Severe P. falciparum malaria in children in a tertiary care center of Allahabad region of india.

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Citation

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Abstract

Background & objectives: Despite a substantial disease burden in this area, little is known about the natural history of complicated falciparum malaria. Therefore, the present prospective study was undertaken to assess the clinical course, complications and outcome i.e. to understand the pattern of morbidity and mortality of falciparum malaria in children in tertiary care center of Allahabad.Methods: This was a prospective hospital based study conducted on 150 consecutive pediatric admissions under the age group of 1-5 years of slide positive complicated falciparum malaria cases between May 2005 to June 2007. The cases were retrieved and scrutinised using a prepared case sheet performa on the basis of patient's detailed history, clinical findings, investigations, treatment and complications.Results: 150 children with complicated Falciparum malaria with a mean age of 4.9±4.08 years to look for occurrence of different complications in younger and older age groups and overall mortality picture. Prostration (49.3%), Severe anemia (48.6%), unarousable coma (27.3%), and Respiratory distress(24.0%) were commonest complications. Under five children had higher risk of development of severe anemia (P<0.05) cerebral malaria (P<0.05), respiratory distress (<0.05) and seizures (P<0.05); whereas above five children had higher risk of prostration (P<0.05), jaundice (P<0.05) and acute renal failure (P<0.05). Over all mortality was 13.7%, cerebral malaria being the commonest cause (14.6%). Conclusion
: Malaria is responsible for major health concern in this region especially in rural areas, particularly in rainy season and is found to affect comparatively the younger children population. High degree suspicion should be maintained to detect these complications in early stage so that malarial mortality and morbidity can be prevented.

INTRODUCTION

Malaria is one of the commonest potentially fatal infections in the world with high incidence in South-East Asia region specially India, Bangladesh, Nepal, Sri Lanka, Thailand and Indonesia.[1] It has been estimated that malaria causes more than 1 million deaths in individuals under 5 years old globally every year.[2]Majority of cases are due to Plasmodium falciparum infection. Recent estimates reveal that the worldwide prevalence of the disease is about 300 to 500 million every year. India contributes 77% of the total malaria in south East Asia. Multiorgan involvement/dysfunction is reported in both Plasmodium falciparum and P.vivax cases.[3]The State of Orissa, followed by West Bengal, Chhattisgarh, Rajasthan, Gujarat, Jharkhand,Uttar Pradesh, Karnataka and Madhya Pradesh, reported the largest numbers of cases in thecountry during 2004. Malaria is one of the most common parasitic infections in our country and up to August 2005, 0.39 million malaria confirmed cases were reported, out of which 0.18 million were caused by P.falciparum. The number of deaths due malaria was 295 up to August 2005.[4] Despite a substantial disease burden in this area, little is known about the natural history of complicated falciparum malaria. Therefore, the present prospective study was undertaken to assess the clinical course, complications and outcome i.e. to understand the pattern of morbidity and mortality of falciparum malaria in children in tertiary care center of Allahabad.

MATERIAL AND METHODS

Study Area: This study was done in Department of pediatrics (Sarojini Naidu Children Hospital) of MLN Medical College Allahabad, important tertiary referral center of whole eastern Uttar Pradesh. Each year a large number of patients with malaria get admitted to this hospital especially in the rainy season. Most of the patients are drained from the rural areas

of Allahabad as well as adjacent part of Madhya Pradesh, Like Chitrakoot and Rewa. The annual range of temperature differs by around 12°C. The temperature varies from a maximum of 45.6°C to a minimum of 1.1°C. Allahabad has an area of about 65 km² and is 98 m/340 ft above sea level. The monsoon season is in June.

Study Design: This was a prospective hospital based study conducted on 150 consecutive pediatric admissions of slide positive complicated falciparum malaria cases (as defined by WHO criteria.[5] between May 2005 to June 2007. Diagnosis was based on thick and thin blood smear examination after staining in Leishman's stain examined by qualified experienced persons. Detailed demographic and clinical evaluation was done. and all the cases devided in to two groups i.e. group 1 as age less than ≤5 years and group 2 years. Routine laboratory tests included complete blood cell count, platelet count , blood sugar, liver and renal tests, coagulation profile was done, hepatitis markers in all jaundiced patients , blood culture and CSF study, chest X-ray, and urine for hemoglobinuria wherever necessary. Patients having clinical or laboratory evidences of other significant illness not attributable to severe malaria were excluded from the study. The outcome of complications with particular reference to number of death (fatal outcome) was documented. The data were subjected to statistical analysis using EPI6 software and in Microsoft excel package.

