International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

A Study of Renal Manifestation of Malaria in Children

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Abstract: ***Background: Malaria is a severe disease of worldwide importance as it afflicts more than ninety nations and territories in the tropical and subtropical regions. The renal manifestation in malaria varies from mild proteinuria to severe renal failure. Aims and Objectives: To evaluate the renal manifestations in children with Malaria. Material and Method: This observational study evaluated 50 children aged <18 years admitted at National Institute Of Medical Science & Research, Jaipur, Rajasthan from January 2019 to June 2020 having malaria. A detailed clinical history, examination and relevant laboratory investigations were recorded on day of presentation. Results: Plasmodium vivax malaria was the predominant form of malaria (50 %). All patients were febrile at admission. The other common presenting complaints were vomiting (28 %) and headache (22 %). Commonest clinical finding were splenomegaly (55 %), pallor (53 %) and hepatomegaly (28 %). Icterus was seen in only 6 % of case. Anemia was present in 44 % of patients, only 4 % of cases had severe anemia. Thrombocytopenia was most common (72 %) hematological abnormality. Severe thrombocytopenia was seen in 17 % of cases. Hematuria was presenting 6 % of cases. Proteinuria was documented in 44 % of case, and it was common with falciparum and mixed malaria than vivax infection. Elevated urine sodium excretion was seen 50 % of cases. Mean urine sodium was high with falciparum infection. Hyponatremia was seen in 64 % of cases. It was common with falciparum and mixed infection. Mean sodium decreases as severity of infection increases. Blood urea and serum creatinine were significantly high in malaria cases. Falciparum cases had higher levels of serum creatinine than vivax and mixed malaria infection. Low glomerular filtration rate was seen 52 % of cases. Conclusion: The evaluation of renal functions in malaria is important as renal involvement is not uncommon and can cause severe morbidity and increase mortality.***

Keywords: Malaria, Plasmodium vivax, Plasmodium falciparum

1. Introduction

Malaria is a serious life threatening protozoal disease known since existence of humans. The symptoms like fever, chills which are observed in malaria, have been in the religious and medical texts of ancient Indian, Assyrian & Chinese civilization.[1] Malaria is a severe disease of worldwide importance as it afflicts more than ninety nations and territories in the tropical and subtropical regions. The major responsible species of Plasmodium for causing malaria[2], commonly parasitize humans are- *P*. vivax , *P*. malariae *P. falciparum, P. knowlesi and P. ovale.* Out of these the most prominent species causing malaria in India are *P. vivax*[2] and *P*. falciparum. Among the five Plasmodium species, P. falciparum causes the most deadly disease.

The renal manifestation in malaria varies from mild proteinuria to severe renal failure. Clinically significant renal and renal related disorders are commonly seen in infection with plasmodium falciparum and in P. vivax infections. The detection of renal pathology is important for clinical management of patients with malaria, including monitoring of drug dosage and fluid balance.

Aims and Objectives

To evaluate the renal manifestations in children with Malaria.

2. Material and Methods

This observational study was carried out at the Department of Paediatrics, National Institute of Medical Sciences & Research, Jaipur, Rajasthan, India from January 2019 to June 2020. In this study 50 children of malaria following inclusion criteria were included, in which the diagnosis was made by rapid diagnostic test (RDT) and confirmation was done by peripheral blood smear (PBF) examination. Categorization and management of the patients were done as per the WHO guidelines. The study plan was approved by the ethical committee of the institute. Information regarding the study was explained to the participants attendants, including the procedures, potential risks, and benefits of the study and a written informed consent was taken from parents. All the information was collected on a standard proforma, which was common for all the age groups.

Inclusion criteria: Children less than 18yrs of age with peripheral blood smear positive for malaria parasite and willing to participate in study.
Exclusion criteria: Children with pre-existing renal disease, children taking any medication which known to cause renal impairment and children with past history of renal disease. Other laboratory investigations done included hemogram, platelet count, blood urea, serum creatinine, serum electrolytes, complete urine analysis, urine sodium, FENa, GFR. Renal function tests were done with Johnson and Johnson- Vitros 5.1/FS auto analyzer. All the clinical syndromes were classified according to WHO criteria[3] and the involvement of two or more than two organs was considered as multiorgan dysfunction (MODS). Specific antimalarial treatment was given in the hospital, according to WHO guidelines.[3]

The sample size was time bound study-sample on convenience. Analyzed for validity statistically with the software SPSS 20.0 (Statistical Package for the Social

Sciences).

