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ORIGINAL ARTICLE

CLINICO-HAEMATOLOGICAL PROFILE AND OUTCOME OF CEREBRAL MALARIA IN A TEACHING HOSPITAL OF SOUTH EAST RAJASTHAN

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ABSTRACT: AIM: Evaluation of Clinico - hematological profile and outcome of cerebral malaria in semi urban hospital situated in endemic area. **MATERIAL AND METHODS:** A cross-sectional hospital-based study was conducted from August to November, 2014 at Department of Paediatrics SRG Zanana Hospital, Jhalawar Rajasthan. Every child, except who was previously abnormal neurologically, of the age of six month to 12 years, presented with a history of fever in the last 7 days, with or without convulsion, and/or impaired consciousness, screened for malaria by peripheral blood smear examination and rapid diagnostic test for malaria parasite. On the basis of this screening examination, these children were classified definite cerebral malaria where the peripheral smear was positive and probable cerebral malaria where the peripheral smear was negative. If the patients presented with fever, convulsion, and/or impaired level of consciousness, they were treated with Artesunate intravenously empirically. Patients were followed-up regularly till they regained consciousness and when, they were able to swallow, treated with oral Artisunate and single dose of Sulphadoxine and Pyrimethamine combination is also given. **RESULTS:** Of the3332 admissions, 869 (26.08%) were admitted for fever. Out of these 869 febrile patients 352 patients were having other obvious clinical diagnosis for fever. In remaining 517(59.49%) cases were suspected to be suffering from malaria, but all of these children who were admitted with the diagnosis of fever, were screened for malaria and 74(08.51%)were found to be positive for malaria parasite either by peripheral blood smear or rapid diagnostic test or both. Cerebral malaria developed in 37 patients. Most cases were of age group of 2-5 years, 14children had definite cerebral malaria and 9 were labelled as suspected to have probable cerebral malaria. Neurological symptoms of altered sensorium, convulsion and abnormal behaviour ranged from 35.7% to 100%. Children presented with Non Neurological symptoms like fever in 23(82.5%), headache in 8(28.5%), abdominal pain in 6(21.4%), vomiting in 12(42.8%), vertigo in 2 and cough in 8(28.5%). All cases recovered without neurological sequelae. **CONCLUSION:** Early detection, prompt management, and adequate supportive therapy may reduce mortality due to falciparum cerebral malaria.

KEYWORDS: Malaria, Quinine, Artesunate, Rapid diagnostic test.

INTRODUCTION: Malaria is one of the most important vector born disease, leading to significant morbidity and mortality, transmission of which occurs in all six WHO regions. Globally, an estimated 3.3 billion people are at risk of being infected with malaria and developing disease, and 1.2 billion are at high risk. High risk population is that who living in sub Saharan Africa and South East Asia. Though malaria incidence and deaths shows a declining trends especially since 2005 (Figure 1), it is still a disease of global importance that resulted in as per WHO estimates 198 million cases and 0.58 Million death in year 2013, out of which 78% deaths were in age group of <5 years.[1-2] Approximately 24 million malaria cases and 41000 deaths were reported in 2013 from South Asia, of which 29% deaths

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were in age group of <5 years of age. WHO believes that these figure may be gross underestimates, these may be 50% higher. In 2011 India contributed for 1.31 million cases and 463 deaths.[3] It is responsible for major morbidity and mortality in rural paediatric population with varying degrees of presentation.[3] Cerebral malaria (CM) is the most dreaded and not uncommon complication of falciparum malaria and occurs in children under five years of age.[4] Infection with this parasite can be lethal in the absence of prompt recognition of the disease and its complications and urgent appropriate patient management.[5] Drug resistance and demographic development will continue to contribute a lot to epidemiological profile of malaria and morbidity and mortality due to malaria. The present study was done to find out the clinico-haematological profile and outcome of cerebral malaria in a teaching hospital of South East Rajasthan (India).

