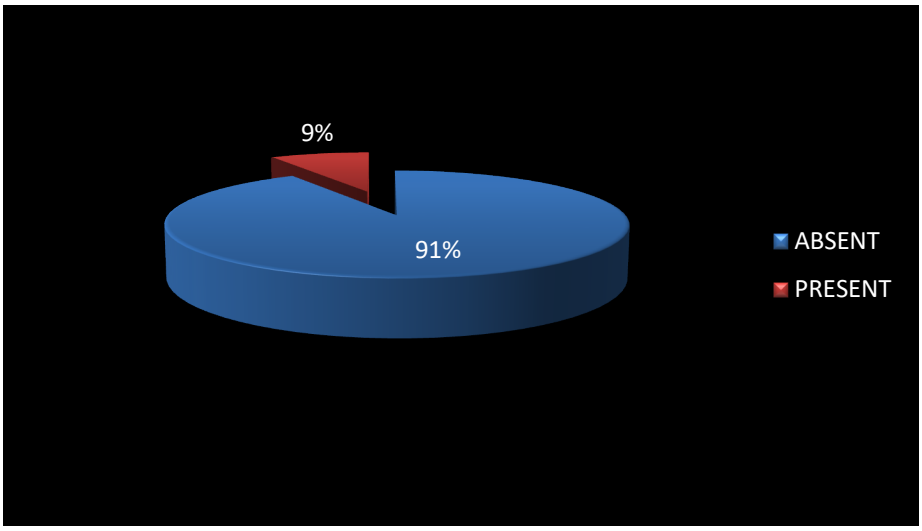

Figure 3: Acute respiratory distress syndrome

Bronchitis was seen in 25 (12.5 %) cases and ARDS was seen in 17 (8.5%) cases, **Figure 3.**

Acute kidney injury

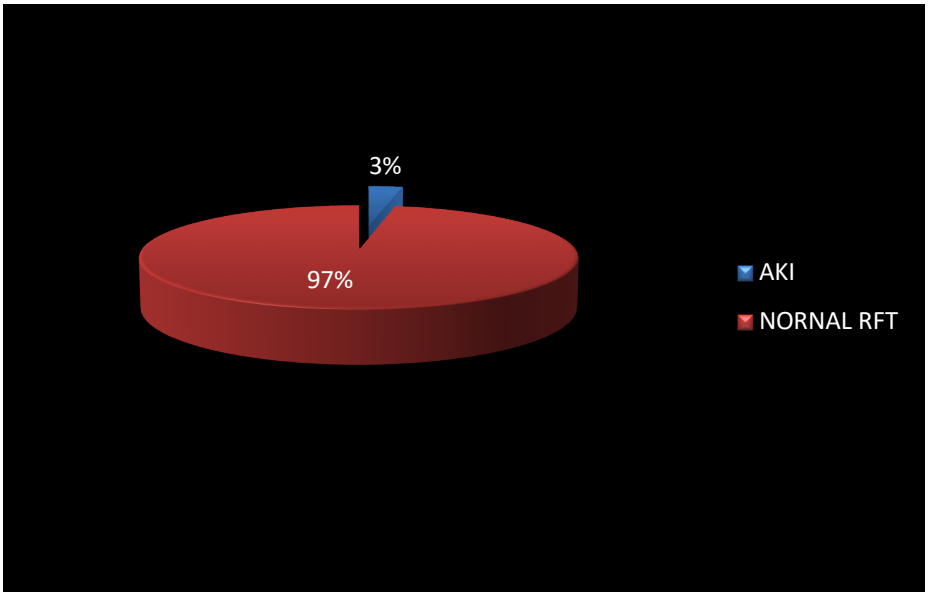

Figure 4: Acute kidney injury

As shown in Figure 4, acute kidney injury was seen in 6(3%) patients.

