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Original Article

Study of Epidemiological Profile, Clinico-Biochemical Spectrum and Prognosis of Malaria-Induced Renal Dysfunction for Appropriate Patients

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ABSTRACT

Introduction: Malaria is one of top ten killer disease in the world. Approximately 40% of the world's population lives in the regions where malaria transmission is endemic, mainly in the tropical and the subtropical regions.
AIM: The objective is to study the epidemiological profile, clinico- biochemical spectrum and prognosis of malaria induced kidney dysfunction for appropriate patients.
Methodology: This study was conducted in the Department of Paediatrics at P.B.M. Hospital during the resurgence of malaria outbreaks in the years 2013 and 2014.
Result: Majority of the cases of malaria-induced renal dysfunction were due to P. vivax infection, with maximum incidence seen in children aged 5–10 years. Fever and oliguria were the most common presenting features, while thrombocytopenia, electrolyte abnormalities, anemia, and raised serum creatinine were frequently observed; mortality was 6.6%, mainly due to respiratory failure, cerebral malaria, and gastrointestinal hemorrhage.
Conclusion: Renal dysfunction is an important and potentially fatal complication of malaria, commonly associated with oliguria and raised serum creatinine at presentation. Early recognition, prompt diagnosis, and timely intervention can significantly reduce morbidity and mortality in children with malaria-induced acute renal failure.

Keywords: *Malaria, Acute Renal Failure, prognosis*

INTRODUCTION

Malaria is one of top ten killer disease in the world. Approximately 40% of the world's population lives in the regions where malaria transmission is endemic, mainly in the tropical and the subtropical regions[1]. About 300 to 400 million clinical cases of malaria are reported annually 1 and mortality estimates ranges between 0.7 and 2.7 million. Most of these deaths are in young children. In Sub-Saharan Africa, where malaria mortality is highest, 90% of the reported malaria-related deaths occur in children younger than the age of five years.[2] By using a combination of epidemiologic, geographic, and demographic data, Snow et al estimated that there were 515 (300-600) million episodes of Plasmodium falciparum malaria in 2002. These global estimates were up to 50% higher than those reported by the World Health Organization[3]. The disease is mainly present in the tropics and countries in sub-Saharan Africa, which account for nearly 90 percent of all malaria cases. The majority of the remaining cases are clustered in India, Brazil, Afghanistan, Sri Lanka, Thailand, Indonesia, Vietnam, Cambodia, and China. Malaria causes 1 to 1.5 million deaths each year in the world and in Africa, it accounts for 25 percent of all deaths in children under the age of five .[4]

In India, the overall yearly incidence is 13 to 17.8% of malarial cases.[5] As its worldwide incidence increases, so are the complications of severe falciparum malaria, including acute renal failure. It is estimated that in 1% of cases , a combination of parasite and host factors will lead to severe malaria, jaundice and acute renal failure, which is associated with 45% mortality. In endemic areas the incidence of ARF may be 4% of all the malarial cases. Worldwide, the incidence of ARF as

a result of malaria varies between 0.6 to 60% depending upon the region. Early intervention, including appropriate antimalarial treatment and renal replacement therapy, is associated with improved survival and recovery of kidney function among patients with ARF as a result of severe malaria.[6]Over a decade ago, cerebral malaria was the predominant manifestation of severe malaria, whereas today the combination of jaundice and renal failure are more common. In Southeast Asia there is an upsurge in the overall incidence of malaria induced acute renal failure and has been reported in between 13% to 17.8%[7].

