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# FREQUENCY OF DERANGED LFT IN PATIENTS WITH FALCIPARUM MALARIA, AT BOLAN MEDICAL COLLEGE AND TEACHING HOSPITALS

***Dr. Abdul Malik Yasinzai, Dr. Qaiser Iqbal, Dr. Muhammad Umar Marri, Dr. Huma Naeem Tareen, Dr. Maqbool Ahmed, Dr. Mohammad Usman and Mir Zaman Kasi**

Classified Surgeon Surgical Department, Ex Combined Military Hospital, Mangla.

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***Corresponding Author**
**Dr. Abdul Malik Yasinzai**
Classified Surgeon Surgical Department, Ex Combined Military Hospital, Mangla.

## ABSTRACT

**Introduction:** According to world health organization (WHO) there has been increasing number of reports of malarial hepatopathy, from Asian countries. The majority of the cases have either isolated infection with P. falciparum or a mixed infection with both P. falciparum and P. vivax. So this study will provides us the latest and updated information regarding frequency of deranged LFT in patients with falciparum malaria. **Objective:** To determine frequency of deranged LFT in patients with falciparum malaria. **Setting and place of study:** Bolan Medical College and Teaching Hospital, Quetta. Cross sectional from 13/2/2017 to 13/2/2018. **Materials And Methods**: In this study a total of 155 patients were observed. Management was done as per standard guidelines with Quinine Sulphate (IV/Oral) 20 mg/kg body weight stat dose followed by 10 mg/kg body weight in three divided doses for seven days. Outcome variable i.e. derangement in LFTs was assessed as operational definition. **Results:** mean age was 33 years ± 13.18. Fifty six percent patients were male while 44% patients were female. More over 12% patients had derangement in LFT while 88% patients didn't had derangement in LFT. **Conclusion**: Our study concludes that the frequency of deranged LFT was 12% in patients with falciparum malaria.

**KEYWORDS**: deranged LFT, falciparum malaria, Quinine Sulphate.

## INTRODUCTION

According to world health organization (WHO) there has been increasing number of reports of malarial hepatopathy, from Asian countries. The majority of the cases have either isolated

infection with P. falciparum or a mixed infection with both P. falciparum and P. vivax. The extent of liver involvement varies from a minimal abnormality in liver function tests to hepatic encephalopathy.[1]

One study conducted in Saudi Arabia has mentioned various derangements in LFTs. Serum alanine amino transferase (ALT) level was more than 3 times of normal level in 11.4% and in 23% of the patients, Serum bilirubin was >3mg/dl.[2]

Recently, the role of apoptosis and oxidative stress in hepatic damage due to malarial infection has been highlighted. Apoptosis in the hepatocyte has been demonstrated by TUNEL assay and Capsase-3 activation. There is significant downregulation of Bcl-2 and upregulation of Bax expression (RT-PCR and confocal microscopy).[3]

It has been proposed that malarial infection in the liver induces generation of hydroxyl radical (OH) which triggers oxidative stress-induced mitochondrial pathway.[4] A host of factors is responsible for the hepatic dysfunction in falciparum malarial infection. This does not appear to be due to direct inflammation of hepatocytes but due to failure of bilirubin excretion due to heavy parasitaemia, endotoxaemia, ischemia, acidosis or a combination of some or all of these factors.[5]

In addition, liver function abnormalities have been reported with administration of mefloquine, chloroguanide, amodiaquine and pyrimethaminesulfadoxine combination.[6]

Since the list of differential diagnoses is long, appropriate tests should be done to rule them out. Liver function tests and ultrasonography are important but liver biopsy is not indicated. Prolonged unexplained jaundice should prompt one to undertake liver biopsy. Quinine is the drug of choice for management of severe falciparum malaria, however, in endemic areas, where resistance is suspected, a combination therapy may be better than single drug.[7]

The hepatitis usually resolves on its own after the subsidence of fever and clearing of the parasite from the body. Since these patients are more prone to complications a careful watch is needed to identify the early signs of pulmonary edema, respiratory failure or sepsis.[6] Serum bilirubin normally starts receding by 72h of starting treatment; however it may be delayed in patients having coexisting renal dysfunction.[7] In one study the frequency of deranged LFT in patients with falciparum malaria was found to be 11.3%.[3,7]

In this study, Patients with hepatocellular dysfunction in falciparum malaria are more prone to develop complications, but have a favorable outcome if hepatic involvement is recognized early and managed properly. It is important to meticulously look for derangement in LFTs as a marker of hepatic dysfunction in patients with falciparum malaria and manage it aggressively.

## MATERIALS AND METHODS

**Data Collection Procedure:** The data collection was started after an approval from the CPSP. After taking ethical committee approval and explaining the procedure informed constant was taken. Patients with biochemical evidence of malaria were recruited from department of medicine Sandeman Provincial hospital, Quetta on the basis of inclusion/exclusion criteria. Patients were interviewed regarding their basic demographics. Liver function tests were done on same day.

