

## Original Research Article

# Observation on relationship of hepatic and renal dysfunction with haemorrhological parameters in plasmodium falciparum malaria in Kosi region, Bihar, India

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### ABSTRACT

**Background:** Malaria contribute to be one of the major public health problem in around 1.5 million contribute per year, of which about 52% due to *Plasmodium falciparum*. The study was designed to assess hepatic and renal dysfunction in plasmodium falciparum malaria, and evaluate if such abnormalities had any bearing with the haemorrhological dysfunction.

**Methods:** Group A comprising 30 cases of plasmodium falciparum positive cases with jaundice or renal failure or both and Group B comprising 30 cases of falciparum malaria and have no complication. Laboratory investigation was done for liver and renal function test, complete blood count and coagulation profile. The data collected was analysed to inter-correlate parameters of hepatic, renal and haemorrhological dysfunction.

**Results:** Fever was the predominant feature in our study, present in 100% patient followed by chill and rigors which was present in 90% cases of both groups. Hepatomegaly was present in 53.33% cases in group A and 16.67% in group B, whereas splenomegaly was present in 43.33% cases in group A and 26.67% in group B. Most common complication in group A was jaundice present in 100% cases followed by renal failure present in 53.33% cases. Overt bleeding was present in only 3.33% cases with complicated falciparum malaria. Anemia was present in 73.33% cases of group A and 50% cases in group B. Thrombocytopenia was present in 50% patient in group A and 23.33% in group B. Bleeding time, clotting time, PT with INR, APTT, FDP and LDH was much higher in group A than group B in our study. The biochemical parameters (serum urea, creatinine, bilirubin, AST, ALT, ALP) in both groups differed significantly. In group A Haemoglobin and platelet count significantly negatively correlated with hepatic and renal parameters where as FDP and LDH significantly positively correlated with all the hepatic and renal parameters. In group B the correlation between hematological and biochemical (hepatic and renal) parameters was not found to be statistically significant.

**Conclusions:** Patients of complicated falciparum malaria have significant subclinical haemorrhological disorders even if they do not manifest as clinically overt DIC.

**Keywords:** APTT, DIC, FDP, Haemorrhological, Hepatic, LDH, Plasmodium falciparum, PT, Renal

## INTRODUCTION

Malaria contribute to be one of the major public health problem in around 1.5 million contribute per year, of which about 52% due to *Plasmodium falciparum*.<sup>1</sup> 0.5-2% *Plasmodium falciparum* case turn into complicated malaria, of which up to 50% fatal if timely treatment is not given. Factors are responsible for jaundice in malaria are multiple including intravascular haemolysis of parasitized erythrocytes, liver dysfunction, associated septicemia. Hepatic dysfunction results from cytoadherence, rosetting and sequestration of erythrocyte containing mature form of *Plasmodium falciparum* in deep vascular bed. These cases are more likely to have acute renal failure and their prognosis is bad.<sup>2</sup>

Renal involvement in *Plasmodium falciparum* malaria may vary from slight proteinuria to overt acute renal failure. Malarial acute renal failure is multi factorial in origin. It is either due to direct effect of parasite on RBC or due to non-specific effect of infection. Direct effect of parasite occur after it attaches to specific receptor site on cell membrane. Its maturation inside the RBC leads to alteration in cell membrane and formation of election dense protrusions or knobs on its surface.<sup>2</sup>

Number of knob increase as the parasite is mature. This reduces the deformity of the RBC and enhances the adherence of RBC with endothelial cell. This lead to occlusion of microcirculation in kidney leading to acute tubular necrosis. The non-specific effects of infection cause several pathophysiological alterations leading to renal ischemia and acute tubular necrosis.<sup>2</sup>

The cause of thrombocytopenia in malaria is not completely understood. Consumption of platelet as a part of disseminated intravascular coagulation has been suggested as possible mechanism<sup>3</sup>. Excessive, removal of normal or immunologically deranged platelet by hypertrophied reticulo-endothelial system could be an alternative explanation.

Studies on hepatic and renal dysfunction in plasmodium falciparum malaria are plenty, but there is a paucity of studies correlating haemorrhological abnormalities with hepatic and renal dysfunction in plasmodium falciparum malaria. Aim of the study was to show the hepatic dysfunction in *Plasmodium falciparum* malaria, to show the renal dysfunction in *Plasmodium falciparum* malaria and to evaluate if such hepato-renal dysfunction in falciparum malaria had any bearing with the haemorrhological dysfunction.

