

RELATIONSHIP OF HEPATIC AND RENAL DYSFUNCTION WITH HAEMORRHOLOGICAL PARAMETERS IN PLASMODIUM FALCIPARUM MALARIA

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HOW TO CITE THIS ARTICLE:

Valluri Satya Prasad, Manavalla Subrahmanyam. "Relationship of Hepatic and Renal Dysfunction with Haemorrhological Parameters in Plasmodium Falciparum Malaria". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 18, May 04, 2015; Page: 2688-2693.

ABSTRACT: The clinical pattern of malaria has changed worldwide including India in last decade. Earlier cerebral malaria was the predominant manifestation of severe malaria, whereas now the combination of jaundice and renal failure are more common. Severe haemorrhage is seen in upto 5% of patients with severe malaria. Studies on renal and hepatic dysfunction in Plasmodium falciparum malaria are a plenty, but there is a paucity of studies correlating haemorrhological abnormalities with hepatic and renal dysfunction in Plasmodium falciparum malaria. **METHODS:** 100 patients of malaria with positive peripheral blood smear for plasmodium falciparum, out of which 50 cases with AKI and Hepatic failure during the period January 2012- June 2013. In department of general medicine, Government General Hospital, Kakinada. **GROUP A:** Comprising 50 consecutive adult patients of all age groups and both genders who had jaundice or renal failure or both at the time of admission. **GROUP B:** comprising 50 consecutive cases of plasmodium falciparum malaria and had no complications. **RESULTS:** In group A patients all parameters are significantly raised as compared to group B patients. **CONCLUSION:** 10% of patients had clinically overt bleeding manifestations, this indicates subclinical haemorrhological dysfunction in patients suffering from falciparum malaria with hepatic and renal dysfunction, high incidence of subclinical DIC, evidenced by prolonged aPTT (56%), low total platelet count (58%), and PT (20%). An observational, screening, analytical prospective study. 100 cases of PF positive complicated and uncomplicated cases during the period - January 2012- June 2013.

KEYWORDS: Plasmodium falciparum, hemorrhological, AKI, Hematological, MODS, PT, APTT.

INTRODUCTION: Earlier cerebral malaria was the predominant manifestation of severe malaria, now the combination of jaundice and renal failure are more common. Das Sidhartha. Falciparum Malaria: a Multi-Systemic Disease in BK Sahay (ed), Medicine Update; Association of Physicians of India 2006; 16: 369-75.⁽¹⁾ Severe haemorrhage is seen in up to 5% of patients with severe malaria. The degree of coagulation derangement is often associated with disease severity. Chawla LS, Sidhu G, Sabharwal BD, Batia KL, Soud A. Jaundice in plasmodium falciparum. J Associate Physicians India 1989; 37(6): 3901. (www.who.int/statistics).⁽²⁾ Studies on renal and hepatic dysfunction in Plasmodium falciparum malaria are a plenty, but there is a paucity of studies correlating haemorrhological abnormalities with hepatic and renal dysfunction in Plasmodium falciparum malaria.

Hence I have taken up this study on relationship of hepatic and renal dysfunction in Plasmodium falciparum malaria, and evaluate if such abnormalities had any bearing with the haemorrhological dysfunction.

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AIM AND OBJECTIVES: To determine the hematological parameters in patients with plasmodium falciparum malaria with hepatic and renal dysfunction.

- (a) To determine the abnormalities in coagulation in patients with plasmodium falciparum malaria with hepatic, renal dysfunction by bleeding time, clotting time, prothrombin time and activated partial thromboplastin time.
- (b) To correlate the haemorrhological parameters with parameters of hepatic and renal dysfunction.

METHODS: The present study was done on 100 patients of malaria with positive peripheral blood smear for plasmodium falciparum admitted in department of general medicine, Government General Hospital, Rangaraya Medical College, Kakinada, Andhra Pradesh during the period January 2012- June 2013.

Group A: Comprising 50 consecutive adult patients of all age groups and both genders who had jaundice or renal failure or both at the time of admission.

Group B: comprising 50 consecutive adult patients all age groups and genders with uncomplicated malaria.

