Original Research Article

Study of renal dysfunction in Malaria

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Abstract

Background: Prevalence of acute renal failure (ARF) in malaria has been reported as 0.57% to 60 % all over the world. An upsurge in the incidence of ARF in malaria also has been reported in India and varies form 13% to 17.8%. **Objective:** To study the frequency, clinical profile and in hospital outcome of ARF in malaria. **Materials and Methods:** In this hospital based observational study 119 cases of fever who were positive for malarial antigen on Histidine rich protein (HRP) and or who has peripheral smear positive foe malarial parasite were enrolled. Cases were categories as having ARF according to RIFLE criteria and were observed for clinical profile, complications, and in hospital outcome. **Results:** Out of 119 cases of malaria studied 40 cases (33.61%) had ARF. Males outnumbered females (Male to Female ration 2:1). Anemia was the most common complication present in 22 cases (55%).Complications like Anemia, jaundice, cerebral malaria, hypotension, algid malaria, ARDS, black water fever, hypoglycemia, and DIC were significantly high in falciparum malaria than vivax malaria ($p<0.05$). Mortality in malaria with ARF was found to be significantly more (11.00% vs.1.27%) ($p <0.001$). **Conclusion:** Malaria being treatable cause of ARF, early detection and prompt treatment can prevent the mortality and morbidity.

Key Words: Acute Renal failure, Malaria, RIFLE criteria.

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INTRODUCTION

Malaria is a protozoan disease transmitted by the bite of infected Anopheles mosquitoes. Malaria is one of the most serious parasitic diseases of the world affecting 300-500 million people and causing over 1 million deaths each year. Of these 89% are in A frican region, followed by the Eastern Mediterranean and the South East Asia Region. Approximately 2.5 million malaria cases are reported annually from South Asia, of which 76% are reported in India[1.2]. Malaria is endemic throughout India with 95% of the population at risk of infection. It is one of the most common parasitic infection in our country and over 1.56 and 1.59 million cases are reported in 2009 and 2010 respectively. In India about 88 percent of malaria cases and 97 percent deaths due to malaria are reported from North-Eastern States, Chhattisgarh, Jharkhand, Madhya Pradesh, Orissa, Andhra Pradesh, Maharashtra, Gujarat, Rajasthan, West Bengal and Karnataka. Recently there is a changing trend not only in the clinical manifestations, but also the complications in malaria. Previously, cerebral malaria was the predominant manifestation of severe malaria, where as today the combination of jaundice and renal failure are more common[2,3]. An upsurge in the incidence of ARF in malaria has been reported in India and varies from 13% to 17.8%. Prevalence of ARF in malaria all over the world has been reported as 0.57% to 60%.Malarial ARF is emerging as an important problem in tropical countries and carries high mortality, especially when the disease in not diagnosed early, the referral to health centre having dialysis facility is late or when dialysis facility is not available[4,5].

MATERIAL AND METHODS

This study is a hospital based observational study conducted in general medicine ward and MICU in our institution. 119 patients with fever who were positive for malarial antigen on FIRP and or who had peripheral smear positive for malarial parasite were included in study. Patients with history of chronic kidney disease were excluded from the study. In all the cases a detailed history and findings on physical examination were

recorded. Biochemical and hematological investigations included KFT, LET, Complete blood count, coagulation profile (where indicated). GFR was calculated using Cockcrofit-Gault formula. According to RIFLE criteria[6] Renal failure is defined as decreased GFR (GFR, 61-90 ml/min, decreased > 25%), acute kidney injury (AKL), (GFR, 31-60 ml/min, decreased >50%) and those with acute renal failure (ARF). (GFR, <30 ml/min, decreased > 75%). Fractional excretion of sodium (FENa) was calculated to classify renal failure into pre-renal and intrinsic renal type.

Statistical Methods: Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. 95% Confidence Interval has been computed to find the significant features. The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc. 9.0.1 and Systat 11.0 were used for the analysis of the data.