## METHODS

Group A comprising 30 cases of plasmodium falciparum positive with jaundice or renal failure or both. Group B Comprising 30 falciparum malaria and have no complication. Detailed history of clinical features had

taken with clinically overt bleeding diathesis and hepatosplenomegaly. Laboratory investigation was done for liver and renal function test, complete blood count and coagulation profile. The data collected was analysed to inter-correlate parameters of hepatic, renal and haemorrhological dysfunction.

## Investigation

Slide test for parasite, immunochromatography, routine haemogram, random blood sugar, prothrombin time (PT) with INR, bleeding time (BT), clotting time (CT), activated thromboplastin time (aPTT), FDP, liver function test (LFT), serum LDH, serum urea, creatinine, serum sodium, potassium, platelet count, peripheral blood smear.

Exclusion criteria of the study were the patients having past history of alcoholism, jaundice, chronic renal failure, bleeding diathesis or coagulopathy. Patients do intake of certain drugs antihypertensive, antidiabetic, antitubercular, thyroid dysfunction, respiratory dysfunction, connective tissue disorder, cardiac disorder, CNS disorder.

## RESULTS

The age of the patients studied ranged between 18 to 75 years. Maximum numbers of patients were in the age group 20-30 years.

In this study hepatomegaly was find in 53.33% of the cases and splenomegaly in 43.33% of patients in complicated falciparum malaria. In our study overt bleeding was a rare manifestation; observe only 1 cases of complicated falciparum malaria and no cases observe in uncomplicated falciparum malaria.

**Table 1: Incidence of clinical symptoms.**

Symptoms	Group A number and percentage	Group B number and percentage
Fever	30 (100%)	30 (100%)
Chill and rigors	27 (90%)	27 (90%)
Headache / Myalgia	24 (80%)	16 (53.33%)
Bleeding manifestation/overt bleeding	1 (3.33%)	0 (0%)
Respiratory distress	5 (16.67%)	0 (0%)
Convulsions	2 (6.67%)	0 (0%)
Disorientation	11 (36.67%)	0 (0%)
Anemia / Pallor	22 (73.33%)	15 (50%)
Icterus	30 (100%)	0 (0%)
Oliguria	16 (53.33%)	0 (0%)
Hepatomegaly	16 (53.33%)	5 (16.67%)
Splenomegaly	13 (43.33%)	8 (26.67%)

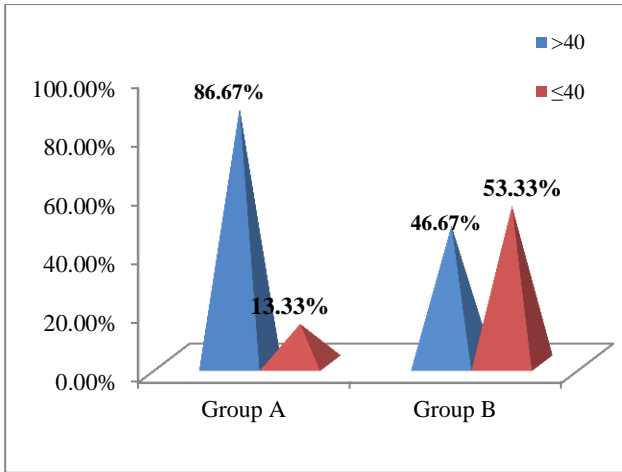


Figure 1: Serum urea value.

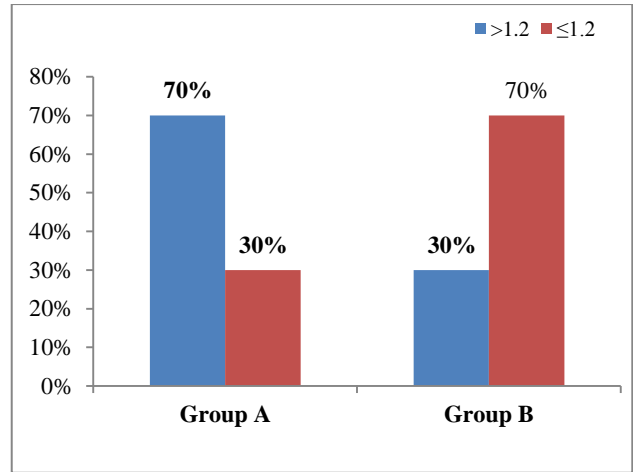


Figure 2: Serum creatinine value.

