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Clinical Profile of Cerebral Malaria in Relation with P arasite Density

KEYWORDS: Cerebral malaria, parasitic index

Dr Sunita Khandelwal

Assistant professor Department of Pediatrics Govt. medical college Kota

ABSTRACT *Plasmodium falciparum malaria is a leading infectious cause of morbidity and mortality in children worldwide. Cerebral malaria (CM) is the most common complication of falciparum malaria. The study was conducted in the department of Pediatric Medicine, Jay Kay Lon Mother and Child Hospital of Government Medical College Kota. Out of 100 patients of cerebral malaria high grade fever 83.33%, convulsion 67.95%, unconsciousness 80.59%, altered sensorium 66.66%, breathlessness 71.42% ,low glasgow coma scale 80.85% ,absent doll's eye movements 55%,extenser planter reflex 75.71% were associated with high parasitic index.*

This study has been an endeavour to assess the severity and clinical profile of cerebral malaria in relation with parasite density of plasmodium falciparum.

Introduction

Plasmodium falciparum malaria is a leading infectious cause of morbidity and mortality in children worldwide. Each year, 300 to 500 million clinical cases of malaria occur, resulting in 1.5 to 2.7 million deaths.[1]Approximately 2.48 million malaria cases are reported annually from South Asia, of which 75% cases are contributed by India alone.[2] Malaria is one of the major public health problems of the india. Around 1.5 million confirmed cases are reported annually by the National Vector Borne Disease Control Programme (NVBDCP), of which 40–50% are due to Plasmodium falciparum. The disease is caused by protozoan parasites of the genus Plasmodium. There are four species of human malaria parasites; Plasmodium vivax, P.falciparum, P.malariae and P.ovale. [3]

Cerebral malaria (CM) is the most common complication of falciparum malaria and occurs in children 3 to 6 years of age. [4]It is the commonest cause of death in infants and children in areas endemic and hyperendemic for malaria. Inadequate immunity results in rapid increase in the parasite count and development of complications. Delay in diagnosis and treatment also contributes to the mortality. [3]Morbidity and mortality have been strongly linked to Plasmodium falciparum parasite density and guidelines have been introduced for etiologic classification of febrile illnesses and for therapeutic regimens based upon density of parasites in the blood.

Manifestations of cerebral dysfunction include any degree of impaired consciousness, delirium, abnormal neurological signs, and focal and generalized convulsions. In severe P. falciparum malaria, the neurological dysfunction can manifest suddenly following a generalized seizure or gradually over a period of hours. A strict definition of cerebral malaria has been recommended for sake of clarity and this requires the presence of unarousable coma, exclusion of other encephalopathies and confirmation of P. falciparum infection. However, all patients with P. falciparum malaria with neurological manifestations of any degree should be treated as cases of cerebral malaria. [3]. The cause of cerebral malaria is not well understood.

Pathophysiology of Cerebral malaria

Currently, there are two major hypotheses explaining its etiology. They are the mechanical and the humoral hypotheses.

Machanical Hypoheses:

The mechanical hypothesis asserts that a specific interaction between a P. falciparum erythrocyte membrane protein (PfEMP-1) and ligands on endothelial cells, such as ICAM-1 or E-selectin, reduces microvascular blood flow and induces hypoxia. This selective cytoadherence of PRBCs and non-PRBCs, also known as rosetting, can apparently better account for CM's histopathological hallmark and its characteristic coma condition. However, this hypothesis is inadequate in explaining the relative absence of neurological deficit even after days of unconsciousness.

