Original Research Article

Study of renal complications of malaria

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Abstract

Background: Plasmodium falciparum malaria is one of the major health problems in many tropical countries including India and due to increase in the drug resistance in India the incidence of complicated malaria has increased.
Objectives: To study the renal complications of malaria.
Materials and methods: 50 malaria positive cases with clinical renal disease were prospectively observed clinically and by laboratory investigations till the discharge.
Results: Among the 50 malaria positive cases 41 (82 %) patients had p. falciparum infection, 4 (8%) had p. vivax and 5 (10%) had mixed infections. P. falciparum and mixed infection found to be responsible for ARF in 25 (89.28%), 3 (10.70%) respectively. Volume depletion was found to be the prominent cause (75%) of ARF, hyperbilirubinemia was noted in 64.28% of patients. Urinary abnormalities were noted in 24 (48%) cases, proteinuria in 20(40%), microscopic haematuria in 20 (40%), granular casts in 7 (14%). In the present study electrolyte abnormalities were noted in 46 (92%) of the patients. The overall mortality in the present study was 5 (10%). The cause of death was multi-factorial. MODS were the commonest cause of death.
Conclusion: Renal complications were seen as the commonest complication of malaria. Early diagnosis, treatment specially the fluid management reduces the overall mortality

Key words

Falciparum malaria, Renal complications, Urinary abnormalities, Hypovolemia.

Introduction

Malaria is a protozoan disease transmitted by the bite of the anopheles mosquitoes and characterized by fever, splenomegaly, anaemia and chronic relapsing course. It is one of the most important parasitic diseases of the humans affecting hundred and three endemic countries

with a population of over 2.5 billion people and causing between one and three million deaths each year worldwide. Studies carried out so far in India revealed that Plasmodium falciparum resistance to chloroquine is widespread in the North eastern and Eastern parts. Severe falciparum malaria may present as cerebral malaria, hypoglycemia, lactic acidosis, non-cardiogenic pulmonary edema, renal impairment, hematological and hepatic abnormalities, petechial hemorrhages in the skin and mucus membranes develop rarely in severe falciparum malaria. Alteration in coagulation profile prolonged PT, thrombocytopenia and presence of fibrin degradation products are common in severe falciparum malaria [1]. Occasionally, disseminated intravascular coagulation occurs in severe falciparum malaria and is associated with cerebral and renal complications [2, 3]. Nephrotic syndrome may occur in chronic P. malaria infections**.**

Acute renal failure (ARF) commonly occur as a complication of plasmodium falciparum infection, occasionally in P. vivax infection [4, 5] and found in the setting of severe infection associated with hemodynamic disturbances, and multi-organ failure [6]. The cause of established ARF is due to acute tubular necrosis or as a part of multi-organ dysfunction. Two mechanisms are involved in the pathogenesis of ARF in falciparum malaria [7, 8] viz, impaired microcirculation due to parasitized erythrocytes resulting in renal ischemia and non-specific effects of infection like hypovolemia, hypotension, Jaundice, intravascular haemolysis, intravascular coagulation and endotoxemia. Vascular endothelial damage, induced by anoxia, complement activation and oxygen radicals released during inflammatory process and circulatory reflow further increases fluid leakage from the intravascular space [9]. Hyperbilirubinemia increases vascular response to catecholamine and increases renin activity [10]. Recently cytokines have been implicated in the production of endotoxin like effect in malaria [11]. Malaria ARF is catabolic in type characterized by rapid rise of plasma urea and creatinine. Mild proteinuria and abnormal urinary sediment occur in patients with falciparum malaria [12]. The urinary proteins consists of albumin and both micro and macromolecule proteins and therefore proteinuria is both glomerular and tubular in origin [13]. Urinary abnormalities in the form of microscopic haematuria and granular caste may be associated with glomerulonephritis in patients with malaria. The prognosis of ARF is favorable in patients who have early diagnosis, early referral and frequent dialysis.

With this background this was the first study conducted at Government Medical College and Hospital Nizamabad, Telangana state, to find out the renal complications of malaria at the earliest so as to take necessary therapeutic measures to decrease the associated mortality and morbidity.

Materials and methods

50 malaria positive cases with clinical renal disease were prospectively observed at Government medical college and hospital, Nizamabad, Telangana state, India, from April 2016 to October 2017 after taking Institutional ethical clearance and written informed consent from the patients.

Inclusion Criteria

Both male and Female patients of age >15 years with clinical renal disease in the form of one or more of any of the abnormalities like abnormal urine analysis, increased urinary protein excretion, acute renal failure, electrolyte abnormalities.

Exclusion Criteria

- Known case of chronic systemic illness involving the CNS, renal, haematological, respiratory, and hepatobiliary systems.
- Patients with history of alcoholism and those taking hepatotoxic drugs.
- Patients with altered renal echo texture on ultrasound abdomen.

