Characteristics of Hepatic Complications In Pf Malaria: A Study In A Tertiary Health Center

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Abstract

Introduction: Malaria significantly impedes economic growth. It is brought on by Plasmodium infection and spread to people through the bite of a female anopheles mosquito. About 20% of the nation's malaria infections come from Orissa, and 85% of those cases are P. falciparum. The state accounts for 40% of malaria-related fatalities nationwide. Out of 39,556 positive cases and 9 fatalities in Odisha in 2019. **Materials and Mathod:** Out of 450 hospitalised patients with acute severe malaria, 60 complex malaria cases presenting with jaundice were studied in this prospective case series research to better understand their clinical characteristics. For a total of seven days, quinine dihydrochloride, 600 mg administered intravenously every eight hours, was administered to all patients.**Results:** The male to female ratio in the current study was 3:1, with 45 cases being men and 15 cases being women. Most instances—around 39 in total—belong to the 15–35 age bracket, or 65% of all cases. In every patient in our investigation, fever was the initial complaint. The temperature was between 100 and 103 °F. Furthermore, the presence of cerebral symptoms in 24 (40%) of the patients would logically support a clinical diagnosis of Falciparum infection. On the other hand, liver enlargement was seen in 12 (20%) instances.39(65%) instances The spleen requires extended exposure to malarial infection. In the current investigation, 39 instances (65%) had elevated S.G.O.T, whereas 42 cases (70%) had elevated S.G.P.T. valves greater than 100 U/L. showing clear hepatocellular damage.In 30 cases (or 50% of the total), the SGOT was above 100U/L, and in 27 cases (or 45% of the total), the SGPT was over 100U/L (Table 9). SGPT and 145 u/1 for SGPT had the greatest value at 200. Only 15 people (or 25%) experienced a little rise in serum alkaline phosphatase. 79.2 U/L was the highest figure ever observed. Histopathology of the liver revealed evidence of swollen hepatocytes in 100% of cases, malarial pigment deposition (also known as "Hemozoin") in 75% of cases, inflammatory infiltrates in 60% of cases, congestion of hepatocytes in 50% of cases, and associated centrizonal necrosis in 25% of cases. **Conclusion:** Sever In malaria, concurrent viral hepatitis or underlying chronic liver disease are frequently linked to hepatic dysfunction. Patients who have malarial hepatopathy also run a higher risk of complications. Malarial Hepatopathy should be identified early on

and vigorously treated since people who have it may do better than those who have the condition from other sources.

Keywords : Malaria, malaria-related hepatitis, and malaria-related jaundice.
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Introduction

In terms of morbidity and death, malaria ranks as one of the leading causes of disease burden in poor nations. [3-5] According to the World Malaria Report 2018, India recorded 9.5 million cases of malaria in 2017, a decrease of around 3 million cases from 2016. Only India has been able to considerably lower its disease burden, with a 24% decline between 2016 and 2017. India is no longer among the top three nations with the greatest malaria burden, and it is the only country to have done so.[8].

The goal year for the eradication of malaria has been established by India at 2030. It contributes 4% to the global burden of malaria. In a similar vein, Odisha was responsible for 40% of all malaria cases in India. In the year 2017, India unveiled its "National Strategic Plan for Malaria Elimination" (NSPEM). By 2022, 571 of India's 678 districts would no longer have malaria as a public health issue, according to this plan. As a result, "disease elimination" has become the primary goal of India's battle against malaria instead of "disease control". [1]

The most dangerous strain of the disease, which accounts for a large majority of complex malaria globally, is falciparum malaria. Over time, changes have been made to the Falciparum malaria clinical profile. Throughout the course of the illness, all main organs may be impacted. Older children and adults are more likely to get acute renal failure and malarial hepatopathy. One of the most frequent severe symptoms of falciparum malaria is malarial hepatopathy. According to various statistics, it affects between 10 and 45 percent of people, mostly adults. Jaundice is a sign of a more advanced stage of Falciparum malaria, which has higher likelihood of problems. Jaundice sufferers have a 40% greater mortality rate. [7]

The occlusion of intrahepatic blood arteries brought on by erythrocytes with parasites adhering to the endothelial cells of liver capillaries results in a shift in blood flow patterns and, ultimately, ischemia. Complications include multi-organ failure and hepatic encephalopathy happen as a result of this. In individuals with malaria hepatopathy, histopathological examinations have found hepatocyte necrosis, cholestasis, granulomatous lesions, and malarial nodules [7]. Jaundice can be brought on by hepatic involvement brought on by a number of illnesses or by severe hemolysis brought on by blood problems. Hepatocyte rupture during the first schizogony may cause cellular damage, albeit this is not always followed by a noticeable hepatic dysfunction. [8] Jaundice has been shown to occur in 2.58% of individuals with severe malaria.[12] Hemolysis brought on by severe P. falciparum infection of red blood cells causes a spike in bilirubin levels. Significant correlations between high bilirubin levels and malarial hepatopathy have also been noted in several investigations.Similar to the sequestration of the parasite-infested red blood cells, blockage of the liver capillaries results in hepatic dysfunction [6].