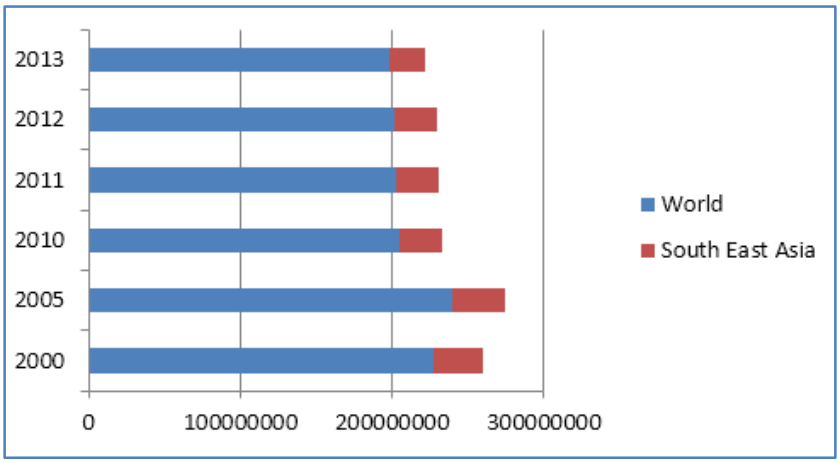

Fig. 1: Estimated cases of malaria from 2000 to 2013 (WHO malaria report 2014)

MATERIAL AND METHODS: This hospital based cross-sectional study was done from August to November 2104 at SRG Hospital attached to Jhalawar Medical College Jhalawar. Every child who was previously neurologically normal, of age six months to 12 years, and presented with a history of fever in the last 7 days, with or without convulsion, and/or impaired sensorium, underwent a peripheral blood smear examination and rapid diagnostic test for malaria parasite. Accordingly, they were grouped as definite cerebral malaria where the peripheral smear was positive and probable cerebral malaria where the peripheral smear was negative. If the patients presented with fever, convulsion, and/or altered sensorium, then inj. quinine or inj. Artesunate was given empirically. A detailed history and examination were done in the study group and observations and relevant details were recorded. All patients with fever were investigated with complete blood counts, serum electrolytes, and blood urea/creatinine and blood culture. In addition, CSF examination, urine examination (microscopic and culture), and abdominal and brain imaging was done where indicated. The complete blood cell count was done with an automated counter, and peripheral smears were examined by a qualified pathologist. Blood films were labelled as negative if there were no asexual forms of P. falciparum in 100 high power fields of a thick film. Severe anaemia was defined as haemoglobin concentration of <6 g/dl and/or haematocrit concentration <15%. Rapid diagnostic test (RDT) Histidine rich protein II, for detection for Plasmodium falciparum, was also done in the study

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cases. Inj. Quinine dihydrochloride in a dose of 20 mg/kg loading dose and then 10 mg/kg 8 hourly was diluted in 10 ml/kg of 5% Dextrose and infused over 4 hours given daily for 7 days. Whereas inj. Artesunate was given in a dose of 2.4 mg/ kg stat by IV injection followed by 1.2 mg/kg after 12 hours, and then 1.2 mg/kg daily for 6 days. After stabilisation of the patients, injectable drugs were replaced by oral drugs; while those patients who developed complications of quinine therapy such as QT prolongation, hypotension, and recurrent hypoglycaemia were given IV Artesunate.[6] In case of suspicion of viral encephalitis, a response to quinine or artesunate therapy and resolution of neurological symptoms were considered, as per Faliseva.[7,8] A diagnosis of malaria can also be based on response to treatment. Supportive cares like IVF, analgesics, sedatives, anti-convulsants, antipyretics, etc., were given to all the patients. Also, all patients with severe anaemia received blood transfusion.

