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Original article

Clinical Spectrum of Renal Involvement in Malaria in Kumaon Region of Uttarakhand

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ABSTRACT

Introduction : Malaria poses a great Public Health menace in India especially in the Gangetic Plains of Uttarakhand, Uttar Pradesh and Bihar, which is now endemic for malaria. The present study reports the serious complications of malaria, like malarial nephropathy. **Material and Methods :** Three hundred sixty patients with acute febrile illness were subjected to various tests of malaria, Routine hematological, biochemical tests and urine examination were performed. The data of their mode of presentation, management and outcome was analyzed. **Results :** Two hundred forty one cases out of three hundred and sixty were positive for malaria and of these positive cases of malaria, 32 patients (13.2%) revealed renal involvement. Their age ranged from 18 to 65 years (mean $\pm$ SD = 45.8 $\pm$ 6.2 years) with male to female ratio being 2.2:1. Plasmodium falciparum alone (50%) or mixed infection with Plasmodium vivax (31.2%) were the causative organism. Oliguria and/or anuria (62.5%) was the commonest mode of presentation. All of them were managed with appropriate antimalarial drugs, fluid and electrolyte replacement and other supportive therapy. Hemodialysis was performed in 10 cases and 8 of them had full recovery. Seven patients(21.8%) expired within 48-72 hours. Multi organ-failure and sepsis were the main causes of death. **Conclusion:** Our study shows that falciparum malaria is an important cause of acute renal failure. Advanced age, oliguria, anuria, hypovolumia, electrolyte imbalance and late referrals were the main bad prognostic factors. So early intervention is required for the favourable outcomes in these cases.

KEYWORDS: Acute renal failure, Falciparum malaria, Nephropathy, Hypovolumia

INTRODUCTION

Malaria is a common health problem in India and it is endemic throughout South East Asia, South America and Africa, largely as a result of warmth and humidity which favours the multiplication of mosquito Anopheles, the principal vector for the transmission of malaria[1]. The disease is caused by haemoparasite protozoa Plasmodium, of which Plasmodium falciparum and Plasmodium vivax are common pathogens. Plasmodium falciparum malaria poses a great public health menace in India especially in the Gangetic balt of Uttarakhand, Uttar Pradesh, Bihar and also Tamilnadu and Orissa[2,3].

Infection with the Plasmodium falciparum produces mainly acute manifestations, ranging from asymptomatic urinary abnormalities and mild electrolyte imbalance to acute renal failure. Renal failure is multifactorial and carries a high mortality and morbidity[1,4] Malaria was not usually seen in the Kumaon region of Uttarakhand in the past but of late due to a significant increase in population, deteriorating hygienic conditions, migratory population, poor sanitation and a large influx of tourists are mainly responsible for the resurgence of malaria in this region.

In view of the increasing incidence of malaria in Kumaon region of Uttarakhand , the present study was undertaken to evaluate the incidence and degree of renal involvement in patient with malaria.

MATERIALS AND METHODS

During the period of January, 2007 to December 2009, three hundred sixty patients of acute febrile illness compatible with malaria were studied. Two hundred forty one cases out of three hundred and sixty were positive for malaria included in study. The study was conducted in the Department of Medicine, Government Medical College Haldwani, Uttarakhand. The diagnosis of malaria was confirmed by the demonstration of malaria parasite on thick and thin peripheral blood smear. Other methods for malaria detection viz. quantitative buffy coat smear, antigen detection, malarial pigment in polymorphonuclear leucocytes were carried out in patients where blood film could not demonstrate malarial parasite. Gradation of parasitaemeia was done by counting number of parasitized red blood cells. One thousand RBC were screened for the presence of parasite and percentage of infected RBC determined the parasite load which was graded as follows-.

-up to 10% mild parasitaemia

-10 to20% moderate parasitaemia

-20 to30% severe parasitaemia

-Above 30% fulminent type parasitaemia, which was usually fatal

Two hundred forty one positive cases (68.7%) of malaria were subjected to detailed history and physical examination. Renal involvement was evidenced by the presence of pyrexia followed by albuminurea, oligurea, anurea and development of uremia within 7 to 10 days. Routine investigations like haemoglobin, total and differential leucocyte counts and urine examination for quantative proteinurea and sediments were performed. Biochemical examination were performed for estimation of blood urea, serum creatinine, serum electrolytes and liver enzymes. Ultrasonography was performed for visualizing the KUB region.

