www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v6i10.75

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

A Study on Incidence and Prognostic Value of Jaundice in Patients of Plasmodium falciparum Malaria in Jharkhand

Authors
Dr Jeewan Kumar Mitra[1], Dr Manmeet Topno[2*], Dr Upendra Prasad Yadav[3]
Dr Rohit Keshav[4], Dr Aman Sinha[5]
[1]Professor & Head Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi
[2,3,4,5]Junior Resident, Rajendra Institute of Medical Sciences, Ranchi
*Corresponding Author
Dr Manmeet Topno
Junior Resident, Rajendra Institute of Medical Sciences, Ranchi
Add: RIMS Boys Hostel No. 5, Room no. 89; Bariatu, PO- R.M.C.H, Ranchi, Jharkhand, Pin 834009, India
Email: *manmeettopno@gmail.com*

Abstract
Introduction: *Malaria is still one the most important protozoan disease causing significant mortality. One of the causes may be because of atypical presentation of the disease resulting in delay in diagnosis and treatment. Jaundice is one the important predictors of severity of the disease. Jaundice when present alone indicates severe disease and when in combination with other complications ARF (Acute Renal Failure) indicates poor prognosis.*
Material and Method: *A hospital based prospective observational study was done on 71 confirmed cases of P. falciparum malaria admitted in our hospital from July 2017 to August 2018.*
Result: *The total no. of cases in the study was 71. The mean age of the patients was 34.76 ± 12.81 years. Majority of the cases (49) were seen in age group 20 -39 years (69.01%). On looking at the sex distribution, total no. of cases among males were 53 (74.64%) and 18 were females (23.35%), no. of males was more than females. Majority of the patients came from rural areas 51 (71.83%) as compared to urban areas 20 (28.17%) this may be due to poverty, lack of proper education and living in unhygienic conditions. 32.39% of the patients (23) were tribal and 67.61 % (48) were non-tribals. According to serum bilirubin levels, patients were classified into two Groups A (53 patients, serum bilirubin <3 mg/dl), B (18 patients, serum bilirubin > 3 mg/dl). Group B patients had total bilirubin, direct bilirubin, indirect bilirubin, serum glutamic oxaloacetic transaminase, SGPT, and alkaline phosphatase levels in the range of 9.67±7.37 mg/dl, 5.22±4.31mg/dl, 4.46±3.85 mg/dl, 119.39± 99.07 IU/L, 62.22±40.18 IU/L, and 126.17±46.12 U/L, respectively.*
Conclusion: *We suggest that jaundice in P. falciparum malaria can serve as an important prognostic factor indicating a severe disease as serum bilirubin rises. When it is associated with ARF prognosis becomes bad. Jaundice with fever in an malaria endemic country like India, P. falciparum malaria should always be ruled out.*
Keywords: *Hyperbilirubinaemia, Malarial hepatitis, Acute Renal Failure, Falciparum malaria.*

Introduction

Malaria is a protozoal disease which is transmitted by the bite of infected female Anopheles mosquitoes. It is one of the most important of the parasitic diseases of humans, with 216 million cases and estimated 445000 deaths worldwide in the year 2016; mortality rates are decreasing as a result of highly effective control programs in several countries. Malaria has now been eliminated from United States, Canada, Europe, and Russia, but despite enormous efforts, has reappeared in many parts of the tropics. The main factors responsible for its resurgence are increase in the drug resistance of the parasite, the insecticide resistance of its vectors, and human travel and migration of humans to different parts of the globe.

The major manifestations of severe falciparum malaria may be cerebral malaria, unarousable coma, acidosis, severe normochromic, normocytic anaemia, renal failure, ARDS, hypoglycaemia, hypotension, shock, bleeding, disseminated intravascular coagulation, repeated seizures, hemoglobinuria and jaundice.[1,2]

It is important to appreciate that these severe manifestations can occur singly or more commonly in combination in some patients. Children and non-immune adults are at most risk in endemic areas. Jaundice is one of the common severe manifestations of falciparum malaria. Its incidence varies between 10 to 45% in different reports, and is seen more in adults than in children. WHO, also states that involvement of liver is not an uncommon presentation in P. Falciparum and it manifests as jaundice (bilirubin ≥3 mg/dl). Hyperbilirubinemia in falciparum malaria results from intravascular haemolysis of parasitized RBCs, hepatic dysfunction and an element of microangiopathic haemolysis due to DIC.[3-8] In severe and complicated malaria, a term "malarial hepatitis" is commonly used to describe hepatocytic dysfunction; however, actual inflammation is almost never seen in the liver parenchyma.[3]An increased level of serum bilirubin along with increased level of serum glutamate pyruvate transaminase (SGPT) to more than three times the upper limit of normal, is main characteristics of malarial hepatitis.[9]

