Clinical profile and complications of acute malaria caused by different species of Plasmodium

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Abstract

Introduction: Malaria is more severe in children than in adults and 78% of all deaths due to malaria occur in children under 5 years. Plasmodium vivax has long been considered to have benign course. However during past few years several studies reported severe complicated cases of vivax malaria. Methodology: Children in the age group of 6 months to 15 years admitted in the Department of Pediatrics with clinical malaria were tested for malaria using peripheral smear, QBC and rapid diagnostic test. Children with positivity of any of these tests were enrolled in the study. Complete clinical profile is noted. Investigations like complete blood counts, LFT, RFT etc., were done. Results: Out of 150 children enrolled in the study 80 had Plasmodium vivax monoinfection. 61 had Plasmodium falciparum monoinfection and 9 had mixed infection. 41% of them were under 5 years of age. The incidence of complications like severe anemia (10% vs. 18%), jaundice (10% vs. 44%), transaminitis (6% vs. 13%), azotemia (6% vs. 36%) and thrombocytopenia (12.5% vs. 26%) were more common in P falciparum than in P vivax malaria with statistical significance (p < 0.05). There was no statistically significant difference in the incidence of hypoglycemia and cerebral malaria in P vivax and P falciparum malaria. Conclusion: The incidence of severe malaria in P. vivax infection is comparable to that in P. falciparum infection and it is no more benign. Hence robust efforts are required for reduction and elimination of P vivax transmission.

Key Words: Plasmodium falciparum, Plasmodium vivax, Clinical Profile, Complicated Malaria,
complications of malaria caused by different species of plasmodium.

Methodology

The present study was a cross sectional observational study conducted over a period of 18 months from December 2011 to May 2013 in the Department of Pediatrics, Government General Hospital, Kakinada. Children in the age group of 6 months to 15 years who were admitted in pediatric wards/ICU with clinical suspicion of malaria were tested for malaria using peripheral smear, QBC and RDT.

Those children with positivity of any of the above mentioned tests were enrolled in the study.

Exclusion Criteria: Children with infections like enteric fever, pyogenic meningitis, tuberculosis etc., with coincidental smear positivity for malaria were excluded in the study.

A predesigned proforma was used to record the socio-demographic details and clinical manifestations of enrolled children. Detailed clinical examination was done and patients were given anti-malarial treatment and complications and outcome were noted. All the enrolled children were subjected to investigations like hemogram, renal function tests, liver function tests and blood sugar. Other investigations like serum electrolytes, ABG, chest X ray etc., were done whenever required. The results were tabulated and statistically analyzed using SPSS version 17.

Results

During the study period 450 cases of clinically suspected malaria were admitted in the hospital, of which 150 cases were positive for malaria either by peripheral smear or QBC or rapid diagnostic tests. P. vivax monoinfection was seen in 80 children (53.3%). P. falciparum was seen in 61 (40.6%) children and 9 (6%) had mixed infection.

The demographic profile of patients included in the study was shown in table I. 41.3%, 34% and 24.6% of children were in the age group of < 5 years, 6-10 years and 11-15 years respectively. 52% of children were males and 48% were females. 35% of them were from tribal areas and rest from rural and urban areas.

Clinical profile and lab parameters of children with malaria caused by P. vivax, P. falciparum and mixed infections were given in table II and table III.

All children presented with fever. History of chills was present in 93% of P. vivax and 95% of P. falciparum malaria cases. Myalgias (40% vs. 70.4%), vomitings (38% vs. 62%), oliguria (12.5% vs. 24.5%), cerebral malaria (25% vs. 33%), jaundice (10% vs. 44%) and organomegaly (54% vs. 84%) were more common in children with P. falciparum malaria than in children with P. vivax malaria. Elevation of AST and ALT (6% vs. 13%), azotemia (6% vs. 36%), severe anemia <5gm % (10% vs. 18%) and thrombocytopenia (12.5% vs. 26%) were more common in children with P. falciparum malaria than with P. vivax malaria.

