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ORIGINAL ARTICLE

Severe Plasmodium vivax Malaria in Children : An emerging threat

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Abstract:

Plasmodium vivax was previously considered a relatively benign infection. This perception, however, has changed in recent years, and P.vivax has become recognized as a cause of severe malarial disease .The current knowledge on severe malaria has focused on P.falciparum and there is little information on the contribution of P.vivax to severe disease especially in children. Hence the present study was designed to study the clinicopathological profile of severe Plasmodium vivax malaria in children. In this study, records of 81 children of suspected severe malaria, 0–15 years of age hospitalized in the Paediatrics Department, S.N Medical College, Agra from January 2010 to December 2011were reviewed. Cases were included if malaria was diagnosed by microscopy(thick and thin smears) and rapid diagnostic tests. The rapid diagnostic test was conducted using one step malaria anti P.f/P.v. serum test using three lines –lateral flow chromatographic immunoassay for qualitative estimation of antibodies. WHO severity criteria for malaria was used to study the complication profile of the patients. Of 81children of suspected severe malaria, P.vivax, P.falciparum and mixed infection were diagnosed by microscopy and rapid diagnostic test in 27, 26 and 4 children respectively. Spontaneous bleeding was the most frequent complication in both P.vivax (29.62%) and P.falciparum (38.46%). Severe anaemia was more common in P.falciparum (30.76%) whereas cerebral malaria in P.vivax(18.51%). Our study emphasizes that P.vivax is a major cause (52.5%) of severe form disease in children. P.falciparum is a known cause of severe malaria but P.vivax is now also emerging as a cause of severe malaria in children.

Keywords: *Severe Malaria, Cerebral Malaria, Plasmodium vivax*

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Introduction

Malaria is one of the most important public health problems worldwide, with an estimated 243 million cases and nearly 863,000 deaths in 2008 [1]. Around 1.5 million malaria cases are annually reported from India [2]. Of the various Plasmodium species affecting humans, Plasmodium vivax was previously considered a relatively benign infection. This perception, however, has changed in recent years, and P.vivax has become recognized as a cause of severe malarial disease in case reports or small case series [3-5]. The current knowledge on severe malaria has focused on P.falciparum and there is little information on the contribution of P.vivax to severe disease especially in children. This study aimed to characterize clinicopathological profile in children with severe malaria especially P.vivax.

Material and Methods

This study is a retrospective review of clinical records of children 0–15 years admitted in

Department of Paediatrics, SN Medical College, Agra with suspected severe malaria between January 2010 to December 2011. The study was approved by the Ethical committee of the institute. Both microscopy (thick and thin smears) and rapid diagnostic test were performed in all suspected cases of malaria. The rapid diagnostic test was conducted using one step malaria anti P.f/P.v. serum test using three lines –lateral flow chromatographic immunoassay for qualitative estimation of antibodies. Blood was collected in a container without anticoagulant and allowed to clot; serum was separated and was used for the test. One drop of specimen serum was transferred to the test device with pipette to which three drops of diluent provided was added. The test was read in 5 to 20 minutes. The test was interpreted according to the colour bands within the result window; negative result showed only control colour band on left side within result window. The presence of not less than two colour bands (p.v, p.f & control)within the result window indicated a positive result for P. vivax and P. falciparum respectively. If no control band developed, the assay was considered as invalid and repeated on a new test device. Cases were included in the study in which malaria was positive by rapid diagnostic test and microscopy. Patients showing evidence of bacterial infection were excluded from the study. Demographic data, clinical history, examination, laboratory investigations were obtained from the records. Patients were labelled as severe malaria in the presence of one of the WHO severity criteria [6]. As blood gas analysis samples were not collected for all patients, hence hyperlactatemia and metabolic acidosis were not used to classify severity.

Results

Clinical records of 81 children, with suspected severe malaria were reviewed. Of these 57 were positive on microscopy and rapid diagnostic tests. (P.vivax-27; P.falciparum-26 and mixed -4).Table I shows the demographic details of these patients. Mean age was 8.17 years, mostly were males (77.19%) with rural predominance (63.15%). Table II describes the severe malaria cases according to WHO criteria. Spontaneous bleeding (36.8%) and severe anaemia (22.80%) were the most common clinical complications followed by cerebral malaria (17.54%), hepatic dysfunction (12.28%) and renal manifestation (3.50%). Severe anaemia was more common in P.falciparum (30.76%) and cerebral malaria was more frequent with P.vivax (18.51%) and mixed infection. Spleenomegaly was the most common examination finding seen in (75.43%) cases followed by hepatomegaly in (66.66%). Amongst laboratory parameters mean haemoglobin in P. falciparum was 7gm% and in P. vivax was 9gm%, leucopoenia was seen in only 1 subject with P. vivax. Liver enzymes were increased in 3 cases (mean SGPT -133.6 IU/dl) in both vivax and falciparum (mean SGPT-69.9 IU/dl). Serum creatinine was more than 3mg/dl in one subject in P. vivax and P. falciparum.

