

Comparative Features of Vivax, Falciparum and Mixed Malarial Infections in a Peripheral Hospital of Mumbai.

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Abstract: *Falciparum malaria is known to cause severe malaria with multiorgan involvement while Vivax malaria is thought to run a benign course. However recent studies have reported complications even in vivax malaria and mixed infections. A prospective observational study was conducted for a period of 2 years on all patients who tested positive for malaria by smear examination or antigen test. A comparative evaluation of clinical features diagnostic methods, hematological profile and biochemical profile of patients presenting with vivax falciparum and mixed infection was done. Appropriate statistical analysis was done to compare the various parameters. There were 197 cases of vivax, 76 cases of falciparum and 27 cases of mixed infection out of the total 300 malaria cases. Headache, diarrhoea, vomiting, hepatomegaly, jaundice, anaemia, raised bilirubin, liver enzymes and creatinine were more common in mixed and falciparum infections than in vivax infection while splenomegaly and thrombocytopenia was more common in P. vivax and mixed malaria. Only falciparum cases showed convulsions and acute renal failure, while respiratory distress was seen in both vivax and falciparum infections. Though falciparum and mixed infections present more frequently with complications and altered laboratory parameters even vivax infection can present with severe malaria in less proportion of the cases.*

Keywords: *Biochemical profile, clinical features, hematological parameters, vivax, falciparum*

I. Introduction

About 3.2 billion people remain at risk of malaria worldwide. In year 2015 alone there were an estimated 214 million new cases of malaria and 4.38 lakhs deaths.⁽¹⁾ Most of these cases occurred in African region(88%) followed by South East Asian region(10%) and Eastern Mediterranean region.(2%). Malaria in humans can be caused by 4 human species Plasmodium vivax, P.falciparum, P.malariae and P.ovale after a bite of female Anopheles Mosquito.⁽²⁾ P.falciparum and P.vivax pose the greatest public health challenge. P.falciparum is most prevalent in the African continent and is responsible for majority of the deaths due to malaria. P.vivax has a wider geographic distribution because it can develop at even lower temperature, higher altitude and has a dormant liver stage. It accounted for an estimated 13.8 million cases in 2015 and caused >50% cases outside Africa. Most cases of vivax malaria occurred in South East Asian Region(74%) region followed by East Mediterranean region(11%) and African region.(10%). More than 80% cases of vivax occurred in 3 countries Ethiopia, India and Pakistan. Though number of deaths due to vivax are estimated to be between 1400 and 14900 globally it causes significant morbidity. In India estimated cases of malaria in 2014 were 1.4 million with 561 deaths. Falciparum contributed to 66% cases followed 34% vivax cases.⁽¹⁾ The ability of falciparum infection in causing severe malaria and organ dysfunction is well known. Though vivax infection was considered to be benign recent studies indicate that even it can cause severe malaria in some cases.⁽³⁻⁶⁾ A considerable number of patients are even presenting with mixed infection. The present study was conducted to do a comparative analysis of clinical presentation, diagnosis, biochemical and hematological profile of patients presenting with vivax falciparum and mixed infections in a peripheral hospital of Mumbai.

II. Material and Methods

The present study was a prospective observational study done in the department of pathology at Dr R.N. Cooper Hospital Mumbai. The duration of the study was a 2 year period between 1st June 2009 till 31st May 2011. Institutional ethics committee permission was obtained. Study included all febrile patients of both sexes who were malaria positive by either thick smear thin smear or antigen detection tests. Thick smears were stained by Jaswant and Bhattacharya Stain and thin smear by fields stain. Smears were examined for malarial parasite in 100 oil immersion fields for at least 5 minutes. A complete clinical history and clinical examination was done with reference to the presence of fever, chills, headache, vomiting, diarrhoea, oliguria, altered mental status/convulsions, jaundice and hepatosplenomegaly. Complete blood count was done on a fully automated cell counter and biochemical profile was done on a fully automated analyzer. Haemoglobin levels, WBC count and

platelet count were noted. Serum bilirubin, liver enzymes and serum creatinine levels were noted. A comparative analysis was done among patients with vivax, falciparum and mixed infections.

2.1 Statistical analysis: Statistical analysis was done by SPSS version 16. The data of the 3 groups of vivax falciparum and mixed infection was analysed using the Fisher or Chi square test appropriate for parameters like splenomegaly hepatomegaly along with hematological and biochemical parameters.