Malaria has been a major public health problem in India since ancient times, with references found in the Atharva Veda and Charaka Samhita. During the latter parts of nineteenth and early twentieth centuries nearly one-fourth of India's population suffered from malaria, with the annual incidence estimated at around 75 million cases in 1953 and about 7-8 lakhs deaths annually, particularly in the states like Punjab and Bengal.At the time of independence in 1947, the direct mortality due to the disease was estimated at 0.8 million per annumFollowing independence, the Government of India launched the National Malaria Control Programme in 1953, which initially achieved a remarkable decline in malaria incidence; however, repeated technical and operational setbacks led to resurgence of the disease.[8] In recent decades, malaria has re-emerged with newer challenges such as insecticide-resistant vectors, drug-resistant P. falciparum, rapid urbanization, irrigation projects, and changing vector behaviour, contributing to increased transmission and persistence of the disease.In 2007, in Rajasthan a state 55,000 malaria cases were reported and 46 deaths were caused by malaria. Between 2002 and 2006 the slide positivity rate ranged between 0.56% and 2.29 % in Jodhpur. Over a hundred cases of malaria have been reported from the Kolayat town in Bikaner, most of them due to the Plasmodium falciparum malaria. There are also reports of a large number of people suffering from fever and similar medical conditions[9]. The incidence of Plasmodium falciparum malaria was brought to notice when 76 cases of the disease were registered within a month in the hospitals of this area. Most of these cases were traced to Kolayat.

AIM

The objective is to study the epidemiological profile, clinico- biochemical spectrum and prognosis of malaria induced kidney dysfunction for appropriate patients.

METHODOLOGY

This study was conducted in the Department of Paediatrics at P.B.M. Hospital during the resurgence of malaria outbreaks in the years 2013 and 2014. The study included pediatric patients of both sexes who were admitted to the pediatric wards with a clinical diagnosis of malaria. Confirmation of malaria was done by examination of thick and thin peripheral blood smears and/or by Optimal test. Only those patients who demonstrated asexual forms of Plasmodium on peripheral smear examination or had a positive Optimal test for Plasmodium were included in the study. Patients with malaria-induced renal dysfunction at presentation were enrolled, where malaria-induced renal dysfunction was defined as derangement in renal function tests at the time of presentation.

Patients suffering from infections known to cause multiorgan dysfunction, such as enteric fever, brucellosis, leptospirosis, hepatitis A, hepatitis B, hepatitis C, hepatitis E, and dengue, were excluded from the study. Patients with a past history of systemic illnesses affecting renal function, those receiving medications likely to alter renal function tests, and unwilling patients were also excluded from the study.

RESULT

Table 1: Geographical Distribution of Patient with Malaria Induced Acute Renal Failure

Area	P. vivax	P. falciparum	Mixed
Bikaner	12	1	4
Sri Ganganagar	14	1	3
Kolayat	6	-	3
Khajuwala	5	-	1
Other	4	-	1
Nokha	4	1	0
Total	45	3	12

Maximum cases were from Sri Ganganagar (30%) district followed by Bikaner (28.33%) and other areas.

Majority of the cases i.e., 45 (75%) patients had P.vivax malaria, mixed infection was present in 12 (20%) patients and P. falciparum malaria in 3 (5%) patients.

Table 2:Relationship of Age group and Malaria Induced Acute Renal Failure

Age group (Years)	P. vivax	P.falciparm	Mixed

<5 yr	13	2	3
5-10 Yr	21	1	5
10-15yr	11	0	4
Total	45	3	12

Twenty seven (45%) patients presenting with malaria induced acute renal failure were in the 5-10 year age group.

Table 3:Major Clinical Manifestations in Malaria Induced Acute Renal Failure Patients

Manifestation		Percentage
Fever	60/60	100%
Vomiting	32/60	53.33%
Unconsciousness	7/60	11.67%
Convulsions	8/60	13.33%
Oligo/Anuria	56/60	93.33%
Abdomen pain	9/60	15%
Dyspnea	6/60	10%
Hypotension	20/60	33.33%
Headache	8/60	13.33%
Jaundice	4/60	6.67%
Hepatosplenomegaly	33/60	55%

Fever and oliguria were observed in all the patients (100%) followed by hepatosplenomegaly and vomiting in 33% & 32% patients respectively. Hypotension was found in 20% of the patients.

