International Journal of Research in Medical Sciences
Mohanty N et al. Int J Res Med Sci. 2018 Jun;6(6):2008-2011
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20182278

Original Research Article

Multiorgan dysfunction (MOD) in falciparum malaria in children: a study from high endemic area of Southern Odisha

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Received: 17 March 2018
Accepted: 25 April 2018

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ABSTRACT

Background: To find out the prevalence of multiorgan dysfunction in cases of severe falciparum malaria in children, correlating the organ dysfunction in different age group and relationship with case fatality rate (CFR).
Methods: This prospective cross-sectional study was conducted from Jan 2014 to June 2016 in the Department of Pediatrics, Maharaja Krushna Chandra Gajapati medical college and hospital (MKCG MCH), Berhampur, Odisha, India. Total 340 cases belonging to <14 yrs having severe malaria (as per the WHO criteria) were included in the study. Mixed malaria and Plasmodium falciparum (Pf) positive cases having other significant disease e.g. chronic hemolytic anaemia, cardiac, renal or other chronic diseases were excluded. The study subjects were thoroughly screened for presence of organ dysfunction clinically and by appropriate laboratory tests and analysed.
Results: Out of 340 subjects, maximum no of cases (56.76%) were found in >5yr age group. Hyperparasitemia (>10%) was detected in 12.35% cases. Cerebral malaria was most common organ dysfunction found in 1-5 years, followed by anaemia in 5-10 years, acute renal failure (ARF) in 10-14 years age group. Multiorgan dysfunction (MOD) was detected in 32.94% cases of severe malaria. Overall CFR was 8.82%, being directly proportional to no. of organ involvement, 31.81% with 4 organs and 100 % with five organs involvement respectively which was statistically significant.
Conclusions: MOD is of grave outcome in severe Pf malaria increasing the case fatality rate proportionate to number of organs involved.

Keywords: Case fatality rate, Endemicity, Multiorgan dysfunction, Pf malaria

INTRODUCTION

Malaria is one of the largest infectious killer disease of the world, having devastating consequences even in 21st century. India being the second most populous country in the world, with 90% of its population living in areas of malarial risk.[1]

According to recent report around 26 million cases and 55,000 malarial deaths occur only in India annually.[1] Inspite of intensive programs and strategies to contain Pf malaria and to reduce mortality, we are far behind achieving success, particularly in case of children.

This part of eastern India, Odisha state, having only 4% of land area and 3% of population of the country contributes to as high as 20% of cases and 17% of all malarial deaths.[2] There is lot of geographical variation in distribution of malaria cases within the state and districts. Our tertiary centre (place of study) caters 10 southern districts, highly endemic for falciparum malaria contributing approx. 64% of malarial deaths in the state.[2]

Areas with API (Annual Parasite Incidence) ≥2 per 1000 population per year have been classified as high-risk area in India.[3] The API of Odisha is 10.24 (2016) whereas the district of Ganjam (study centre) was having an API of 3.18.[4]

Severe malaria is well defined by WHO.[1] Severity leads to multiorgan dysfunction (MOD) syndrome landing in higher mortality. MOD is defined as dysfunction of 2 or more organs requiring intervention to maintain homeostasis.[5] Involvement of vital organs increases the mortality risk which is directly proportional to number of organs affected.[6] But it is worthwhile to mention that timely rational antimalarial treatment along with appropriate supportive management can reduce the mortality risk significantly.

METHODS

This cross-sectional study was carried out in the Department of Pediatrics of Maharaja Krushna Chandra Gajapati Medical College (M.K.C.G Medical College), Berhampur, Odisha-the only tertiary care teaching hospital in the southern part of Odisha, during the period from January 2014 to June 2016 to find out the prevalence of multi organ dysfunction (MOD) and observe the clinical outcome of severe *Plasmodium falciparum* (Pf) malaria in children in correlation with the case fatality rate (CFR).

Convenient sampling technique was used to select the study participants. The W.H.O criteria for severe Pf malaria was used to select the study participants. Out of all the patients ≤14 years of age admitted to the in-patient of the Department of Pediatrics with a clinical and laboratory diagnosis (positive blood smear for asexual form and/or rapid diagnostic test) of malaria, only cases of severe Pf malaria were selected for inclusion in the present study.