Table 2: Liver function parameters value.

Parameter	Value	Group A		Group B	
		No of patients	Percentage	No of patients	Percentage
Serum bilirubin	> 1.2 mg/dl	30	100%	11	36.67%
	≤ 1.2 mg/dl	0	0%	19	63.33%
AST	> 48 mg/dl	30	100%	12	40%
	≤ 48 mg/dl	0	0%	18	60%
ALT	> 55 mg/dl	28	93.33%	3	10%
	≤ 55 mg/dl	2	06.67%	27	90%
ALP	> 115 mg/dl	23	76.67%	14	46.67%
	≤ 115 mg/dl	07	23.33%	16	53.33%

Table 3: Decrease or normal haemorrhheological : parameters in Group A and Group B.

Parameter	Group A				Group B			
	Decrease		Normal		Decrease		Normal	
	No of patients	Percentage	No of patients	Percentage	No of patients	Percentage	No of patients	Percentage
Hb% (gm/dl)	22	73.33%	8	26.67%	15	50%	15	50%
Platelet count/mm <sup>3</sup>	15	50%	15	50%	7	23.33%	23	76.67%

Table 4: Increase or normal haemorrhheological parameters in Group A and Group B.

Parameter	Group A				Group B			
	Increase		Normal		Increase		Normal	
	No of patients	Percentage	No of patients	Percentage	No of patients	Percentage	No of patients	Percentage
Reticulocyte count (%)	12	40%	18	60%	0	0%	30	100%
BT (Sec)	8	27.33%	22	72.67%	3	10%	27	90%
CT (Sec)	15	50%	15	50%	8	26.67%	22	73.33%
PT (Sec)	15	50%	15	50%	10	33.33%	20	66.67%
INR (ratio)	13	43.33%	17	62.67%	7	23.33%	23	76.67%
aPTT (Sec)	16	53.33%	14	46.67%	8	26.67%	22	73.33%
FDP (ng/ml)	13	43.33%	17	56.67%	4	13.33%	26	86.67%
S. LDH (IU/ml)	22	73.33%	8	26.67%	17	56.67%	13	43.33%

**Table 5: Correlation between hepato renal and haemorrhological parameters in Group A.**

Parameter		Urea	Creatinine	Bilirubin	AST	ALT	ALP
HB%	r	-0.584	-0.5942	-0.5865	-0.4919	-0.6779	-0.7408
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Platelet	r	-0.589	-0.7327	-0.6538	-0.5712	-0.4992	-0.6898
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Reticulocyte	r	-2064	-3738	-0.4492	-0.285	-0.2858	-0.448
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
BT	r	0.7495	0.7657	0.7006	0.7084	0.5213	0.7344
	p	>0.05	<0.05	<0.05	>0.05	>0.05	>0.05
CT	r	0.5258	0.6811	0.5983	0.5471	0.571	0.6871
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
PT	r	0.4467	0.4554	0.5294	0.4732	0.5744	0.5301
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
INR	r	0.4273	0.4636	0.5257	0.4666	0.5856	0.5501
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
aPTT	r	0.6657	0.7679	0.7598	0.7187	0.6346	0.7514
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
FDP	r	0.7389	0.7655	0.7046	0.7127	0.5975	0.7799
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
S.LDH	r	0.7098	0.8262	0.7131	0.6747	0.5996	0.748
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