Table 4:Association of hematological profile with Malaria Induced Acute Renal Failure

hematological profile		P. vivax	P. falciparum	Mixed	Total
Hb	**<5 g/dl**	5	0	1	6(10%)
	5-10 g/dl	26	1	6	33(55%)
	>10 g/dl	14	2	5	21(35%)
TLC	<4000/mm3	11	0	2	13(21%)
	4000-11000 mm3	25	2	8	35(58%)
	>11000mm3	9	1	2	12(20%)
Thrombocytopenia	<50,000	10	0	3	13(21.66%)
	50,000-100,000	13	0	4	17(28.33%)
	100,000-150,000	22	3	5	30(50%)

Thirty three (55%) patients with malaria induced acute renal failure had Hb level between 5-10 g/dl.
Thirty five (58%) patients had TLC in the normal range (4000-11000/mm3), while 13 (21%) had leucopenia and 12 (20%) had leucocytosis.Severe Thrombocytopenia was found in 13 (21.66%) patients.

Table 5:Electrolyte Abnormalities in Patients of Malaria Induced Acute Renal Failure

Malarial Species	Electrolyte abnormality			
	Hypokalemia <3.5mg/dl	Hyperkalemia >5.5mg/dl	Hyponatremia <135mg/dl	Hypernatremia >145mg/dl
P. vivax	8	2	12	3
P. falciparum	0	0	3	0
Mixed	2	1	5	0
Total	10	3	20	3

- Hypokalemia was found in 10(16.66%) patients. Hyperkalemia was found in 3 (5%) patients.
- Hyponateremia was found in 20 (33.33%) patients. Hypernatremia was found in 3 (5%) patients.
- Electrolyte abnormalities were found in 36 (60%) patients.

Table 6:Association of Serum Creatinine levels with Malaria Induced Acute Renal Failure

Malarial Species	Serum Creatinine 1.5-3mg/dl	SerumCreatinine >3mg / dl
P. vivax	41	4
P. falciparum	2	1
Mixed	12	0
Total	55(91.66%)	5(8.33%)

S. Creatinine >3mg/dl was observed in 5 (8.33%) patients.Majority of the patients i.e., 55 patients (91.66%) had S.Creatinine levels <3 mg/dl.

Table 7:Total Duration of Illness After Hospitalization in Malaria Induced Acute Renal Failure Patients

Malarial species	Duration <5 days	Duration 6-10 days	Duration >10 days
P. vivax	35	6	4
P. falciparum	3	0	0
Mixed	7	4	1
Total	45(75%)	10(16%)	5(8.3%)

75% patients recovered in < 5 days,16 % had a hospital stay of 6-10 days and, 8.3% patients stayed for > 10 days.55 patients (91%) recovered in <10 days of illness .

Table 8:Cause of Mortality in Patients with Malaria Induced Acute Renal Failure

Cause	P. vivax	P. falciparum	Mixed
Cerebral Malaria	0	0	1
Respiratory Failure	2	0	0
GI hemorrhage	0	0	0
Multiorgan failure	0	0	1
Total	2	0	2

The cause of death was respiratory failure in two patients, Multiorgan failure in one patient and cerebral malaria in the fourth patient.

DISCUSSION

The desert region of Bikaner has traditionally been hypoendemic for malaria, but developmental activities, climatic changes, irrigation through the Indira Gandhi Canal, migration of laborers, and increased rainfall have significantly altered

the epidemiological and clinical profile of malaria in recent years. Complications such as jaundice and acute renal failure are now increasingly observed not only in P. falciparum malaria but also in P. vivax malaria. Severe malaria, as defined by the World Health Organization, is associated with high mortality, especially among children, elderly individuals, and pregnant women, and annual report from the Government of India has reported that 38.6% of all cases from different parts of the country were due to P.falciparum.

Our study do not reflect the true prevalence of P.falciparum and P.vivax malaria in the community as most of our patients were from districts of Bikaner and Shri Ganganagar, while some serious and complicated cases were referred from primary health centres situated in the rural areas with semi developed medical facilities.