Management was done as per standard guidelines with Quinine Sulphate (IV/Oral) 20 mg/kg body weight stat dose followed by 10 mg/kg body weight in three divided doses for seven days. Unstable and patients with vomiting was treated by IV infusion. On day three, almost all patients were also receive 3 Sulphadoxine+Pyrimethmine combination tablets stat. Outcome variable i-e derangement in LFTs was assessed as operational definition. Results were noted in proforma.

**Statistical Analysis:** Data was analyzed using software of Statistical package of Social Sciences (SPSS version 20). Mean + SD was calculated for continuous variable of age, serum ALT level, serum bilirubin level and duration of disease. Results on categorical variables of gender, anemia, thrombocytopenia, leucopenia and outcome variable i-e deranged LFTs (ALT and bilirubin). Stratification of age, gender, anemia, thrombocytopenia, leucopenia was done to see their effect on outcome variable. Assuming the P value of $<0.05$ as significant, Chi-Square was.

## RESULTS

In this study age distribution was analyzed as 45(29%) patients in the age range of 18-25 years, 48(31%) patients of age range of 26-35 years, 33(21%) patients in the age range of 36-45 years, 15(10%) patients in the age range of 46-55 years and 14(9%) patients in the age range of 56-65 years. Mean age was 33 years ± 13.18. (table no 1).

Gender distribution was analyzed as 87(56%) patients were male and 68(44%) patients were female. (table no 2).

Duration of disease was analyzed as 110(71%) patients had duration of disease <4 days while 45(29%) patients had duration of disease >4 days. mean duration of disease was 4 days with SD ± 2.892. (table no 3) mean serum ALT level was 140 mg/dl with SD ± 15.461 while mean serum bilirubin level was 2 with SD ± 1.08.

Status of anemia was analyzed as 116(75%) patients were anemic while 39(25%) patients were non anemic. (table no 4).

Status of thrombocytopenia was analyzed as 141(91%) patients had thrombocytopenia while 14(9%) patients didn't had thrombocytopenia. (table no 5).

Status of leucopenia was analyzed as 8(5%) patients had leucopenia while 147(95%) patients didn't had leucopenia. (table no 6).

Frequency of derangement in LFT was analyzed as 19(12%) patients had derangement in LFT while 136(88%) patients didn't had derangement in LFT. (table no 7).

Stratification of derangement in LFT with respect to age, gender, duration of disease, anemia, thrombocytopenia, leucopenia is given in table no 8,9,10,11,12,13.

**Table 1: Age Distribution (n=155).**

| AGE | FREQUENCY | PERCENTAGE |
|---|---|---|
| **18-25 years** | 45 | 29% |
| **26-35 years** | 48 | 31% |
| **36-45 years** | 33 | 21% |
| **46-55 years** | 15 | 10% |
| **55-60 years** | 14 | 9% |
| **Total** | **155** | **100%** |

Mean age was 33 years with SD ± 13.18

**Table 2: Gender Distribution (n=155).**

| GENDER | FREQUENCY | PERCENTAGE |
|---|---|---|
| **Male** | 87 | 56% |
| **Female** | 68 | 44% |
| **Total** | **155** | **100%** |

**Table 3: Duration of Disease (n=155).**

| DURATION | FREQUENCY | PERCENTAGE |
|---|---|---|
| **< 4 days** | 110 | 71% |
| **≥ 4 days** | 45 | 29% |
| **Total** | **155** | **100%** |

Mean duration was 4 days with SD ± 2.892

**Table 4: Status of Anemia.**

| ANEMIA | FREQUENCY | PERCENTAGE |
|---|---|---|
| **Yes** | 116 | 75% |
| **No** | 39 | 25% |
| **Total** | **155** | **100%** |

**Table 5: Status of Thrombocytopenia**

| THROMBOCYTOPENIA | FREQUENCY | PERCENTAGE |
|---|---|---|
| **Yes** | 141 | 91% |
| **No** | 14 | 9% |
| **Total** | **155** | **100%** |

**Table 6: Status of Leucopenia**

| LEUCOPENIA | FREQUENCY | PERCENTAGE |
|---|---|---|
| **Yes** | 8 | 5% |
| **No** | 147 | 95% |
| **Total** | **155** | **100%** |

**Table 7: Derangement in LFT (Alt and Bilirubin)**

| DERANGEMENT IN LFT | FREQUENCY | PERCENTAGE |
|---|---|---|
| **Yes** | 19 | 12% |
| **No** | 136 | 88% |
| **Total** | **155** | **100%** |

**Table 8: Stratification of derangement in lft w.r.t age distribution.**

| Derangement IN LFT | 18-25 years | 26-35 years | 36-45 years | 46-55 years | 55-60 years | Total |
|---|---|---|---|---|---|---|
| **Yes** | 6 | 6 | 4 | 2 | 1 | 19 |
| **No** | 39 | 42 | 29 | 13 | 13 | 136 |
| **Total** | **45** | **48** | **33** | **15** | **14** | **155** |