All the cases of mixed malaria, Pf positive cases with other co-morbid conditions like hemolytic anaemia or any chronic illness were excluded. As per the current management protocols appropriate investigation and management were instituted in all the cases. The cases of mortality were analysed to find out the cause of death.

Assuming the prevalence of multi-organ dysfunction to be 58 % in severe Pf malaria as per available literature and a desired confidence level of 95% the sample size was calculated to be 309 at an absolute precision of 5.5%.[7] To account for drop outs the sample size was further increased by 10%. Finally, 340 patients of severe Pf malaria were included in the study.

Case definition

For the present study, severe malaria is defined as one or more of the following, occurring in the absence of an identified alternative cause and in the presence of P. falciparum asexual parasitaemia as per WHO criteria.[1]

Clinical and laboratory criteria

Impaired consciousness

A Glasgow Coma Scale score <11 in adults or a Blantyre Coma Scale of <3 in children.

Prostration

Generalized weakness so that the person is unable to sit, stand or walk without assistance.

Multiple convulsions

More than two episodes within 24hr.

Metabolic acidosis

A base deficit of >8mEq/L or, if unavailable, a plasma bicarbonate of <15mmol/L or venous plasma lactate >5mmol/L. Severe acidosis manifests clinically as respiratory distress (rapid, deep and laboured breathing).

Hypoglycaemia

Plasma or blood glucose concentration of less than 2.2mmol/l (less than 40mg/dl).

Severe anaemia

A haemoglobin concentration <5g/dl or a haematocrit of <15% in children <12 years of age (<7g/dl and <20%, respectively, in adults) together with a parasite count >10000/µl.

Renal impairment

Plasma or Serum creatinine >265µmol/l (> 3.0mg/dl) or blood urea >20mmol/L.

Jaundice

Plasma or Serum bilirubin >50µmol/L (3mg/dl) together with a parasite count >100000/µl.

Pulmonary edema

Radiologically confirmed, or oxygen saturation <92% on room air with a respiratory rate >30/min, often with chest indrawing and crepitations on auscultation.

Significant bleeding

Including recurrent or prolonged bleeding from nose gums or venepuncture sites; haematemesis or melaena.

Shock

Compensated shock is defined as capillary refill ≥3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure <70mmHg in children or <80mm Hg in adults with evidence of impaired perfusion (cool peripheries or prolonged capillary refill) Hyperparasitemia *P. falciparum* parasitaemia >10%. Data was collected and were recorded in a case record form. Prior approval of the Institutional Ethics Committee was obtained for the study and the participants were included only after obtaining the written informed consent of the accompanying parents. The accompanying parents were explained about the implications of the present study and were assured that the information collected shall be used for the research purpose only and confidentiality shall be maintained.

Descriptive inferential statistics was used to analyse the data. Chi square test was used to analyse the discrete outcome variables and a p value of ≤0.05 was considered to be statistically significant. The free trial version of GraphPad Prism 7.0 was used to for statistical analysis.

RESULTS

340 cases of Pf malaria were included in our study. As depicted in Table 1, the male to female ratio was 1.5:1. Maximum no of cases were found in >5yr age group (56.76%). Pallor was found to be the most common manifestation followed by splenomegaly and hepatomegaly as shown in Table 2. Hyperparasitemia (>10%) which is an indicator of severity was detected in only 12.35% cases. This low percentage in presence of significant multi organ involvement could be due to prior usage of free artesunate injection available in different levels of health care.

Table 1: Age wise distribution.

Age group (yrs)	Male	Female	No. and%
<1	13	9	22(7.23%)
1-<5	77	48	125(36.76%)
5-<10	61	46	107(31.47%)
10-14	54	32	86(25.29%)
Total	205(60.3%)	135(39.7%)	340

Table 3 aptly describes that cerebral malaria and shock were common presentation of organ involvement in 1-5yr age group whereas severe anaemia and jaundice were most frequent in 5-10yr age group. In contrast acute renal failure was most frequent in a higher age group (10-14yrs). The age specific differential manifestations could be due to the host-parasite interaction in relation to the malarial endemicity of this area.

Table 2: Clinical and important lab profile (n=340).

