VOLUME-8, ISSUE-10, OCTOBER-2019 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

LIVER AND RENAL DYSFUNCTION IN PLASMODIUM FALCIPARUM MALARIA

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ABSTRACT

BACKGROUND – Malaria still continues to be a major killer of mankind especially in developing countries.Almost all deaths and severe disease are due to plasmodium falciparum. It is observed that the patients of falciparum malaria with liver, renal and hematological abnormalities are more vulnerable to development of complications like cerebral malaria, anaemia, acute respiratory distress syndrome etc.

METHODS – 50 cases of plasmodium falciparum malaria diagnosed by peripheral smear examination or by immunochromatographic tests were included in the study. All these patients are subjected to blood investigations like renal function test,liver function test, random blood sugar level(BSL).

RESULTS- 68% patients were males with sex ratio M:F was 2.12: 1. Majority of patients (26%) belong to age group of 21-30 years. Most common presentation was fever in 100% of patients, followed by headache in 48% of patients, vomiting in 46% of patients. 42% patients were showed increased in serum creatinine more than 1.2mg% with mean was 2.14+/-2.23 mg% with range of 0.6 – 9.5 mg%. 38% patients were having increased in serum bilirubin more than 1.2mg%. with mean was 2.87+/-4.72 mg% with range of 0.58 – 25 mg%. Mean RBSL level was 98.3+/- 23.47 mg % with range of 54 – 190 mg%. 08% patients were having RBSL less than 60mg%.44% were having splenomegaly and 28% were having hepatomegaly on USG report. Only 12% patients showing both hepatomegaly and splenomegaly on USG report. .P Falciparum malaria with renal and liver dysfunction mostly associated with coagulation abnormality with or without bleeding diathesis having bad prognosis.

KEYWORDS :

INTRODUCTION-

Malaria is an Italian word composed of "*mala*" and "*aria*," derived from *malus* (bad), and *aeris*(air)[1].Several species affect humans, leading to different patterns of the disease. The most important are *Plasmodium falciparum*, which causes falciparum malaria, *P. malariae*, which causes Quartan malaria, and *P. vivax and P. ovale*, which cause tertian malaria. Genetic interspecies differences explain the variance in the clinical syndromes caused by these sporozoans. These include the rate of multiplication, expression of different antigenic and ligand proteins on the host's parasitized cells, influence of host factors on the parasite's antigenic variability, and others. A striking expression of this divergence is the ability of different strains to invade human red cells of different ages. Thus, *P. vivax and P. ovale* infect only young red cells, whereas *P. malariae* infects only aging cells. *P. falciparum* invades erythrocytes at any age, which explains the heavy parasitemia associated with this species. In contrast, erythrocytes with haemoglobin S typically are resistant to this species.[2]

Malaria is widely spread throughout the world and affects close to 400 million people, most of whom live in Africa, India, Southeast Asia, and Latin America. With the increasing immigration of natives from those regions to Europe and North America, "imported malaria" imposed itself on the list of differential diagnosis of many medical conditions in the West as recurrent fever, jaundice, hemolytic anemia, acute renal failure (ARF), systemic inflammatory response (SIR) syndrome, and posttransplantation pyrexia.[1,5]

Malaria affects almost all organ systems but acute kidney and liver injury are the most dreaded complications of severe malaria.[4]

A study based on 31 American soldiers in Vietnam with chloroquine-resistant falciparum malaria noted that the patients with more severe thrombocytopenia also had DIC and that there was correlation between platelet count and C3 protein levels. However, the reduction in C3 was proportional to that in parasitaemia, suggesting that thrombocytopenia was not independently associated with C3 . In Manaus 2004, a study with falciparum and vivax patients demonstrated a negative correlation between platelet counts, thrombin-anti-thrombin complex and D-dimers, suggesting that the activation of coagulation could be partially responsible for thrombocytopenia.[14]

MATERIAL AND METHODS

The present study was carried out in department of medicine at tertiary care hospital for one year. Patients selected those who got admitted in department of medicine at tertiary care hospital for one year with either peripheral smear or RMT positive for plasmodium falciparum. Patients with past history of alcoholism, jaundice, chronic renal failure,bleeding diathesis or coagulopathy were excluded. Patients with mixed malaria, plasmodium falciparum and other malarial parasites infection i.e. P Vivax, P Ovale, P. Malariae were excluded from studies.Aim of our study is to study the relationship of Hepatic and Renal Dysfunction with Hematological Parameters in Plasmodium falciparum Malaria.