Detailed history, clinical examination and treatment received were noted from malaria positive cases, which were confirmed by demonstration of malarial parasite by the peripheral smear or by HRP2 antigen. Other laboratory investigations done were complete hemogram, urine examination for albumin and microscopy- red cells, WBC's casts, crystals and sugar, blood suagr, blood urea, serum creatinine, serum electrolytes, prothrombin time, APTT, liver function tests. Arterial blood gas analysis, X-ray chest, lumbar puncture, CT brain, blood and urine cultures were done if required. Hematological and bio-chemical investigations were done at the time of diagnosis and at the time of remission of symptoms or disappearance of parasitemia. As per W.H.O. Guidelines renal failure was defined as urine output of <400ml in 24 hours in adults, failing to improve after rehydration, and with serum creatinine >3 mg/dl.

Statistical Methods

The Excel and SPSS (SPSS Inc., Chicago) software packages were used for data entry and analysis.

Results

Total 50 Malaria positive cases with clinical disease were studied with M: F ratio of 43:7, of which 41 patients had pl. falciparum infection. **Table – 1**.

Table - 1: Sample composition.

Total no of patients	50
Age group	15-70
M: F	43:7
P. Falciparum	41
Mixed infections	5
P. Vivax	4

Patients' age ranged between 15 to 70 years. The maximum number 17 (34%) of the patient were in the group of 21-30 years (**Table – 2**). Sex distribution was as per **Table – 3**. Etiology of ARF was as per **Table – 4**. Systemic involvement was as per **Table – 5**. Clnical renal disease was as per **Table – 6**.

Table - 2: Age Distribution.

Age (years)	No	%	Mortality%
0-10	0	0.00	0.00
11-20	06	12.00	0.00
21-30	17	34.00	0.00
31-40	08	16.00	25.00
41-50	07	14.00	0.00
51-60	09	18.00	0.00
61-70	02	4.00	33.3%

Table - 3: Sex Distribution.

Sex	Number	Died	Mortality (%)
Male	43	4	9.30%
Female	7	1	14.28%

Table - 4: Etiology of ARF.

Etiology	Number (%)
Volume Depletion	21 (75.00)
Intravascular Hemolysis	19 (67.85)
Hyper-bilirubinemia	18 (64.28)
Sepsis	8 (28.57)
Hypotension	5 (17.86)

Table - 5: Systemic Involvement.

Systems Involved	No of Cases
Renal	50
Hepatic	26
Circulatory	25
Endocrine	19
Respiratory	6
CNS	5

Table - 6: Clinical Renal Disease.

Clinical renal disease	No of patients (N=50)
Urinary Abnormalities	24 (48.00%)
Urinary protein excretion (>500 mg/24 hours)	10 (20.00%)
Electrolyte abnormalities	46 (92.00%)
ARF	28 (56.00%)

Urine examination was as per **Table – 7**. Hypoglycemia cases were as per **Table – 8**. Renal parameters were as per **Table – 9**. Mean RFT vs Mortality was as per **Table – 10**. Serum creatinine as prognostic factor was as per **Table – 11**. Cause of death was as per **Table – 12**.

Table - 7: Urine Examination.

Urine Examination	No. of Cases
Protein	24
Sugar	0
RBC	20
WBC	0
Casts	7
Crystals	0

Table - 8: Hypoglycemia.

	Range	Hypoglycemic Patients	Mortality
RBS (mg%)	24-105	12 (<40 mg%)	25%

Table - 9: Renal Parameters.

Renal Parameters	Mean	Range
BU (mg%)	74.34	32-134
Serum Creatinine (mg%)	3.7	0.6-12.1
Serum Na+ (meq/lt)	134.6	125-157
Serum K+ (meq/lt)	5.02	2.8-7.0

Table - 10: Mean RFT vs Mortality.

RFT Mean	Blood Urea (mg%)	Serum Creatinine (mg%)
Recovered	70.11	3.33
Expired	112.4	6.96

Table - 11: Serum Creatinine as Prognostic Factor.

Serum Creatinine	Cases	Deaths	Mortality
0.2-6	38	0	0%
6.1-12.1	12	5	41.60%

Table - 12: Cause of Death.

Cause of the death	No of Cases	Cases in %
MODS	2	40%
Hepatic failure	1	20%
Cerebral Malaria	1	20%
Sepsis	1	20%

Discussion

In present study 50 malaria positive cases with clinical renal disease were prospectively observed with M: F ratio of 43:7, of which 41 (82%) patients had p. falciparum infection, 4 (8%) had p. vivax and 5 (10%) had mixed infections. Maximum number of patients, 17 (34%) were in the age group of 21-30 yrs.

