Prospective Study Of The Clinical Profile Of Hospitalized Patients Of Malaria

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Abstract : Background & Objectives: To study the clinical profile of hospitalised patients of malaria aged 15-60 years. Methods: This was a prospective analysis of patients suffering from malaria diagnosed by malaria serology and/or peripheral smear. The mode of presentation, clinical course, treatment history, laboratory investigations and complications were recorded and the data statistically analyzed.Results: P. vivax was the most common (80.39%) plasmodium species, the rest (19.61%) being P. falciparum. The mortality rate was 6.54%. A fall in hemoglobin (p=0.005) and platelet count (p=0.040) was observed in the patients who expired. There was an improvement in the final platelet counts in both the groups (p=0.00052). The mean total bilirubin at admission was higher in P. falciparum group than P. vivax group (p = 0.00789). Renal failure was observed in 16.34% patients. The mean systolic and diastolic blood pressure in patients who expired was lower than patients who were discharged (p=0.007, 0.001). The mean heart rate was higher (109.40) in patients who expired (p = 0.002). Conclusion: Factors associated with poor prognosis in malaria are moderate grade fever, hypotension, tachycardia, anaemia, thrombocytopenia, hyperbilirubinemia, high transaminase and renal failure. A high clinical suspicion, early diagnosis and treatment is recommended in highly prone areas. [Jain N et al NJIRM 2013; 4(4) : 92-97]

Key Words: Malaria, Plasmodium falciparum, Plasmodium vivax.

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Introduction: Malaria is an important parasitic infection with considerable morbidity and mortality. This disease was almost eradicated in 1960's and has re-emerged as a major public health problem in the last few decades. About 110 million cases are reported. It is one of the most endemic disease, especially in African tropical countries and India. [1]

A prompt and early diagnosis is key to effective management in malaria. Many acute febrile illnesses like viral fever, arboviral infections, enteric fever and leptospirosis occur in the tropics and it is difficult to distinguish malaria from these illnesses on clinical grounds alone. Microscopic examination by peripheral smear is used for diagnosis.

A variety of haematological alterations like anaemia, decreasing RBC counts, thrombocytopenia and leukopenia or leukocytosis occur in malaria.[2,3]

The mortality in Malaria is mainly due to Plasmodium falciparum. The mortality and morbidity in falciparum malaria is due to its protean manifestation, multiorgan involvement, delay in diagnosis and failure of administration of treatment promptly and adequately. The emergence of drug resistance adds to the seriousness of the problem.[4]

Malaria ranks third among the major infectious diseases in causing deaths-after pneumococcal acute respiratory infections and tuberculosis. It is expected that by the turn of the century malaria would be the number one infectious killer disease in the world. It accounts for 2.6 per cent of the total disease burden of the world. It is responsible for the loss of more than 35 million disability-adjusted life-years each year. Every year ~ 30,000 visitors to endemic areas develop malaria and 1% of them die[5]. Since 1994 focal outbreaks of malaria have been reported from various parts of the country. Hence a hospital based prospective study of clinical profile of malaria was aimed at in patients aged 15 – 60 years.

Material And Methods : A prospective analysis of patients suffering from malaria was carried out in the department of Medicine at Dayanand Medical College and Hospital, Ludhiana over a period of 18 months (01.01.2009 to 30.06.2010) after obtaining approval from the ethical committee. All the cases which tested positive for malaria parasite (Plasmodium antigen positive or peripheral smear positive) in the age group 15-60 were included in the study. Patients presenting with fever (malaria smear negative), but treated empirically for malaria, those presenting with clinical features mimicking malaria (malaria parasite test negative) as in leptospirosis, dengue fever and sepsis and those having any

concomitant infection were excluded from the study.

A detailed history was taken and data collected regarding the demographic details, history of fever, associated localizing or general symptoms. Investigations were broadly divided in the following groups.

Basic investigation: Complete Blood Count, ESR, Peripheral Blood Film, Liver Function Test and Urine Routine.