Chotanagpur plateau of Jharkhand is an endemic area of malaria. There is a large area of hills and dense forests distributed widely all over the state of Jharkhand. The population residing here is basically tribal dominated and the people are socioeconomically backwards living in villages. It has been observed that complicated cases of falciparum malaria are being admitted in gradually increasing numbers at the Rajendra Institute of Medical Sciences, Ranchi. There is no data regarding jaundice in malaria from Jharkhand.

The prolonged hospital stay, the serious complications associated with falciparum malaria, the exhaustive management add to the economic burden of the community.

In the light of above factors, I have carried out my present study amongst the admitted patients at the Dept. of Medicine, RIMS in favour of the suffering population of Jharkhand state.

Material and Methods

This was hospital based prospective observational study done on 71 confirmed cases of severe falciparum malaria admitted in hospital from July 2017 to August 2018 after taking informed consent. The approval of institutional ethics committee was taken prior to the commencement of this study. A case sheet proforma was prepared and data regarding demographic profile, clinical features, investigations, treatment, and complication were recorded. Severe falciparum malaria was diagnosed as per guidelines of WHO.[4]

Inclusion criteria: Only those cases whose blood was found to be positive for plasmodium falciparum by peripheral blood smear examination or antigen test were considered for the study.

Exclusion criteria

- Pre-existing neurological disease
- Pre-existing hematological disease
- Pre-existing acute or chronic renal failure
- Pre-existing liver disease

Two Groups were studied

Group A included 18 patients who were P. falciparum positive cases with hyperbilirubinaemia (i.e. serum bilirubin > 3 mg/dl) & Group B included 53 P. falciparum positive patients with serum bilirubin < 3 mg/dl.

The following investigations have been done in cases under study:

1) Blood for TC & DC of WBCs, Hb% estimation.
2) Peripheral blood smear, both thick and thin for the presence of P. falciparum.
3) Rapid diagnostic kit test for P. falciparum.
4) Random blood sugar
5) Renal function test – Blood urea and serum creatinine.
6) Liver function test – Sr. Bilirubin (Total, Direct and Indirect), SGOT, SGPT, alkaline phosphatase.
7) Routine examination of urine.
8) USG Abdomen – Only those cases with relevant findings suggestive of deranged renal function.

Statistical Analysis

Microsoft office 2010 was used for the statistical analysis. Descriptive statistics like mean, standard deviation and percentages were used in the analysis.

Result

The total no. of case studied were 71(n=71). The mean age of patients were 34.76 ± 12.81 years. Majority of the cases (49) were seen in age group 20 -39 years (69.01%). On seeing the sex distribution, total no. of cases among male patients were 53(74.64%) and amongst females were 18(23.35%), no. of males was more than females. Majority of the cases were from rural areas 51(71.83%) as compared to urban areas 20(28.17%) due to poverty, lack of proper education and living in unhygienic conditions. 32.39% of the patients (23) were tribal and 67.61 % (48) were non-tribals.

Fever with chills (100%) was the leading symptom noted followed by altered sensorium (57.14%). Neck rigidity was seen in 76.17% of cases. Oliguria/Acute renal failure was seen in 14 cases. Splenomegaly in 30 cases & hepatomegaly in 26 cases. Hypoglycaemia was seen in 04 cases. High serum bilirubin(> 3mg/dl) was seen in 25.35;% of cases which is similar with incidence of 23.41% in a study by G. Lalitha Murthy et al.[10]

Table 1 Different clinical manifestations observed in patients of P. Falciparum malaria under study

Clinical Presentation	No. of Cases N = 71 (%)	No. of cases with Jaundice N = 18(%)
Fever With Chills	71(100)	18(100)
Altered Sensorium	19(26.76)	12(57.14)
Neck Rigidity	42(59.15)	16(76.19)
Convulsion	04(5.63)	03(14.29)
Coma	12(16.90)	05(23.81)
Severe Anaemia	07(9.86)	05(23.81)
Hypoglycaemia	04(5.63)	03(14.29)
Oliguria/Renal Failure	14(19.72)	10(47.62)
ARDS	01(1.41)	00
Shock	04(5.63)	03(14.29)
Splenomegaly	07(9.86)	00
Hepatomegaly	03(4.23)	01(4.76)
Acidosis	14(19.71)	09(42.86)
Hemoglobinuria	06(8.45)	03(14.29)
DIC	02(2.82)	01(4.76)

Hyperbilirubinaemia was predominantly of conjugated bilirubin. However, unconjugated bilirubin was also seen in many cases. Patients were divided in two groups: Group A included 18 patients, mean age 40.22 ± 17.43 yrs, 12 males & 06 females, having hyperbilirubinaemia (Sr. Bilirubin > 3mg/dl). Group B included 53 patients with serum bilirubin < 3mg/dl.