Analysis of 577 cases of ARF of diverse aetiology revealed that 93 patients (16%) developed ARF complicating malaria (P. falciparum 74 and p. vivax 19). Thus among malarial ARF, plasmodium vivax infection 20.5% was due to P. vivax infection [14]. In the present study P. falciparum and mixed infection found to be responsible for ARF in 25 (89.28%), 3 (10.70%) respectively. None of the vivax malarial developed ARF. The onset of ARF was 4-7 days after the appearance of fever and non-oliguric ARF was found to be more common (50-70%) [15, 16]. In the present study non oliguric ARF was found in 66.66% of cases and remaining 33.33% of patients had oligo-anuric ARF, similar to the findings of above studies [15, 16].

In present study volume depletion resulting from various causes such as high grade pyrexia, vomiting and poor intake was a prominent cause (75%) of ARF. Evidence of volume depletion which was present in 21 (75%) of cases and may be due to decreased fluid intake, sweating from pyrexia and increased vascular permeability due to catecholamine release in severe infection [17]. Five patients had documented hypotension i.e. (systolic blood pressure below 90mm of Hg) at the time of admission, hyperbilirubinemia was noted in 64.28% of patients .Incidence of jaundice in malaria has been reported to range from 20% -30% and it was predominantly haemolytic rather than cholestatic [18].

In the present study sepsis was reported in 8 (28.57%) patients, no other source of infection has been found in these patients on clinical and laboratory examination. Five (17.86%) had documented hypotension resulting in renal ischemia due to decreased perfusion of the kidney. The hypotension was related to volume depletion in 4 cases and to sepsis in 1 case. In

the present study evidence of DIC was not observed in any case as occasionally disseminated intravascular coagulation occur in severe falciparum malaria and is associated with cerebral and renal complications [2, 3].

In the present study urinary abnormalities were noted in 24 (48%) cases, proteinuria in 10 (20%), microscopic hematuria in 20 (40%), granular casts in 7 (14%) respectively. This proteinuria was transient. Mild proteinuria and abnormal urinary sediments occur in patients with falciparum malaria [12]. Transient proteinuria usually less than 1g/24 hours was seen in 20-70% of patients in various studies [19]. The urinary proteins consist of albumin and both micro and macromolecule proteins, therefore proteinuria are both glomerular and tubular in origin [13]. Urinary abnormalities in the form of microscopic hematuria and granular cast may be associated with glomerulonephritis in patients with malaria.

Renal involvement in the form of electrolyte abnormalities is seen during malarial infection [20]. In the present study electrolyte abnormalities were noted in 46 (92%) of the patients. These electrolyte abnormalities were hyponatremia 30 (60%), hyperkalemia 16(32%), hypernatremia 2 (4%), hypokalemia 1 (2%), Hyperkalemia observed was attributed to haemolysis, rhabdomyolsis and acidosis. Hyponatremia was asymptomatic and may be dilutional as a result of intravenous fluid administration or due to true wastage that occurred before the onset of oliguria. Hypernatemia may be severe due to severe water depletion which resulted from blunted thirst and inadequate intake of water.

In present study nine cases (32.15%) required dialysis. If 9 cases are taken as 100% out of which eight (88.88%) had full recory of renal function, one patient (11.11%) died in the dialysis group. Nineteen (67.85%) were managed on conservation treatment with artemisinin derivatives. Three (15.78%) patients died in the conservative group. So mortality was almost similar in both groups. The reported mortality of malarial ARF in various studied ranged between 10% to 45% [4, 15, 21]. The overall mortality in the present study was 5 (10%). The cause of death was multi-factorial. However prognosis was grave when multiple organs were involved. In the present study MODS (Multi Organ Dysfunction Syndrome) was found to be the commonest cause of death (40%). Hepatic failure as a result of malarial hepatitis, as evidenced by raised serum transaminases was noted in 13.3%. The other factors contributing to mortality in present study were cerebral malaria 1 case and sepsis 1 case.

Conclusion

Malaria presents with protean manifestations, commonest symptoms being fever. On analysis 12 out of 50 patients are migrant labourers from Northern coastal AP and Orissa. Most of the patients were in the age group between 20-40 years. Renal complications were seen as the commonest complication of malaria with electrolyte abnormalities being the commonest manifestations. ARF was seen in 56% of cases but dialysis was required in only 18% of cases. Mortality in both dialysed and conservatively managed patients was nearly the same, but morbidity was prolonged in RRT group. MODS was the commonest cause of death. Poor prognostic factors being, old age, Patients with multi organ involvement i.e. evidence of more than 5 organs involvement invariably died ,Late diagnosis, late referral, delayed RRT. Serum creatinine >6.1 mg%, X-ray chest showing pulmonary infiltrates and hypoglycemia whereas good prognostic factors being early diagnosis, early referral, early treatment, especially the fluid management. Young age less than 2 organ involvement, serum creatinine <6.0 mg%, clear X-ray chest and RBS/GRBS > 60 mg%.

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