RESULTS

Present study included 119 diagnosed eases of malaria. Males were out numbering the females (80) (67.23 %) and 39 (32.77%). Male: Female ratio was 2:1.90 cases (75.63%) out of 119 were positive for Plasmodium falciparum, 15 (12.60%) were positive for Plasmodiurn vivax. and 14 (11.76%) cases had mixed Plasmodium infection.40 cases (33.61%) had ARF,18 cases (15.13%) had AKI and 28 cases (23.52 %) had reduced GFR and were at risk of developing renal failure. Out of 90 cases of falciparum malaria, 32 (35.55%) had ARF. Out of 15 cases of vivax malaria, 4 (26.66%) had ARF. Even though renal failure was observed in 40 cases (33.61%), large number of cases (34 out of 90, 37.77%) of falciparum and (4 out of 15, 26.66%) of vivax were at risk for development of renal failure. Risk for development of renal failure was significantly higher in cases with falciparuin malaria than vivax malaria (p <0.05). Sixty six (73.33 %) out of 90 cases of falciparum malaria had renal involvement in the form of ARF/AKI/ risk of renal failure which was significantly higher as compared to 8 cases out of 15 (53.33%) of vivax malaria. (p value < 0.01, O.R. 2.62) (Table 1) Amongst clinical manifestations, Headache, Vomiting, Jaundice and oliguria were the most common symptoms observed in significantly higher number of cases of Malaria with *ARF (Table 2)* Complications observed were significantly more in cases of Malaria with ARF. *(Table 3)* Mortality of cases of malaria with acute renal Failure was 15.00% (6 out of 40 cases of malaria with ARF) which was significantly higher than cases of malaria without ARF (15.00% vs. 1.27%) (p<0.01). Two out of 6 cases (33.33%) expired in spite of renal replacement therapy. Four out of 6 cases (66.66%) expired on mechanical ventilation (Table 4) Factors associated with ARF in malaria were young age, high mean parasite index, hyperkalemia, hyponatremia, jaundice, increased AST, increased ALT, increased ALP, ARDS, Cerebral malaria, anemia, DIC, thrombocytopenia, algid malaria and black water faver. (Table 5)

Table 1: Malaria with ARF, AKI, Risk of renal failure and normal GFR according to Plasmodium species

GFR (ml/min)	p.falci n= 90	p. vivax n = 15	p-value	OR (95%CI)	Mixed n=14
ARF + AKI+ GFR (GFR < 90 ml/min)	66 (73.33%)	8 (53.33%)	< 0.001	2.627 1.449 to 4.762)	12 (85.71%)
Normal (GFR>90ml/min)	24 (26.66%)	4 (46.66%)			2 (14.29%)

Table 2: Clinical manifestations in malaria with ARF

Symptoms	Total no. of cases of Malaria cases (n=l19)	Total no. of of malaria (n=40)
Fever	116(97.47%)	37(90.00%)
Headache	88(73.94%)	31(77.50%)
Myalgia	57(47,89%)	16(40.00%)
Nausea and Vomiting	72(60.50%)	21(52.50%)
Jaundice	25(21.00%)	18(45.00%)
Diarrhoea	19(15.96%)	8 (20.00%)
Cough	7(5.88%)	4(10.00%)
Oliguria	26(21.84%)	26(65.00%)
Altered sensorium	18(15.12%)	14(35.00%)
Breathlessness	9(7.56%)	9(22.50%)
Convulsions	6(5.04%)	6(15.00%)
Bleeding	3 (2.52%)	3(7.50%)