All Patients were treated with antimalarial drugs along with other supportive measures. Hemodialysis was appropriately performed in clinically and biochemically indicated patients viz; patients in uremia, acidosis, hyperkalemia, fluid overload, oligurea, anurea and raised creatinine level. The duration and number of dialysis were determined as per clinical and/or biochemical improvement. All patients were followed-up till discharge from hospital or death. The complications were analyzed in each patient and possible cause of death was noted.

RESULTS

Thirty two cases (13.20%) with male to female ratio of 2.2:1, revealed clinical evidences of renal involvement (smear positive malaria cases = 211, serologically positive cases = 30). Their age ranged from 18 to 63 years with mean ± SD=30.4 ± 5.2 years (Table:1). Plasmodium falciparum either alone 16 cases or 50% or in mixed infection with Plasmodium vivax was seen in 50% and 31.2% of cases respectively (Table:2) Degree of parasitaemia in 27 cases (malaria parasite positive in blood film) revealed severe degree parasitaemia in 12 cases (44.4%) and fulminant in 4 cases(4.8%). Pyrexia with body ache and prostration (85.5%) was usual presentation and often associated with nausea and vomiting (43.7%), followed by hypovolumia (56.2%), oligurea (68.7%) and anurea (6.2%) (Table:3).

Table :1 Demographic profile of study subjects

Age groups in years	Number of cases (%)	Sex	
		Male	Female
11-20	19 (7.8%)	10	9
21-30	60 (24.8%)	41	19
31-40	49 (20.3%)	33	16
41-50	68 (28.2%)	48	20
51-60	33 (13.7%)	24	9
Above 60 Years	12 (5.2%)	9	3
Total (%)	241 (100%)	165	76

Table:2 distribution of cases according to the type of malaria and renal involvement

Age groups in years	P. Falciparum		P. Falciparum + P. Vivax		P. Vivax		Serum Positive malaria cases	
	No. of cases	Renal involvement	No. of cases	Renal involvement	No. of cases	Renal involvement	No. of cases	Renal involvement
11-20	9	1	1	0	8	0	1	1
21-30	40	3	7	2	6	1	7	1
31-40	30	5	5	3	8	0	6	1
41-50	34	6	11	4	15	0	8	1
51-60	17	0	3	1	8	0	5	1
Above 60	5	1	0	0	4	0	3	0
Total %	135	16	27	10	49	1	30	5
	56	6.6%	11.2	4.1	20.3	0.4	12.4	2.1%

Table:3 Presenting Clinical Features of Malarial Nephropathy Patients (n=32)

Clinical Features	Number of Cases	%
Fever	28	87.5
Body ache, Myalgia, Headache	22	68.7
Hypothermia (Temp. <36.5^{0}c)	2	6.8
Nausea, Vomiting	14	43.7
Oliguria	22	68.7
Anuria	2	6.8
Beeding	3	9.4
CNS symptoms	12	37.5
Convulsion	3	9.4
Dehydration or hypovolumia	18	56.2
Jaundice	14	43.7
Hepatosplenomegaly	10	31.2
Splenomegaly	9	28.5
Oedema Over Feet & Face	7	21.8
Respiratory distress	3	9.4
Hypotension (Systolic B.P. <90 mmHg)	5	15.6

Routine investigations revealed mild (31.2%) to moderate (46.9%) degree of anaemia with leucocytosis in 14 cases. Thrombocytopenia (platelets<80000/c.mm) was seen in 37.5% of cases and 5 of them showed evidences of bleeding with platelets<40000/c.mm. Functional renal changes was observed in the form of proteinurea >500mg/day in 15 cases (46.9%) with raised specific gravity (>1020) in 13 cases and various types of urinary sediments in 17 cases (53.1%).(Table:4)