Clinical manifestations	No. of cases	Percentage
Fever	340	100%
Pallor	267	78.52%
Icterus	104	30.58%
Oedema	42	12.35%
Hepatomegaly	248	72.94%
Splenomegaly	253	74.41%
Oliguria	54	15.88%
GCS≤11	139	40.8%
Shock	25	7.3%
Bleeding	24	7.05%
Chest signs	20	5.88%
Pretreatment hypoglycemia	37	10.88%
Hyperparasitemia (>10%)	42	12.35%

Table 3: Organ involvement according to age.

Organ involvement (WHO criteria)	<1yr (No. and %)	1-5yr (No. and %)	5-10yr (No. and %)	10-14yr (No. and %)	Total (No. and %)	P value
Cerebral malaria (CNS)	7 (5.03%)	76 (57.67%)	35 (25.17%)	21 (15.10%)	139 (100%)	<0.00001
Anaemia (Hematological)	12 (4.48%)	86 (32.70%)	102 (36.20%)	67 (25.96%)	267 (100%)	
ARF (Renal)	2 (3.70%)	10 (18.51%)	14 (25.92%)	28 (51.85%)	54 (100%)	
Jaundice (Hepatic)	10 (9.61%)	27 (25.96%)	56 (53.85%)	11 (10.57%)	104 (100%)	
Shock (CVS)	2 (8%)	17 (68 %)	3 (12 %)	3 (12%)	25 (100%)	
ARDS	0	0	3 (42.85%)	4 (57.15%)	7 (100%)	

Table 4: Distribution of organ dysfunction.

Organ dysfunction	No. of cases	No. of survivor	No. of nonsurvivor	Case fatality rate
Single organ	118 (51.30%)	116 (58%)	2 (6.66%)	1.69%
2 organs	54 (23.47%)	40 (20%)	14 (46.66%)	25.92%
3 organs	33 (14.34%)	29 (14.5%	4 (13.33%)	12.12%
4 organs	22 (9.56%)	15 (7.5%)	7 (23.33%)	31.81%
5 organs	3 (1.30%)	0	3 (10%)	100%
Total	230 (100%)	200 (100%)	30 (100%)	
P value is <0.00001				

The prevalence of organ dysfunction in our study as shown in Table 4 was 67.64%, while the multi organ dysfunction was present in 32.94% of total subjects. The overall CFR was 8.82% which rose to 31.81% with 4 organ and 100% with five organ involvement respectively indicating that the CFR was proportionate to the number of organs involved (P value: <0.00001).

DISCUSSION

In the present study maximum no. of cases (56.76%) were found in >5yr age group which was similar as reported by Satapathy SK et al, (62.8%) whereas Kumar et al found maximum cases (68%) in ≤5 years.[7,8] In clinical presentation fever was present in all cases whereas Chander V et al, reported absence of fever in 7.3% cases.[9] Other prominent symptoms as observed by us were altered sensorium (45%), convulsion (35%), jaundice (30.8%) and oliguria(15.88%) whereas Merchant S et al, reported fever in 100 %, altered sensorium in 66.47%, convulsion in 34%, Breathlessness in 22.9%, Jaundice in 18.23% and oliguria in 7% cases.[10]

In the present study, 78.52 % cases had anemia , which is similar to the observation by Allen et al and Marsh et al.[11,12] Hepatopathy was a significant finding in 30.58% cases in the present series which is in agreement to the finding of N Mohanty et al (33.3%).[13] Renal failure was found in 15.88% cases which is consistent with the study of R.tripathy et al.[14] Our series detected multiorgan involvement occuring in 32.94% cases of Pf malaria in comparision to 90% cases reported by Nagaraj et al.[15] The overall CFR is 8.82% in comparison to 9.9% as reported by Satpathy et al.[8]

CONCLUSION

To conclude multiorgan involvement in Pf Malaria is relatively common in children. The risk of mortality being proportionate to the number of vital organs involved. Thus, in the context of sustainable development goals (SDG) by 2030, mortality prevention due to Pf malaria in children should be the thrust area.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mohanty N, Patro D, Dhal S. Multiorgan dysfunction (MOD) in falciparum malaria in children: a study from high endemic area of Southern Odisha. Int J Res Med Sci 2018;6:2008-11.