OBSERVATION AND DISCUSSION

Present study (2013) comprised of 50 patients with P Falciparum malaria, of which 34 are males and 16 are females with M:F ratio 2.12.Similarly, in Manan et al (2006)[15] studied 46 patients with P Falciparum malaria out of that 36 were males and 10 were females with M:F ratio 3.6 ; Abro et al(2009)[11] studied 103 patients with P Falciparum malaria out of that 94 were males and 9 were females with M:F ratio 10.44;Singh et al (2010)[10] studied 82 patients with P Falciparum malaria out of that 56 were males and 26 were females with M:F ratio 2.15. M : F ratio of present study(2013) i.e 2.12 correlates with Singh et al study(2010)[10] (M:F ratio=2.15). It was lower than Abro et al (2009)[11] ie 10.44 and Manan et al(2006)[15] i.e3.6.

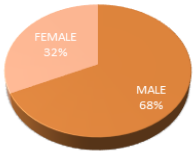

Chart no. 1. Sex distribuction

Table No. 1 Comparisons of sex distribution in various studies

STUDY	Males N(%)	Female N(%)	Total	M:F ratio
Manan et al (2006) 15	36(78.26%)	10(21.74%)	46	3.6
Abro et al (2009) 11	94(91.5%)	9(8.5%)	103	10.44
Singh et al (2010) 10	56(68.29%)	26(31.71%)	82	2.15
Present study(2013)	34(68%)	16(32%)	50	2.12

In Present study (2013) ,age range between 13-85 years with mean ± SD is 38 ± 16.74 years. Similarly, Manan et al (2006)15 study mean age ± SD was 32 ± 12.61 years and age range between 16-65 years. Ahsan et al (2008)12 study range age between 14-70 years with mean ± SD was 33.74±14.89 years, Abro et al (2009)11 study age range between 14- 68 years with mean ± SD was 31±9.39 years , Singh et al (2010)10 study age range between 16-57 years with mean ±SD was 28 ±7.23 years. Age range and mean ±SD of present study (2013) i.e 13-85 years and 38±16.74 years respectively was higher than Manan et al (2006)16 (age range 16-65 years, mean ± SD 32± 12.61 years) and Ahsan et al (2008)13 (age range 14-70 years , mean ±SD 33.74±14.89 years).It was also low in Abro et al (2009)12 (age range 14 -68 years and mean ± SD was 31± 9.39 years) and Singh et al (2010) 11 (age range 16-57 years and mean ± SD 28+/-7.23 years.)

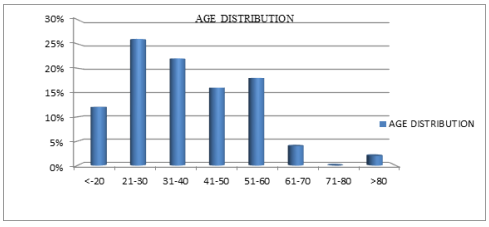

Chart no 2. Age distribution

Table No. 2 Comparison of age distribution in various studies.

Study	Age range(years)	Mean±SD(years)
Manan et al(2006) 15	16-65	32+/- 12.61
Ahsan et al (2008) 12	14-70	33.74+/-14.89
Abro et al (2009) 11	14 -68	31+/- 9.39
Singh et al (2010) 10	16-57	28+/-7.23
Present study (2013)	13-85	38+/- 16.74

Present study(2013) of P Falciparum malaria showing most common clinical symptoms of fever with rigor [50(100%)] followed by headache[24(48%)] and vomiting [23(46%)]. Manan et al (2006)15 studied acute renal failure associated with malaria. Study comprised of 237 patients with acute renal failure(ARF) of which 46(19.4%) had malarial acute renal failure. Plasmodium Falciparum was responsible for all cases of malarial ARF. Fever was the leading symptom. 43(93.48%) patients were febrile at the time of admission while the remaining 03(6.52%) had a history of fever in the preceding one week. Oliguria (76.09%), jaundice (71.73%), hepatomegaly (67.39%), and impaired consciousness (63.04%), were the most common presenting abnormalities. Although impaired consciousness was present in 29 patients, only 09 fulfill the WHO criteria for cerebral malaria. Rasheed et al (2009)16 studied 311 patients of P Falciparum showing most common clinical symptoms of fever with rigor (99.04%) followed by headache (73.63%) and vomiting (52.73%).Present study (2013) correlates with Rasheed et al(2009)16 showing most common clinical symptoms of fever with rigor followed by headache and vomiting.

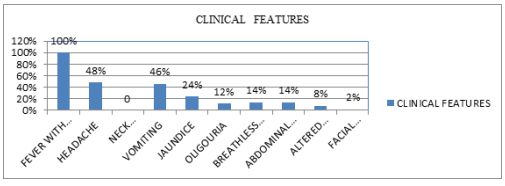

Chart no 3. Clinical features in P Falciparum malaria patients.

Table No 3 Comparison of clinical features in various studies.