Table: 4 Haematological and Urinary Findings Patients with Nephropathy Patients (n=32)

Haematological Findings	Number of Cases	%
Haemoglobin		
< 8 gm / dL	6	18.7
8-10 gm / dL	9	28.2
10-12 gm / dL	10	31.2
Total Leucocyte Counts – > 10,000 / c.mm	14	43.7
Platelet Counts –		
< 40,000 / c.mm	5	15.6%
40,000 – 80,000 / c.mm	7	21.9%
Prothombin Time		
> 15 seconds	5	15.6
Urinary Findings		
Specific gravity > 1.020	13	40.6
Proteinura	17	53.1
< 500mg / day	15	46.9
> 500mg / day	6	12.5
Haematuria (RBC>10/HPF)	13	40.6
Pus Cells(above 25 cells/HP)	5	15.6
Hyaline Cast	2	6.2
Granular Cast	4	12.5
Cylinduria		

Biochemical changes revealed raised blood urea and serum creatinine in 20 (62.5%) and 14 (43.8%) cases respectively. Five cases revealed hyperbilirubinemia (serum bilirubin > 5 mg/dl), whereas there was more than two fold increase in serum transaminases in 12 cases (37.5%). Electrolyte imbalance in the form of hyponatremia and hyperkalemia was seen in 50% and 34.4% of cases respectively. (Table:5), Renal biopsy could be performed in two cases only and histopathological findings was suggestive of proliferative glomerulonephrites in one and acute tubular necrosis with pigmented cast in other case.

Table:5 Biochemical Findings in Malaria Patients with Nephropathy Patients (n=32)

Biochemical Findings	Number of Cases	%
Blood Sugar < 60 mg / dL	9	28.2
Blood Urea –		
up to 80 mg / dL	12	37.5
> 80 mg / dL	20	62.5
Serum Creatinine –		
up to 2.6 mg / dL	18	56.2
> 2.6 mg / dL	14	43.8
Serum Bilirubin –		
2.0 – 5.0 mg / dL	9	28.2
> 5 mg / dL	5	15.6
SGPT or ALT, above two fold increase	12	37.5
SGOT or AST, above two fold increase	11	34.4
Serum Sodium <130 meq / L	16	50
Serum Potassium > 5.5 meq / L	11	34.4
LDH > 500 IU / L	12	37.5

All patients were managed with standard course of antimalarial drugs (chloroquine, artimesnin-derivatives, mefloquene) and conservatively, with special attention to maintain the fluid electrolyte balance and euglycemia (9 cases with blood sugar < 60mg/dl). Fluid was administered slowly and titrated against central venus pressure and urine output to avoid fluid overload. Hemodialysis was performed in 10 cases and 8 of them showed full recovery of renal function. Two patients expired, who were in anurea with severe degree of renal impairment.There was no significant difference in number of session of dialysis between oliguric and non-oliguric cases.

Table:6 Risk factors identified with malarial nephropathy and correlation with mortality

Risk factors*	**Number of Cases**	**Expired Cases**	
		number	%
Age above 40 years	14	6	42.5
Oliguria	18	4	22.5
anuria	2	2	100
coma	1	1	100
Hemoglobin <10gm/dL > 10gm/ dL	15 17	3 4	20 23.5
Platelets < 80,000 / c.mm	7	4	57.1
Blood Urea > 80 mg / dL	24	6	25
Serum Creatinine > 2.5 mg / dL	14	6	42.8
Serum Biliriubin > 5 mg / dL	5	3	60
Hyponatremia (Sodium < 130 meq / L)	16	5	31.2
Hyperkalemia (Potassium > 5.5 meq/ L)	11	6	54.5
Hypotension (Systolic B.P. < 90 mm Hg)	5	3	60

***majority of patients had more than one risk factors**

Table:6, revealed the various risk factors. Mortality was 21.8% ,comatosed patients expired within 48 hours. Advance age (death in 6 aged cases, 42.5%), late referral, acute illness with septicaemia were main prognostic factors. Three out of 5 cases (60%) with hepato-renal failure expired within 2-3 days. Overall it can be concluded that advance age, oligurea, anurea, hypovolumea, hepato-renal failure and respiratory distress, had a bad prognosis.