Conjugated bilirubin was seen in 08 cases, unconjugated bilirubin was seen in 04 cases whereas mixed type of hyperbilirubinemia was seen in 06 cases. Serum bilirubilin was above the reference range in 25.35% (18) of patients whereas serum alanine aminotransferase (ALT or SGPT) was raised in 49.30% (35) patients above the reference value. Total no. of cases developing jaundice (jaundice +ARF) was 10. Among those patients only developing jaundice were 08 & those only developing ARF were 04. Total No of deaths were 05; among those 04 had developed jaundice. Three had developed ARF (Acute Renal Failure). (Table-3)

Table 2 Demographic characteristics of Group A (study group) and Group B

Parameters	Group A (N= 18) (Mean ± SD)	Group B (N= 53) (Mean ± SD)	p value
Age (yrs)	40.22 ± 17.43	32.72 ±10.20	0.0064
Total bilirubin (mg/dl)	9.67 ± 7.37	1.14±0.71	<0.0001
Conjugated bilirubin (mg/dl)	5.22 ± 4.31	0.48±0.33	<0.0001
Unconjugated bilirubin (mg/dl)	4.46 ± 3.85	0.68±0.44	<0.0001
SGOT (U/L)	119.39±99.07	54.36±42.28	0.0002
SGPT (U/L)	62.22±40.18	49.74±32.67	0.1914
Alkaline phosphatase (U/L)	126.17±46.12	94.42±37.90	0.0050

Table 3 Clinical manifestations & prognosis

Clinical manifestations	No. of cases	cured	Death
Only Jaundice	08	06	02
Only ARF	04	03	01
Jaundice+ARF	10	08	02

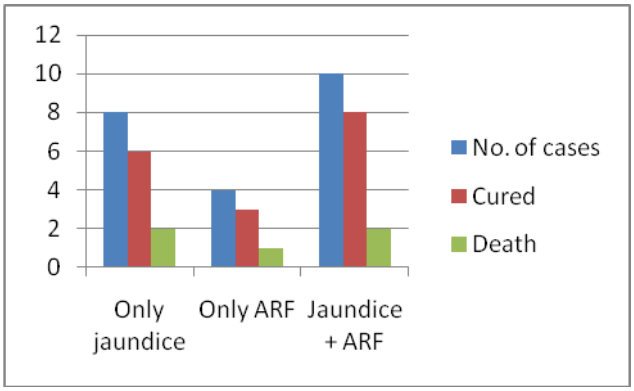

Fig. 1 showing clinical manifestations with prognosis among patients

Discussion

In our study it was seen that most of the P. Falciparum infection, 49 cases were seen in the age group 20-39 yrs which is comparable to study by Rathod et al.[11] Also if we see the sex distribution males were more frequently infected with P. Falciparum. This is similar to study by Abro et al.[12] This may be attributed to the fact that in Indian subcontinent people aged 20-39 yrs are involved in outdoor activity. In Jharkhand, males are involved in agricultural activities in villages in swampy areas making them prone to malaria. On the other hand females are involved in household activities indoors beside 'chulha' (cooking fire) which protects them from malaria.

P. Falciparum malaria is characterized by unconjugated hyperbilirubinaemia which is due to hemolysis of parasitized and non-parasitized RBCs and partly due to damage to liver.[13,14] In our study, serum bilirubin was raised in 25.35 % of patients and ALT level was raised in 49.30% patients while in the study of Abro et al.[12] 67.6% patients had ALT level above the reference range and in 81% patients serum bilirubin level was found to be higher than the normal reference value. In a study from Vietnam it was seen that 63% of patients of malaria had jaundice when acute renal failure was present whereas only 20% had jaundice when acute renal failure was absent.[15] In our study 55.56% of patients had jaundice when ARF was associated and 44.44% had jaundice when ARF was absent. Thus, complications like ARF are more common in patients with jaundice.