STUDY	Manan et al (2006)[15]	Rasheed et al (2009)[16]	Present study (2013)
FEVER WITH RIGOR	43(93.48%)	99.04%	50(100%)
HEADACHE	NOT SPECIFIED	73.63%	24(48%)
VOMITING	NOT SPECIFIED	52.73%	23(46%)
NECK STIFFNESS	NOT SPECIFIED	NOT SPECIFIED	0(0%)
JAUNDICE	33(71.73%)	NOT SPECIFIED	12(24%)
OLIGURIA	35(76.09%)	NOT SPECIFIED	6(12%)
BREATHLESSNESS	NOT SPECIFIED	NOT SPECIFIED	7(14%)
BLEEDING DIATHESIS	NOT SPECIFIED	NOT SPECIFIED	0(0%)
ALTERED SENSORIUM	29(63.04%)	NOT SPECIFIED	4(8%)
ABDOMINAL PAIN	NOT SPECIFIED	11.58%	7(14%)
FACIAL SWELLING	NOT SPECIFIED	NOT SPECIFIED	1(2%)

Present study comprised of 50 patients with P Falciparum malaria having serum creatinine range between 0.6 – 9.5mg% with mean of 2.14±2.23 mg%. Manan et al(2006)15 study comprised of 46 patients of ARF due to P Falciparum malaria showed mean serum creatinine level was 7.304±3.16 mg/dl. Positive correlation was found between duration of illness and impairment of renal function. Over all, haemodialysis treatment was performed in 36(78.26%) of the patients. The remaining 10(21.74%) patients were treated conservatively. Among 36 patients requiring the haemodialysis 32(88.89%) were oliguric and 04(11.11%) non-oliguric . Compared with nonoliguric subjects, the oliguric patients had higher need of dialysis(p=0.001). Abro et al(2009)11 study comprised of 105 patients with P Falciparum patients showing serum creatinine mean± SD was 1.8± 0.8 mg/dl.Creatinine was increased in 38(36.1%) patients.Maximum serum creatinine level was 6.7 mg/dl.Singh et al (2010)10 study comprised of 82 patients with P Falciparum malaria with hepatic involvement having mean ± SD of serum creatinine level of 1.8± 0.8 mg/dl.Creatinine was increased in 32(39.02%) patients. Hussain et al(2012)18 study comprised of 42 patients with P Falciparum malaria having serum creatinine range between 0.5-2.3 mg% with mean of 1.36 ± 0.07mg%. Present study(2013) has higher mean ±SD of serum creatinine than Hussain et al (2012)18 i.e 1.36± 0.07 mg% but lower than Manan et al(2006)15 i.e 7.304±3.16 mg%.

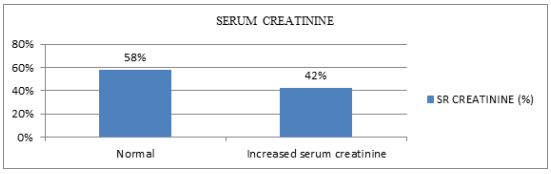

Chart no. 4 Serum creatinine

Table No 4.Comparison of serum creatinine in various studies.

STUDY	RANGE (mg/dl)	MEAN ± SD (mg/dl)
Manan et al(2006)15	NOT SPECIFIED	7.304±3.16
Abro et al (2009)11	NOT SPECIFIED	1.8±0.8
Singh et al (2010)10	NOT SPECIFIED	1.8±0.8

Hussain et al (2012)18	0.5-2.3	1.36±0.07
Present study	0.6 – 9.5	2.14 ± 2.23

In Present study (2013) of P Falciparum having serum bilirubin (total) range between 0.58 – 25 mg% with mean 2.87±4.72 mg%. Out of 50 patients of P Falciparum malaria , 19(38%) patients were having serum bilirubin more than 1.2mg% . Manan et al(2006)15 study comprised of 46 patients of ARF due to P Falciparum malaria having serum bilirubin level range between 0.57 – 37mg/dl with mean±SD was 11.22 ±9.34 mg/dl. This was predominantly of the conjugated variety. Serum transaminases were not significantly raised, in comparison with serum bilirubin.Serum alanine aminotransferase (ALT) <128 IU/L and serum aspartate aminotransferase (AST) <321IU/L was noted in all patients.Ahsan et al(2008)12 studied jaundice in P Falciparum malaria. Study comprised of 76 patients of P Falciparum , 35(46.05%) developed jaundice. Fifteen(42.86%) patients had bilirubin 3-10mg/dl while 20(57.14%) had bilirubin >10mg/dl. In Group- A (serum bilirubine between 3-10 mg/dl),only 27.23% patients had renal failure as compared to Group-B (serum bilirubine more than 10mg%) with high bilirubin where 77.27% patients developed renal failure(p= 0.001). Serum transaminases, Prothrombin time (in seconds) and serum albumin were not significantly raised in comparison with rising serum bilirubin. Impaired consciousness, hepatomegaly and renal failure were most common and significantly associated with rising bilirubin. Singh et al(2010)10 studied hepatic involvement in P Falciparum malaria showing serum bilirubin range between 1-32 mg/dl with mean of 5.65 mg/dl in 82 patients.41.46% patients had serum bilirubin of <3 mg%, 40.24% patients had 3-10 mg/dl and 18.29% patients had >10 mg/dl.Abro et al(2009)11 studied jaundice with hepatic dysfunction in P Falciparum malaria in 105 patients.Bilirubin level was raised above normal level in 85 (81%) patients,with mean bilirubin level of 2.45± 2.22 mg/dl.In 24 (23%) patients, bilirubin was >3 mg/dl(maximum – 11.4 mg/dl).The patients with increased ALT level had predominant conjugated hyperbilirubinemia, whereas patients with normal liver function tests had unconjugated hyperbilirubinemia. There was no significant change in levels of serum albumin and prothrombine time.Hussain et al(2012)18 studied 42 patients with P Falciparum malaria having serum bilirubin (total) ranged between 0.9 – 5.8 mg/dl with mean±SD of 2.35±0.1 mg/dl. Present study(2013)i.e 2.87 ± 4.72 mg correlates with Hussain et al(2012)18 in terms of mean±SD serum bilirubin i.e 2.35± 0.1 mg% but lower than Manan et al(2006)15 i.e 11.22 ±9.34 mg/dl and Singh et al(2010)10 i.e 5.65 mg/dl.