Table I: Demographic characteristics

|                | No of children | Percentage |
|----------------|----------------|------------|
| **Age**        |                |            |
| 6 m - 5 yrs    | 62             | 41.4       |
| 6 - 10 yrs     | 51             | 34         |
| 11 – 15 yrs    | 37             | 24.6       |
| **Sex**        |                |            |
| Male           | 78             | 52         |
| Female         | 72             | 48         |
| **Residence**  |                |            |
| Tribal         | 52             | 34.7       |
| Urban & rural  | 98             | 65.3       |
Table II: Clinical profile of children with malaria

| Clinical Features | P. vivax | % | P. falciparum | % | mixed | % | total | % |
|-------------------|---------|---|--------------|---|-------|---|-------|---|
| Fever             | 80      | 100| 61           | 100| 9     | 100| 150   | 100|
| Chills            | 74      | 92.5| 58           | 95 | 8     | 88.8| 140   | 93.3|
| Myalgias          | 32      | 40 | 43           | 70.4| 6     | 66.6| 81    | 54 |
| Vomittings        | 30      | 37.5| 38           | 62.2| 6     | 66.6| 74    | 49.3|
| Oliguria          | 10      | 12.5| 15           | 24.5| 3     | 33.3| 28    | 18.7|
| Hepatomegaly      | 11      | 13.7| 28           | 46 | 8     | 89  | 47    | 31.3|
| Splenomegaly      | 43      | 53.7| 51           | 83.6| 9     | 100 | 103   | 68.6|
| Cerebral malaria  | 20      | 25 | 20           | 32.7| 2     | 22.2| 42    | 28 |
| Jaundice          | 8       | 10 | 27           | 44.2| 2     | 22.2| 37    | 24.7|

Table III: Lab parameters in children with malaria

| Parameter                  | P. vivax | %   | P. falciparum | %   | P value |
|---------------------------|---------|-----|--------------|-----|---------|
| Anemia                    | 30      | 37.5| 46           | 75.4| 0.000   |
| Thrombocytopenia          | 10      | 12.5| 16           | 26.2| 0.037   |
| Deranged RFT              | 5       | 6.25| 22           | 36  | 0.000   |
| Elevated transaminases    | 5       | 6.25| 8            | 13.1| 0.000   |
| Hypoglycemia              | 2       | 2.5 | 3            | 4.9 | 0.442   |
| Hyperbilirubinemia (TSB >1.5 mg/dl) | 8 | 10 | 27 | 44.2 | 0.000 |

Table III shows comparison of morbidity profile of P. vivax and P. falciparum infections. All the complications of malaria were more common with P. falciparum than with P. vivax infection.

It was observed that severe anemia, thrombocytopenia, azotemia, transaminitis and jaundice were more common with P. falciparum with statistical significance (p value <0.05). There was no statistically significant difference in the incidence of hypoglycemia and CNS manifestations in P. vivax and P. falciparum malaria.

Table IV: Clinical features and lab parameters in children of different age groups with P. vivax and P. falciparum infection

| Parameter                  | 6 m – 5 years | 6 – 10 years | >10 years |
|---------------------------|----------------|--------------|-----------|
|                           | Pv            | Pf           | Pv        | Pf         | Pv       | Pf       |
| Splenomegaly              | 17(21%)       | 15(24%)      | 14(17.5%) | 23(37%)    | 12(15%)  | 13(21%)  |
| Hepatomegaly              | 6(7.5%)       | 6(9.8%)      | 3(3.75%)  | 14(23%)    | 2(2.5%)  | 8(13%)   |
| Cerebral malaria          | 6(7.5%)       | 5(8%)        | 7(8.7%)   | 9(15%)     | 7(8.8%)  | 6(10%)   |
| Raised bilirubin          | 3(3.7%)       | 8(13%)       | 4(5%)     | 13(21%)    | 1(1.2%)  | 6(10%)   |
| Elevated transaminases    | 1(1.2%)       | 3(4.9%)      | 3(3.75%)  | 3(4.9%)    | 1(1.2%)  | 2(3.2%)  |
| Abnormal RFT              | -              | 6(9.8%)      | 4(5%)     | 11(18%)    | 1(1.2%)  | 5(8%)    |
| Anemia                    | 8(10%)        | 14(23%)      | 12(15%)   | 21(34%)    | 10(12%)  | 11(18%)  |
| Thrombocytopenia          | 3(3.7%)       | 4(6.5%)      | 3(3.75%)  | 8(13%)     | 4(5%)    | 4(6.5%)  |
Table IV shows the age wise incidence of various complications of *P. falciparum* and *P. vivax* malaria. There was no significant difference in the incidence of complications of *P. falciparum* and *P. vivax* malaria in different age groups.