EXCLUSION CRITERIA:

- Patients less than 15 years of age.
- Plasmodium vivax smear positive and mixed smear positive.
- Patients with chronic liver disease, chronic kidney disease and bleeding. Diathesis or coagulopathy.
- Patients with past history of alcoholism.
- Dengue and leptospirosis.

INVESTIGATIONS:

- These investigation were done in all cases.
- Complete haemogram
- Coagulation profile (BT, CT, PT, INR and aPTT)
- LFT (Serum bilirubin, AST, ALT, ALP).
- Serum urea, Serum creatinine, random blood sugar.
- Ultrasound abdomen.

OBSERVATIONS:

1. Age and sex distribution:

Group A: Cases of falciparum malaria with hepatic/renal dysfunction.

Group B: Cases of uncomplicated falciparum malaria.

In group A, 74% of the patients are below the age of 45 years 68% of the patients are male and 32% are female. In group B 52% are males 48% are females.

2. Clinical features:

Group A: Cases of falciparum malaria with hepatic/renal dysfunction.

Group B: Cases of uncomplicated falciparum malaria.

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All cases of complicated falciparum malaria included in the study had fever and icterus, 60% oliguria, 30% disorientation, 10% convulsions, 18% respiratory distress, 10% bleeding manifestations, 52% hepatomegaly, 44% splenomegaly, 32% hypotension and 80% presented with pallor respectively.

In the group B with uncomplicated falciparum, all had fever, 28% splenomegaly and 60% presented with pallor.

3. BIOCHEMICAL PARAMETERS:

	Group				p-value
	A		B		
	Mean	SD	Mean	SD	
S. Urea	76.82	42.24	31.84	6.36	<0.001 sig
S. Creatinine	3.21	2.31	1.02	.17	<0.001 sig
RBS	96.42	25.19	117.40	34.03	0.004 sig
S. Bilirubin	7.67	4.67	1.01	.30	<0.001 sig
AST	111.64	59.09	30.40	4.73	<0.001 sig
ALT	99.88	48.84	28.80	3.59	<0.001 sig
ALP	215.58	173.80	99.52	31.20	<0.001 sig
Biochemical Parameters: (Mean Values with standard deviation):					

4. HEMATOLOGICAL MANIFESTATIONS:

	Group				p-value
	A		B		
	Mean	SD	Mean	SD	
HB	8.27	2.66	10.30	1.78	0.001
PLT	1.30	.81	2.14	.85	<0.001
RC	1.74	.62	1.14	.22	<0.001
BT	97.02	47.07	130.36	23.30	<0.001
CT	460.50	151.25	457.92	87.98	0.937
PT	14.41	1.95	12.68	1.50	<0.001
INR	1.11	.15	.99	.11	0.001
aPTT	35.00	6.29	31.20	4.25	0.003
Mean values with standard deviation					

In Group A, Mean value of Hb 8.27 (± 2.66), PLT 1.30 ($\pm .81$), PT 14.41(± 1.95), 35.00 (± 6.29) Statistically significant difference was observed between the values of Group A and Group B except CT.

5. Correlation between Haematological parameters, liver function test and renal function test- Group A:

Group A		S. Urea	S. Creatinine	S. Bilrubin	AST	ALT	ALP
HB	r	-.435**	-.479**	-.539**	-.464**	-.418**	-.421**
	p	.002	<0.001	<0.001	.001	.002	.002
PLT	r	-.254	-.363**	-.306*	-.307*	-.343*	-.323*
	p	.076	.010	.030	.030	.015	.022
BT	r	.033	.133	.157	.114	.178	.083
	p	.822	.359	.276	.431	.217	.566
PT	r	.541**	.596**	.558**	.280*	.388**	.454**
	p	<0.001	<0.001	<0.001	.049	.005	.001
aPTT	r	.536**	.624**	.575**	.464**	.494**	.459**
	p	<0.001	<0.001	<0.001	.001	<0.001	.001

GROUP A: Cases of falciparum malaria with hepatic/renal dysfunction; r; r. value, p; p-value.

