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Clinical Profile of Malaria and its Complication in Magadh Zone of Bihar: A Study

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Abstract
Introduction: *Malaria continues to be one of the most important cause of fever and related sufferings of human beings. While nearly eliminated from many countries like United states, Canada, Europe, and Russia, it still remains a heavy burden on tropical countries despite continued preventive strategies. In recent times Malaria is presenting new challenges in terms of changing clinical profile especially p.vivax infection causing severe malaria thereby defying early diagnosis and so the early institution of antimalarial therapy.*
Aims and Objectives: *Evaluation of clinical profile and its complication will assist in early recognition of malaria helping timely treatment thereby reducing the morbidity and mortality and so the present study is undertaken.*
Materials and Methods: *96 patients were enrolled from indoor and outdoor section of Magadh medical college hospital, Gaya. Rapid tests and peripheral blood smear examination used for diagnosis of malaria. Detailed clinical examination done and presenting clinical features noted, routine and specific lab. Investigation done, proper treatment instituted and regular follow up done. WHO criteria utilized for defining sever malaria. Statistical data analysed with 2016 Microsoft Excel.*
Results: *54% suffered p.vivax infection, 47% from p. falciparum and 9% from mixed infection. More than 30% patients presented with uncommon clinical features , 8.6% showed warning sign , 31% developed severe malaria out of which P vivax contrary to the usual belief also developed complication. 3 patients with more than one complication died despite best treatment.*
Discussion: *The burden of malaria varies in different zones of India so also the proportion of p. vivax and p. falciparum. P. vivaxdominates in Magadh zone of Bihar. Cough, severe headache, severe vomiting, abdominal pain, malena, oliguria are some of the uncommon presenting features recognized in the present study. Cerebral malaria, severe hypotension, ARDS were found to be the important cause of mortality as also reported from other studies.*
Conclusion: *Malaria remains a major public health problem. Changing clinical profile and increasing virulence of p. vivax is a matter of concern. Acknowledging these patterns helps in early diagnosis and better outcome.*
Keywords: *Malaria, Complications, prevalence, clinical profile.*

Introduction

Malaria is an age old disease, present throughout most of the tropical regions and despite continued effort to eradicate, it continues to be a major public health problems not only in India, but around the world. It is caused by plasmodium

parasites spread by infected Anopheles mosquito bites.It can be fatal and even in uncomplicated cases causes high fever, anaemia with severe malaise and is specially dangerous for pregnant women and young children. Plasmodium vivax is the most common prevalent species and plasmodium falciparum remains the most virulent worldwide[1,2]. WHO estimates 300-500 million malaria cases annually with 90% burden being born by Africa and 7lacs – 2.7 million malaria deaths globally every year with > 75% affecting African children and expectant mothers[3]. However only 2.5 million cases of this global burden is born by south east Asia. Out of thisIndia contributes 76% of malaria cases and 69% of malaria deaths in this South-East Asia Region[3]. However WHO projection showed a decreasing trend, a decline in the rate of incidences from 2010 to 2016, from 76 down to 63 cases per thousand population at risk. WHO 2017 World malaria report registers 216 million new cases in 2016. According to the global health body, Nigeria accounted for the highest proportion with 27% cases, India has the 4th highest number of malaria with 6% cases of global load and accounts for 7% of malaria deaths in world .National Vector Born Disease Control Program (NVBDCP) in India assesses about 1.5 million cases per year[4]. Distribution of malaria in different states of India reveals that Gujrat, Karnataka, Goa, Southern Madhya Pradesh, Chattisgarh, Orissa and Jharkhand are worst affected (Annual parasite incidence >5). NVBDCP provides technical and operational guidelines to every state for preventing malaria. Early detection and complete treatment together with selective vector control, and behavioural change communication are the key components of malaria control strategy Thus early diagnosis and speedy treatment is of the utmost significance However in recent times besides difficulties in vector control, malaria like other infectious disease, has also presented new challenges not only in the field of management but also in the pattern of presentation and severity of disease posing difficulty in diagnosis. Contrary to the usual belief P. vivax infection caused many complications[5,6,7] traditionally thought to be associated with p. falciparum or mixed infection thereby delaying the proper and timely diagnosis resulting in delayed institution of proper management leading to increased mortality and morbidity. Thus defining clinical profile of malaria in a given geographical area is the need of the hour and so this clinical evaluation is undertaken.

Material and Methods

Study design and ethical issues

96 patients of age more than 14 years were enrolled from outdoor and indoor section of Anugrah Narayan Medical College Hospital, Gaya between 2014 to 2016. This medical college hospital receives patients from all the area of Magadh zone of Bihar which makes it a true representative of the area around. LDH based Rapid diagnostic tests used for identifying the cases and Malaria infection was confirmed by microscopic examination of Giemsa-stained thick blood smears. All were given information about the study and written informed consent was taken. Standard treatment was given to all, severe malariaand falciparum and mixed malaria were treated by artesunate combination therapy with appropriate supportive therapy[8].