DISCUSSION

More than one billion people are infected with malaria and disease causes 0.5 to 3 million deaths each year [1,3,4,5]. Severe malaria is mostly caused by Plasmodium falciparum which is the only species of malaria that causes parasatised red blood cells to adhere to endothelial cells and produce micro-vascular changes. These changes often result in multisystem disorder presenting with different complications. Renal involvement in malaria is a well recognized complication. It is usually found in patients with severe malarial infection associated with hemodynamic disturbances, acidosis and multiogran failure[1,3,6,7]. Acute renal failure is a serious complication of falciparum malaria and carries a high mortality of 15 to 45% [1,3,4]. In the present series of cases, the mortality was 21.8%.

Plasmodium vivax is also incriminated in acute nephropathy[8,9] . We observed one patient with Plasmodium vivax out of 49 cases of Plasmodium vivax infection had renal failure, whereas 10 cases with mixed infection had renal impairment out of 27 cases (37%). Acute renal failure in malaria is multifactorial and two mechanisms are involved in the pathogenesis of nephropathy in malaria[1,3,8,9] viz; impaired microcirculation due to parasitized red blood cells which resulted to renal ischemia and non-specific effect of infection like hypovolumea, hypotension, jaundice, intravascular hemolysis, coagulation and endotoximea.

Hypovolumia (18 cases or 56.26%) was the commonest cause of acute renal failure in the present series of cases which resulted from nausea/vomiting (43.7%), decreased fluid intake, fever (87.5%) and severe infection which caused increased vascular permeability because of release of catecholamines. In malaria the hyperbilirumbinemia (unconjugated) was mostly seen which is due to hemolysis and conjugated element elevation resulted from cholestasis[3,10].Malarial hepatitis was present in 14 cases (jaundice, 43.7%) which was hallmarked by raise serum transaminase(37.5%) and incidence was reported up to 20% or even more[3,4,11]. Hyperbilirubinemia increases a vascular response to catecholamine and increase renin activity[3,12].

Hemolytic process is mostly responsible for hyperbilirubinemia but majority of opinion is that both hemolytic and cholestatic factors may be responsible for hyperbilirubinemia (present series 43.7%). Malarial parasite mimics the effect of endotoxin through activation of monocytes. Recently, cytokines have been implicated in the production of endotoxin like product in malaria[3]. In the present series 43.7% cases had clinical and laboratory evidences of sepsis, 15.6% of cases had hypotension (BP<90mmHg, systolic) resulting in renal ischaemia due to decreased perfusion of kidney. Hyponatremia (50%) and hyperkalemia (34.4%) are typical biochemical findings in malarial acute renal failure and incidence reported upto 55%[4,13,14] Although internal dilution is the usual mechanism but the, true sodium wastage occurs before the onset of oliguria.

Hyperkelamia is striking feature and often fatal. It is attributed to hemolysis, rhabdomyolysis and acidosis, particularly in the presence of impaired renal function. Lactic acidosis is reflecting the degree of tissue hypoxia. Histological picture is a variable mixture of acute tubular necrosis (ATN), interstitial nephritis and glomerulo-nephritis, thereby displaying the three major pathogenic mechanisms described. ATN is most consistent histologic finding. Tubular changes includes cloudy swelling, hemosiderin, granular deposits and variable degree of cell necrosis. In the present series the histopathologic finding is available in only two cases which consists of ATN and proliferative glomerulonephritis.

Acute interstitial inflammation is well recognized pattern of malarial nephritis with clumps of parasitized erythrocytes in the venules in experimental animals. Glomerular lesions are characterized by proximal mesangial proliferation with many transit cells. Deposition of an eosionphillic granular material has been noticed along the capillary walls with in mesangium and in Bowman's capsule. The glomerular capillaries often are empty, but they may contain a few parasitized cells or giant nuclear masses in patients who develop intravascular coagulation. The prognosis in acute renal failure (ARF) is favourable in patients who have early diagnosis, early referral and underwent dialysis as and when needed. Approximately 60% of malarial ARF required dialysis[3,15].