Table 3: Complications in malaria with ARF and without ARF

Parameters	With ARF n=40	Without ARF n=79	p-value OR (95%CI)
Jaundice (Bilirubin ? 3.00 /g/dl) n=25	18 (45.00%)	7 (8.86%)	p<0.0001 OR -8.27 (3.753 to 18.23)
Anemia (Hb%<13gm/dl in men and < 12gm/dl in women) (n=32)	22(55.00%)	10 (12.65%)	p<0.0001 OR -8.17 (4.047 to 16.53)
Thrombocytopenia (<l lakh/mm^3) (n=36)	19 (47.50%)	17 (21.51%)	p<0.0001 OR = 3.33 (1.792 to 6.209)
Hypoglycemia (RBS 40 gm/dl) (n=7)	4(10.00%)	3 (3.79%)	p<0.05 OR = 2.667 (0.8072 to 8.809)
Hypotension (SBP 80 mm Hg) (n=8)	8(20.00%)	0 (0.00%)	p<0.0001 OR 51.19 (3.047 to 859.9)
Hyponatremia (135 m Eq/L) (n=46)	21 (52.50%)	25 (31.64%)	p<0.01 OR =2.30 (1.295 to 4.091)
Hyperkalemia (5.5 mEq/L) (n=10)	10 (25.00%)	0 (00.00%)	p<0.0001 OR =67.89 (4.065 to 1134)
ARDS (PaO2/FiO2 200) n=8	6 (15.00%)	2 (2.53%)	p<0.01 OR =5.706 (1.597 to 20.39)
DIC n=3	3 (7.5%)	0 (00.00%)	p<0.05 OR =16.12 (0.9076 to 286.4)
Cerebral malaria n=18	14 (35.00%)	4 (5.06%)	p<0.0001 OR =10.23 (3.805 to 27.51)
Algid malaria n=18	8 (20.00%)	2(2.53%)	p<0.001 OR =8.08 (2.317 to 28.20)
Black water fever n=5	5 (12.50%)	0(00.00%)	p<0.001 OR 28.39 (1.656 to 486.8)

Table 4: Comparison of outcome of cases of malaria with ARF and without ARF

Outcome	Cases with ARF (n=40)	Cases without ARF (n=79)	p-value	OR (95% CI)
Survived	34 (85.00%)	78 (98.73%)	0.0003	0.05724 (0.007403 to 0.4426)
Expired	6 (15.00%)	1 (1.27%)		
Total	**40**	**79**		

Table 5: Factors associated with Acute Renal failure

Factors	ARF n=40	Without ARF n=79	p-value, OR (95% CI)
Mean Age ± SD (Range)	32.05 ± 14.23 (13 64)	39.10 ± 15.49 (13-76)	p<0.05
Gender (M:F)	2:1	2:1	p>0.05
Mean parasite index ± SD % (Range)	8.87 ± 8.73 (0-45)	0.74 ± 1.15 (1-5)	8.16, p<0.001
Hyperkalemia	10 (25.00%)	0 (00.00%)	P<0.0001; OR=67.89 (4.065 to 1134)
Hyponatremia	21 (52.50%)	25 (31.64%)	P<0.01; OR=2.30 (1.295 to 4.091)
ARDS	6 (15.00%)	2 (2.53%)	P<0.01; OR=5.706 (1.597 to 20.39)
Cerebral malaria	14 (35.00%)	4 (5.06%)	p<0.000; OR=10.23 (3.805 to 27.51)
Anemia	22 (55.00%)	10 (12.65%)	p<0.0001 OR-8.17 (4.047 to 16.53)
Jaundice	18 (45.00%)	7 (8.86%)	P<0.0001; OR-8.27 (3.753 to 18.23)
Increased ALT (>2 times of upper limit of normal)	14 (35.00%)	12 (15.18%)	p<0.01; OR=3.05 (1.537 to 6.058)
Increased AST (<2 times of upper limit of normal	12 (30.00%)	11 (13.92%)	p<0.0; OR=2.63 (1.296 to 5.348)
Increased ALP (>2 times of upper limit of normal)	20 (50.00%)	8 (10.12)	p<0.0001; OR=9.0 (4.200 to 19.28)