The no. of deaths increased with the no. of complications. The total no of deaths observed in our study was 7.04% (05) whereas mortality in others Indian studies were in range of 12.4 to 50%.[16,17,18]Our hospital is a tertiary care centre so most of the patients who died of malaria who were referred patients from either PHCs or private hospitals when patients had developed complications. Unfortunately, infrastructure provided at the level of PHCs by our government may not be adequate to deal with complication of P. falciparum. Thus delay in diagnosis and referral resulted in mortality of patients.

Conclusion

Thus, we conclude that P. falciparum malaria is still an important cause of mortality. Delay in diagnosis due to atypical presentation can be fatal. Early referral should be made to tertiary should be done promptly at PHCs level when complications are seen. Jaundice can serve as an indicator to rule out P. falciparum malaria especially when accompanied by fever. Also village people should be educated about use of bed nets, to use insecticide, elimination of breeding places of mosquitoes through mass media. Most villagers are unaware that stagnant water bodies such as ponds, ditches harbours mosquitoes.

They should be encouraged to keep such places clean. Further there are limitation to this study such as this is a single centered study, sample population was small also duration of study was less. Thus it may not be representative of actual population of community. More of studies are needed to address the situation in future.

References

1. Harrison's principle of internal medicine 19th edition page -1368-1384.
2. World Health Organisation. World malaria report 2017, Geneva.
3. Anand AC, Puri P: Jaundice in malaria. J Gastroenterol Hepatol 2005, 20:1322 – 1332.
4. World Health Organisation: Severe falciparum malaria: Communicable Diseases cluster. Trans R Soc Trop Med Hyg 2000, 94 (Suppl) : 51-590.
5. Mishra SK, Mohapatra S, Mohanty S. Editorial. Jaundice in falciparum malaria. J Ind Acad Clin Med 2003;4(1):12-3.
6. Bhalla A, Suri V, Singh V. Malarial hepatopathy. J Postgrad Med 2006; 2:315-20.
7. Singh R, Kaur M, Arora D. A prospective study of hepatic involvement in plasmodium falciparum malaria. Jour Clin Diag Res. 2010; 4: 2190-2197.
8. Kochar DK, Agarwal P, Kochar SK, Jain R, Rawat N, Pokharm RK, Kachawa S, Srivastava T. Hepatocyte dysfunction and hepatic encephalopathy in Plasmodium falciparum malaria. Q Journal of Medicine 2003; 96: 505-512.
9. Anand AC, Ramji C, Narula AS, Singh W. Malarial hepatitis: A heterogeneous syndrome? Natl Med J India 1992;5:59-62.
10. Murthy GL, Sahay RK, Srinivasan VR, Upadhaya AC, Shantaram V, Gayathri K. Clinical profile of falciparum malaria in a tertiary care hospital. J Indian Med Assoc. 2000 Apr;98(4):160-2.
11. Rathod CC, Deshpande SV, Himanshu RM, Varsha GY, Amul P, Vaibhav D, et al. Plasmodium falciparum versus Plasmodium vivax: Which is a lesser evil? Natl J Community Med 2012;3:541-6.
12. Abro AH, Ustadi AM, Abro HA, Abdou AS, Younis NJ, Akaila SI. Jaundice with hepatic dysfunction in P. falciparum malaria. J Coll Physicians Surg Pak 2009;19:363-6.
13. Harinasuta T, Bunnag D. The clinical features of malaria. In: Wernsdorfer WH, McGreogor IA, editors. Malaria: Principles of Practice of Malariology. Vol. 1. Edinburgh: Churchill Livingstone; 1988. p. 721.
14. Molyneux ME, Looareesuwan S, Menzies IS, Grainger SL, Phillips RE, Wattanagoon Y, et al. Reduced hepatic blood flow and intestinal malabsorption in severe falciparum malaria. Am J Trop Med Hyg 1989;40:470-6.
15. Trang, Phu NH, Vieh H et al. Acute renal failure in patients with severe falciparum malaria. Clin Inf Disease 1992;15: 874-80.
16. Ahsan T, Rab SM, Shekhani MS. Falciparum malaria or fulminant hepatic failure? J Pak Med Assoc 1993;43:206-8.
17. Srivastava A, Khanduri A, Lakhtakia S, Pandey R, Chaudhri G. Falciparum malaria with acute liver failure. Trop Gastroenterol 1996;17:172-4.
18. Sarkar S, Prakash D, Marwaha RK, Garewal G, Kumar L, Singhi S, et al. Acute intravascular haemolysis in glucose-6-phosphate dehydrogenase deficiency. Ann Trop Paediatr 1993;13:391-4.