Dialysis

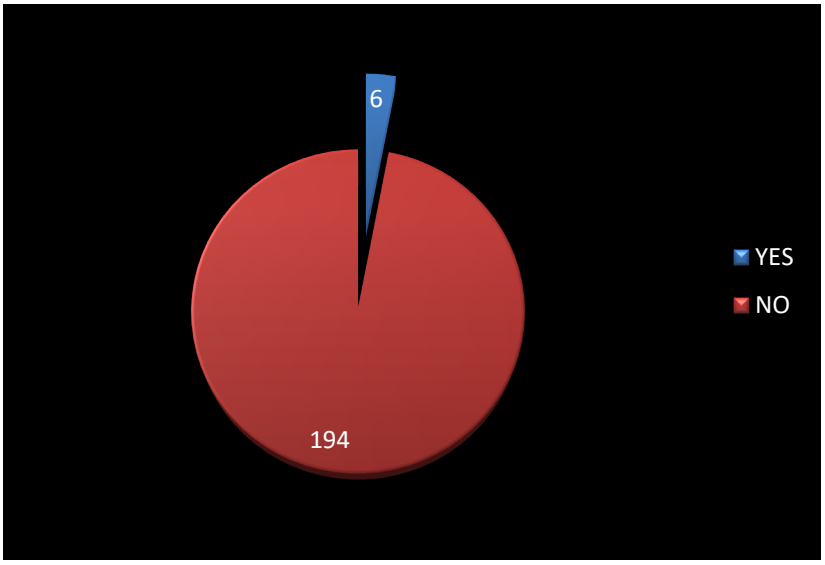

Figure 5: Dialysis

Dialysis was done in all the 6 (3%) patients who developed acute kidney injury, Figure 5.