RESULTS

1. Patient characteristics and demographic:

150 cases of severe malaria that had symptoms consistent with severe malaria and were found peripheral smear positive to falciparum infection.102(68.0%) were ≤5 years of age and 68(32%) >5 years of age. The mean age was 4.9±4.08 years. Males were 89(59.0%) out numbered females 61(40.6%). The mean duration of complaints was 4.7±4.89 days, and hospital stay was 5.0±2.1 days. 80% cases were admitted from adjacent rural area and belong to lower socioeconomic status. Although patients presented to hospital throughout the years but about two third cases were admitted from July to October months.

2. Clinical features and examination

A. Central nervous system:

Cerebral malaria was occurred in 27.3% of cases on admission. the incidence was statistically high ($p<0.05$) in less than 5 years of age as compared to > 5 year age, as shown in table no.3.Seizures and altered sensorium was statistically significant in < 5 year of age group of children, on follow up 2.7 % cases developed residual neurological sequelae in form of hemiparesis and one patient developed dystonic movements.

B. Respiratory system: Cough was noticed in 32% of cases which was significantly more common in ≤5 year age group children ($p<.05$). Among them 50% cases were associated with evidences of lower respiratory tract infection and received antibiotics along with anti malarial drugs.

C. Gastrointestinal system: Diarrhoea and vomiting was documented in 56.0% and 50.0% cases in group1 and group 2 respectively. Signs of dehydration were present in 9.3 % of cases. On admission Clinical icterus was noticed in 10.6% of cases but as per WHO criteria jaundice was documented in 11.3% of cases. Which was significantly more common in group1 ($P<.05$). 5(3.3%) patients developed jaundice during the hospital stay. 8(5.3%) cases had conjugated and associated with deranged ALT/ AST and PT. Hepatomegaly was noticed in 59.3% of cases which was significant in group 1(74.5 Vs 27.0,$P<0.001$).Palpable spleen was second most common sign after pallor and was noticed in 77.3% of cases.

D. Renal involvement: on time of admission oliguria was found in 6.6 % cases with raised level of S. creatinine in these all these cases. In 3(2%) cases urine output was improved after giving initial fluid boluses, but in rest of the cases it was improved over 3 to5 days of conservative treatment. Hemoglobinuria was a less common finding and noticed in 6.6 % of cases. 2(1.3%) patients of acute renal failure were also had associated with clinical jaundice.

3. Lab investigations: Most common sign was pallor and noticed in 82.6% cases. But severe anemia as per WHO definition was noticed in 48.6% of cases which was more common in group 1. Leucocytosis was more common (26.6%) than leucopenia (8.6%), with out any significant age group difference. Similarly thrombocytopenia was noticed in 26.6% cases but severe thrombocytopenia (<50,000) was found in 10(6.6%) cases which was associated with patechial rashes in 8 (5.3%) cases. Low blood glucose and serum albumin was found significantly low in group1 while raised levels of AST/ALT and serum creatinine was significantly high in group2. In CSF study, abnormally raised protein (>40mg/dl) was found in 4(2.6%) patients of cerebral malaria in group1.

4. Outcome: 14(13.7%) child died in this study. The mortality in group1 and group2 were 10(9.8%) and 4(8.3%) respectively without any statistically significant difference age group difference. 6 (14.6%) cases were died due to cerebral malaria. other extra cerebral complications responsible for deaths were pulmonary edema for 3, anemia for 3 and hypoglycemia for 2 deaths. All these children had more than two complications of severe malaria.