III. Results

A total of 6366 patients were tested for malarial parasite out of which 300 were positive for malaria and included in the study. There were 197(66%) cases of vivax, 76(25%) cases of falciparum and 27(9%) cases of mixed infections. The age and sex distribution is given in Table-1. There were 200 males(66.67%) and 100(33.33%) females with a male female ratio of 2:1. Majority of the cases were in the 21 to 30 (31.67%) years age group followed by 11 to 20(24.33%) years age group. This trend was seen in vivax and mixed infections while falciparum was more common in 11 to 20(30.26%) years age group.

3.1 Clinical features. The clinical presentation of patients with vivax, falciparum and mixed infections is given in Table 2. Fever was present in all (100%) patients followed by chills and rigours in 92.7% patients and headache in 57% patients. Chills and rigour was most common in patients with mixed infection 27(100%) whereas it was similar in patients with P.vivax 179(90.86%) and P.falciparum 72(94.73%). Headache was more common in mixed 23(85.2%) and falciparum malaria 48(63%) than in vivax malaria 101(51%). Vomiting was seen in 60(20%) of the cases. It was more frequently observed in mixed(48.2%) and falciparum(36.8%) infections than in vivax(11.2%) infection. Diarrhoea was observed in 61(20.33%) of all the cases. It was more common in mixed infection 48.15% followed by falciparum 36.84% and vivax infections(10.15%). One case each of falciparum and vivax presented with respiratory distress, while 2 cases of falciparum presented with convulsions. Jaundice was more common in mixed infections 10(37.03%) than in falciparum 14(18.42%) and vivax malaria 17(8.63%). Out of the total patients 38(12.66%) had hepatomegaly and 51(17%) had splenomegaly. Hepatomegaly was significantly ($p < 0.0005$) more common in mixed malaria(40.74%) than in falciparum(18.42%) and vivax infections.(6.6%). Similarly splenomegaly was also present significantly ($p = 0.015$) more in mixed infection(40.74%) than in vivax (15.29%) and falciparum cases(14.47%).

3.2 Diagnosis. All cases were subjected to thick smear, thin smear and rapid antigen test. 196 cases(99.49%) of vivax were positive by thick smear, 137 (69.54%) by thin smear and 183(92.89%) by kit method. 75 cases (98.68%) of falciparum were diagnosed by thick smear 45(59.21%) by thin smear and 70(92.10%) by kit method. 27 cases (100%) of mixed infection were diagnosed by thick smear and 26(96.29%) each by thin smear and antigen method. The sensitivity of thin smear in diagnosis of vivax and falciparum malaria was 73.09% and 69.61% while the sensitivity of antigen test was 91.03% and 90.2%.

3.3 Laboratory parameters. Table 3 shows the various laboratory parameters in different Plasmodium species. Anaemia was significantly ($p = 0.003$) more common in mixed 19(70.4%) than in falciparum 45(59.2%) and vivax cases 84(42.6%). However severe anaemia (Hb < 7 mg%) was seen in only 40(13.33%) cases. Severe anaemia was seen in 25.93% of mixed infection 17.11% of falciparum infection and only 10.15% of vivax infection. Out of 300 patients 226(75%) had thrombocytopenia. Incidence of thrombocytopenia was significantly ($p < .001$) more in mixed infection (100%) than in vivax (74.10%) and falciparum (69.70%) malaria. Bilirubin was raised (> 1.2 mg) in 79(26.3%) cases. It was significantly ($p < .0005$) higher in mixed malaria 15(55.56%) and falciparum malaria 26(34.21%) than in vivax monoinfection. 38(19.29%). Liver enzymes were raised in 93(31%) cases. They were increased in 24 cases (88.88%) of mixed infection, 27 cases(35.53%) of falciparum infections and 42 cases (21.31%) of vivax infections. 29 patients (9.6%) had raised serum creatinine. High creatinine levels were seen in 7(3.55%) cases of vivax 16(21.05%) cases of falciparum and 6(22.22%) cases of mixed infection and the difference was statistically significant ($p < .005$). Two cases of falciparum had acute renal failure.

