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A STUDY ON PLASMODIUM FALCIPARUM MALARIA IN CHILDREN IN A TERTIARY CARE CENTRE IN EASTERN BIHAR.

Dr. Pawan Kumar Yadav* Senior Resident, Department of Pediatrics, JLNMCH, Bhagalpur, Bihar. *Corresponding author.

Dr. Anil Kumar Junior Resident, Department of Pediatrics, JLNMCH, Bhagalpur, Bihar.

Dr. Brajesh Kumar. Senior Resident, Department of Pediatrics, JLNMCH, Bhagalpur, Bihar.

ABSTRACT

INTRODUCTION: Severe malaria is a potentially fatal condition encountered in all age groups, especially in children and if not treated timely can cause mortality. Malaria in its severe form is one of the leading cause of mortality in all ages in tropical countries. Across the world, South East Asian Region bears the second largest burden of malaria, being next only to African region.

OBJECTIVES: 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, Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar.

METHODS: This was a prospective hospital based study conducted on 300 consecutive pediatric admissions under the age group of 1-5 years of slide positive complicated falciparum malaria cases between January 2017 to March 2018. The cases were retrieved and scrutinised using a prepared case sheet proforma on the basis of patient's detailed history, clinical findings, investigations, treatment and complications.

RESULTS: 300 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%), 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 ($P<0.05$). Overall mortality was 13.7%, cerebral malaria being the commonest cause (14.6%) in the present study.

CONCLUSION: P. falciparum infection is a major public health concern amongst the children residing in these malaria endemic region i.e. rural areas of Eastern Bihar. Therefore, region specific sustainable intervention measures need to be initiated for the prevention and control of malaria and malaria related deaths in children in this region.

KEYWORDS : Malaria, Plasmodium falciparum, Children.

INTRODUCTION:

Malaria is a life-threatening protozoal infection and India has the highest malaria burden in South East Asia. India is the major contributor to malaria burden in Southeast Asia [1]. In a recent study by "million death collaboration", it was estimated that malaria accounts for 205,000 deaths per year in India, with 55,000 deaths occurring in early childhood [2]. It 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 [3]. It has been estimated that malaria causes more than 1 million deaths in individuals under 5 years old globally every year [4].

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. Multi-organ involvement/dysfunction is reported in both Plasmodium falciparum and P.vivax cases [1].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 the country 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 [5]. 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 Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, in eastern part of Bihar.

MATERIALAND METHODS:

This study was done in Department of Pediatrics, Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar, important tertiary referral center of whole eastern Bihar. 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 Bihar. This was a prospective hospital based study conducted on 300 consecutive pediatric admissions of slide positive complicated falciparum malaria cases (as defined by WHO criteria [6] between January 2017 to March 2018. 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 were divided 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, blood sugar, platelet counts , liver and renal function 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 present study. The outcome of complications with particular reference to number of deaths (fatal outcome) was documented. The data were subjected to statistical analysis.

RESULTS:

300 cases of severe malaria that had symptoms consistent with severe malaria and were found peripheral smear positive to falciparum infection, 204(68.0%) were ≤5 years of age and 136(32%) >5 years of age. The mean age was 4.9±4.08 years. Males were 178(59.0%) outnumbered females 122(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.

In our study, Cerebral malaria 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. 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 two patients developed dystonic movements.

In the present study 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.

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. 16(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 in the present study.

Oliguria was found in 6.6 % cases with raised level of S. Creatinine. Out of these cases in 6(2%) cases urine output was improved after giving initial fluid boluses, but in rest of the cases it improved over 3 to5 days of conservative treatment. Hemoglobinuria was a less common finding and noticed in 6.6 % of cases. 4(1.3%) patients of acute renal failure were also had associated with clinical jaundice.

In the present study, 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%), without any significant age group difference. Similarly thrombocytopenia was noticed in 26.6% cases but severe thrombocytopenia (<50,000) was found in 20(6.6%) cases which was associated with patechial rashes in 16 (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 8(2.6%) patients of cerebral malaria in group1.