**Table 6: Correlation between hepato renal and haemorrhological parameters in Group B.**

Parameter		Urea	Creatinine	Bilirubin	AST	ALT	ALP
HB%	r	0.2254	0.0148	-0.015	-0.4672	-0.2279	-0.4672
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Platelet	r	0.0612	0.1027	-0.2347	0.4936	0.4501	0.938
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Reticulocyte	r	-0.0519	0.1227	-0.0034	0.1356	0.1855	0.287
	p	<0.05	>0.05	>0.05	<0.05	<0.05	<0.05
BT	r	-0.0228	0.0274	0.1994	0.0711	0.5223	0.4862
	p	<0.05	<0.05	<0.05	<0.05	<0.05	>0.05
CT	r	-0.017	-0.0992	0.0292	0.4128	0.3671	0.5669
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
PT	r	0.0732	0.1467	0.1739	0.3044	0.489	0.403
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
INR	r	0.0894	0.1764	0.1706	0.2954	0.4804	0.394
	p	<0.05	>0.05	<0.05	<0.05	<0.05	<0.05
aPTT	r	-0.0317	-0.0317	0.0655	0.5242	0.2481	0.3392
	p	<0.05	<0.05	<0.05	<0.05	>0.05	<0.05
FDP	r	0.97	-0.185	-0.0262	0.4193	0.3289	0.27
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
S.LDH	r	-0.0522	0.0754	-0.0156	0.6266	0.4224	0.7505
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Renal derangement was observed in 70%-80% cases of complicated falciparum malaria in our study. Blood urea was raised in 86.67% cases and serum creatinine was raised in 70% cases in complicated falciparum malaria whereas in uncomplicated malaria blood urea raised in only 46.67% cases and serum creatinine raised in 30%

cases. Also maximum level of blood urea and serum creatinine were much higher (maximum blood urea up to 240mg/dl and serum creatinine 11.2 mg/dl) in complicated falciparum malaria whereas the maximum rise of blood urea was up to 70 mg/dl and serum creatinine was only 1.8 mg/dl in uncomplicated malaria.

Patients in group A serum bilirubin was raised in 100% cases, serum AST, ALT, ALP were raised in 100%, 93.33% and 76.67% of cases respectively. In group B in our study serum bilirubin, AST, ALT, ALP were raised in 33.33%, 40%, 10%, 46.675% cases respectively. Maximum level of bilirubin was 25 mg/dl in group A where as in group B 2.2 mg/dl.

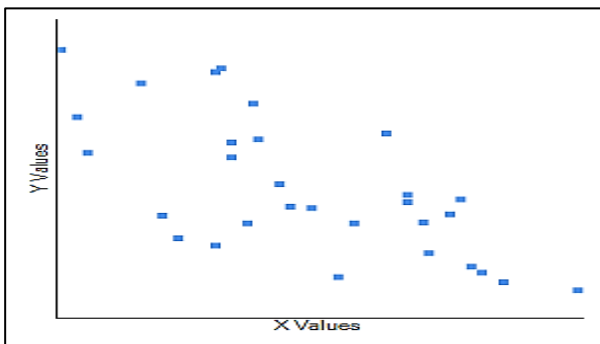
Assessment of the haemorrhological parameters had shown that in group A, 73.33% had anemia, majority were normocytic normochromic, total platelet count were reduced in 50% cases, reticulocytosis was observed

in 40% cases, clotting time was prolonged in 50% with prolongation of PT 50% and INR 43.33% cases respectively. aPTT was prolonged in 53.33% cases while positive serum FDP was found in 43.33% cases. Serum LDH was raised in 73.33% cases.

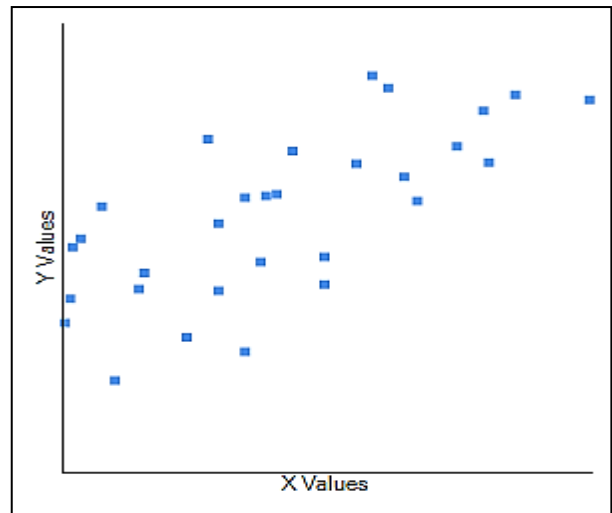
Comparison of similar parameters studied in group B revealed that, anemia was present in 50% (normocytic normochromic) cases, thrombocytopenia in 23.33%, prolonged Clotting Time 26.67%, PT prolongation 33.33%, prolonged aPTT 26.67, FDP positive in 13.33% and raised serum LDH in 56.67% cases respectively.