Figure 1

Table no 1. Symptom and signs of severe malarial cases

Symptoms	Group 1 n=102(%)	Group2 n=48(%)	Total n=150(%)	χ2	P
Fever	102(100)	48(100)	150(100)	-	-
Chills & rigors	20(19.6)	36(75.0)	56.0(39.3)	42.8	0.000
Cough	40(39.2)	8(16.6)	48(32.2)	7.63	0.005
vomiting	60.(58.8)	24(50.0)	84(56.0)	1.03	0.309
Diarrhoea	36(35.2)	14(29.1)	50(33.3)	0.55	0.457
Breathing Difficulty	34(33.3)	8(16.6)	42(28.8)	4.5	0.033
Seizures	25(24.5)	4(8.3)	29(19.3)	5.48	0.019
Icterus	10(9.8)	4(8.3)	14(9.3)	0.00	0.990
Vomiting	60(58.8)	24(50.0)	84(56.0)	1.03	0.309
Cola colored urine	8(7.8)	4(8.3)	12(8.0)	0.05	0.826
Oliguria	4(3.9)	6(12.5)	10(6.6)	2.6	0.106
Edema	20(19.6)	8(16.6)	28(18.6)	0.19	0.666
Signs					
Pallor	92(90.1)	32(66.6)	124(82.6)	12.6	0.000
Hepatomegaly	76(74.5)	13(27.0)	89(59.3)	30.4	0.000
Palpable spleen	82(80.3)	34(70.8)	116(77.3)	1.78	0.192
Altered sensorium	38(37.2)	10(20.8)	48(32.0)	4.05	0.044
Abnormal posture	6(5.8)	6(12.5)	12(8.0)	0.14	0.707
Petechial rashes	4(3.9)	4(8.3)	8(9.3)	0.05	0.826
Abnormal jerks	20(19.6)	12(25.0)	22(14.6)	0.57	0.452
CHF	8(7.8)	3(6.2)	11(7.3)	0.00	0.989
Dehydration	14(13.7)	5(10.4)	19(12.6)	0.32	0.569

Figure 2

Table no.2 Laboratory features of severe malaria cases

Lab. investigations	Group 1 n =102(%)	Group 2 n=48(%)	Total n=150(%)	χ2	P
Hemoglobin	58(56.8)	15(31.2)	73(48.6)	8.57	0.003
Blood glucose	28(27.4)	6(12.5)	34(22.6)	4.16	0.041
WBC >11000	30(29.4)	10(20.8)	40(26.6)	1.23	0.267
<4000	9(8.8)	4(6.2)	13(8.6)	0.05	0.826
Platelet count<150000	30(29.4)	10(20.8)	40(26.6)	1.23	0.267
S. bilirubin	8(7.8)	9(18.7)	17(11.3)	3.86	0.049
Deranged AST/ALT	8(7.8)	10(20.8)	18(12)	4.00	0.045
S. creatinine	4(3.9)	7(14.5)	11(7.3)	4.00	0.045
Hemoglobinuria	6(5.8)	4(8.3)	10(6.6)	0.04	0.833
S. Albumin	10(20.8)	8(7.8)	24(16.0)	5.22	0.022
Hyperparasetemia	39(38.2)	17(35.5)	56(37.3)	0.11	0.739

Figure 3

Table no.3 Complications of severe malaria according to WHO

Symptoms	Group 1 n=102(%)	Group 2 n=48(%)	Total n=150(%)	χ2	P
Severe anemia	58(56.8)	15(31.2)	73(48.6)	8.57	0.003
Cerebral malaria	33(32.3)	8(16.6)	41(27.3)	4.5	0.033
Prostration	44(43.1)	30(62.2)	74(49.3)	4.9	0.026
Respiratory distress	30(29.4)	6(12.5)	36(24.0)	5.12	0.023
Multiple seizures	24(23.5)	4(8.3)	28(18.6)	4.96	0.025
Jaundice	8(7.8)	9(18.7)	17(11.3)	5.22	0.022
Hemoglobinuria	6(5.8)	4(8.3)	10(6.6)	0.04	0.833
Circulatory collapse	8(7.8)	4(8.3)	12(8.0)	0.05	0.826
Abnormal bleeding	10(9.8)	4(8.3)	14(9.3)	0.00	0.990
Pulmonary edema	8(7.8)	2(4.1)	10(6.6)	0.24	0.623
ARF	4(3.9)	7(14.5)	11(7.3)	4.00	0.045

Figure 4

Table no.4 Mortality in different complications.

Complications	No. of total patients	No. of deaths	Case fatality
Cerebral malaria	41(27.3)	6	14.6
Hypoglycemia	34(33.3)	2	5.8
Pulmonary edema	10(6.6)	3	30.0
Severe anemia	120(80)	3	4.1
		14	13.7

DISCUSSION

Since 1977, there is a consistently declining trend in the annual malaria incidence in our country. During 2005 about 1.8 million cases were reported with 940 deaths. There were 0.79 million cases of falciparum malaria. Infants, young children and pregnant women have been identified as malaria high risk groups. In this study ≤5 year of age group were commonly affected with severe malaria than older children similar to previous studies.[6] The difference in the age of presentation in severe malaria might be the result of multiple factors including differential parasite organ sequestration in young children as compared to older children and adults.[7] Low level of complementary regulatory proteins leading to increased red cell destruction in young children.[8] Satpathy et al[9] reported 40.5% cases of cerebral malaria whereas we reported 27.3% cases, this is because of strictly applied WHO definition of cerebral malaria who had altered sensoriium. Though malaria with impaired consciousness is a well-recognized syndrome, although the exact definition of cerebral malaria is controversial.[10] Seizures and altered sensorium was significantly present in children 19.3% and 32.o% respectively which was comparable with the Tripathy R.at eL.[11]