Depending on the severity of the condition, artesunate is either administered intravenously or orally to the majority of patients with malarial hepatopathy. The data at hand points to artesunate as being preferable to intravenous quinine for treating adults with severe malaria. [2] The aims of this investigation on patients with malaria-related hepatopathy were as follows.

Objectives:

- What is the clinical behavior of patients?
- How it affects the outcome of the disease?
- What is pattern of abnormalities in liver function tests results?
- What is the influence of treatment on jaundice and comparison of response to the treatment?
- Comparison of Outcome between jaundiced and non -jaundiced patients with falciparum malaria

Material and Method:

The MKCG Medical College and Hospital in Berhampur, an eastern coastal city in India with a high malaria incidence, was the site of this study.

With a greater malaria prevalence, the hospital serves a sizable population. A peripheral smear test for malaria was used to register patients who had a fever and had tested positive for the disease. After ruling out alternative causes of liver illness, the goal of the current investigation was to identify Hepatic involvement in malaria. The study comprised patients who were admitted to the internal medicine department of the M.K.C.G. medical college and hospital in Berhampur, Odisha. between October 2006 and October 2008. For the investigation, a manageable sample of 60 patients was collected. All subjects were given written informed consent prior to being enrolled in the trial. The first author's institution's Institutional Ethics Committee gave its permission.P-values less than 0.05 (p0.05) were regarded as significant for analysing the data, which were gathered in accordance with Performa and analysed using SPSS 22.0.

Inclusive Criteria

- All patients who presented with fever and/or icterus were initially checked for plasmodium falciparum in their peripheral smear.
- Cases with positive smear results were included in the research.

Exclusive Criteria

- Careful effort was made to rule out any individuals who had a history of drunkenness, were on other hepatotoxic medications, or had confirmed instances of infectious hepatitis.
- Younger than 15-year-olds were not allowed to participate in the research.

Results

60 cases were included, including 45 (75%) men and 15 (25%) females. The younger age group, between 15 and 34 years, accounted for more than half of cases (65%).

Table. 1.0 Age And Sex Wise Distribution Of Study Subjects

Age (Years)	Male	Female	Total (%)
15-24	16	4	20(33.33)
25-34	14	5	19(31.66)
35-44	6	6	9(15)
45-54	5	2	7(11.6)
>55	4	1	5(8.3)
Total	45(75%)	15(25%)	60(100)

Table 2: Symptoms With Which The Cases Presented

Symptom	No. of Cases	Percentage
Fatigue	26	46.66
Poor appetite	25	41.66
Nausea/vomiting	28	46.66
Upp. abd. discomfort	22	36.66
Headache	52	86.66
Fever	60	100.00
Yellow discoloration of eyes	60	100.00
Dark urine	28	46.60
G1 bleeding	4	6.66
Joint pain	20	30.00
Diarrhoea	10	16.66
Altered sensorium.	24	40.00

Table no. 2 shows that maximum proportion of patients were with fever and yellow discoloration of eyes 60(100%) followed by Headache 52(86.66%) and least number of cases reported G1 bleeding 4(6.66%).

Table. 3: Clinical Features Of The Cases

Sign	No. of cases	Percentage
Pallor	21	35.00
Icterus	60	100.00
Hypotension	9	15.00
Hepatomegaly	39	65.00
Splenomegaly	12	20.00
Altered level of consciousness	24	40.00
Meningeal signs	3	5.00
Respiratory signs	3	5.00
Brisk deep reflex	45	75.00
Extensor plantar	30	50.00

From the above table no.3 it is observed that icterus 60(100%) was present in all the cases studied. Pallor was present in most of the cases of malaria with jaundice. Hypotension even after correction of dehydration was present in 9(15%) cases. Hepatomegaly was present in 39(65%) cases and splenomegaly in 12(20%) cases. Altered level of consciousness at different levels was observed in 24(40%) cases. Meningeal signs and respiratory signs were present in few cases (around 5% cases). Divergent squint of eyes was also seen in some cases. Plantar was Extensor in 30(50%) cases.