Inclusion and exclusion criteria

Patients with confirmed diagnosis of malaria who satisfied exclusion criteria were included.

Patients with a history of systemic illness like hypertension, diabetes, tuberculosis, chronic kidney or liver disease, nephritis, acute or chronic viral hepatitis etc were excluded. Patients taking medicines likely to affect renal and liver function tests were also excluded.

Clinical assessment and laboratory tests

Standard Clinical evaluation of all patients at the time of enrolment were done and then regular follow up carried out with standard treatment protocol.

Whole blood (7 to 10cc) was drawn and properly collected into Vacutainer tubes containing EDTA.

Giemsa stained thick blood smear prepared and was examined for the type of malarial species and density by a trained malaria macroscopics. Complete blood cell counts were done by automated haematology analyser, blood chemistry for urea and creatinine, bilirubin, liver enzymes, blood sugar and urine analysis were performed in clinical laboratory of the institution.

Patients were classified as uncomplicated or severe malaria cases as per the clinical and laboratory criteria laid down by WHO: severe malaria-unarousable coma with convulsions together with exclusion of other causes for cerebral malaria. Acidaemia, severe anaemia, renal failure, jaundice, hypoglycaemia were diagnosed when plasma bicarbonate level was < 15 mmol/L, haemoglobin < 5gm/dl, serum creatinine > 3.0 mg/dl, serum bilirubin > 3 mg/dl, random blood glucose was <40 mg/dl respectively[8]. Hypotension was defined as systolic blood pressure <70 mmHg and respiratory distress diagnosed when patient presents with tachypnoea with rate of > 30/ min[8].

Statistical analysis

The observed data were analysed with the help of Microsoft excel 2016. A p- value of < 0.05 was taken as statistically significant.

Results

96 patients with acute malaria enrolled, 4 left in between the study. Out of 92 with 54 male and 38female, 50 suffered P. vivax (54%), 34 from P. falciparum (37%) and 8 suffered mixed infection (9%). The average age was 33years, the range being 14 to 64 years. Fever, malaise and body ache found to be the presenting complain in 100% of cases but the classical intermittent fever with chills/rigor and sweating was present in only 56% (76% of p. vivax, 35% p. falciparum and in 25% of mixed infection).

Table- 1: Clinical features at the time of presentation

Symptoms	P V 50	P F. 34	Mix 8	Total 92	Signs	p. vivax	p. fal.	mixed	total
Fever	50 (100%)	34 (100%)	8 (100%)	92 (100%)	splenomegaly	18*(36%)	2(6%)	1(12.5%)	21(225%)
intermittent	38(76%)*	12(35%)	2(25%)	52(56%)	Hepatomegaly	14*(28%)	1(3%)	1(12.5%)	16(17%)
Irregular	12(24%)	22(65%)	6(75%)	40(44%)	dehydration	11(22%)	7(20.5 %)	2(25%)	20(21%)
Chills/rigor	40(80%)	20(58%)	6(75%)	66(71%)	tachycardia	9(18%)	5(14%)	1(12.5%0	15(16%)
Cough	+11(22%)*	4(11%)	0	17(18%)	Jaundice	15(30%)	9(26%)	1(12.5%)	25(27%
severe headache	5(10%)	4(11.7%)	1(12.55)	10(10.8%)	pallor	17(34%)*	6(17%)	2(25%)	25(27%)
severe myalgia	2(4%)	1(3)	0	**3(3%)**	**Warning signs**				
weakness	36(72%)	25(73.5%)	6(75%))	67(72%)	Tachypnoea without fever	2(4%)	1(2.9%)		3(3.2%)
anorexia	30(60%)	21(61%)	5(62)	56(61%)	Alteration in consciousness	2(4%)	2(5.8%)		4(4.3%)
vomiting	15(30%)	8(23%)	2(255)	25(27%)	Persistent vomiting	1(2%)	2(5.8%)	1(12.5%)	4(4.3%)
diarrhoea	9(18%)	5(14%)	1(12.5%)	15(16%)	convulsions	.0%	3(8%)		3(3.2%)
Abd pain	10(20%)	2(6%)	0	12(14%)	choluria	0	1(2.9%)		1(1%)
Malena	0	1(2.9%)		1(1%)					
Severe arthralgia	6(12%)	3(8%)	0	9(11%)					
Oliguria	5(10%)	6(17%)		11(12%)					

*p value between p. vivax and p. falciparum <0.01

Uncommon symptoms like vomiting(27%), cough (18%), diarrhoea(16%), abdominal pain(12%) were present more frequently in p. vivax patients. 11% patients presented with arthralgia, 10.8% with severe headache, 1patient of p . falciparum complained of malena. Splenomegaly (22%), hepatomegaly (17%) and mild pallor(27%) were found usually in patients with p. vivax(p value <0.05) . Dehydration, Tachycardia and jaundice (21%, 16%, 27% respectively) were present with near equal distribution among different species.