Optional investigations (if considered necessary by the treating unit) included:

- Malarial serology - The malaria rapid test is a chromatographic immunoassay for qualitative determination of malarial parasite infection in human blood sample. It detects antigen of malarial parasites.
- Malarial parasite antigens, LDH (Lactate Dehydrogenase) and aldolase levels, Widal, Leptospira, Dengue, Anti HIV, Anti HCV, HBsAg, Blood Culture, Urine Culture, Radiological Investigation - Chest X-ray, Ultrasound abdomen, CT Scan head

The mode of presentation, clinical course, treatment history, laboratory investigations reports and complications were recorded. The data was analysed using chi square test. A p value of less than 0.05 was considered significant.

Results : Over a period of 18 months (January 2009 to June 2010), a total of 171 patients admitted with a diagnosis of malaria were a part of the study. Of these, 153 were included and the rest excluded as 10 patients were pregnant, 5 had positive dengue serology and 3 patients had concomitant viral hepatitis (2 had HAV hepatitis and 1 had HEV hepatitis).

A large number of patients belonged to the relatively younger age group of 15-35 years (62.10%), 18 (11.76%) were in the age group 36-45 years and 25 (16.34%) were in the age group 46-55 years. Among those who expired, 3(30%) were in the age group 36-45 years. The number of male patients were 91 (59.48%) and the male: female ratio was 1.47:1. Of the 10 patients who expired, 60% were females.

Malaria showed a seasonal trend with most of the patients presenting in the month of July to September (62.09%). First quarter of the year (Jan-March) showed least incidence.

Among the patients who were discharged, the average length of stay was 6.84 days, with stay being more in the ward (5.99 days) than in the ICU (0.85 days). In contrast, the stay of patients who expired was more in the ICU (2.4 days) but this was statistically insignificant (p=0.075). However the total length of stay was less in patients who expired (4.7 days).

The average length of stay for patients with P. vivax malaria in the ward was 5.59 days in comparison to 6.4 days for patients with P. falciparum malaria but this was statistically insignificant (p=0.132). The average stay in the ICU was more for patients with P. falciparum malaria (1.50 days) as compared to patients with P. vivax malaria (0.82 days) and this was also statistically insignificant (p=0.13). 143 (93.46%) patients were discharged and 10 (6.54%) died or went LAMA (left against medical advice). Of the 153 patients, 123 (80.39%) had P. vivax malaria and 30 (19.6 %) had P. falciparum malaria.

Of the 123 patients in the P. vivax group, 116 (94.31%) were discharged and 7 (5.69%) patients expired. In the P. falciparum group, 3 (10%) expired and 27 (90%) patients were discharged.

Fever was the presenting complaint in 100% of the patients. In 96.08% patients it was intermittent and in 77.78% associated with chills and rigors. Myalgias were present in 31.37% patients, vomitings in 37.25%, pain abdomen in 24.84% and jaundice in 16.34% of the patients. Headache was present in 16.34% patients, altered sensorium in 11.11% and dyspnea also in 11.11% of the patients.

Low grade fever was observed in 63 patients (41.18%), moderate grade in 60 (39.22%) and high grade in 30 (19.61%). 90% of the patients who

expired had moderate grade fever as compared to 35.66% of those who were discharged. Duration of between 6 to 10 days, in 51 (33.33%), it was 1-5 days.Of the 123 patients who had P. vivax malaria, 54 (43.90%) had low grade fever, 46 (37.40%) had moderate grade and 23 (18.70%) had high grade fever. In the P. falciparum group, 14 patients (46.67%) had moderate grade fever in contrast to 37.40% in the P. vivax group.

The mean systolic blood pressure in patients who expired was 97.78 mm Hg and mean diastolic blood pressure was 63.33 mm Hg as compared to the mean SBP of 113.76 mm Hg and mean DBP of 72.45 mm Hg in patients who were discharged and this was statistically significant (p=0.007, 0.001). The mean heart rate was significantly higher (109.40 per minute) in patients who expired (p = 0.002).

fever was of average 8 days. In 49.67%, it was

On clinical examination, 37 (24.18%) patients had hepatomegaly and 30(19.61%) had splenomegaly. In the P. falciparum group, 8 (26.67%) patients had hepatomegaly whereas in P. vivax group, 29 (23.58%) had hepatomegaly.

A statistically significant difference (p=0.005) was observed in the mean hemoglobin of the patients in the discharge group (11.13 gm/dl) and the expired group (9.05 gm/dl). A significant fall in mean hemoglobin levels was observed in both the groups (discharged and expired).