IV. Discussion

A total of 300 malaria positive cases were included in the study. There were 197 (66%) cases of vivax 76(25%) cases of falciparum and 27(9%) cases of mixed infection. The proportion of vivax and falciparum cases varies in different parts of India. Jadhav et al⁽⁷⁾ conducted a study in Navi Mumbai and found vivax in 44.7% cases falciparum in 42% cases and mixed infections in 12.9% cases. Kochar et al⁽⁸⁾ in a study from Bikaner in north western India found 58% cases of falciparum and 41% cases of vivax infection. Overall there were 200 males and 100 females positive for malaria with a male female ratio of 2:1 which is similar to studies conducted by Muddaiah et al⁽⁵⁾, Mishra et al⁽⁹⁾ and Jadhav et al.⁽⁷⁾ High infectivity in the male population has been attributed to high mobility and outdoor activities of males as compared to the females. Overall maximum

cases of malaria were in the 21 to 30 years age group(31.67%).In a study conducted by Farogh et al⁽¹⁰⁾ and Muddaiah et al⁽⁵⁾ majority patients belonged to 21 to 30 years age group followed by 11 to 20 years as in our study.Maximum cases of vivax 68(34.5%) and mixed infections 11(40.8%) were in the 21 to 30 years age group while maximum cases of falciparum 23(30.26%) were in the 11 to 20 years age group. Symptom analysis showed that fever was the commonest symptom in all the cases followed by chills and rigours in all types of malaria.Headache was most common in mixed infection followed by falciparum and vivax infections. Vomitting and diarrhoea were common in falciparum and mixed infections than in vivax infections.Similar findings have been reported from studies from bundelkhand and Pakistan.^(11,12) There were 2 patients presenting with oliguria and 2 with convulsions and all had falciparum infection while one patient with vivax presented with respiratory distress.Hence multiorgan involvement is more common in falciparum than vivax as has been reported by other studies⁽¹³⁾. Vivax malaria does not have a benign course and this has been reported in several recent studies.^(3-6,14) .17% of our patients had splenomegaly while 13% had hepatomegaly. Splenomegaly was more common in mixed and vivax infections than in falciparum infections while hepatomegaly was more common in mixed and falciparum infections than in vivax infections. Similar findings have been reported by a study by Verma et al.⁽¹⁵⁾ Splenomegaly was more common in vivax infections probably because of relapses.Proportion of cases with splenomegaly is very variable in different studies because of differences in immune status of patients in different malaria transmission regions .Anaemia and thrombocytopenia(TCP) are the most frequently found abnormality in patients suffering from malaria⁽¹⁶⁾.

Anaemia was present in 49.33% of the cases. Adedapo et al⁽¹⁷⁾ and Ahmed et al⁽¹⁸⁾ have reported anaemia in 43.8% and 42% of their cases which is similar to our study.It was more common in falciparum(50%) and mixed infections(73.6%) than in vivax infections(42.13%).Severe anaemia with haemoglobin <7gm% was seen more commonly in mixed (25.93%) and falciparum (17.1%) than in vivax infections(10.2%).Similar findings have been reported in studies by Singh et al⁽¹¹⁾ and Kochar et al⁽⁸⁾.This shows that even vivax can present with severe anaemia and can no longer be considered benign.Severe anaemia may be due to red blood cell destruction, phagocytosis of non parasitized red cells, increased splenic clearance and dyserythropoiesis in the bone marrow. Thrombocytopenia was present in 75% cases.It was more common in mixed(100%) and in vivax(74.1%)infections than in falciparum (69.7%)infections. Faseela et al⁽¹⁹⁾ have reported TCP in 82.77% cases while Colonel et al⁽²⁰⁾ found it in 72% their of cases.TCP has been reported more frequently in vivax and mixed infections than in falciparum infections by Gupta et al⁽²¹⁾ and Verma et al⁽²¹⁾ which is similar to our study. Leucopenia was seen in 13% cases while leucocytosis was seen in only 2.6% cases. Jadhav et al⁽⁷⁾ found leukopenia in 14% of their cases and leucocytosis in 4.9% cases.In our study both were more common in mixed infections.In our study raised bilirubin was seen in 26% cases while increased liver enzymes were seen in 31% cases.Bilirubin was raised in only 19.29% cases of vivax 34.21% cases of falciparum and 55.56 % cases of mixed infections.Similarly liver enzymes were raised more in mixed infections followed by falciparum and vivax infections. Similar findings have been reported by Limaye et al⁽⁶⁾ et al in their study.Increased creatinine levels are seen in falciparum and mixed infections as reported by Piplani et al.⁽¹³⁾.ARF was seen only in 2 cases of falciparum in our study while other studies have reported cases even in vivax infection.⁽¹⁴⁾.ARDS was seen in 1 each case of falciparum and vivax infection.Cho Naing et al⁽²²⁾ have reported ARDS in cases of vivax malaria.we had only 2 cases of falciparum with cerebral malaria .Other studies have reported a higher incidence and even in vivax infections⁽¹⁴⁾.Hence though hepatic renal and hematological parameters are more deranged in falciparum and mixed infections they are also seen in vivax infection indicating that vivax infection does not always have a benign course.