In the present series 10 cases (31.2%) were dialyzed out of which the eight case (80%) had full recovery of renal functions. Twenty two cases (68.8%) were managed with conservative treatment with anti malarial drugs and other supportive measures and 5 of them expired (22.7%) because of hypotension, fluid and electrolyte loss and old age. The mortality in malarial ARF in various studies varies from 10-45%[1,3,8,10]. The overall mortality in the present series of cases was (21.8%). The cause of death was found to be multifactorial. Prognosis was unfavourable when multiple organs are involved and in the present series of cases (Table-5) multi organ involvement was found to be the commonest cause of death.

CONCLUSION

It can be inferred from our study that falciparum malaria is an important cause of acute renal failure. Nephropathy varies widely from mild proteinuria in association with urinary sediments to acute renal failure. Advanced age, oliguria, anuria, hypovolumia, electrolyte imbalance and late referrals were the main bad prognostic factors. The favourable outcome can only be achieved by early diagnosis treatment with appropriate anti malarial drugs with supportive measures and early dialysis.

REFERENCES

1. Naqvi R, Ahmed E, Akhtar F, Naqvi A, Rizvi A. Out come in severe acute renal failure associated with malaria. Nephrology Dialysis Transplantation 2003; 18:1820-1823.
2. Mishra KC, Baliarsinha AK, Panda R, Das S, Mohanty SC. Renal Changes in falciparum malaria. J. Assoc Physicians India 1982; 30:723-24.
3. Maheshwari A, Singh AK, Singh DK, Tripathi K, Prakash J. Spectrum of renal disease in malaria. J. Indian Med. Assoc 2004; 102:144-150.
4. Dash SC, Bhuyan UN, Gupta A, Sharma LC, Kumar A, Agarwal SK. Falciparum malaria complicating cholestatic jaundice and acute renal failure. J Assoc Physicians India 1994; 42(2):101-102.
5. Guerin PJ, Olliar P, Nosten; Current status of control, diagnosis, treatment and a proposed agenda for research and development. Lancet Inf Dis, 2002; 2:564-573.
6. Nicholas JW, Joel GB. Malaria, in "Harrison's Principles of Internal medicine". Ed. 18th. Editors Fauci AS, Kaspar DL, Longo DL, Hauser SL, Jameson JL, Loscalzo J, MC Graw Hill Medical, New York, New Delhi. 2012 Vol-1, Ch-210, PP 1288-1705.
7. Agarwal AK, Chatterjee S; Dilip R Karnad : Malaria, in "API Text book of Medicine" 9th Edition, Eds : Munjal YP, Sharma S K, Agarwal AK et al. The Association Physician of India Mumbai, 2012, Vol-2, Ch-52, PP 1177-1184.
8. Prakash J, Singh AK, Kumar AS, Sexana RK. Acute renal failure in Plasmodium vivax malaria. J Assoc Phys Ind 2003; 51:265-267.
9. Myang Dono, Shinlt, Shin D, Uiscok KJM. Clinical features of vivax malaria. Am J Trop Med Hyg 2001;65:143-146.
10. Barsoum R. Malarial acute renal failure. J Am Soc Nephrol 2000; 11:2147-2154.
11. Wilairatama P, Looareesuwans; Charoenlap P. Liver Profile Changes and complication in Jaundice Patient with falciparum malaria. Trop Med Parasitol 1994; 45:298-302.

12. Bloom D, MC Calden TA. Effect of jaundiced plasma on vascular sensitivity to nor-adrenaline. Kidney Int 1975;8:149-57.

13. Hilton Rachel. Acute Renal failure. Brit. Med. J 2006; 333 : 786-790

14. Prakash J. Acute renal failure in malaria (Letter to Editor) J Assoc Phys Ind 2005; 55:656-658.

15. Stone WJ, Hanchett JE, Knephshield JH. Acute renal insufficiency due to falciparum malaria : review of 42 cases. Arch Intern Med 1987;46:167.

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