Table 4: Level of Hemoglobin in cases of Malarial Hepatitis

Hb (gm%)	Male		Female	
	No of cases	%	No of cases	%
<6	6	15.00	4	20.00
6-8	12	30.00	6	30.00
8-10	16	40.00	7	35.00
>10	6	15.00	3	15.00
Total	40	100.00	20	100.00

Anemia was found to be common in case of malaria with jaundice. As observed out of 60 cases around 10 cases (6 male and 4 female) had hemoglobin below 6 gm % and 18 cases (12 male and 6 female) had Haemoglobin between 6-8 gm%, and 23 cases (16 male and 7 female) had Haemoglobin between 8-10 gm% and only 9 cases (6 male and 3 female) had Haemoglobin above 10 gm %. (Table no.4)

Table 5: Platelet count

Platelet counter cubic mm	Number of cases	Percentage
<1 lakh	8	13.33
1-1.5 lakh	18	30.00
>1.5 lakh	34	56.66
Total	60	100.00

A tendency for Thrombocytopenia was observed in malarial hepatitis cases as shown in the table -5 around 8 patients (13.33%) had platelet count less than 1 lakh, 18 patients (30%) had platelet count between 1-1.5 lakhs and 34 patients (56.66%) had platelet count more than 1.5 lakh. (Table no.5)

Table 6: Levels of blood urea and serum creatinine

Levels	No of cases	Percentage
Blood urea(mg/dl)		

20-39	14	23.33
40-59	18	30.00
60-79	10	16.66
80-99	10	16.66
>100	8	13.33
Total	60	100.00
Serum creatinine (mg/dl)		
<1.6	30	50.00
1.7-3.0	25	41.66
>3.0	5	8.33
Total	60	100.00

Impaired renal function in the form of elevated blood urea and Sr. creatinine levels were found in around 50% of malaria cases indicating multi organ dysfunction.

Table 7: Type of presentation

Types of presentation	No of cases	Percentage
Fever + altered sensorium+ icterus	24	40.00
Fever + icterus	36	60.00
Fever+ ARF+ icterus	5	8.33

24(40%) cases had fever, lcterus with altered sensorium; where as 36(60%) cases had fever and lcterus. Renal dysfunction was seen in 5(8.33%) cases.

Table 8: Level of serum bilirubin

Sr. Billirubin level (ma/dl)	No of cases	Percentage
<5	36	60.00
5-10	18	30.00
>10	6	10.00
Total	60	100.00
Mean ± SD	3.33±1.32	
Range	0.7 to 11 mg/dl	

From the above Table 8, we found that the maximum cases i.e.36(60%) had Sr. Billirubin below 5mg/dl, 18(30%) cases had Sr. Billirubin between 5-10 mg/di and 6(10%) cases had Billirubin more than 10 mg/dl. The highest value of Sr. Billirubin was 11 mg%. The mean Sr. Billirubin value on admission was found to be 3.33 mg/dL.

Table 9: SGOT level

SGOT(IU/L)	NO. OF CASES	PERCENTAGE
<40	21	35
41-100	9	15
>100	30	50
TOTAL	60	100
MEAN	93.7±59.4	
RANGE	15-200	

Out of all, 21(35%) cases had normal SGOT value (40 IU/L),9(15%) had SGOT value between 41-100 and 30(50%) cases had SGOT level more than 100 U/L. The

highest value recorded was 200U/L. The mean value was found to be93.7 ±59.4 IU/L.

Table 10: SGPT level

SGPT(IU/L)	NO. OF CASES	PERCENTAGE
<40	18	30
41-100	15	25
>100	27	45
TOTAL	60	100
MEAN	86.45±48.12	
RANGE	18-145	

Among all study subjects, 18 (30%) cases had normal SGPT values (40U/L), 15(25%) cases had SGPT between 41-100 and 27(45%) cases had SGPT more than 100 U/L. The mean SGPT value was 86.45 ±48.12 IU/L

Table 11: Sr. Alkaline phosphatase level

Sr. Alkaline phosphatase	No. Of cases	Percentage
<42	45	75
>42	15	25
Total	60	100
MEAN	33.47±19.18	
RANGE	10-79.2	

Serum Alkaline phosphatase was raised (>42 u/I) only in 15(25%)cases. But the rise was minimal. The highest value of Alkaline phosphatase was 79.2 U/L. 45(75%) cases had normal Alkaline phosphatase value. The mean value was recorded was 33.47 ±19.18 U/L