**Table 7: Correlation between hepatic and renal parameters.**

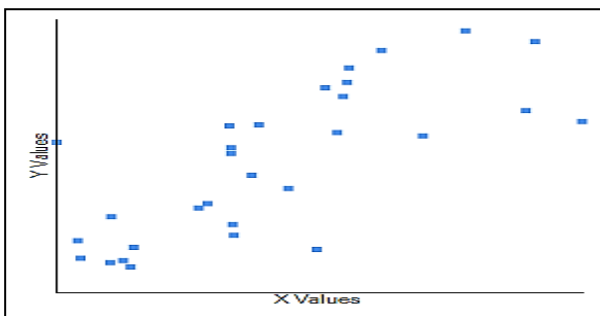
Group A			Group B				
Para Meter		Urea	Creatinine	Parameter	Urea	Creatinine	
Bilirubin	r	0.4537	0.6299	Bilirubin	r	-0.2602	0.1408
	p	<0.05	<0.05		p	<0.05	<0.05
AST	r	0.6632	0.5676	AST	r	-0.3499	-0.0744
	p	<0.05	<0.05		p	>0.05	<0.05
ALT	r	0.4373	0.6704	ALT	r	0.0771	0.2123
	p	<0.05	<0.05		p	>0.05	<0.05
ALP	r	0.507	0.7316	ALP	r	0.0612	0.1027
	p	<0.05	<0.05		p	<0.05	<0.05



**Figure 3: Pearson correlation coefficient (a)-In group A Hb negatively correlated with serum ALT (r= -0.6779).**



**Figure 5: In group A Serum LDH positively correlated with serum bilirubin (r = +0.7131).**



**Figure 4: In group A Serum FDP positively correlate with serum urea (r = +0.7389).**

**DISCUSSION**

The age of the patients studied ranged between 18 to 75 years. Maximum numbers of patients were in the age group 20-30 years. All cases of complicated falciparum malaria included in the study had fever and icterus followed by chill and rigors, headache and myalgia in

maximum cases. Study conducted by Mishra DP et al observe the same clinical features.<sup>4</sup>

Table 1 showing hepatomegaly was found in 53.33% of the cases and splenomegaly in 43.33% of patients in complicated falciparum malaria. Prasad VS et al in his study observe hepatomegaly in 52% cases and splenomegaly in 44% cases.<sup>5</sup> In our study overt bleeding was a rare manifestation, observe only 1 (3.33%) cases of complicated falciparum malaria and no cases observe in uncomplicated falciparum malaria. Balaraju G et al also observe overt bleeding in only 3.33% of cases.<sup>6</sup>

Renal derangement was observed in 70%-80% cases of complicated falciparum malaria in our study. Blood urea was raised in 86.67% cases maximum up to 240 mg/dl and serum creatinine was raised in 70% cases up to 11.2 mg/dl where as in uncomplicated malaria blood urea raised in only 46.67% cases upto 70 mg/dl and serum creatinine raised in 30% cases up to 1.8mg/dl. D P Misra et al also observed raised serum creatinine in 57% cases of complicated falciparum malaria.<sup>4</sup>

Jaundice is a common presentation of falciparum malaria.<sup>7</sup> In group A serum bilirubin was raised in 100% cases, serum AST, ALT, ALP were raised in 100%, 93.33% and 76.67% cases respectively. In the studies of Misra DP et al, had the similar finding. In group B in our study serum bilirubin, AST, ALT, ALP were raised in 33.33%, 40%, 10%, 46.67% cases respectively.<sup>4</sup> Maximum level of bilirubin were 25 mg/dl in group A where as in group B 2.2 mg/dl. Jaundice in falciparum malaria is due to malarial hepatitis, intravascular hemolysis and disseminated intravascular coagulation.<sup>8</sup>

In group A, 73.33% had anemia, majority were normocytic normochromic, platelet count were reduced in 50% cases, positive serum FDP was found in 43.33% cases. Serum LDH was raised in 73.33% cases. In group B anemia was present in 50% cases, thrombocytopenia in 23.33% cases, FDP positive in 13.33% and raised serum LDH in 56.67% cases. The values of reticulocyte count, PT, aPTT, serum FDP and serum LDH differed in the two groups to a degree of statistical significant ( $p < 0.05$ ). Our observation regarding such haemorrhological abnormalities in subjects with falciparum malaria having hepatopathy and ARF are comparable with publications by other investigators on this subject, like Misra DP et al and Prasad VS et al.<sup>4,5,7</sup> Thrombocytopenia may be a cause of marked bleeding diathesis in falciparum malaria.