In this study, 28(13.7%) child died. The mortality in group1 and group 2 were 20(9.8%) and 8(8.3%) respectively without any statistically significant difference age group difference. 12 (14.6%) cases died due to cerebral malaria. Other extra cerebral complications responsible for deaths were pulmonary edema for 6, anemia for 6 and hypoglycemia for 4 deaths. All these children had more than two complications of severe malaria in the present study.

Table 1: Symptoms of Severe Malarial Cases.

Symptoms	Group 1 N=204(%)	Group 2 N=96(%)	Total N=300(%)	X^2	P
Fever	204(100)	96(100)	300(100)	-	-
Chills and Rigors	40(19.6)	72(75)	112(39.3)	42.8	0.000
Cough	80(39.2)	16(16.6)	96(32.2)	7.63	0.005
Vomiting	120(58.8)	48(50.0)	168(56.0)	1.03	0.309
Diarrhoea	72(35.2)	28(29.1)	100(33.3)	0.55	0.457
Breathing Difficulty	68(33.3)	16(16.6)	84(28.8)	4.50	0.033
Seizures	50(24.5)	8(8.3)	58(19.3)	5.48	0.019
Icterus	20(9.8)	8(8.3)	28(9.3)	0.00	0.990
Cola Coloured Urine	16(7.8)	8(8.3)	24(8.0)	0.05	0.826
Oliguria	8(3.9)	12(12.5)	20(6.6)	2.60	0.106
Edema	40(19.6)	16(16.6)	56(18.6)	0.19	0.666

Table 2: Signs of Severe Malarial Cases.

Signs	Group 1 N=204(%)	Group 2 N=96(%)	Total N=300(%)	X^2	P
Pallor	184(90.1)	64(66.6)	248(82.6)	12.6	0.000
Hepatomegaly	152(74.5)	26(27.0)	178(59.3)	30.4	0.000
Palpable Spleen	164(80.3)	68(70.8)	232(77.3)	1.78	0.192
Altered Sensorium	76(37.2)	20(20.8)	96(32.0)	4.05	0.044
Abnormal Posture	12(5.8)	12(12.5)	24(8.0)	0.14	0.707
Petechial Rashes	8(3.9)	8(8.3)	16(9.3)	0.05	0.826
Abnormal Jerks	40(19.6)	24(25.0)	44(14.6)	0.57	0.452
CHF	16(7.8)	6(6.2)	22(7.3)	0.00	0.989
Dehydration	28(13.7)	10(10.4)	38(12.6)	0.32	0.569

Table 3: Laboratory Features of Severe Malarial Cases.

Laboratory Investigations	Group 1 N=204(%)	Group 2 N= 96(%)	Total N=300(%)	X^2	P
Haemoglobin	116(56.8)	30(31.2)	146(48.6)	8.57	0.003
Blood Glucose	56(27.4)	12(12.5)	68(22.6)	4.16	0.041
WBC>11000	60(29.4)	20(20.8)	80(26.6)	1.23	0.267
WBC<4000	18(8.8)	8(6.2)	26(8.6)	0.05	0.826
Platelet Count< 1.5 Lakh	60(29.4)	20(20.8)	80(26.6)	1.23	0.267
Serum Bilirubin	16(7.8)	18(18.7)	34(11.3)	3.86	0.049
Deranged AST/ALT	16(7.8)	20(20.8)	36(12)	4.00	0.045
Serum Creatinine	8(3.9)	14(14.5)	22(14.6)	4.00	0.045
Hemoglobinuria	12(5.8)	8(8.3)	20(6.6)	0.04	0.833
Serum Albumin	20(20.8)	16(7.8)	48(16.0)	5.22	0.022
Hyperparasitemia	78(38.2)	34(35.5)	112(37.3)	0.11	0.739

Table 4: Complications of Severe Malaria according to WHO.