Thrinvictopenia	19 (47.50%)	17 (21.51%)	p<0.001; OR=3.33 (1.792 to 6.209)
DIC	3 (7.5.00%)	0 (00.00%)	p<0.01; OR=16.12 (0.9076 to 286.4)
Algid malaria	8 (20.00%)	2 (2.53%)	p<0.001; OR=8.08 (2.317 ro 28.20)
Ourcome (Expired)	6 (15.00%)	1 (1.27%)	p<0.001;OR=0.05724 (0.007403 to 0.4426)

DISCUSSION

Malarial ARF is emerging as an important problem in tropical countries and carries a high mortality, especially when the disease is not diagnosed early, the referral to health centre having dialysis facility is late or when dialysis facility is not available. ARF in malarial being a treatable cause early detection and prompt treatment can prevent the mortality and morbidity of ARF in malaria. In the present study 90 out of 119 (75.63%) cases of malaria were due to Plasmodium falciparum, 15 cases (12.60%) were due to plasmodium vivax and 14 eases (11.76%) were due to Mixed (Plasmodium falciparum and plasmodium vivax both positive) malaria cases. The higher frequency of falciparum malaria than vivax malaria is a reflection of hospitalization policy, as falciparum malaria patients arc more likely to get hospitalized, since these patients are more serious than vivax malaria patients who can be managed as out-patients. In the present study, prevalence of Acute renal failure in malaria was found to be 33.61%, liven though established renal in lure was observed in 40 cases, (33.61%), large number of cases (34 out of 90, 37.77% cases of faiciparurn) and (4 out of 15, 26.66% cases of vivax) were at risk for development of renal failure. Risk for development of renal failure was significantly higher in cases with falciparum malaria than vivax malaria. An upsurge in the incidence o1ARF in malaria has been reported in India arid varies from 13% to 17.8%[6]. ARE is usually associated with intravascular haemolysis or heavy parasitaemia. Prevalence of ARF in malaria all over the world has been reported as 0.57% to 60%[7.8]. ARF lasts from few days to several weeks. Several factors including various chemical mediators, catecholamine release, cytoadherence of parasitized erythrocytes and associated haemorrhaeologic changes, intravascular coagulation, intrava- scular haemolysis, hyperbilirubinaemia a and severe hyperpyrexia have been implicated in the pathogenesis of ARF in Malaria[8]. ARF occurs commonly in plasmodium falciparum malaria, although it's rare occurrence has been reported in plasmodiurn vivax malaria[9]. The disease is more common in adults in those areas of the tropics where transmission of malaria is low or unstable and where symptomatic disease occurs at all ages[9,10]. Established ARE is usually oliguric, but urine output may also be normal or even increased in the presence of increasing serum creatinine values[11,12]. In the study conducted by Prakash *et al*' 3 from Jan. 1995 to Dec. 1999, showed an alarming increase in the incidence ARF in malaria from 6.66% in 1995 to 27% in 1999. Mortality in cases of malaria with ARE was 15.00% in the present study. Mortality was fhund to be significantly higher in patients of malaria with ARE as compared to patients of malaria without ARE (15.00% vs. 1.27% p<0.001. Similar observation is made by Mishra *et al*[14]. In the present study, flictors associated with malaria and ARE were young age, high mean parasite index, hyperkalemia, hyponatremia, jaundice, increased AST, increased ALI, increased ALP, presence of ARDS, cerebral malaria, anemia, DIC, thrombocytopenia, algid malaria and black water fever (p<0.05). Mortality of cases of malaria with ARF was significantly higher than cases of malaria without ARF (15.00% vs. 1.27%, p<0.003). Similar observation was reported by Tangpukdee *et al*[15].

CONCLUSION

It is concluded that malaria is an important cause of ARE. ARE in malaria being a treatable cause early detection and prompt treatment can prevent the mortality and morbidity of ARF in malaria.

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