Original Article

Changing clinicohematological spectrum of *Plasmodium vivax* malaria

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Background: Malaria is one of the most common public health problems in India, with estimated mortality of mortality of 0.7–2.7 million per year globally among which 15,000 per year in India. Mortality is due to complicated malaria which was previously believed to be caused only by *Plasmodium falciparum* malaria. This study was done to observe the changes in clinicohematological spectrum of *Plasmodium vivax* malaria. **Materials and Methods:** Total of 80 indoor patients were taken according to inclusion and exclusion criteria. The patients were investigated for malaria by rapid antigen test and peripheral smear. Routine hematological and biochemical investigations were done. Observations were recorded, and result was obtained. **Results:** Our study revealed symptoms such as fever, hepatosleenomegaly, seizure, altered sensorium, anemia, thrombocytopinea, deranged liver function, and deranged coagulopathy among the patients selected for the group following inclusion and exclusion criteria**.** **Summary:** Among the total study group, it was observed *P. vivax* can also cause complicated malaria leading to severe symptoms and mortality. Hence, a change in clinicohematological spectrum of *P. vivax* malaria is observed.

KEY WORDS: Rapid antigen test, anemia, thrombocytopenia

INTRODUCTION

Malaria is one of the most important public health problems in India. As per the World Health Organization (WHO) report 2015, Southeast Asian (SEA) region bears the second largest burden of malaria (10%), only being next to African region (88%). Among South east Asian Region, India shares almost two-third of the burden (66%), followed by Myanmar, (18%) and Indonesia (10%).[1] The WHO estimates approximately 300–500 million malaria cases annually. The estimated, mortality attributed, to malaria, ranges from 0.7 to 2.7 million/year, globally.[2] Malaria is caused by a protozoan parasite of the genus plasmodium. Five species of the plasmodium such as *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi* causes malaria in humans which is transmitted by the bite of infected female anopheles mosquito.[1] One of major species causing malaria in human species is *P. vivax*. Although more emphasis has been given on *P. falciparum*, attention should be given to *P. vivax* malaria also due to increase in the severity of coarse of infection. This study aims to find the evidence on severe malaria in children <18 years of age which is caused by *P. vivax* infection.[1] *P. vivax* is responsible for 70–390, million infections every year. In continents other than Africa, vivax malaria, accounts for more than, 50% of all, malarial cases, yet the morbidity associated with malarial infection, and the changing spectrum of this disease is less studied.[3] There is growing evidence that *P. vivax* is responsible for a significant burden of disease worldwide. The clinical paradigm of "benign tertian malaria" has been challenged recently by various reports of severe disease and deaths due to *P. vivax* monoinfection.[2]

P. vivax infection has been considered to be benign and self-limiting disease for a long time. Previously, complicated *P. vivax* malarial cases have been rare in the and documented exclusively by case studies and small case series. Due to increasing, resistance to chloroquine and other antimalarials in

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P. *vivax* parasitic infection, the recent reports with involvement of this species in complicated malaria suggests the need for further research in vivax malaria.[4] With this background, a study in tertiary care center to find the clinical and laboratory profile of patients who are admitted with severe vivax malaria with its complications and outcome will help to bolster the new *P. vivax* which for long had engaged reputation of being benign does no longer hold true. The contribution of *P. vivax* versus *P. falciparum* to severe morbidity has not been properly assessed for children in India. Most of available literatures are pertaining to adult studies. Clinical profile with potentially life threatening complication would be of immense value and when diagnosed early might show improvement in the outcome with patients infected with *P. vivax.* Therefore, this study was planned to look for the profile of severe malaria and contribution of *P. vivax* related morbidity in children of western U.P. This study aims to focus on the changes in clinicohematological spectrum of *P. vivax* malaria in to selected sample of children aging less than 18 years.

MATERIALS AND METHODS

Study was held in Rohilkhand Medical College for a period of 1 year, study population included admitted patient aged <18 years with *P. vivax* positive malaria by rapid antigen test. This was an observational type of study with sample size of 85. The sample was selected based on following inclusion and exclusion criteria:

Inclusion Criteria

1. Patients testing positive for *P. vivax* malaria presenting below 18 years of age
2. Patients giving informed and signed consent for the study.

Exclusion Criteria

1. Patient with mixed malarial infection
2. Clinically suggestive but negative for malaria
3. Known case of bleeding disorders
4. Patients with other infections like enteric fever, tuberculosis along with malaria.