3. Results

There was a slight male preponderance for malaria with male to female to ratio being 1.16:1. Majority of the cases were from rural areas. Highest numbers of cases were seen in school going children. Plasmodium vivax malaria was the predominant form of malaria. It was seen in 50% of cases. All patients were febrile at admission. The other common presenting complaints were vomiting (28%) and headache (22%). Commonest clinical finding were splenomegaly (55%), pallor (53%) and hepatomegaly (28%). Icterus was seen in only 6% of case. Anemia was present in 44% of patients, only 4% of cases had severe anemia. Thrombocytopenia was most common (72%) hematological abnormality. Severe thrombocytopenia was seen in 17% of cases. Hematuria was presenting 6% of cases. Proteinuria was documented in 44% of case, and it was common with falciparum and mixed malaria than vivax infection. Elevated urine sodium excretion was seen 50% of cases. Mean urine sodium was high with falciparum infection. Hyponatremia was seen in 64% of cases. It was common with falciparum and mixed infection. Mean sodium decreases as severity of infection increases. Blood urea and serum creatinine were significantly high in malaria cases. Falciparum cases had higher levels of serum creatinine than vivax and mixed malaria infection. Low glomerular filtration rate was seen 52% of cases.

Table 1: Demographic data and baseline characteristics of study subjects

Characteristics		Observations	
		No. of Study Subjects	% Study Subjects
Sex	Male	26	52
	Female	24	48
P. vivax		25	50
P. falciparum		12	24
Mixed Infections (P. vivax+P. falciparum)		13	26

Table 2: Distribution of clinical symptoms in different types of malaria

Clinical Symptoms	Vivax	Falciparum	Mixed	Total	Percentage
Fever	25	12	13	50	100
Vomiting	08	03	03	14	28
Headache	03	04	04	11	22
Abdominal Pain	05	00	00	05	10
Dysuria	00	00	00	00	00

Table 3: Clinical sign in different cases of malaria

Clinical Sign	Number		Percentage	
	Present	Absent	Present	Absent
Pallor	32	18	64	36
Icterus	03	47	06	94

Table 4: Distribution showing abdominal examination findings in study population

Abdominal Examination	Vivax	Falciparum	Mixed	Total	Percentage
Hepatomegaly	7	4	5	16	32%
Splenomegaly	13	9	10	32	64%
Hepatosplenomegaly	5	3	2	10	20%

4. Discussion

In our study the male to female ratio was 1.16:1 male population is slightly more effected All other studies also showing male predominance which could be attributed to higher health seeking behavior for male children.[4,5,6,7,8,9] Children between 5-12 years of age were commonly affected by malaria in our study. This may be due to increased exposure to mosquito bites outdoors compared to children less than 5 yrs. Jasani JH et al[10] observed similar results in their study. Studies by Okwara FN et al[6] and Marsh K et al[11] reported that preschool children were more commonly affected by malaria. Presenting symptoms of our study showed similarity to the presenting symptoms of the study group of Muddaiah M et al.[12]

Percentage of children having vomiting, headache and pain abdomen in our study was less compared to studies done by Sownumi A[13] and Rasheed A et al.[14] The higher incidence of these symptoms in their study may be due to the fact that, the study was conducted in patients with falciparum infection only and these symptoms are found to be more common with falciparum malaria. Hematuria was noted in 6% (3 patient) which is similar to study conducted by Meena M. Hari et. al.[15] where they observed hematuria in 7.2% (4 patient). Patients of our study had dysuria.

Commonest clinical findings in our study were pallor, splenomegaly and hepatomegaly. Incidence of pallor was 52% in our study in comparison to 75% in study carried out by Malhotra OP et al[16]. Splenomegaly was seen in 64% of the patients in our study. Similar rate was observed in study by Taha K et. al.[17] and Rasheed A et. al.[14] where the percentage of patients with splenomegaly was 60% and 67% respectively. Hepatomegaly was noted in 32% of the patients in the present study. Study by Taha K et. al.[17] had shown a similar incidence of hepatomegaly (30%) in their work. Sowunmi A[18] has reported that hepatomegaly was more common than splenomegaly in acute falciparum infection in children. This observation is contrary to our findings wherein splenomegaly was more common. The clinical findings in vivax, falciparum and mixed infections were more or less similar. There was no statistically significant difference in clinical presentation of various types of malaria.