Thrombocytopenia was observed in 141 patients (92.16%). It was seen in 93.71% patients who were discharged and 70% who expired. It was significantly lower in the expired group than in the discharge group. There was a significant improvement in the final platelet counts in both the groups (Table 1)

Table 1: Trends in platelets

Platelets (thousand /cmm)	**Discharged**		**Expired**		**Total**		**p-value**	**P. vivax**		**P. falciparum**		**p-value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**		**Mean**	**SD**	**Mean**	**SD**	
On admission	57.98	70.14	11.90	7.14	54.97	68.77	0.040	50.30	57.83	74.10	101.2	0.096
On discharge	189.47	116.82	73.88	72.75	183.26	117.6	0.006	172.48	107.5	227.86	146.3	0.041
p-value	0.0005		0.010		0.0005			0.0005		0.001		

In the P. vivax group, thrombocytopenia was observed in 114 patients (92.68%) where as in the P. falciparum group, thrombocytopenia was observed in 27 patients (90%). (p = 0.154).

The mean final bilirubin levels in patients who were discharged was significantly lower than in those who expired. The mean total bilirubin at admission was significantly higher in P. falciparum than P. vivax group. (Table 2). The mean SGOT in patients who got discharged was 71.68 and it was 139.9 IU/ml in those who expired and this result was statistically significant (p=0.013). Also there was a declining trend observed in the level of SGOT at discharge in both the groups of patients but this was statistically significant only in the discharged group of patients.

Table: 2 : Trends in total bilirubin levels

S.Bilirubin levels (mg/dl)	Discharged		Expired		Total		p-value	P. vivax		P. falciparum		p-value
	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
On admission	3.36	4.60	1.10	0.57	4.04	6.32	0.0001	3.23	3.93	7.28	11.32	0.007
On discharge	1.76	1.36	3.74	3.55	1.90	1.65	0.009	1.55	1.04	2.76	2.43	0.006
p-value	0.007		0.042		0.006			0.006		0.046		

The mean level of SGPT in patients who got discharged was lower at admission (54.42 IU/ml) as compared to those who expired (87.20 IU/ml) and this was statistically significant (p=0.048). However, the mean SGPT of both the groups combined was almost the same at admission and at discharge.

Renal failure was observed in a total of 25 patients (16.34%). Out of the 10 patients that expired, 8 had renal failure at the time of admission and this was statistically significant (p=0.00458). 17 out of 123 patients (13.82%) in the P. vivax group and 8 out of 30 patients (26.67%) in the P. falciparum group had renal failure.

Table 3 shows the trends in the serum creatinine levels. The mean serum creatinine in patients who were discharged was significantly lower than in those who expired. There was a statistically insignificant decrease in the level of mean creatinine in both the P. vivax and P. falciparum groups at discharge (when compared to creatinine at admission)

Table 3 : Trends in serum creatinine

S.Creatinine levels (mg/dl)	Discharged		Expired		Total		p-value	P. vivax		P. falciparum		p-value
	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
On admission	1.34	1.20	3.16	1.91	1.46	1.33	0.0001	1.41	1.20	1.65	1.11	0.187
On discharge	0.97	0.41	4.87	2.77	1.25	1.29	0.0001	1.12	0.41	1.58	1.69	0.089
p-value	0.0074		0.102		0.116			0.090		0.868		

Discussion: In our study, 93.46% patients were discharged and 6.54% died or went LAMA (left against medial advice were taken as expired due to their critical condition). In the P.vivax group, 94.31% were discharged and 5.69% expired. In the P.falciparum group, 10% expired and 90% were discharged. Murthy GL et al[4] reported a mortality of 20.25% and Koh et a1[6] of 35.7% which is probably higher because of inclusion of only P. falciparum malaria.

We recorded P. vivax malaria in 80.39% patients and P. falciparum malaria in 19.61%. Mehta et al[7] reported P. falciparum infection in 36.6%, P.vivax in 54.5% and mixed infection in 8.9%. However this study was done in Mumbai where P.falciparum is more common.