Methodology

This hospital-based observational study was conducted in the Department of Paediatrics, Rohilkhand Medical College, Bareilly. All patients were informed about the study, and informed consent was taken. Approval of the Institutional Ethical Committee was taken. Data from all indoor patients were filled and analyzed on a preformed pro forma. All children who satisfied the WHO criteria of malaria and severe malaria guidelines 2015,[5] admitted in Paediatric Intensive Care Unit and ward were enrolled. All cases underwent peripheral blood smear test for malarial parasite and malarial antigen test to confirm malaria. Routine hematological and biochemical investigations were done. Patients were followed up until discharge.

RESULTS

The onset of malaria was observed to be mostly during rainy season that is from August to October in Uttar Pradesh and neighboring regions. Total of 85 confirmed cases of *P. vivax* malaria was included in this study after inclusion criteria was satisfied. Among all the cases, 28% were seen to be uncomplicated and 72% cases showed features of complicated malaria in this study. The study cases were diagnosed on the basis of rapid diagnostic test and peripheral smear. All 85 patients showed rapid test and peripheral smear to be positive with *P. vivax* malaria. For peripheral smear, giemsa stain was used. The principle behind rapid antigen test was based on immunochromatographic principle with formation of antigen antibody complexes with specific malarial antigen that are released from lysed blood.

Descriptive Statistics

Among total number of 85 cases, all the cases showed positive for *P. vivax* malaria by rapid diagnostic test as well as in peripheral smear. Among the study group 70.6% males and 29.4% of female, 91.8% were hindus, 7.1% muslims, 1.2% Christian, all patients presented with fever as initial symptom. Other clinical feature observed were headache in 78.8%, paleness of body in 81.2%, yellowish discoloration in 5.9%, 21.2% of the patients presented with respiratory distress,71.8% had petechiae with 16.5% of cases having bleeding from any other site, 7% had complain of hematuria, and 3% had oliguria. On examination, almost 68.2% had hepatomegaly whereas spleenomegaly was observed in all the patients with *P. vivax* malaria. It was observed that 36% of the patients had convulsion during the hospital course. Based on the of laboratory investigations, maximum patients showed thrombocytopenia with anemia. Thrombocytopenia stays no longer differentiating feature between *P. vivax* and *P. falciparum* malaria.

DISCUSSION

The incidence and virulence of vivax malaria had been underestimated until the previous decade, when severe or complex malaria was synonymous with *P. falciparum* infection. The severity of *P. vivax* malaria has grown considerably and has been studied by Price *et al.*,[4] although the majority of the public literature on severe *P. vivax* malaria is made up of case reports or simple summary clinical series with no denominators. It was still lately that the severe illness produced by *P. vivax* was documented in bigger research on malaria from the South East Asia area, which covered all ethnicities and all Plasmodium species as studied by Tjitra *et al.*,[5] Barcus *et al.* [4] For example, according to a research conducted in Indonesia, 3.2 percent (36/1135) of the Patients infected with *P. vivax* had severe malaria as reported by Barcus *et al.*,[6] in this study, the proportion of malarial admissions caused by *P. vivax* had a rate of 23%, while *P. vivax* had a rate of 20%. Falciparum hospitalizations, with blended infection having the greatest incidence (31 percent) been reported by Tjitra *et al.*,[5] study. An Indian study of children hospitalized with malaria found

	n	Minimum	Maximum	Mean	Std. Deviation
Age	85	1	15	10.26	3.962
Hemoglobin (G/DL)	85	7	14	8.33	1.672
Total leukocyte count (cells/cumm)	85	4000	15000	10635.29	2953.396
Platelet count	85	1.2	90000.0	36718.439	25858.1942
Serum creatinine	85	0.5	2.0	0.847	0.4689
Urea	85	15	57	31.52	10.186
RBS	85	40	120	91.62	17.560
Serum bilirubin -D	85	0.10	26.00	1.3505	4.87709
Serum bilirubin - T	85	1.5	3.7	1.635	0.4519
SGPT	85	8	180	39.59	26.899
SGOT	85	7	432	50.02	83.167
PT	85	12.0	84.0	28.815	17.0206
INR	85	1.00	3.05	1.4218	0.33456
APTT	85	24	74	38.51	10.401