4.1 Diagnosis:Thick smear was able to diagnose vivax falciparum and mixed infections in 99.3% cases.The sensitivity of thin smear was low in both vivax and falciparum infections but high in mixed infections.The sensitivity of rapid antigen test in diagnosis of all three infections was around 90%.Similar results have been found in studies by Parija et al⁽²³⁾ and Panigrahi et al ⁽²⁴⁾ who reported a sensitivity of thin smear for vivax and falciparum as 69.9% and 60%.Hence when only thin smear is done one can miss many cases of both vivax and falciparum infections.

V. Conclusion

P.vivax is more common than P.falciparum and mixed infections in Mumbai.Though complicated malaria with alterations in haematological and biochemical parameters is more common in falciparum and mixed malaria it can also occur in vivax malaria hence even these patients need to be monitored.

Table-1:Age And Sex Distribution Of Various Species Of Malaria

Age group-years	Males	Females	Total	%	P.vivax	%	P.falciparum	%	Mixed infection	%
0-9	6	4	10	3.33	6	3.05	4	5.26	0	0

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10-20	35	38	73	24.33	46	23.35	23	30.26	4	14.8
21-30	69	26	95	31.67	68	34.52	19	25	11	40.8
31-40	43	14	57	19	40	20.30	13	17.11	4	14.8
41-50	19	16	35	11.67	24	12.18	7	9.21	4	14.8
51-60	17	5	22	7.33	10	5.07	8	10.52	2	7.4
61-70	6	0	6	2	2	1.01	2	1.02	2	7.4
71-80	1	0	1	0.33	1	0.51	0	0	0	0
Total	200	100	300	100	197		76		27	
%sex	66.67	33.33								
	P.vivax			P.falciparum			Mixed infection			
Males	124			53			19			
Female	72			23			8			

Table 2: Comparison Of Clinical Features In Different Species Of Malaria

CLINICAL PRESENTATION	P.Vivax (n=197)	P.falciparum (n=76)	Mixed Infection(n=27)	Total
FEVER	197(100%)	76(100%)	27(100%)	300(100%)
CHILLS	179(90.9%)	72(94.7%)	27(100%)	278(92.7%)
HEADACHE	101(51.3%)	48(63.2%)	23(85.2%)	172(57.3%)
VOMITING	22(11.2%)	26(36.8%)	12(48.2%)	60(20%)
DIARRHOEA	20(10.2%)	28(36.8%)	13(48.2%)	61(20.3%)
OLIGURIA	0	02(0.66%)	0	02(0.66%)
RESPIRATORY DISTRESS	01(0.33%)	01(0.33%)	0	02(0.66%)
CONVULSIONS/NEUROLOGICAL DEFICIT	0	02(0.66%)	0	02(0.66%)
JAUNDICE	17(8.6%)	14(18.4%)	10(37%)	41(13.7%)
PALLOR	16(8%)	10(13.2%)	07(26%)	33(11%)

Table:3 comparison Of Diagnostic Technique In Diagnosis Of Malaria

	THICK SMEAR	THIN SMEAR	ANTIGEN TEST
PV(P.VIVAX)	196 (99.49%)	137 (69.54%)	183(92.89%)
PF(P.FALCIPARUM)	75 (98.68%)	45 (59.21%)	70 (92.10%)
PV,PF	27 (100%)	26(96.29%)	26 (96.29%)
TOTAL	298 (99.33%)	208 (69%)	279 (93%)

Table:4 Statistical Analysis Of Various Parameters In Vivax ,Falciparum And Mixed Infections

PARAMETERS	P.Vivax (n=197)	P.Falciparum (n=76)	Mixed infection(n=27)	P value
SPLENOMEGALY	30(15.12%)	11(14.5%)	10(37%)	0.015
HEPATOMEGALY	13(6.6%)	14(18.4%)	11(40.7%)	<.0005
ANAEMIA	84(42.6%)	45(59.2%)	19(70.4%)	0.003
THROMBOCYTOPENIA	146(74.1%)	53(69.7%)	27(100%)	<.001
RAISED BILIRUBIN	38(19.3%)	26(34.2%)	15(55.6%)	<.0005
RAISED LIVER ENZYMES	42 (21.3%)	27(35.5%)	24(88.9%)	<.0005
RAISED CREATININE	7(3.6%)	16(21.1%)	6(22.2%)	<.0005

N=total no of cases p value-<0.05 is significant

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