In Group A Serum urea and creatinine were found to have statically significant negative correlation with Hb and PLT(Platelet count) Jadhav UM, Patkar VS, Kadam NN.⁽³⁾ Wher eas positive correlation with PT and aPTT. Serum bilirubin, AST, ALP, were found to have significant negative correlation with Hb and PLT and positive correlation with PT, aPTT.

Correlation of liver function and renal function tests.

GROUP A: In group A, Serum bilirubin was found to have statistically significant positive correlation with Serum creatinine ($r = +.920$, $p < .001$) and Serum urea ($r = +.890$, $p < .001$), similarly AST with Serum creatinine ($r = +.762$, $p < .001$) and Serum Urea ($r = +.762$, $p < .001$), ALT with serum creatinine ($r = +.745$, $p < .001$) and Serum urea ($r = +.720$, $p < .001$) and ALP with serum creatinine ($r = +.777$, $p < .001$) and serum urea ($r = +.718$, $p < .001$). In group B, no such significant correlation was observed between renal function test and liver function test.

DISCUSSION: 50 cases of Plasmodium falciparum malaria with hepatic or renal dysfunction or both Group A, and 50 cases of uncomplicated falciparum malaria Group B were included as subjects, with a mean age of 38.04 (± 15.09) years in Group A and 30.32 (± 10.62) years in the Group B. Maximum number of patients were in the age group 21-30 years. Falciparum malaria is usually a disease of the young. Earlier studies conducted by Das Sidhartha et al.,⁽¹⁾ (2006), Kochar et al.,⁽⁴⁾ (2003) and Misra et al., (2011)⁽⁵⁾ have shown similar age of incidence.

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Comparison of abnormal Haematological Parameters:

	Misra et al., Study 2011 Group A	Present study Group A	Misra et al., Study 2011 Group B	Present study Group B
HB%	87%	80%	80%	60%
PLT	26%	58%	15%	14%
RC	12%	14%	-	-
CT	44%	46%	35%	14%
PT	16%	20%	5%	8%
aPTT	67%	56%	65%	20%

Group A: Cases of falciparum malaria with hepatic/renal dysfunction;

Group B: Cases of uncomplicated falciparum malaria.

CONCLUSIONS:

1. Majority of plasmodium falciparum patients with hepatic dysfunction presented with anemia and renal failure.
2. Thrombocytopenia is very common in falciparum malaria, but spontaneous bleeding is rare. Jadhav UM, Patkar VS, Kadam NN. Thrombocytopenia in Malaria.⁽³⁾
3. Our study revealed that, even though 10% of patients studied had clinically overt bleeding manifestations, R Clemons, C Pnamoolsinsap, R Lorinz, S pokrittayakane, H.L. Bock et al;⁽⁶⁾ Activation of coagulation cascade in severe falciparum malaria through the intrinsic pathway. Br. J Haematol vol.87; 100-105. Moxon CA, Heyderman RS, and Wassmer SC. Dysregulation of coagulation in cerebral malaria. Mol Biochem Parasitol. 2009; 166: 99–108⁽⁷⁾ there prevailed significant burden of subclinical haemorrhological dysfunction in patients suffering from falciparum malaria with hepatic and renal dysfunction.
4. As observed in patients of falciparum malaria with hepatic and renal dysfunction, there prevailed high incidence of subclinical DIC as evidenced by prolonged aPTT (56%), low total platelet count (58%), and PT (20%).
5. In patients with hepatic and renal involvement, the parameters of haemorrhological dysfunction (PT, aPTT) had significant positive correlation with parameters of renal dysfunction & parameters of liver dysfunction (serum ALP, AST, ALT and serum bilirubin). Harrison's principles of internal medicine, 18th EDITION; 1688-1705⁽⁸⁾
6. The parameters of hepatic dysfunction had significant positive correlation with the parameters of renal dysfunction (serum urea and creatinine) in patients of plasmodium falciparum with hepatic and renal involvement.
7. In this study prolonged duration of illness, oliguria, higher concentration of bilirubin, severity of AKI (higher urea and creatinine with acidosis), ARDS and DIC were associated with poor prognosis.

ORIGINAL ARTICLE

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Date of Submission: 11/04/2015.
Date of Peer Review: 12/04/2015.
Date of Acceptance: 16/04/2015.
Date of Publishing: 29/04/2015.