that highest risk of severe illness was associated with *P. vivax*. Vivax infections were the most common (63.1%), followed by Infections caused by *P. falciparum* (42.7%) and mixed infections (40%) in study by Kochar *et al.*,[7] *P. vivax* malaria was shown to account for a significant number of hospitalized patients in Asia and the Pacific area, as well as contributing to death as observed in the studies of Vannaphan *et al.*,[8] and Rodríguez-Morales *et al.*,[9] According to a similar research conducted by Chandra and Chandra[10] in Uttarakhand, India, 69.8% of patients tested positive for *P. vivax* and only 27.5 percent tested positive for *P. falciparum*, with 2.7% of cases reporting mixed infection. According to two other research undertaken by Rajendra Kumar Verma *et al* [11] from Kanpur, North India and Gaurav I. Patel *et al* [12] from Vadodara, Gujarat, India, 76.74 percent of cases of *P.vivax*, 13.95 percent of cases of *P.falciparum*, and 9.3 percent cases of mixed infection were reported, and 61 percent of cases of *P.vivax*, 29 percent of cases of PF, and 9.43 percent of mixed infection were reported, respectively. Kumbhar *et al* [13] in their study discussed children who have severe malaria are more likely to have one or more of the following symptoms: severe anaemia, respiratory distress due to metabolic acidosis, or cerebral malaria, among other issues. Adults are also more likely than children to have multiple organ involvement. It is possible to develop partial immunity to malaria in malaria-endemic areas, allowing for the development of asymptomatic infections. Patients in Kumbhar *et al.*[13] research reported 98.3% cases to be of *P. vivax* whereas one case of *P. falciparum* had been observed. Patient with severe *P. vivax* malaria showed symptoms such as fever, widespread body weakness (malaise), headache, nausea/vomiting, shortness of breath, abdominal discomfort, pallor, bleeding signs, hepatomegaly, and splenomegaly eleveted ESR was observed in 78%of the cases. In this study, *P. vivax* was observed to be causing more number of complicated cases of malaria. *P. falciparum* infection has been extensively researched; however, new research has revealed that similar alterations can also occur in infection with *P. vivax*, as demonstrated by the study conducted by Saurabh Srivastava *et al.*[14] In this study, among 74 patients 50 had *P. vivax* mono infection in which 41 presented as complicated malaria with thrombocytopenia being the most common symptom. The study concludes by stating *P. vivax* monoinfection no longer holds true for benign tertian malaria. The most significant hematological alteration seen in the present research was thrombocytopenia as been depicted by Patel *et al.*,[13] Erhart *et al.*[15] The same conclusion was reached by a number of additional investigations where thrombocytopenia has been observed in *P. vivax* malaria which was also seen in study by Agnihotri *et al.*[16] Regarding male and female children in the study, Rao *et al.*[17] found that 76% of the participants were male youngsters, while Kashinkunti and Alevoor[18] study found that the male to female ratio was 3.76:1. Male youngsters participating in outdoor activities may be the cause of an increase in the number of males who contract malaria. Whereas in the present study out of 85 patients 29% were males and 70% were observed to be females. In another study by Mitra *et al.*[19] included comparision of severity of malaria caused by vivax, falciparum and dual manifestation. The study observed out of 131 cases of malaria 83 cases was found to be *P. vivax* malaria. As per the study clinical manifestations caused by *P. vivax* was no different than that of *P. falciparum*. Hence, the study concluded *P. vivax* malaria can no longer be considered as benign. An investigation by Prasad *et al.*[1] discovered that children had a greater prevalence of malaria than adults due to their undeveloped immune systems. Adults are more successful in clearing parasites than youngsters at doing so, according to research. 67% of the children are between the ages of 4 and 12 years, and 11 percent of the children are between the ages of 3 and 12 years.

CONCLUSION

Our study included the cases suffering from *P. vivax* positive malaria. This study observed all the cases to show atleast one complication such as bleeding from any site, fast breathing, convulsion, jaundice, thrombocytopenia, anemia, deranged liver function and deranged coagulopathy. Therefore, it is notable that *P. vivax* can no more be labeled as a benign malaria and is emerging as an important cause of morbidiy in endemic regions.

In addition, the present study also shows the changings trend of clinicohematological spectrum of *P. vivax* malaria. Considering the reported trend in severity of the disease caused by *P. vivax*, there is need to strengethen and initiate more control programs targeted toward severity, control and prevention of the disease. Along with this kind of hospitalized study, and a large number of multi-centric prospective regional studies are needed to confirm the findings of this study and to determine the extent of complication of *P. vivax* malaria, after the exclusion of other associated infections and mixed malarial infections, with the use of the most up-to-date diagnostic methods and practices. Furthermore, required is an understanding of the reasons for the shift in virulence and whether any genetic mutation in *P. vivax* is responsible for the shift in virulence trend. As with this the research was carried out in an acute care hospital with solely admitted patients, the rate of malaria cases was rather significant in this study. Obtaining an accurate estimate of the real risk of progression vivax malaria and its complications would need large-scale population-based study.