RESULTS: Out of 3332 admissions, 869(26.08%) were admitted for fever. Peripheral smears were obtained in 517(59.49%) patients for malarial parasites (MP); others had some definitive localising cause for fever. Of the 517 peripheral smears, 43(08.31%) were positive for MP, of these 21(04.06%) were Plasmodium falciparum, 22(04.25%) were Plasmodium vivax. Rapid diagnostic test (RDT) was positive in 26(05.02%) patients. In rapid diagnostic positive group 9 positive for falciparum and 10 for vivax and 7 were shown positive for both type. 20 patients were positive for both peripheral smear and rapid diagnostic test, whereas 6 patients had only rapid diagnostic test positive with peripheral smear negative. Thus, malaria (peripheral smear positive; and RDT positive with peripheral smear negative) accounted for 49(05.63%) of the febrile patients. Cerebral malaria developed in 23 patients. 14 had definite cerebral malaria, and 9 had probable cerebral malaria. Cerebral malaria as a complication in falciparum malaria was seen in 11(36.66%) out of 30 positive cases for Plasmodium falciparum. The maximum number of cases were encountered below the age group of 5 years (47.82%). The male to female ratio was 1:1.4. All cases belonged to rural areas. Most of them had low socioeconomic status. 16(69.56%) patients were falling in PEM (protein-energy malnutrition) grade II, and 1(04.34%) in PEM grade III according to Indian Academy of Paediatrics classification. Children presented with neurological symptoms like impaired sensorium convulsions and abnormal behaviour in 100, 82 and 43% of these cases respectively. Non neurological symptoms like fever in 17(73%), headache in 8(34%), abdominal pain in 4(17%), vomiting in 8(34%), and cough in 7(30%) as shown in Table I. On physical examination18 (78%) patients had pallor, 4(17%) had petechiae, and 1(4%) had icterus. Splenomegaly and hepatomegaly were noted in 17(73%) and 8(34%) patients respectively. “Blantyre Coma Scale” (score <3) was seen in 19(67.8%) patients. Haemoglobin between 5-10 gm was seen in 18(64.2%) cases, and the 11(47.8%) patients who received blood transfusion had <6 gm% of haemoglobin. 8 (28.5%) patients had leucocytosis, and 5(17.8%) had leucopenia. Haematocrit was low in 4(14.2%) patients. Thrombocytopenia was seen in 10(35.9%) cases. The haematological parameters of probable cerebral malaria and definitive cerebral malaria cases are shown in Table II. No statistically significant difference was seen in haematological parameters between definitive cerebral malaria and probable cerebral malaria. Blood sugar was normal except in 2(08.69%) cases who documented hypoglycaemia (RBS < 40 mg %) on admission.

CSF was examined in all cases having a suspicion of CNS involvement, and it did not reveal any abnormal findings. 12(52.1%) cases received antimalarial drug before admission. In 73.9% patients, symptoms were relieved as treatment was started (inj. quinine or inj. artesunate) within 48

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hours of hospitalisation and remaining patients improved after 48 hrs. All study cases recovered without neurological sequelae.

Table I: Presenting features of cerebral malaria.

A. Symptoms	DCM (n = 14)	PCM (n = 9)	Percentage (%)
I. Neurological			
Impaired consciousness	14	9	100
Convulsions	11	8	82.6
Abnormal behaviour	7	3	43.47
II Non Neurological			
Fever	12	8	86.95
Headache	6	2	34.78
Abdominal pain	3	1	17.39
Vomiting	4	4	34.78
Cough	6	1	30.43
Vertigo	2	0	8.6
B. Physical signs			
I. General examination			
Pallor	10	8	78.26
Petechiae	2	2	17.39
Icterus	1	1	8.69
II. Systemic examination (per abdomen)			
Splenomegaly	9	8	73.91
Hepatomegaly	5	3	34.78

(DCM: Definite cerebral malaria; PCM: Probable cerebral malaria).

Table II: Haematological parameters of cerebral malaria.

Haematological parameters	DCM (n = 12) Means ± SD	PCM (n = 16) Means ± SD
Haemoglobin (gm/dl)	6.75 ± 2.01	7.08±2.22
WBC (per cu mm)	8.01 ± 1.33	7.38 ±1.4
Haematocrit (%)	26.14 ± 4.32	26.9 ± 3.17
Platelet count (lac/cu mm)	1.61 ± 0.38	1.8 ± 0.69

DISCUSSION: Malaria especially falciparum malaria is having significant morbidity and mortality. Severe falciparum malaria is associated with many life threatening complication in children some time with unusual presentations. Hence it is imperative for paediatricians to remain alert and have high index of suspicion for falciparum malaria infection and its various complications, in order to prevent mobidity and mortality, and effective management of this major rural disease of tropics.[9,10,11] Brewester et al[12] reported an incidence of 45% malaria admissions of which 11.3% had PCM; whereas in the present study, malaria positive cases accounted for 01.47% of total admissions and 09.53% of fever without any focus, of which 04.44% had either definite or probable cerebral malaria.