**Discussion**

In the present study highest prevalence of malaria was seen in children of age less than 5 years (41%). This is in contrast with the studies done by Ragini et al[6] and Pankiti D Desai et al[7], where children above 6 years are more commonly affected; this can be explained by high endemicity in this area.

*Plasmodium falciparum* accounted for 40% of hospitalized malaria cases in the present study, whereas Koushik et al[8] from Delhi and Ragini et al from uttarakhand[6] showed lower prevalence of *Plasmodium falciparum* (7.9% and 28% respectively).

In the present study hematological, renal and hepatic complications were noted more commonly in *P. falciparum* infection. The incidence of CNS complications was similar in *P. vivax* and *P. falciparum* infections.

Jaundice was seen in 44% and 10% of *P. falciparum* and *P. vivax* malaria whereas transaminitis was seen in 13% and 6% of *P. falciparum* and *P. vivax* malaria. These results indicate that besides hemolysis, hepatocellular injury is important factor for jaundice.

Thrombocytopenia was seen in 26% and 12% of *P. falciparum* and *P. vivax* malaria in present study. Earlier observations found that thrombocytopenia is quiet rare in *P. vivax* malaria but recently thrombocytopenia has been noted in *P. vivax* monoinfection from many parts of world including India [11,12,13,14].

Renal dysfunction was seen in 6% of *P. vivax* infection in this study. A study from Bikaner reported 10% incidence of renal dysfunction in *P. vivax* malaria. Several other studies [11, 15] reported acute renal failure in *P. vivax* infection.

The present study analysis shows that the incidence of severe malaria (including cerebral malaria) in vivax infection is comparable to that in *P. falciparum* infection.

The inability of the infected RBC to adhere to vascular endothelium and the parasite’s strict preference for invading reticulocytes could explain the benign nature of *P. vivax* infection.

Infected RBC in *P. vivax* is not as rigid as observed in *P. falciparum* infection which makes capillary blockage in organs less likely in *P. vivax* infection. But several reports of occurrence of severe malaria with *P. vivax* show the need to decipher the pathogenesis of severe malaria caused by *P. vivax*.

The geographical areas that reported severe *P. vivax* malaria are the same that demonstrated *P. vivax* chloroquine resistance [16]. Hence further studies are required to find out the relation between the pathogenesis of severe malaria and its relation to emergence of multidrug resistant strains of *P. vivax*.

The WHO severity criteria formerly only validated for *P. falciparum* infection seem to be applicable to most of the *P. vivax* patients. But certain criteria need to be re-addressed. Severe disease with *P. falciparum* is considered with parasitemia of >2, 00,000/µl, while parasitemia exceeding 50,000/µl is rare in severe *P. vivax* malaria[17]. *P. vivax* causes potentially life threatening infection at relatively low grade parasitemia.

There are abundant data showing that transmission of *P. falciparum* is actually more responsive to malaria control measures. As a result, in areas where two species co-exist, the scale up of integrated malaria control measures generally result in a shift, such that *P. vivax* becomes dominant species [18]. Globally malaria control strategies and action plan needs to re-address the fallacy that *P. vivax* is ‘benign’, not fatal. More robust efforts are required for reduction and elimination of *P. vivax* transmission to achieve Millennium Development Goal 6 (the goal of no deaths from malaria and malaria free world), which specifically addresses malaria. Malaria control also helps to achieve other MDGs.
Conclusion

The present study shows that P. vivax monoinfection can result in severe malaria in children and more robust measures are required to reduce the transmission of P. vivax malaria to achieve MDGs.

Abbreviations

QBC: Quantitative buffy coat
RDT: rapid diagnostic test
LFT: liver function tests
RFT: renal function tests
HIV: human immunodeficiency virus
AIDS: acquired immune deficiency syndrome
RBC: red blood cell

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