Table 1. Demographic profile of patient with severe malaria

		P. vivax (n = 27)	*P.falciparum* (n =26)	*Mixed* (n=4)
Mean Age (years)		7.7	8.75	8
Age (years)	**0-5**	8	6	2
	>5-10	12	10	1
	>10	7	10	1
Male / Female		21/6	19/7	4/0
Rural /Urban		15/12	17/9	4/0

Discussion

There are few studies on the clinical aspects of complicated P. vivaxmalaria in pediatric age group. In this study P. vivax and P.falciparum contributed to almost equal number of severe malaria cases which is like the study of Kochar et al. [5], and Barcus et al [7]. Children more than five years were more frequently affected unlike study of Kochar et al. [5]. There is male predominance, as health facilities are more often seeked for male children in our region.

The complication profile of P. vivax in our study showed spontaneous bleeding (38.09%) cases

Table 2. Clinico-pathological profile of patient with severe malaria (As per WHO Guidelines for the treatment of malaria Second edition 2010)

	P. vivax (n=27)	*P. falciparum* (n=26)	*Mixed* (n=4)
Clinical features			
- Impaired Consciousness	5(18.51%)	3(11.53%)	2(50%)
- Prostration	5(18.51%)	3(11.53%)	2(50%)
- Failure to feed	5(18.51%)	3(11.53%)	2(50%)
- Multiple Convulsions	2(7.40%)	1(3.84%)	2(50%)
- Respiratory Distress	-	-	-
- Shock	-	-	-
- Jaundice	3(11.11%)	3(11.53%)	1(25%)
- Spontaneous bleeding	8(29.62%)	10(38.46%)	-
- Pulmonary edema	-	-	
Laboratory Findings			
- Hypoglycemia (blood glucose < 2.2 mmol/l or < 40 mg/dl)	1(3.70%)	2(7.69%)	-
- Anemia (Hb < 5 g/dl, packed cell volume < 15%)	3(11.11%)	8(30.76%)	2(50%)
- Renal impairment (serum creatinine >265 µmol/l or >3mg/dl)	1(3.70%)	1(3.84%)	-

followed by severe anaemia (22.80%), cerebral malaria (17.54%), hepatic dysfunction (12.28%) and renal impairment (3.5%) which were similar to case series of Arboleda et al, presenting with severe anaemia (51.8%), severe spontaneous bleeding (15.6%), and hyperbilirubinemia (7.2%) [3]. Srivastava et al. in his case series reported spontaneous bleeding as most common complication as seen in our study [4]. Cerebral involvement (5/26 cases) was more common in our study as compared to study of Srivastava et al. reporting (2/50 cases), the probable reason could be that being a tertiary centre, referral were more for fatal forms of malaria [4].

Although haematological complications observed with P. falciparum (Table II) were also encountered with P. vivax, but their distribution was different. The proportion of P. vivax cases as compared to P. falciparum with severe anaemia and spontaneous bleeding was much less in our study as also reported by Ellen et al. [8]. These observations are understandable since we know that P. vivax malaria patients have lower densities than P. falciparum patients, and therefore the likelihood of having profound anaemia is less.

Cerebral malaria, the most fatal complication of malaria was found more frequently with P. vivax (18.51%) as compared to P. falciparum (11.53%) in our study. There have been scattered reports of cerebral malaria with P. vivax in studies by Beg et al. and Ozen [9,10]. Cerebral malaria in P. falciparum is due to rossetting and cytological adherence. The increasing number of severe manifestations of P. vivax infections, similar to those observed for severe falciparum malaria, suggests that key pathogenic mechanisms (eg. cytoadherence and sequestration) might be shared by the two parasites [11]. But the study conducted by Laurens et al. does not support the hypothesis that P. vivax sequestration occurs in human brain. The mechanism of cerebral involvement in P.vivax is not well understood [12].

Other less common complications included acute case in both the species inour study unlike the

renal failure which was observed in only one study of Prakash et al. who reported renal manifestation in 79.61% in falciparum and 20.4 % in vivax cases [13]. Hepatic involvement has been reported not only in P.falciparum but also in P.vivax in our study (3 cases each) as also reported by Arboleda [3], and Nautiyal et al. [14].

We found in this study that patients with mixed infections presented with more severe form of malaria than those infected with a single Plasmodium species as seen in study of Blaise et al. [15].

Biochemical parameters of hepatic dysfunction as evident by elevated bilirubin and liver enzymes was lower in our study as compared to study of Nautiyal et al. [14] and Sharma et al. [16]. Leucopenia, very uncommon complication as reported in few case studies [17] was seen in only one P. vivax case in our study.

Conclusion

Present study showed that, P. vivax infection was responsible for complicated malaria in almost equal number of cases as P.falciparum. Spontaneous bleeding, anaemia and cerebral malaria were the major complications associated with P. vivax infection. Though it is a well known fact that P. falciparum is responsible for most of the serious forms of malaria, P. vivax which was earlier thought to be a relatively benign infection is recently emerging as a cause of severe forms of malaria in pediatric age group.

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