Humoral Hypotheses:

The humoral hypothesis suggests that a malarial toxin may be released that stimulates macrophages to release TNF-a and other cytokines such as IL-1. The cytokines themselves are not harmful, but they may induce additional and uncontrolled production of nitric oxide. Nitric oxide would diffuse through the blood-brain barrier and impose similar changes on synaptic function as do general anesthetics and high concentrations of ethanol, leading to a state of reduced consciousness. The biochemical nature of this interaction would explain the reversibility of coma. [5]

Although the importance of the parasite density has been recognized for a long time, few field studies have used it systematically. This, in our opinion, is because most of the proposed counting methods are time-consuming and unsuitable for mass screening. [6]

Based on a review of the literature and a series of complementary investigations, we have tried to define a method permitting a relatively precise measure of parasite density that is simple and rapid enough to be used during large field surveys.

AIMS AND OBJECTIVES

1. To correlate the clinical profile of the cerebral malaria with P. falciparum parasite density in pediatric patients.
2. To study the complications and outcome of cerebral malaria in relation with parasitic index.

MATERIAL AND METHODS

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The study was conducted in the department of Pediatric Medicine, Jay Kay Lon Mother and Child Hospital of Government Medical College Kota between April 2008 to July 2009.

SAMPLE

This study was done in 100 smear positive (30 cases positive from hospital lab & 70 cases positive from outside labs) children of cerebral malaria upto the age of 18 years admitted in Jay Kay Lon hospital.

INCLUSION CRITERIA

Cerebral malaria present in a patient who ;

- Has altered sensorium or unconsciousness.
- Has peripheral asexual P falciparum parasitaemia.
- Has no other identified cause of an encephalopathy.

EXCLUSION CRITERIA

Only proved cases of cerebral malaria by PBF examination included. All other cases who have had a single seizure and children with other causes of cerebral dysfunction, such as bacterial or viral meningitis or toxic or metabolic encephalopathy excluded.[7] .

Thick and thin films prepared. Thick film used for species identification and thin film used to see parasite load.

Parasite density

Parasite density determined by counting the number of trophozoites in 100 oil immersion fields and multiplying by four thousand to give parasites per µl, assuming a blood volume of approximately 0.25 ml per 100 microscopic fields. This method of parasite enumeration has been validated and found to be more accurate than relating the number of parasites to leucocytes. [8-9].

According to Parasite density patients were divided in two groups-

Patients with high parasitic index (>2, 50,000/µl or >5%) designated as 'B'

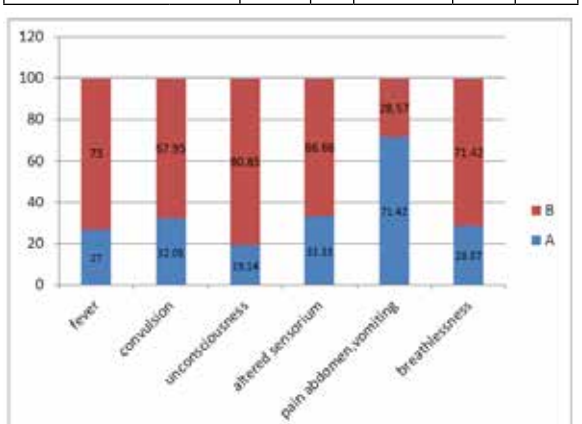
Patients with low parasitic index (≤2, 50,000/µl or ≤5%) designated as 'A'

Results

Fever was most common clinical feature at the time of admission N=100(100%) as compare to other symptoms like convulsion N=78(78%), unconsciousness N=67(67%), altered sensorium N=33(33%), pain abdomen N=7(7%), breathlessness N=7(7%).

Out these symptoms 83.33% children of high grade fever were associated with high parasitic index.Other CNS symptoms like convulsion 67.95%, unconsciousness 80.59%, altered sensorium 66.66%, breathlessness 71.42% were also associated with high parasitic index.