In the present study the incidence of vivax malaria was 50% falciparum was 24% and mixed infection had incidence of 26%. In a study by Shetty G[19] et al had similar results compare to our study. Jadav UM[20] et al, Lathia TB[21] et al and Goyal S et al[19] had similar incidence of vivax malaria in their studies. Rasheed A et al[52] had higher incidence of falciparum infection, which was attributed to higher incidence of falciparum infection in the area in which study was conducted. Study by Faseela TS et al[57] observed higher incidence of mixed infection like our study, which was attributed to endemicity for malaria in that area. From these observations we can conclude that the incidence of particular species varies with geographical area. The area where we have conducted the study is known to be endemic for vivax infection and hence the higher incidence of vivax infection in our study.

44% of the study population had Hb less than 10gm%, only 1% had severe anemia i.e. Hb less than 7gm%. In our study mean haemoglobin was less compare to Rasheed A et al[14] study, where mean Hb was 12.87±1.88gm%. Marsh K[22] had reported an incidence of 17% of severe anemia in his study group, which is higher than what we observed. In our study thrombocytopenia was observed in 72% of the patients. 32% had mild thrombocytopenia, 22% had moderate and 20% had severe degree thrombocytopenia. Shetty G et al[19] and Jamal et al[23] had similar results in their work, but few studies[24,25] have reported slightly lower incidence of thrombocytopenia like 40% and 58.97% respectively.

Proteinuria was documented in 44% percent of malaria cases in our study, which is similar to study done by Sowunmi A[13] in which proteinuria was reported in 40% acute falciparum malaria cases. Ahmad SH et al[26] has documented 4 out of 23 patients having proteinuria in his study. In contrary Buchard GD et al[27] and Nityananda et al[28] reported higher incidence proteinuria in their studies. Incidences of proteinuria in these studies were 85% and 78% respectively. In these studies proteinuria was estimated quantitatively, but in the present study only qualitative testing of urine protein was done. Karom AEGO and Mohammed AB[29] documented urinary changes in 71% of malaria cases in their work. In that same study 84% had proteinuria, 53% had pyuria and 45% had hematuria. In our study proteinuria was documented in 42% cases, pyuria in 13% cases and hematuria in 6% cases.In present study proteinuria was significantly more common with falciparum and mixed infection. Ugwuja EI[30] had reported similar result in his study. Ekeanyanwu RC et al[31] reported significant higher incidence of proteinuria in age group between 1 to 5 years in children affected with malaria, but in our present study such difference was not found. Ogbadoyi EO[32] et al and Ekeanyanwu RC et al[31] in their studies reported that presence of proteinuria in malaria depends on severity of infection. But in our study such difference was not found. Studies have shown that proteinuria in malaria is both tubular and glomerular types due to aggressive immune mediated glomerular and tubulointerstitial dysfunction.[33] This immunopathogenetic hypothesis is supported by microscopic examination of renal biopsy tissue in adult patient with malaria showing mesangial proliferation and mesangial deposition of immunoproteins.[34]

In our study mean urine sodium level was significantly higher in malaria cases. Mean urine sodium was significantly high in falciparum malaria cases. Sowunmi A[13] had reported similar results in his study. In that same study there was a positive correlation between urine sodium excretion and degree of parasitemia, both during and after recovery from the illness, but such relation was not found in our study.

In our study 76.7% of the cases had FeNa less than one. 13.3% cases had FeNa between 1 to 2 and 10% case had FeNa more than 2. There was no statistical difference in FeNa between different species or severity of malaria infection. Sowunmi A[13] has reported FeNa value greater than 2 in 25% of cases and Ahmad SH[26] has reported in 4% of cases.