Metabolic acidosis

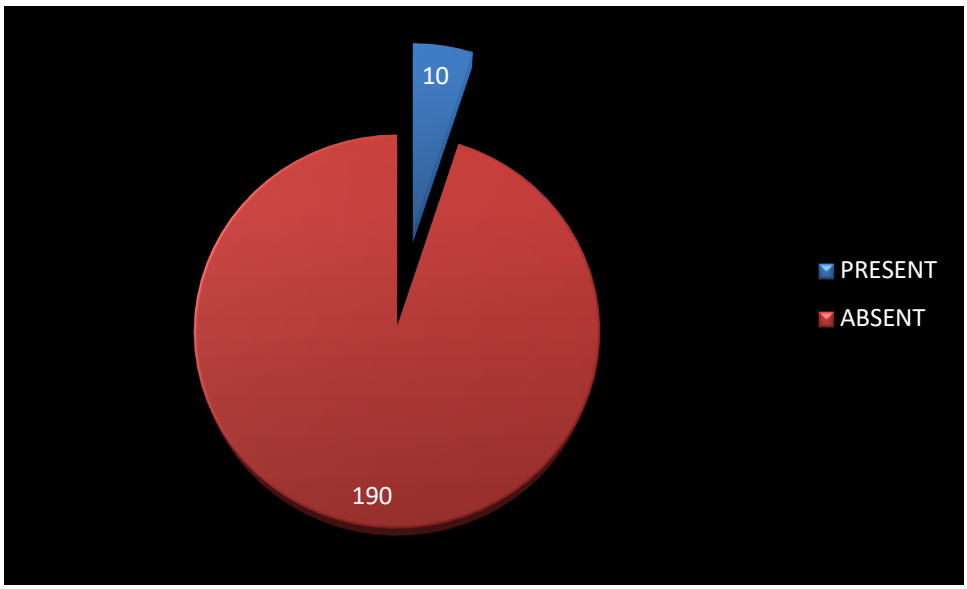

Figure 6: Metabolic acidosis

Metabolic acidosis was seen in 10 (5%) cases, **Figure 6.**

Treatment received

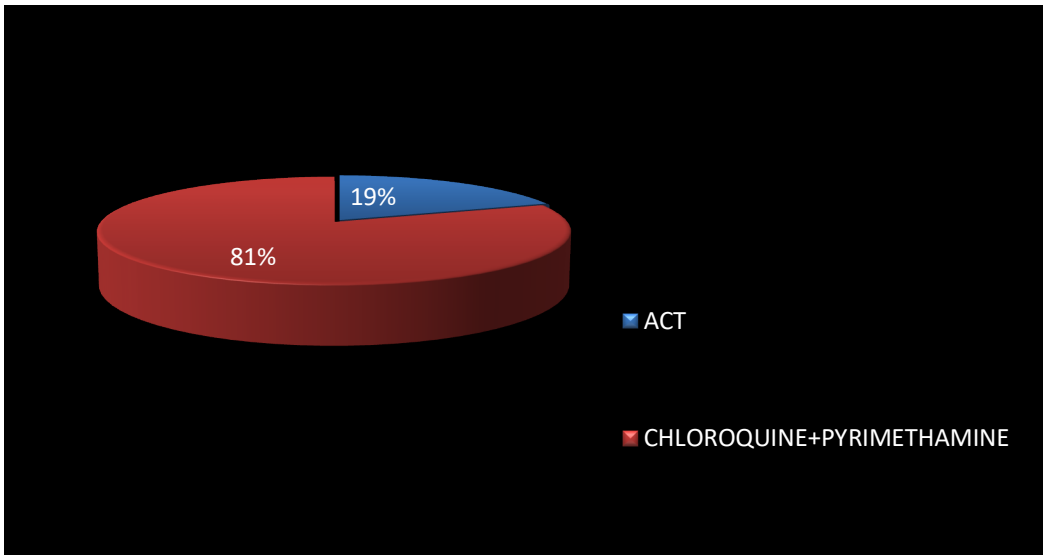

Figure 7: Anti-malarials received

80 % received chloroquine as the first line of treatment while the remaining 20 % were treated with artemisinin combination therapy as per WHO guidelines, Figure 7.

Manifestations of severe malaria

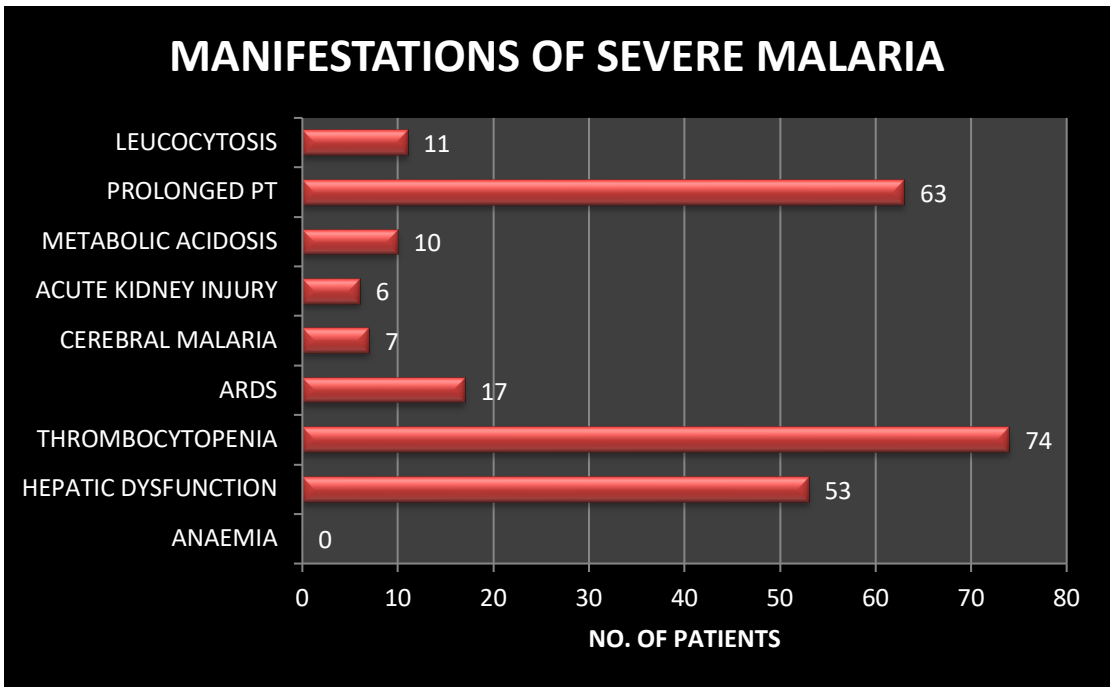

Figure 8: Manifestations of severe malaria

The above Figure 8 shows the manifestations of severe malaria as per the WHO criteria in the present study.

Discussion

This research involved 200 *P. vivax* malaria patients who were admitted at Father Muller Medical College in Mangalore between May 2010 and April 2012. The male to female ratio in the current research was 2.125:1. It correlated with numerous other studies that were conducted [6–8].