REFERENCES

1. Prasad PL, Rai PL, Hussain MS. A study of haematological profile of malaria in a tertiary. Pediatrics 2018;5:1115.
2. Yadav D, Chandra J, Aneja S, Kumar V, Kumar P, Dutta AK. Changing profile of severe malaria in north Indian children. Indian J Pediatr 2012;79:483-7.
3. Sarkar D, Ray S, Saha M, Chakraborty A, Talukdar A. Clinico-laboratory profile of severe *Plasmodium vivax* malaria in a tertiary care centre in Kolkata. Trop Parasitol 2013;3:53.
4. Price RN, Tjitra E, Guerra CA, Yeung S, White NJ, Anstey NM. Vivax malaria: Neglected and not benign. Am J Trop Med Hyg 2007;77:79-87.
5. Tjitra E, Anstey NM, Sugiarto P, Warikar N, Kenangalem E, Karyana M, *et al.* Multidrug-resistant *Plasmodium vivax* associated with severe and fatal malaria: A prospective study in Papua, Indonesia. PLoS Med 2008;5:e128.
6. Barcus MJ, Basri H, Picarima H, Manyakori C, Sekartuti, Elyazar I, *et al.* Demographic risk factors for severe and fatal vivax and falciparum malaria among hospital admissions in northeastern Indonesian Papua. Am J Trop Med Hyg. 2007;77:984-91.
7. Kochar DK, Tanwar GS, Khatri PC, Kochar SK, Sengar GS, Gupta A, *et al.* Clinical features of children hospitalized with malaria-a study from Bikaner, northwest India. Am J Trop Med Hyg 2010;83:981-9.
8. Vannaphan S, Saengnetswang T, Suwanakut P, Kllangbuakong A, Klinnak W, Rungmatcha P, *et al.* The epidemiology of patients with severe malaria who died at the hospital for tropical diseases, 1991-2004. Southeast Asian J Trop Med Public Health 2005;36:385-9.
9. Rodríguez-Morales AJ, Sánchez E, Vargas M, Piccolo C, Colina R, Arria M. Anemia and thrombocytopenia in children with *Plasmodium vivax* malaria. J Trop Pediatr 2006;52:49-51.
10. Chandra S, Chandra H. Role of haematological parameters as an indicator of acute malarial infection in Uttarakhand state of India. Mediterr J Hematol Infect Dis 2013;5:e2013009.
11. Verma RK, Giri R, Singh N, Gupta C, Jain A. A study on clinical presentation and outcome of concurrent malaria and dengue infection from a malaria endemic zone of North India. J Med Sci Clin Res. 2016;4:15116-27.
12. Patel GI, Muley P, Vadher A, Suthar PP, Shah GV, Patel AB. A comparative study of clinical, biochemical and hematological profiles in smear positive malaria patients: At a tertiary care center located in rural part of Gujarat, India. Int J Res Med Sci 2015;3:2561.
13. Kumbhar SS, Kanetkar SR, Mane A, Agarwal G, Bansal S. Clinico-hematological profile of malaria cases in a tertiary care hospital. Galore International Journal of Health Sciences and Research. 2019;4:79-89.
14. Srivastava S, Ahmad S, Shirazi N, Verma SK, Puri P. Retrospective analysis of vivax malaria patients presenting to tertiary referral centre of Uttarakhand. Acta Tropica. 2011 Feb 1;117(2):82-5.
15. Erhart LM, Yingyuen K, Chuanak N, Buathong N, *et al.* Hematologic and Clinical indices of malaria in a semi-immune population of Western Thailand. Am J Trop Med Hyg 2004;70:8-14.
16. Agnihotri DV, Soni KS. Parasitemia and its relation to blood indices and liver function among malarial patients. Int J Biomed Adv Res 2017;8:222-7.
17. Rao VT, Rao BB, Chikkala R. Clinical profile of *Plasmodium falciparum* case presenting to a tertiary care teaching institution in south India: An observational study. IAIM 2016;3:159-65.
18. Kashinkunti M, Alevoor S. Clinical, hematological and coagulation proflile in malaria. Sch J App Med Sci 2014;2:584-8.
19. Mitra S, Abhilash KP, Arora S, Miraclin A. A prospective study from South India to compare the severity of malaria caused by *Plasmodium vivax*, *P. falciparum* and dual infection. J Vector Borne Dis 2015;52:281.