Thirty one percent of total cases were from Shri Ganganagar, 28% cases were from Bikaner, 15% cases were referred from Kolayat tehsil in Bikaner district which is the main pockets of existence of malaria followed by 8% cases from Nokha and 4% from other area . Out of total 60 cases,45 (75%) were of P.vivax, 12 (20%) were of mixed infection and 3 (5%) cases were of P. falciparum infection .Two parasite species can develop in the same vector species and infection can be transferred with a single bite. So patients with mixed infection have their clinical pictures mixed up and fever might occur daily. In India about 70% of the infections are reported to be due to P.vivax, 25-30% due to P.falciparum and 4-8% due to mixed infection. [10]

The majority of the patients (45%) were between 5-10 years of age followed by 25% patients in the 10-15 year age group and 30% patients were in the 0-5 year age group.This lower incidence among 0-5 year may be due to maternal immunity in infants and more care and attention given by parents to the young children. Higher incidence among the age group 5-10 years is due to more mobility and unawareness of the preventive aspects of the disease.

Fever and oliguria were observed in all the patients (100%) followed by HSM and vomiting in 33% &32% respectively. Hypotension was observed in 20% of patients. In a study conducted at tertiary care center at Asarwa, Ahmadabad, Gujarat, India the presenting features were fever (100 %), nausea-vomiting (89%), oligo/anuria (82%), abdominal pain/tenderness(55%), jaundice (55%), dyspnea (30%), altered sensorium (31%),convulsions (18%), diarrhea (17%), Splenomegaly (69%) and hepatomegaly (39%) , which nearly correlates with our study.[11]

Thirty three out of 60 patients of malarial renal dysfunction were having moderate anemia with hemoglobin levels between 5 to 10 gm/dl and only 6 had Severe anemia having hemoglobin below 5 gm/dl.Severe anemia is a common feature of P. falciparum malaria; however, in vivax-endemic areas, P. vivax is a major risk factor for severe anemia, particularly in young children [12]

twelve (20%) patients of renal failure had leukocytosis (TLC >11000/cu mm) and 13 (21%) had leukopenia which suggests some superimposed infection or endotoxemia and 35 (58%) patients had normal leukocyte count.

Out of 60 cases of Malaria induced acute renal failure 10 (16.66%) patients had hypokalemia & 3 (5%) patients had hyperkalemia and hypernatremia & 20 (33.33%) patients had hypernatremia. The Total Electrolyte abnormality was observed in 36(60%) of the patients. Renal involvement in the form of electrolyte abnormalities has also been seen during malaria infection.

Out of the 60 patients, 13 patients, had severe thrombocytopenia, 17 patients had moderate thrombocytopenia, and 30 patients had mild thrombocytopenia. A rare case of idiopathic thrombocytopenic purpura triggered by P. vivax infection has also been described by Lacerda et al [13]

S. Creatinine >3mg/dl was observed in 5(8.33%) patients and 55 (91.66%) had S.Creatinine level <3 mg/dl which found to be statistically significant.

Out of 60 patients with malaria induced Acute Renal Failure 45 patients were hospitalized for less than 5 days, 10 for 6-10 days, and 5 patients needed more than 10days of hospitalization. Out of these 4 patients expired during treatment. Stone et al also found that the average duration of symptoms after hospitalization was eight days. [14]

Out of 60 patients present as renal dysfunction 4 patients expired due to complications of Malaria induced acute renal failure. Causes of death in 2 patients were respiratory failure and in the other two patients it was gastrointestinal hemorrhage and cerebral malaria.William J stone et al [14](1972) found that mortality was 29% in patients of P.falciparum malaria with renal failure and the major causes of mortality were cerebral and pulmonary complication. These finding are identical to those of our study.

CONCLUSION

In spite of high prevalence of renal dysfunction in malaria it is not reported early due to lack of awareness among healthcare providers because of lack of suspicion of malaria and shortage of rapid and sensitive diagnostic facilities. The specific

reason for presenting our observation is to develop awareness regarding the early complication of malaria and to prevent these, prompt actions must be taken.In this hospital based observational study we observed that ARF was more common in subjects who have high serum creatinine and oliguria at the time of presentation.Early diagnosis of ARF and intervention in subject who have malaria with acute complication can save many lives.In the light of our study further studies are recommended with a large sample size to see the association of renal dysfunction in malaria.

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