In group A only 1 patient was present with bleeding manifestation (petechiae, purpura in all over body) but raised BT, CT, PT with INR, aPTT and serum FDP most patients than group B indicate subclinical DIC and raised bilirubin, decreased haemoglobin and raised serum LDH indicate subclinical intra vascular haemorrhage in patient with hepato renal dysfunction.

In group A of our studies haemoglobin was negatively correlate with serum urea ( $r = -0.584$ ;  $p < 0.05$ ), serum creatinine ( $r = -0.5942$ ;  $p < 0.05$ ), serum bilirubin ( $r = -0.5865$ ;  $p < 0.05$ ), AST ( $r = -0.4919$ ;  $p < 0.05$ ), ALT ( $r = -0.6779$ ;  $p < 0.05$ ), ALP ( $r = -0.7408$ ;  $p < 0.05$ ). This correlation is found in studies of Misra DP et al, Prasad S et al and Balaraju et al.<sup>5,6</sup> Platelet negatively correlate with serum urea ( $r = -0.589$ ;  $p < 0.05$ ), serum creatinine ( $r = -0.7327$ ;  $p < 0.05$ ), bilirubin ( $r = -0.6538$ ;  $p < 0.05$ ), AST ( $r = -0.5712$ ;  $p < 0.05$ ), ALT ( $r = -0.4992$ ;  $p < 0.05$ ), ALP ( $r = -0.6898$ ;  $p < 0.05$ ). This correlation is found in studies of Balaraju G et al, Prasad VS et al.<sup>5,6</sup> BT positively correlate with serum urea, serum creatinine, bilirubin, AST, ALT, ALP similarly correlate with the studies of Balaraju G et al.<sup>6</sup>

CT positively correlates with all renal and hepatic parameters. PT with INR positively correlates with all renal and hepatic parameters. This finding similar with the studies of Balaraju G et al, Prasad VS et al. aPTT positively correlated with serum urea ( $r = +0.6657$ ;  $p < 0.05$ ), serum creatinine ( $r = +0.7679$ ;  $p < 0.05$ ), serum bilirubin ( $r = +0.7598$ ;  $p < 0.05$ ), AST ( $r = +0.7187$ ;  $p < 0.05$ ), ALT ( $r = +0.6346$ ;  $p < 0.05$ ), ALP ( $r = +0.7514$ ;  $p < 0.05$ ). The studies of Misra DP et al, Prasad VS et al had the similar correlation. Serum FDP correlate positively with serum urea ( $r = +0.7389$ ;  $p < 0.05$ ), serum creatinine ( $r = +0.7655$ ;  $p < 0.05$ ), bilirubin ( $r = +0.7046$ ;  $p < 0.05$ ), AST ( $r = +0.7127$ ;  $p < 0.05$ ), ALT ( $r = +0.5975$ ;  $p < 0.05$ ), ALP ( $r = +0.7799$ ;  $p < 0.05$ ).<sup>4,5</sup>

The studies of Balaraju G et al, Misra GP et al had the similar correlation. Serum LDH had positive correlation with serum urea ( $r = +0.7098$ ;  $p < 0.05$ ), serum creatinine ( $r = +0.8262$ ;  $p < 0.05$ ), bilirubin ( $r = +0.7131$ ;  $p < 0.05$ ), AST ( $r = +0.6747$ ;  $p < 0.05$ ), ALT ( $r = +0.5996$ ;  $p < 0.05$ ), ALP ( $r = +0.748$ ;  $p < 0.05$ ).

In group B of our study platelet had negative correlation with AST ( $r = -0.4936$ ;  $p < 0.05$ ) and ALT ( $r = -0.4501$ ;  $p < 0.05$ ). Serum ALP positively correlate with CT ( $r = +0.5669$ ;  $p < 0.05$ ) and aPTT ( $r = +0.3392$ ;  $p < 0.05$ ). This finding had similarity with studies of Misra DP et al and Balaraju G et al. Serum FDP had positive correlation with serum urea ( $r = +0.97$ ;  $p < 0.05$ ). serum LDH had positive correlation with AST ( $r = +0.6266$ ;  $p < 0.05$ ) and ALP ( $r = +0.7505$ ;  $p < 0.05$ ). Serum AST had positive correlation with CT ( $r = +0.4128$ ;  $p < 0.05$ ) and aPTT ( $r = +0.5242$ ;  $p < 0.05$ ). This finding had similarity with the study of DP Misra et al.<sup>4</sup>

The highly significant positive correlation between values of bilirubin and serum urea ( $r = +0.4537$ ;  $p < 0.05$ ) and serum creatinine ( $r = +0.6299$ ;  $p < 0.05$ ) in patients of complicated falciparum malaria. This finding has previously been reported Pati SS et al.<sup>9</sup> With increasing renal impairment there appears to be a fall in the renal excretion of conjugated bilirubin. This leads to a disproportionate rise in the plasma concentration of conjugated bilirubin and this may further worsen the

renal impairment since bilirubin can be toxic to renal tubules.