Table No. 1					
Clinical Features at the time of admission					
Clinical Features	No.	%	Parasite Index		%
Fever	High	48	48	8	A	16.66
				40	B	83.33
	Mod.	20	20	10	A	50
				10	B	50
	Mild	12	12	9	A	75
				3	B	25
Convulsion		78	78	25	A	32.05
			53	B	67.95	
Un Consciousness		67	67	13	A	19.40
			54	B	80.59	
Altered Sensorium		33	33	11	A	33.33
			22	B	66.66	
Pain abdomen & Vomiting		7	7	5	A	71.42
			2	B	28.57	
Breathlessness		7	7	2	A	28.57
			5	B	71.42	



Low Glasgow coma scale was seen in 47 (47%) patients of cerebral malaria

Most of the children 80.85% with low Glasgow coma scale (<8) were having high parasitic index.

Doll's eye movement was absent in 20 patients,out of these 55% patient were associated with high parasitic index.

Cranial nerve involvement was present only in 5 patients and all were associated with high parasitaemia.

Tone was increased in 50 patients, out of them 80.85% patients were associated with high parasitic index.

Deep tendon reflexes were brisk in 25 patients and de-

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pressed in 20 patients. there was no significant correlation with parasitic index.

Extensor planter reflex was present in 70 patients, out of them 75.71% were associated with high parasitic index.

Abdomen reflex was absent in 25 patients, out of them 60% with high parasitaemia.

Table No. 2						
Examination of Study Group				Cranial Nervous System		
On Examination		N	%	Parasite Index		%
Glasgow Coma Scale	< 6	47	47	9	A	19.14
				38	B	80.85
	>6	53	53	38	A	71.69
				15	B	28.3
Doll's Eye Movement	Absent	20	20	9	A	45
				11	B	55
Cranial Nerve involvement	Present	5	5	5	B	100
Tone	increased	50	50	10	A	20
				40	B	80
	decreased	23	23	20	A	86.95
				3	B	13.04
Power	increased	77	77	27	A	35.06
				50	B	64.93
DTR	Brisk	25	25	20	A	80
				5	B	20
	Depressed	20	20	10	A	50
				10	B	50
Planter Reflex	Extenser	70	70	17	A	24.28
				53	B	75.71
Abdominal Reflex	Absent	25	25	10	A	40
				15	B	60

Discussion

High grade fever, convulsion, unconsciousness, altered sensorium, and breathlessness in malaria were associated with high parasitic density. **Paul Bouvier**, [10] **etal** (1993) found that the risk of fever was increased in children of ages 1-3 years in those with an initial parasitemia >15,000/ fJ (with increasing parasitic index). It was consistent with our study.

Beadle C. [11] etal in Kenya found that 64% of children with > or = 20,000 parasites/microL versus 10% with 1-4999/ microL were febrile when parasitemic.it was also consistent with our study that fever is associate with high parasitaemia then low level of parasitaemia in blood.

Amar Taksande et al[12] (2005) Sevagram found that CNS symptoms of impaired consciousness, convulsion and abnormal behaviour ranged from 35.7% to 100% children of cerebral malaria.In our study CNS symptoms range was 21% to 78% on admission.

Hyperparasitemia was associated with severely deranged Glasgow coma scale, cranial nerve involvement, hypotonia, and extensor planter reflex. . **Amar Taksande** et al[12] (2005) Sevagram found that Blantyre Coma Scale" was deranged in all patients, but severe derangement (score < 3) was seen in 19 (67.8%) patients. In our study severely deranged Glasgow coma scale was seen in 47% patients.

Conclusion

This study has been an endeavour to assess the severity and clinical profile of cerebral malaria in relation with parasite density of plasmodium falciparum. Parasitic index is very sensitive index to assess the severity of the disease. By this index we can assess the complication and outcome of disease so that aggressive and proper management can be started to decrease the mortality and morbidity as early as possible.

High parasite density was associated with severe clinical illness, complications and mortality. As parasite density is very sensitive index, preparation of good quality PBF and proper assessment (parasite density) can help to assess the disease severity and outcome. So the trained staff and good equipments (microscope) should be arranged at the primary health center. High parasitaemia can be prevented by general measures in the form of proper education, good sanitation, and good awareness about illness.

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