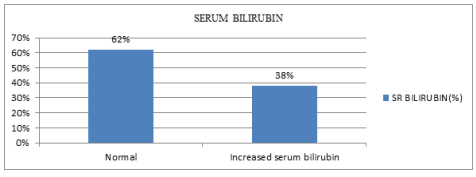

Chart no 5. showing serum bilirubin level (total)

Table No 5. Comparison of serum bilirubin in various studies.

STUDY	RANGE(mg/dl)	MEAN ±SD (mg/dl)
Manan et al (2006)15	0.57 - 37	11.22±9.34
Ahsan et al (2008)12	NOT SPECIFIED	NOT SPECIFIED
Singh et al (2010)10	1-32	5.65
Abro et al (2009)11	NOT SPECIFIED	2.45±2.22
Hussain et al (2012) 18	0.9-5.8	2.35±0.1
Present study (2013)	0.58 - 25	2.87± 4.72

In the present study(2013) comprised of 50 patients, 22(44%) patients having splenomegaly and 14(28%) patients having hepatomegaly.Kocher et al(2003)19 studied hepatocyte dysfunction and hepatic encephalopathy in Plasmodium falciparum malaria.The detailed ultrasonography done in 29 patients having serum bilirubin>10mg% revealed hepatomegaly in 25, splenomegaly in 24 and both hepatomegaly and splenomegaly in 20. Seven patients with hepatomegaly also had decreased echogenicity. Gall bladder wall thickness was increased in five patients. There was no evidence of intrahepatic or extrahepatic bile duct dilatation.Rasheed et al(2009)16 study comprised of 502 males patients with P Falciparum malaria , out of which 21(6.75%) patients showed hepatomegaly and 213(68.81%) patients showed splenomegaly. Singh et al(2010)10 study comprised of 82 patients with P Falciparum malaria, out of which 48(58.54%) patients showed hepatomegaly and 42(51.22%) patients showed splenomegaly. In all the patients with hepatomegaly and/or decrease echogenicity on ultrasonography,transaminases were found to be more than thrice normal. Present study (2013) has low incidence of hepatomegaly and splenomegaly than Singh et al(2010)10.

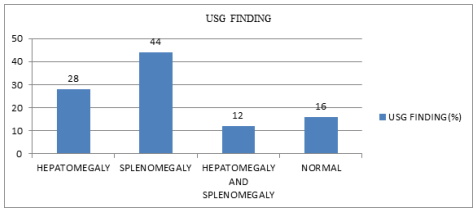

Chart no 06. USG Finding

Table No 06.Comparison of sonographic finding in various studies.

STUDY	HEPATO MEGALY	SPLENO MEGALY	HEPATO MEGALY SPLENO MEGALY
Kocher et al (2003)19	05	04	20
Rasheed et al (2009)16	21(6.75%)	213(68.81%)	NOT SPECIFIED
Singh et al (2010)10	48(58.54%)	42(51.22%)	NOT SPECIFIED
Present study (2013)	14(28%)	22(44%)	06(12%)

CONCLUSION

P Falciparum malaria is more common in young males patients. Most common symptoms of P Falciparum malaria is fever with rigor.Splenomegaly and/or hepatomegaly most common in P Falciparum malaria.P Falciparum malaria most commonly presented with acute renal failure.P Falciparum malaria with renal and liver dysfunction mostly associated with coagulation abnormality with or without bleeding diathesis having bad prognosis.

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