In this study, the second decade (34%) and third decade (20.5%) had the highest incidence rates. Age at presentation was 37.32 years on average. The findings are consistent with those of studies done at Columbia [9–11]. All of the individuals in our research had fever as their primary presenting symptom. This discovery is consistent with the findings of other investigations done [6–8]. Thirty-six percent of the patients in our research reported vomiting, and 25.6 percent reported abdominal discomfort. In the Columbia University research, it was observed in 39% and 34% of the participants [9].

In our study, headache was present in 22.1% of patients, whereas it was present in 83.2% of cases in the Republic of Korea study [12]. 8.5% of the individuals in our research experienced coughing and shortness of breath. It is consistent with the Bikaner trial, where 10% of the patients experienced similar symptoms [13]. In our investigation, neurological involvement was identified in 3.5% of patients in the form of seizures and altered sensorium, whereas it was seen in 1.41% of cases in the Mangalore study [14]. The research conducted in Bikaner, where the incidence was 12.5%, produced a variety of outcomes [13]. In contrast to our analysis, which included all *P.vivax* malaria cases, their study only included patients who met the WHO criteria for severe malaria, which resulted in a greater prevalence of cerebral malaria. Throughout their hospital stay, 2.5% of the patients experienced oliguric symptoms. This was different from the research done in Bikaner, where the incidence was 45% since they only included cases of severe *P. vivax* malaria [3].

In our study, pallor and icterus were observed in 20.5% and 40.5% of participants, whereas they were found in 46% and 15% of participants in the Columbia study, respectively [9]. In this study, hepatomegaly and splenomegaly were detected in 53% and 47% of participants, respectively. In the research conducted in the Republic of Korea [12], it was seen in 15.8% and 42% of people, respectively.

In the current research, 18.5% of patients experienced ARDS at some point throughout their illness. In a research conducted at Buritus, the prevalence of ARDS was 21.05%, and other investigations produced comparable findings [15]. Renal failure was discovered in 3% of individuals in our research and 10.5% of cases in the Buritus study [15]. In our research sample, 3.5% of participants experienced neurological symptoms, compared to 1.41% of cases in the Mangalore 14 study. In our investigation, there were no patients with haemoglobin levels below 5 g/dl. In the Mangalore research, 0.47% of subjects had severe anaemia [14].

In our study, 6.5% of the patients showed leucocytosis whereas 27.5% had leucopenia. Leucocyte count was 6634 cells/cumm on average. Leucopenia and 2.9% leucocytosis were found in the Republic of Korea research. [12]. 91% of the study population had thrombocytopenia (1.5 lakh/L), which was consistent with the findings of the Delhi research. In 37% of patients, severe thrombocytopenia as defined by WHO criteria was discovered [16].

In our research, there were 26.5% of subjects with hepatic impairment. This was consistent with the Delhi research [16]. In

our investigation, 3% of instances of acute renal damage were observed. There were no individuals with renal impairment in the Columbia research. Our findings diverged from those of the Bikaner investigation, which found a high frequency of 45% [9, 13].

In our study, 8.5% of patients had ARDS. 10% of the patients in the Bikaner research experienced ARDS. All 17 patients required ventilatory support; 15 of them had successful outcomes, while the other two passed away from the disease [13]. In our investigation, multi-organ dysfunction was seen in 3% of individuals, whereas it was found in 47.5% of cases in the Bikaner study [13]. While only patients who met the WHO criteria for severe malaria were included in the research at Bikaner, but our study included all vivax malaria cases, their study had a greater incidence of all sequelae (ARDS, AKI, cerebral malaria, and MODS) [13]. In our investigation, the mortality rate was 2% (n=4), which was consistent with a study conducted in Delhi [16]. The four patients each exhibited sepsis-related symptoms. One patient died from AKI and ARDS, another from sepsis and AKI, and two more patients from AKI, ARDS, and hepatic dysfunction.

Conclusion

This study emphasizes the possibility of P. vivax malaria having a severe and difficult course, which is typically connected to P. falciparum malaria, despite the fact that it has historically been thought of as a benign disease. Hepatic dysfunction and thrombocytopenia are frequent symptoms that signal the severity of the illness. According to our study, life-threatening complications such ARDS, AKI, cerebral malaria, and MODS do aggravate benign tertian malaria.

Ethical Approval: The study was approved by the Institutional Ethics Committee

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