ORIGINAL ARTICLE

CHANGING TRENDS IN CLINICAL PRESENTATION OF PEDIATRIC MALARIA

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Abstract

Aim: This retrospective study was undertaken to determine incidence of different clinical presentations in pediatric malaria and its correlation with parasitology of disease.

Methods: Case records of 100 children admitted in pediatric ward of a tertiary care hospital from June 2010 to September 2011were studied. All children below 12 years of age with any of the following diagnosis based on peripheral smear examination were included: a) P. vivax malaria, b) P. falciparum malaria, c) Mixed infection (both vivax and falciparum) and d) Those who responded only to antimalarials despite their peripheral smears being negative for malarial parasite. Complete history, clinical examination, relevant investigations and treatment given were recorded and findings were analyzed using statistical tests.

Results: Out of 100 cases reviewed, 53 had P.vivax malaria, 20 had P.falciparum, 1 had mixed infection (both vivax and falciparum) and 26 patients had clinical features suggestive of malaria (fever with chills, malaise, pallor, hepatosplenomegaly) with their peripheral smears being negative for malarial parasite but responded only to single dose of antimalarials. The average age of presentation of vivax malaria was 6.9 $\pm$ 3.6 years and of falciparum was 7.0$\pm$ 3.5 years. The average duration of hospital stay was 5.3 $\pm$ 3.6 days for P.vivax and 5.4 $\pm$ 2.9 days for P.falciparum. Cerebral malaria, splenomegaly were seen more in falciparum; whereas respiratory problems, severe anemia, thrombocytopenia and low blood pressure were similar in both vivax and falciparum malaria. Seventy five percent of children with vivax and 55% of children with falciparum malaria responded to single dose of chloroquine only.

Conclusion: P. Vivax can also lead to unusual and serious complications thus defying its stereotype as a benign disease. Most of the prevalent strains of plasmodia are still sensitive to chloroquine monotherapy.

Key Words: Malaria, Vivax, Unusual clinical presentations.

Introduction

Presently, about two million cases and a thousand deaths due to malaria are reported annually in India. (1) Among the four species of plasmodium, P. falciparum and P. vivax are commonly found in our country. Of the two, P. falciparum has always garnered more attention due to its association with severe complications, high mortality, and multidrug resistance while P. vivax has classically been treated as benign. However, recent studies show that many complications are now being seen with increasing frequency in P. vivax. (2,3) The relative contribution of P. vivax to significant morbidity has not been properly analyzed as yet. This study highlights the changing trends in clinical presentation of malaria in children and its relation to species of malarial parasites.

Materials and Methods

This retrospective study was conducted by reviewing case records of 100 patients admitted in a tertiary care hospital from June 2010 to September 2011. Case records were obtained from the medical records department. The objectives were to determine the incidence of different clinical presentations in pediatric malaria and its correlation with the parasitology of the disease. All children below 12 years of age with any of the following diagnosis based on peripheral smear examination were included: a) P. vivax malaria, b) P. falciparum malaria, c) Mixed infection (both vivax and falciparum) and d)those children presenting clinically as malaria and who responded only to antimalarials despite their peripheral smears being negative for malarial parasite. Case details were enrolled in a pre-decided proforma. Complete history, clinical examination, relevant investigations and treatment given were recorded. Central nervous system (CNS) complications recorded were altered sensorium and seizures. Respiratory complications included breathlessness and pleural effusion. Severe anemia was defined as hemoglobin level less than 6 gm/dl and these children required packed cell transfusion. Thrombocytopenia was defined as platelet count less than 1,50,000/ml and severe thrombocytopenia as a platelet count less than 50,000/ml. Low blood pressure was defined as systolic and/or diastolic blood pressure less than 5th centile. Clinical and laboratory features were analyzed with parasitology.

Statistical Methods

Findings were analyzed using Fischer's exact test and Chi square test. P-values less than 0.05 were considered statistically significant.

Results

Out of 100 cases reviewed, 53 had P. vivax malaria, 20 had P. falciparum, 1 had mixed infection (both vivax and falciparum) and 26 patients had clinical features suggestive of malaria (fever with chills, malaise, pallor, hepatosplenomegaly) with their peripheral smears being negative for malarial parasite but responded only to single dose of antimalarials. The average age of presentation of vivax malaria was 6.9 $\pm$ 3.6 years and of falciparum malaria was 7.0 $\pm$ 3.5 years. The average duration of hospital stay was 5.3 $\pm$ 3.6 days for P. vivax and 5.4 $\pm$ 2.9 days for P. falciparum malaria.

CNS complications were seen in 10 (50%) with falciparum malaria and in 7 (13.2%) children with vivax. (p = 0.016). Out of 17 children with cerebral malaria, 2 (11.7%) were below 5 years of age. Respiratory complications were seen in 11 (20.7%) with vivax malaria and 3 (15%) with falciparum malaria (p=0.49). Seven (13.2%) with P.vivax and 3 (15%) with P.falciparum malaria had severe anemia (p=0.919). Thrombocytopenia was seen in 27 (52.7%) with vivax malaria and 10 (50%) with falciparum malaria (p=1.000). Severe thrombocytopenia was found in 12 (22.6%) children with P.vivax and 5

(25%) children with P. falciparum malaria (p=0.1). Hypotension was seen in 33 (62.2%) children with vivax and 12 (60%) children with falciparum malaria. (p=1.00) Splenomegaly was seen in 39 (73.5%) with vivax malaria and all children (100%) with falciparum malaria (p value-0.008). Hepatomegaly was found in 26 (49.1%) children with vivax and 14 (70%) children with falciparum malaria (p=0.123).