Chi square test was applied in which P value was 0.9817

**Table 9: Stratification of derangement in lft w.r.t gender distribution.**

| DERANGEMENT IN LFT | Male | Female | Total |
|---|---|---|---|
| **Yes** | 11 | 8 | 19 |
| **No** | 76 | 60 | 136 |
| **Total** | **87** | **68** | **155** |

Chi square test was applied in which P value was 0.8684

**Table 10: Stratification of derangement in lft w.r.t duration of disease.**

| DERANGEMENT IN LFT | < 4 days | ≥ 4 days | Total |
|---|---|---|---|
| **Yes** | 13 | 6 | 19 |
| **No** | 97 | 39 | 136 |
| **Total** | **110** | **45** | **155** |

Chi square test was applied in which P value was 0.7940

**Table 11: Stratification of derangement in lft w.r.t anemia.**

| DERANGEMENT IN LFT | Yes | No | Total |
|---|---|---|---|
| **Yes** | 14 | 5 | 19 |
| **No** | 102 | 34 | 136 |
| **Total** | **116** | **39** | **155** |

Chi square test was applied in which P value was 0.9014

**Table 12: Stratification of derangement in lft w.r.t thrombocytopenia.**

| DERANGEMENT IN LFT | Yes | No | Total |
|---|---|---|---|
| **Yes** | 17 | 2 | 19 |
| **No** | 124 | 12 | 136 |
| **Total** | **141** | **14** | **155** |

Chi square test was applied in which P value was 0.8083

**Table 13: Stratification of Derangement in Lft W.R.T Leucopenia.**

| DERANGEMENT IN LFT | Yes | No | Total |
|---|---|---|---|
| **Yes** | 2 | 17 | 19 |
| **No** | 6 | 130 | 136 |
| **Total** | **8** | **147** | **155** |

Chi square test was applied in which P value was 0.2591

## DISCUSSION

According to world health organization (WHO) there has been increasing number of reports of malarial hepatopathy, from Asian countries. The majority of the cases have either isolated infection with P. falciparum or a mixed infection with both P. falciparum and P. vivax. The extent of liver involvement varies from a minimal abnormality in liver function tests to hepatic encephalopathy.[1]

Our study shows that mean age was 33 years ± 13.18. Fifty six percent patients were male while 44% patients were female. Mean duration of disease was 4 days with SD ± 2.892.

More over 12% patients had derangement in LFT while 88% patients didn't have derangement in LFT.

Similar results were observed in another study conducted by Abro AH et al,[8] in which On clinical examination, 23% patients were found to be jaundiced. Serum alanine amino transferase (ALT) level was above the reference range in 67.6%, but in only 11.4%, ALT was more than 3 times of normal level. Serum bilirubin was found to be higher than normal level in 81%, however, only in 23% of the patients, Serum bilirubin was >3mg/dl. Predominantly conjugated hyperbilirubinemia was observed in patients with high ALT. There was no significant change in serum albumin and prothrombin time. In comparison to normal bilirubin level, the patient with bilirubin >3mg/dl had high frequency of raised ALT 87.5% vs. 45% (p<.0001), thrombocytopenia 91.6% vs. 65% (p<.01), anemia 70.8% vs. 25% (p<.05) and renal impairment 50% vs. 20% (p>.05). Overall, 5 (4.7%) patients died and mortality rate was high among the patients with bilirubin level>3mg/dl than with normal bilirubin level 4 (16.6%) vs 1 (5%).

Similar results were observed in another study conducted by Woodford J et al[9] in which among 861 cases with LFT evaluated, an elevated bilirubin level was identified in 12.4% (*N* = 107/861), whereas elevated alanine transaminase (ALT) and aspartate transaminase levels were observed in 15.1% (*N* = 130/861) and 14.8% (*N* = 127/861) of cases, respectively. All peak bilirubin results occurred in the early period, whereas ALT elevations were biphasic, with elevations in the early and delayed periods, with 35.4% (*N* = 46/130) of cases delayed.

In the study series of Gopinathan VP et al, serum bilirubin 2 mg/dL was seen in 4.43% of patients.[10] In the study series of Bajiya HN et al serum bilirubin >2.5 mg/dL was seen in 30.8% and in the study series of Chawla LS et al serum bilirubin > 2 mg/dL was seen in 100% of patients.[11,12] In the present study serum bilirubin level higher than normal found in 66% of cases however, only 28% of cases had serum bilirubin >3 mg/dL.

In the study series of Nityanand et al,[13] and Chawla et al,[12] raised ALT values were seen in 100% and 21.11% of patients respectively. In the present study raised ALT values above the reference range are seen in 78% of patients, but ALT values 3 times more than normal are seen in 22% of patients.

In the study of Nityanand et al[13] mortality was 37.5% of these 31.25% died due to renal involvement and 6.25% due to hepatic coma. Bajiya HN et al,[14] revealed mortality rate in 33.5% patients.6 In the study of Dash SC10 et al,[15,16,17,18] mortality rate was 22.2% due to cerebral malaria and multi-organ dysfunction, Deb T et al showed mortality rate of 14.3% due to cerebral malaria.

## CONCLUSION

Our study concludes that the frequency of deranged LFT was 12% in patients with falciparum malaria.

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