Symptoms	Group 1 N=204(%)	Group 2 N=96(%)	Total N=300(%)	X2	P
Severe Anemia	116(56.8)	30(31.2)	146(48.6)	8.57	0.003
Cerebral Malaria	66(32.3)	16(16.6)	82(27.3)	4.50	0.033
Prostration	88(43.1)	60(62.2)	148(49.3)	4.90	0.026
Respiratory Distress	60(29.4)	12(12.5)	72(24.0)	5.12	0.023
Multiple Seizures	48(23.5)	8(8.3)	56(18.6)	4.96	0.025
Jaundice	16(7.8)	18(18.7)	34(11.3)	5.22	0.022
Hemoglobinuria	12(5.8)	8(8.3)	20(6.6)	0.04	0.833
Circulatory Collapse	16(7.8)	8(8.3)	24(8.0)	0.05	0.826
Abnormal Bleeding	20(9.8)	8(8.3)	28(9.3)	0.00	0.990
Pulmonary Edema	16(7.8)	4(4.1)	20(6.6)	0.24	0.623
ARF	8(3.9)	14(14.5)	22(7.3)	4.00	0.045

Table 5: Mortality in Different Complications.

Complications	No. Of Total Patients	No. Of Deaths	Case Fatality
Cerebral Malaria	82(27.3)	12	14.6
Hypoglycemia	68(33.3)	4	5.80
Pulmonary Edema	20(6.6)	6	30.0
Severe Anemia	240(80)	6	4.10
		28	13.7

DISCUSSION:

Even in the 20th century,malaria continues to be major health concern for India. This deadly disease is completely curable if effective treatment started early before the complications of this disease start appearing.In this study ≤5 year of age group were commonly affected with severe malaria than older children similar to previous studies [7]. 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 [8]. Low level of complementary regulatory proteins leading to increased red cell destruction in young children [9]. Satpathy et al [10] 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 [11]. Seizures and altered sensorium was significantly present in children 19.3% and 32.o% respectively which was comparable with the Tripathy R.at eL[12].

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 [13].Vipin Chandra et al [14] reported associated cough in malarial children was 5.5% whereas 32% of cases were present in our study. Recent African study shows that

cough was a dominant symptom of severe malaria [15]. Cough without the evidence respiratory distress and crackles on auscultation indicates that it can occur without LRTI [13].

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 [14] reported 44.5% and 40.9%. This was caused 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 [16].

Presence of raised AST/ALT in these patients indicate that not only hemolysis but liver dysfunction were also responsible to the raised serum bilirubin level. ARF complicates falciparum malaria in less than 1 to 4.8% of native patients in endemic areas, yet it is much more frequent in non immune Europeans; reported figures usually are 25 to 30%[17]. 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[10] , and Olanrewaju WI et al. [18], Show RW et al. [19]).

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%)[14]. 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. [14]). 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. [15]).

Aduragbenro D. et al [20] 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 [10], (9.3%) but similar to Tripathy R et al [12]. The majority of children, especially those with circulatory collapse and respiratory distress, died within 24 hours after admission similar to Mockenhaupt FP et al. [21] 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 [12](17.7%). but less than and African studies Mockenhaupt FP et al [21] (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 [10](80%). Renal manifestations of malaria can range from prerenal azotemia to acute renal failure, nephrotic syndrome and acute glomerulonephritis[22-24].

Our study had certain limitations as it catered to the cases which presented to the hospital. Thus, the complication rates cannot be generalized to the population at large.

CONCLUSION:

In the present study we found that falciparum malaria is a major problem affecting the health of children in Eastern Bihar. Severe anemia, Cerebral malaria, Prostration,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.. The present study highlighted the change in the epidemiology of childhood severe malaria in Eastern Bihar. However, annual reporting with multicentric design of prospective studies is required to establish and confirm this trend. To conclude that P. falciparum is emerging as an important cause of malarial morbidity and mortality. There is an urgent need to strengthen our strategies at National level to overcome the complications of this deadly disease so that mortality and morbidity due to P.falciparum can be brought down.

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