In our study 30% cases had mild hyponatremia (Na level between 131-135 meq/l), 32% patients had moderate hypoantremia (Na level between 125-130meq/l) and only 2% patients had severe hyponatremia (Na<125meq/l). Hyponatremia was more common with falciparum and mixed infection than vivax infection. In our work serum sodium less than 130meq/l was seen in 64% of cases in comparison to studies by English MC et al[35], Wolfswinkel ME et al[36] and Yadav KS et al[35], in which it was seen in 55%, 46% and 34% of malaria cases respectively. A Sowunmi's study[13] on 40 uncomplicated falciparum malaria positive children for renal dysfunction showed Hyponatremia in 12.5% during acute illness. Study done by Ekeanyanwu RC et al[31] had failed to show any significant association between electrolyte changes and presence of malaria. Studies done by Ogbadoyi EO et al[32] and Uzuegbu UE[37] showed that, there was no significant difference between the levels of sodium in male malaria patients and individuals without malaria. However in females, there was significant variation in sodium compare to controls. But our study failed to show any such relationship with gender of the child. Ebele JI et al[38] in their study reported that hyponatremia is common with children aged less than 10yrs. But our study does not show any such relationship. Recent systematic analysis on Dysnatraemia in malaria by Brown S[72] showed that hyponatremia is common in falciparum malaria and less frequently reported in non- falciparum malaria. The extent of hyponatremia is also more extreme in falciparum malaria than it is in non-falciparum malaria. Even our study showed similar results. Our study also showed that mean sodium decreases as severity of malaria increases.

In our work 41.66% of falciparum cases had hyperkalemia (>5meq/l) but it is documented only in 12% cases of vivax malaria. Mean potassium increases as severity of infection increases in our study. Study by Sowunmi A[13] also showed higher serum potassium level during acute falciparum illness. They also estimated fractional excretion of potassium and demonstrated decreased potassium excretion during acute illness. In contrary to our study, studies had done by Jasani JH et al[10] and Ebele JI et al[38] documented hypokalemia in children with malaria. Impaired renal function might be the cause for hyperkalemia in our study, but it requires further studies to know the exact pathogenesis.

In present study mean blood urea, mean serum creatinine was significantly high in malaria cases. Similar results were reported by Ekeanyanwu RC et al[31], Ogbadoyi EO et al[32] and Idonije BO et al[73] in their studies with respect to serum urea, but Ogbadoyi EO et al[32] in their study failed to show any significant difference between the serum creatinine levels in malaria patients when compare to healthy controls. Studies by Ogbadoyi EO et al[32] and Idonije BO et al[39] had also reported that serum urea changes seen commonly with female patients who had malaria. This observation was not seen in our study. Ekeanyanwu RC et al[31] in their study also observed that Children between 1 - 5 years had higher levels of serum urea and creatinine when compared with children between 6 - 12 years. Such relationship between age group and serum urea or serum creatinine levels were not observed in our study. Study done by Umboh A et al[40] had reported

that blood urea increases with severity of infection, but not creatinine. However our study showed mean Blood urea and mean serum creatinine increases as severity of malaria increases. In contrary, study done by Adenosun OG et al[41] showed that there was no significant correlation between blood urea with severity of infection. Our study also showed that Falciparum malaria had significantly increased level of serum creatinine compare to vivax and mixed infection. It is said that renal impairment is commonly seen with falciparum cases, but none of the studies have been compared renal function between vivax and falciparum malaria.

In our study 52% of cases had renal impairment during acute illness. This is contrary to study done at Aligarh (India) by Ahmad SH[26], where 83% of cases had impairment of renal function during acute illness. However the study conducted by Sowunmi A[13] revealed that impairment of renal function was seen in 45% of cases. Our study has not showed any significant relationship between low GFR (<90ml/kg/1.73m^2) level and malaria species or severity of infection. This is in concurrence with findings of Umboh A et al.[40]

5. Conclusion

The evaluation of renal functions in malaria is important as renal involvement is not uncommon and can cause severe morbidity and increase mortality. In our study Proteinuria, hematuria, derange electrolyte balance, anemia and thrombocytopenia are the common manifestations found in malaria. In our study deranged renal functions were observed in both plasmodium vivax and plasmodium falciparum. Proteinuria was common with falciparum and mixed malaria, urine sodium excretion was high with falciparum infection. Hyponatremia was common with falciparum and mixed infection., Blood urea and serum creatinine were high in falciparum cases.

Further extensive clinical studies and research focused on renal functions derangement in different species of malaria is required to make the picture more clear. Timely detection and appropriate management can helpful to prevent and decrease the severity and mortality due to malaria.

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