Table 12: Descriptive statistics of Parameters

Parameter	D1(Mean ± SD)	D8 (Mean ± SD)
Sr. Billirbuni (mg%)	3.33±1.42	0.80±0.82
SGOT	93.7±59.4	23.1±5.1
SGPT	86.45±48.12	23.1±5.12
Sr. Alkaline phosphatase	33.47±19.18	28.47±11.67

The mean level of Sr. Billirubin on 1st day in malaria cases was 3.33±3.42 mg% and on day 8 it was 0.8 0±0.82 mg%. In mean regression of Billirubin in malaria with jaundice was 2.53 mg%. The mean value of SGOT / AST was 93.7±59.4 U/L on day 1 and 23.1±5.1 on day 8. The mean regression was 36.3 U/L. The mean level of SGPT/ALT on day 1 was 86.45 and 23.1 U/L on day 8. The mean regression was 63.35 U/L. Value of Alkaline phosphatase also reduced after 8 days of treatment.

Table 13: Different value of parameter studied

Studied	Value	No.	%	MEAN±SD	Range
Sr. Protein	<5	60	100	6.32±0.35	5.9-7.0
	>5				
Sr. Albumin	3.5-5.5	60	100	3.87±0.27	3.5-4.5

	>5.5				
Sr. Globin	2-3.5	60	100	2.45±0.33	2-3
	>3.5				

Serum protein, serum Albumin and serum Globulin levels in all the cases were within normal limits. The mean value of these parameters was found to be 6.32±0.35 gm/di, 3.87±0.27 gm/di, and 2.45±0.33 gm/di respectively.

Table 14: Distribution of USG Finding:

USG findings		**No. of cases**	**percentage**
LIVER	Size enlarged	28	46.66
	Altered Echo pattern	14	23.33
	Normal architecture	60	100
GALL BLADDER	Increased wall thickness	14	23.33
	Lumen with sludge	20	33.33
	Clear lumen	40	66.66
SPLEEN	Enlargement	24	40

The USG finding in patients of malaria with jaundice showed enlarged liver size in 28 (46.66%) cases, altered Echo pattern in 14 (23.33%) cases. Normal architecture was seen in all the cases. Gall bladder wall was thickened in 14 (23.33%) cases and lumen with sludge was seen in 20 (33.33%) cases and clear lumen in 40 (66.66%) cases. Spleen enlargement was seen in 24 (40%) cases.

Table 15: Survival status of subjects:

Falciparum malaria with malarial hepatitis	**No of cases**	**Percentage**
Expired	**8**	**13.33**
Survived	**52**	**86.66**
Total	**60**	**100**

Out of 60 cases of Falciparum malaria with liver involvement, 8(13.33%) patient expired and 52(86.66%) patients survived and the morality rate was around 13%.

Discussion

From October 2006 to October 2008, researchers at the M.KC.G. Medical College and Hospital in Berhampur, Orissa, studied how the liver contributes to malaria. For the purpose of detecting and evaluating hepatic involvement and its response to antimalarial medication, sixty P. falciparum cases were chosen for observation.

Quinine dihydrochloride IV 600 mg 8 hourly for 3–4 days, followed by oral administration for a total of 7 days, was used to treat all patients. Malaria afflicted people in this research from all age groups. The most often represented age range was 21 to 30. The age incidence was found to be comparable. [13] The male to female ratio in the current research was 3:1, with 45 cases being men and 15 cases being women (Table 1). Most cases—around 65%—involve people in the 15–35 age range.

In every patient in our investigation, fever was the initial complaint. The fever might manifest in several ways, such as continuous, remittent, or intermittent. Fever might last from one to ten days. The temperature ranged from 100 to 103 degrees Fahrenheit. Additional to this, the presence of cerebral symptoms in 24 (40%) of the patients would logically support a clinical diagnosis of Falciparum infection. But Unless a thorough search for the presence of malaria parasite in peripheral blood is done to confirm the diagnosis, the presence of various degrees of icterus in all instances might mislead the diagnosis into acute fulminant Hepatitis or simple viral Hepatitis.

A limited percentage of patients (20-30%) with right upper quadrant discomfort, nausea, and vomiting, which are symptoms frequently associated with viral hepatitis, were observed. In several situations when the sensorium was disrupted, an extended plantar reaction was observed. Meningeal symptoms were hardly seen. Although splenomegaly is frequently linked to malarial infection, in the current investigation, it was only found in 12 (20%) patients, while 39 (65%) individuals had enlarged livers (Table 3). Since most of the patients in this research had a 2 week or less sickness duration and splenic enlargement was not seen in majority of the cases, extended exposure to malarial infection is necessary for the spleen to grow.