Altered pulmonary function in malaria is common and includes airflow obstruction, impaired ventilation, impaired gas transfer, and increased pulmonary phagocytic activity, and its occurrence in both vivax and falciparum malaria suggests that there may be common underlying inflammatory mechanisms.[12] Vipin Chandra et al[13] reported associated cough in malarial children was 5.5% whereas 32% of cases was present in our study. Recent African study shows that cough was a dominant symptom of severe malaria.[14] Cough without the evidence respiratory distress and cracles on auscultation indicates that it can occur without LRTI.[12]

Vomiting and diarrhoea were the frequent symptom found in this study. Hepatomegaly and splenomegaly were documented in 59.3% and 77.3% respectively whereas Chander V. et al[13] reported 44.5% and 40.9%. This cause by vascular congestion and reticuloendothelial proliferation. High spleen palpable rate in this study indicates the disease endemicity in this area. Jaundice was seen in 11.3% and it was hepatocellular as well as cholestatic type. it is one of the common severe manifestation of falciparum malaria. Its incidence varies between 10-54% in different reports, and is seen more in adults than in children.[15] Presence of raise AST/ALT in these patients indicate that not only hemolysis but liver dysfunction were also responsible to the raised serum bilirubin. ARF complicates falciparum malaria in less than 1 to 4.8% of native patients in endemic areas, yet it is much more frequent in nonimmune Europeans; reported figures usually are 25 to 30%.[16] In our study we found acute renal failure were more common in >5 age group of children, which was highly correlated with the other studies. (Satpathy et al.[9] , and Olanrewaju WI et al.[17] Show RW et al.[18])

Severe anemia was observed in 48.6% of cases especially ≤5 years of age group children which is quite similar to that of reported by Chander V.et al.(36.4%). The pathophysiology of anemia is far from clear the mechanism are multifactorial reflecting an extremely complex series of interaction involving parasites red cell destruction ,erythrophagocytosis ,inhibition of reticulocyte release ,depressed or ineffective erythropoesis ,immune mechanism and dyserythropoesis (chander V,et al.[13]). It was rapidly reversible after giving timely blood transfusion, and had better tolerability. Prostration was unique feature found in 49.3% of the cases and an important cause of admission in severe falciparum malaria. The exact pathogenesis is not known, but it is considered as a sign of CNS disease, the mechanisms by which malaria leads to inability to sit, stand or feed are poorly understood (Richard Idro et al[14]).

Aduragbenro D. et al[19] concluded that thrombocytopenia (53.3%) was the most common haematological finding in uncomplicated falciparum malaria whereas we found thrombocytopenia in 26.6%of cases. Petechial hemorrhage was seen in 5.3% of cases which was due to severe thrombocytopenia. Thrombocytopenia in malaria is both non-immunologically mediated and also immune mediated. Immune complexes are formed which activate and thus enhance platelet phagocytosis by macrophages in the spleen.

Overall mortality in our study was 13.7%, slightly higher than Satpathy et al[9]. (9.3%) but similar to Tripathy R et al[11]. The majority of children, especially those with circulatory collapse and respiratory distress, died within 24 hours after admission similar to Mockenhaupt FP et al.[20] emphasizing the need for triage and early treatment. Cerebral malaria responsible for majority of the deaths (case fatality rate14.6%), similar to other Indian studies satpathy et al (16.1%) , Tripathy R et al[11](17.7%). but less than and African studies Mockenhaupt FP et al[20] (36.2%). Severe anemia though highly prevalent complication but had less mortality rate 4.1%, could be due to better tolerance as the high prevalence of nutritional anemia in this area and a rapidly reversible manifestation after timely blood transfusion. Although pulmonary edema was less common finding in this study but has high case fatality rate (30%) but much less than Satpathy et al[9](80%).

CONCLUSION

Severe falciparum malaria is a major problem affecting the health of children in this area.Prostration, Severe anemia, cerebral malaria,and Respiratory distress are the commonest complications in children with severe malaria presenting to hospital. Under five children have higher risk of development of severe anemia, cerebral malaria, respiratory distress and seizures,whereas above five children have higher risk of prostration, jaundice and acute renal failure. High degree of suspicion should be maintained to deferentiate these complications so that by early detection and prompt management morbidity and mortality can be reduced.

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