Serum ALP levels had a positive correlation with values of serum urea ( $r = +0.507$ ;  $p < 0.05$ ) and serum creatinine ( $r = +0.7316$ ;  $p < 0.05$ ). The raised serum ALP level indicate that the hepatic stage of the parasite's life cycle in the human host is accompanied by significant perturbation of the hepatocyte membrane leading to leakage of alkaline phosphatase from the hepatocytes, this leads to impaired drainage capacity of the liver and consequently hyperbilirubinemia. Such hyperbilirubinemia positively correlates with impaired renal function.

Serum AST was positively correlate with with serum urea ( $r = +0.6632$ ;  $p < 0.05$ ) and creatinine ( $r = +0.5676$ ;  $p < 0.05$ ). Serum ALT was positively correlate with serum urea ( $r = +0.4373$ ;  $p < 0.05$ ) and serum creatinine ( $r = +0.6704$ ;  $p < 0.05$ ). In group B there was no any correlation hepatic and renal parameters. Above correlation in hepatic and renal parameter had similarity with the studies of Misra DP et al, Balaraju G et al, Prasad VS et al.<sup>5</sup>

ALT is mainly found in the liver and acts as catalyst in the transfer of amino acid from donor molecule to recipient molecule. ALT is the prime indicator of ongoing liver cell damage.<sup>10</sup> Synthesis of clotting factor is hampered in liver cell damage. Bleeding time and aPTT was found to have significantly positive correlation with serum ALT levels in group A. Such an observation in patient of falciparum malaria is an interesting finding and not met with in earlier studies. Serum LDH had positive correlation with all the renal and hepatic parameters in group A in our study but it was not previously observed.

In this study as observed in patients of complicated falciparum malaria ( Group A ) , only 3.33% had overt bleeding but prevailed high incidence of subclinical DIC as evidenced by raised FDP (Group A 43.33%, Group B 13.33%), prolonged aPTT (Group A 53.33% , Group B 26.67%), prolonged PT (Group A 50%, Group B 33.33%), raised INR (Group A 43.33%, Group B 23.33%), low total platelet count (Group A 50%, Group B, 23.33%) and decreased haemoglobin levels (Group A, 73.33%, Group B 50%) whereas intravascular hemolysis also prevailed in a significant number of patients as evidenced by decreased haemoglobin, hyperbilirubinemia (Group A 100%, Group B 36.67%) and raised serum LDH (Group A 73.33%, Group B 56.67%).

Thus, from the above findings we may conclude that there was a relationship between hepatic and renal dysfunction with haemorrhological parameters in plasmodium falciparum malaria in KOSI region.

## CONCLUSION

Majority of plasmodium falciparum patients with hepatic dysfunction presented with anemia and renal failure. Thrombocytopenia is very common in falciparum malaria, but spontaneous bleeding is rare. Our study revealed that, even though 3.33% of patients studied had clinically overt bleeding manifestations, there prevailed significant burden of subclinical haemorrhological dysfunction in patients suffering from falciparum malaria with hepatic and renal dysfunction.

As observed in patients of falciparum malaria with hepatic and renal dysfunction, there prevailed high incidence of subclinical DIC as evidenced by raised FDP (43.33%), prolonged aPTT (53.33% ), prolonged PT (50%), raised INR (43.33%), low total platelet count (50%) and decreased haemoglobin levels (73.33%) whereas intravascular hemolysis also prevailed in a significant number of patients as evidenced by decreased haemoglobin, hyperbilirubinemia (100%) and raised serum LDH (73.33%). In this study prolonged duration of illness, higher concentration of bilirubin, oliguria, and severity of ARF, acidosis, respiratory distress, severe anemia, disorientation and DIC were associated with poor prognosis.

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