Chloroquine was given as first line therapy in 43 patients (81.1%) with vivax malaria, while remaining 10 (18.8%) patients received artesunate combination therapy (ACT) as first line treatment because they presented with complications like severe anemia and cerebral malaria. Out of the 43 patients receiving chloroquine, 40 (93.2%) responded to chloroquine (CHQ) and 3 (6.9%) did not respond to chloroquine but responded to ACT, highlighting possibility of chloroquine resistance in vivax malaria. With falciparum malaria, 12(60%) were given chloroquine as first line treatment and remaining 8(40%) received ACT as first line treatment because they presented with complicated malaria. Out of the 12 patients receiving CHQ, 11 (95%) responded to chloroquine and 1 (5%) did not respond to chloroquine but responded to ACT. The decision to administer either chloroquine or artesunate combination therapy (ACT) as the first line treatment was based upon the clinical severity of the child on the first day of admission according to the World Health Organization (WHO) guidelines for treatment of malaria. (4)

Discussion

This study highlights that vivax malaria is more common than falciparum in pediatric age group. In our study, CNS complications of malaria were more common with P. falciparum infection; whereas severe anemia, thrombocytopenia and hypotension were almost similar in P.vivax and P.falciparum infection. In our study, even though CNS manifestations were found significantly more in falciparum malaria, considerable number of children with vivax malaria also presented with CNS manifestations (13.2%). This coincides with another study conducted by Tanwar et al who showed that P. vivax mono-infection can cause cerebral malaria. (5) Recently, many more studies have shown increasing association of cerebral malaria with P.vivax monoinfection. (2,6) These findings challenge the usual perception of vivax malaria as a benign entity and therefore should be treated cautiously. Respiratory complications such as breathlessness, cough and pleural effusion were seen both in falciparum malaria and in vivax malaria also. A similar case report by Tanois et al has depicted acute respiratory distress syndrome complicating infection with P. Vivax. (7) Pulmonary complications of P. vivax are rare but occur more frequently than generally acknowledged. (8) A large number of children presented with thrombocytopenia with both falciparum and vivax malaria. Infact over half the children with vivax malaria had thrombocytopenia. This is in contrast to a study conducted by Martelo et al who found that out of 173 reported cases of malaria, 93% had P. vivax of which only 15% had thrombocytopenia. (9)

However, recently many studies have shown that thrombocytopenia was the most common hematological finding in vivax malaria. (10,11). Direct lytic effects, oxidative stress, splenic sequestration and immunological reactions are some of the proposed mechanisms for thrombocytopenia in malaria. (12,13)

We found that severe anemia was seen equally in vivax and falciparum malaria. This is in contrast to a study conducted by Rodriguez-Morales et al who suggested that anemia in vivax malaria may be more severe and frequent than falciparum. (14) Anemia results from accelerated red blood cells (RBC) removal by spleen, obligatory RBC destruction at parasite schizogony and ineffective erythropoiesis. Increased splenic clearance of RBCs results in splenomegaly which plays an important role in defence against malaria. In our study, splenomegaly was present invariably in all cases of falciparum malaria but also seen significantly in vivax (73.5%). A similar study conducted by Ozsoy et al showed that spontaneous splenic rupture was dramatically more pronounced in fatal cases of vivax monoinfection than in those with falciparum. (15) This reflects that more virulent strains of P.vivax are emerging which trigger the body's immune mechanisms. Butler and Weber found that orthostatic hypotension was a prominent feature of vivax and falciparum malaria and attributed it to the relative bradycardia and peripheral vasodilatation that occurs in malaria. (16) Our study showed that hypotension was also a feature in vivax malaria similar to falciparum malaria, seen in over sixty percent of patients.

Treatment with effective anti-malarial agents is the only therapeutic intervention that has been shown to reduce mortality in severe malaria. Recently, many cases of chloroquine resistance in different parts of the world have forced the policy makers to consider ACT first line therapy for both vivax and falciparum malaria, as also suggested by Sutanto et al in their study. (17) However, in our study majority of children with vivax and falciparum malaria responded to single course of chloroquine as first line therapy implying that many of the plasmodium strains are still sensitive to chloroquine. Also, extensive use of ACT may lead to development of resistance to these drugs. Therefore we suggest that its use should be restricted to chloroquine resistant and severe complicated malaria.

Conclusion

This study highlights that even vivax malaria can present with atypical clinical features which may sometimes be serious enough to add to the significant morbidity and mortality caused by malarial fever in an endemic country like India. Therefore, a high index of suspicion is required. Also, most of the malarial parasites are still sensitive to chloroquine as a first line therapy.

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