The study from Dakar found a statistically significant connection (p 0.001) between hypoglycemia and malarial hepatopathy. Of all the patients, 38% had hypoglycemia (fasting blood sugar 70 mg/dl); no controls reported having this condition. Thus, hypoglycemia is more likely to occur in individuals with malarial hepatopathy, particularly those with P. falciparum infection.[14] In a different research, S.G.O.T. levels were elevated in 39 (65%) instances, whereas S.G.P.T. levels were up in 42 (70%) cases. showing clear hepatocellular damage. Twenty-seven instances (45%) had SGPT valves with more than 100U/L, while 30 cases (50%) had SGOT over 100U/L. SGPT and 145 u/1 for SGPT had the greatest value at 200. Serum alkaline phosphatase levels were just slightly elevated in 15 (25%) of the patients. The highest measurement was 79.2 U/L. This is consistent with liver disease and may also involve an intrahepatic blockage.

In a different research, which included 121 cases of malaria, histological analysis of the liver revealed activation of mononuclear phagocyte system cells, particularly Kuppfer's cells, along with the appearance of granules of brownish-black "malarial pigent" and iron deposits. All of the participants in this research had normal blood albumin and globulin levels. Hepatic damage brought on by malaria has been documented to result in a decrease in serum albumin and an increase in serum globulin. None, however, showed abnormal serum albumin and globulin concentrations in the current investigation. [15]

They also underwent liver histopathology, which revealed evidence of enlarged hepatocytes in 100% of instances, malarial pigment deposition known as "Hemozoin" in 75% of cases, inflammatory infiltrates in 60% of cases, congestion of hepatocytes in 50% of cases, and related centrizonal necrosis in 25% of cases. On electron microscopy, it is possible to identify hepatocyte enlargement, Kupffer's cell hypertrophy, sinusoidal macrophage hypertrophy, alterations in the ER and mitochondria, the loss of microvilli, and damage to the membranes of the canaliculi. Less than 50% of patients have evidence of parasites on histology. When it occurs, centrizonal necrosis may be caused by sepsis, hypotension, or a malarial infection.

Due to unforeseen circumstances, liver histology could not be performed in our study. Sr. Bilirubin typically begins to decline 72 hours after the commencement of the medication; however, it may take longer in individuals who also have renal problems. As seen by the significant decline in serum billirubin and enzyme levels, liver function dramatically improved following the start of anti-malarial medication. This shows that the degenerative alterations taking place in the liver are entirely reversible.

Conclusion

From October 2006 to October 2008, the study was carried out in the M.K.C.G. Medical College, Berhampur, Department of Medicine. The presence of liver damage was thoroughly examined in 60 patients of P. falciparum infection that had no history of consuming alcohol or hepatotoxic medications and were HBsAg and HCV negative. All of them received the regular anti-malarial treatment. Changes in liver function were evaluated in addition to clinical response.

In twenty-four patients (40%) the symptoms of fever, icterus, and altered sensorium were evident. 36 instances (15%) had fever and icterus, while 5 cases (8.33%) had fever, icterus, and ARF.The patients with AII all exhibited fever, rigour, and chills. In 28 (46.6%) of the sixty instances, nausea and vomiting were observed. Only 12 patients exhibited splenomegaly, but all cases had icterus, hepatomegaly, and icterus. 39 instances (65%) had increased SGOT levels, whereas 42 cases (70%) had elevated SGPT values. Less than 200 U/L of serum enzymes were present. In all of the patients examined, the serum protein level and albumin-to-globulin ratio were within normal bounds.

Increased liver enzymes like the SGPT value were shown to be correlated with a higher parasite count. The majority of them have conjugated hyperbilirubinemia and elevated SGPT and SGOT levels, both of which indicate hepatocellular injury. Clinically and biochemically, antimalarial therapy was effective in all instances. Most liver functions were back to normal by the eighth day. very five of the instances of acute jaundice resulted in mild icterus that lasted very briefly after the eighth day.

In the context of malaria, the presence of elevated liver enzyme levels with nearly normal coagulation indicators implies the existence of malarial hepatopathy. Malaria-related severe hepatic dysfunction is typically accompanied by concurrent viral hepatitis or underlying chronic liver disease. Although patients with malarial hepatopathy are more likely to experience complications, they nevertheless have a better prognosis than those with other types of liver failure.

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