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Children do not present with classical features of malaria but may have protean manifestations like gastroenteritis, pneumonia, meningitis, encephalitis, or hepatic dysfunction.[13] The atypical presentation in paediatric age group is further compounded by the irregular and incomplete treatment taken prior to hospitalisation. Most of the children received chloroquine as part of National Malaria Eradication Programme (NMEP), as they were referred from primary health centre and private practitioners; 78.5% cases received an antimalarial drug before admission. Cerebral involvement, a well-known entity of falciparum malaria, was encounterd in 46.9% of MP positive patients in this study which is lower to that reported previously.[4,11,14] It occurs as a consequence of hypergesic vasculomyelinopathy in the brain, contrary to the popular belief of there being a mechanical plugging of blood vessels by the parasites. It usually presents with coma, convulsion, delusion, and psychotic state[9.] Kamble et al[8] reported that 66.6% patients presented with convulsion, whereas in our study it was 82.6%. Fever is a characteristic feature of P. falciparum infection, but a not very small, proportion of these children (13.04%) with cerebral malaria were afebrile on admission as observed.[15,16] Self-medication with antipyretic or antimalarial agents was common (about 70% of the children) and may contribute to this finding. Faiz et al[14] reported intermittent fever (83%), vomiting (80%), headache (75%), and convulsion (60%) in children with cerebral malaria. A similar finding was present in our study, except vomiting is less common in our study. Malnutrition predicted death in children with severe malaria. Some dehydrated children may have been categorised as malnourished and thus biased this association. Nevertheless, the limited data available suggests that malnutrition in fact increases the risk of dying from severe malaria.[17-19] 14.28% children fell in PEM grade III in our study. According to Blantyre coma scale5, all patients had impaired consciousness, and 32% developed coma after convulsion. It is a known fact that coma in cerebral malaria can be sudden, often follows convulsion, or can be gradual[18] Blantyre coma score has long been established in children as a good indicator of cerebral dysfunction in malaria.[20] Anaemia is the important cause for morbidity and mortality in falciparum malaria. The pathogenesis of anaemia in malaria is multifactorial. A complex chain of pathogenetic processes involving mechanical destruction of parasitized RBCs, marrow suppression, ineffective erythropoiesis, and accelerated immune destruction of non-parasitised RBCs have been implicated.[21] Anaemia was observed in 82.6% cases, whereas Kamble et al5 reported this in around 60% cases. Petechiael haemorrhages seen in 17.39% were propably due to thrombocytopenia observed in 30.4% cases.

Hepatic and splenic enlargement seen in 34.78% and 73.91% cases respectively were similar to those reported earlier.[7-9] Thrombocytopenia was a common observation in falciparum malaria with spontaneous recovery on treatment. Both leucopenia[22] and leukocytosis[23] have been described in malaria. Histidine-rich protein II is actively secreted by asexual stages and young gametocytes of Plasmodium falciparum but not by mature gametocytes.[24] Two cases of CM had peripheral smear negative but RDT was positive, this happens because in severe and complicated malaria, peripheral parasitaemia may be negative due to sequestration, whereas RDT provides evidence of antigenaemia.[25] No mortality was seen in our study group. Artesunate is as effective as quinine in the treatment of cerebral malaria in children.[25]

CONCLUSION: Most dreaded complication of severe falaciparum malaria is cerebral malaria. Though incidence and mortality due to malaria and its complications seems to be declining globally but still there is need for high index of suspicion. Early recognition and management of falciparum malaria

along with its complications will further improve the outcome from cerebral malaria and other form of severe malaria.

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