A large number of patients belonged to the relatively younger group (mean 34.11+/- 14.06 years) which is comparable to other studies [4,8] It is because malaria is a disease of the younger and the middle age group as they are more involved in outdoor activities. We noted the age pyramid in our country where the base is formed by young people and apex by the older age who constitute lesser percentage of the population.

The length of hospital stay of discharged patients was 6.84 days, more in the ward (5.99 days) and less in the ICU. In contrast, the stay of expired patients was more in the ICU (2.4 days). Koh et a1[6] reported the average length of hospital stay of 11.2 days in patients with falciparum malaria.

Fever was the most predominant complaint (in 100%) and 77.78% patients had chills and rigors in our study which was comparable to other studies.[8,9] Moderate grade fever was seen in 90% of expired and 35.66% of the discharged patients which was statistically significant probably because fever is directly associated with the level of parasitemia.[10] Duration of fever of average 8 days in our study was comparable to 6 days by Abisheganadan et a1[11].

Cough and breathlessness in 11.11% patients in our study as compared to 4.4 % by Mehta et al[9] signifies that the number of complicated malaria cases were more in our area and also because ours is a tertiary referral centre.

Malhotra et al[8] reported altered sensorium in 50% which was higher than ours (11.1%) because they

studied only complicated malaria cases. Splenomegaly in 19.61% of our patients was comparable to 14.3% by Koh et al[6] but lower than Murthy et al[12] (50%) probably because our patients presented relatively early in the course of illness and splenomegaly occurs in the second week of illness.

Lower incidence of hepatomegaly (24.18%) in our study than by Murthy et al[12] (91%) might be because they mainly concentrated on the subjects with malarial hepatitis and jaundice in malaria. The mean hemoglobin observed was 11.13 gm % in discharged patients and 9.05 gm% in expired. A significant fall in the mean hemoglobin was observed in both the groups (discharged and expired). Sharma et al[13] reported anemia in 86.7% and higher mortality with severe anemia (Hb < 6gm%). We noted a poor outcome with hypotension and tachycardia as observed by Koh et al.[6]

92.16% patients in our study had thrombocytopenia at admission and a statistically significant rise at discharge was observed as reported by various authors [14-17]. Platelets were much lower in expired than in the discharged patients. Thrombocytopenia was observed in 92.68% patients in the vivax and 90% in the falciparum group. Jadhav et a1[16] observed a lower count with falciparum than vivax malaria.

A statistically significant difference in the mean final bilirubin levels was observed in patients who were discharged as compared to those who expired. We also observed a declining trend in the level of SGOT at discharge in both the groups but this was statistically significant only in the discharge group. The mean SGPT levels in the discharge group was lower at admission as compared to the expired. Ignatius et al[18] observed a positive correlation between the liver enzyme activities and the degree of parasitaemia.

Renal failure was observed in 16.34 % patients; 13.82 % of the P.vivax and 26.67% of the P. falciparum group. 8 out of 10 patients who expired had renal failure at the time of admission. The mean serum creatinine at admission in discharge group was lower than in the expired group. Renal failure has been reported as a key prognostic indicator in many studies[4,6] Kanodia et al[19] reported a 10.43% incidence of ARF in malaria and Mehta et al[7] reported 5.9%. ARF necessitating dialysis was seen in 92% of patients [7]. P.falciparum infection, severe ARF, DIC and ARDS were poor prognostic factors. 29% of total 24 patients succumbed to the disease. Serum creatinine value was higher in them compared to those who survived[7] (P <0.05). Higher mortality has been associated with presence of complications like anaemia, jaundice, renal failure, DIC, adult respiratory distress syndrome (ARDS) and septicaemia in other studies also[4,6] .

Conclusions: Malaria is a potentially life threatening disease, which is transmitted by the infectious bite of the female Anopheles mosquito. In India, malaria has been a major publichealth problem since ages. Many malaria deaths occur outside of hospitals and thus aren't easily recorded. And unlike more prolonged diseases, malaria can strike fast, making it even harder to track. Factors associated with poor prognosis include moderate grade fever, hypotension, tachycardia, anaemia, thrombocytopenia, hyperbilirubinemia, higher levels of transaminases and renal failure. A high clinical suspicion, early diagnosis and treatment is recommended especially in highly prone areas.

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