3 % to 4% patients presented with warning signs (convulsions, persistent vomiting, altered consciousness, choluria and tachypnoea (Table 1)

17% Patients had severe hypotension (BP < 70 mmHg), 3.2% presented with feature of ARDS and 9.7% came with clinical features of cerebral malaria. (Table 2)

Table-2: Type of malaria and no of patients with following presentation

	Hypotension -SBP<70	ARDS	Cerebral malaria
Total			
P. vivax	9(18%)	1(2%)	2(4%)
P. falciparum	6(17%)	2(5.8%)	6(17.5%)
Mixed(pv/pf)	1(12.5%)		01(12.5%)
total	16(17%)	3(3.2%)	9(9.7%)

Haematological Parameters

Thrombocytopenia appeared as a common finding (57.6%), however only 13% showed severe effect (<50000).43% patient showed anaemia, severe anaemia more common in p.falciparum however lower MCV and MCHA were more common in p.vivax cases, more than 70% showed Leukocyte alterations predominantly in p. falciparum patients. (Table 3)

Table 3: Haematological Findings

	platelet		Hb		MCV	MCHC	Leukocyte		
	50000-150000	<50000	5-10mg/dl	<5 mg/dl	lower	lower	Leukopaenia	Neutrophilia	monocytosis
P.VIVAX,n-50	24 (48%)	8 (16%)	19 (38%)	1 (2%)	9 (18%)	25 (50%)	12 (24%)	26(52%)	8 (16%)
P FAL N=34	16 (47%)	4 (11.7%)	10 (29.4)%)	7 (20.%)*	3 (8.8%)	3 (8.8%)	13 (38%)*	21 (61%)*	10 (29%)*
PF/PV N=8	1 (12.5%)	0	2 (25%)	1(12.5%	0	0	1 (12.5%)	1 (12.5%)	0
Total N=92	41 (44.5%)	12 (13.2%)	31 (33%)	9 (9.7%)	12 (13%)	30 (32.6%)	26 (29%)	48 (52%)	18 (19.5%)

P Value between p. vivax and p. falciparum <0.01)-sinificant

Biochemicals Parameters

Renal parameters in 65% of patients and hepatic parameters in 52% are within normal range. 28% patients showed mild to moderate alteration in bilirubin level predominantly affecting p. vivax patients(p <0.01) however out of 18% patients with > 3mg serum bilirubin, p. falciparum and mixed infection patients suffered more(p<0.01) with AST level alterations also more frequent in p. falciparum (p<0.05).Mild to moderate alterations in renal parameters affected 27% patients with near about equal distribution among different species, however 7% patients showed serum creatinine > 3 mg significantly affecting p. falciparum patients (p<0.01); haematuria, leukocyturia and proteinuria also observed in 7 to14% patients mainly affecting p. falciparum group. 7.6% patients suffered severe hypoglyc-aemia more frequent in p. falciparum (p<0.05). 3% recorded acidosis compounding the severity.

Table -4: Laboratory Parameters and no of patients with different malarial species

	S. Bilirubin		S. Creatinine		B. sugar	Raised AST			Acidosis
	1.2-3 mg/dl	>3.0 mg/dl	1.5-3 mg/dl	>3 mg/dl	<40 mg/dl	AST raised	Proteinuria	Haematuria	Bicarbonate
p. vivax n=50	19 (38%)*	4(8%)	14 (28%)	1(2%)	2(2%)	4(8%)	6(12%)	2(4%)	1(2%)
p. falciparum n=34	7 (20.5%)	11 (32.3%)*	10 (29%)	6 (17%)*	5 (15%)**	10 (29%)**	8 (24%)*	4 (11%)*	2 (6%)
Mixed N=8	1 (12.5%)	2 (25%)	1 (12.5%)	0	0	1(12.5%)	0	1(12.5%)	0
Total	27 (28%)	17(18.4%)	25 (27%)	7 (7%)	7 (7.6%)	10(16.3 %)	14 (15%)	7 (7.6%)	3 (3%)

P value for the no. of patients with lab. Findings for p. vivax vs p. falciparum *<0.01 **<0.05

Uncomplicated/ Complicated Malaria

Analysing the data referred above, 31% patients suffered complicated/severe malaria mainly involving p. falciparum ($p<0.05$); 18% with one complication and 10% with two or more than two complications.

Table -5: Clinical profile of all patients studied (male-54, female38)

classification		P .vivax No/(%)	p. falciparum	Mixed (PV/PF)	total
Total number		50	34	8	92
Uncomplicated malaria					
	Warning signs	02(4%)	05(14.7%)	01(12.5%)	08(8.6%)
Complicated malaria		09(18%)	16(47%)**	4(50%)	29(31%)
	One complication	7(14%)	9(26.4%)	2(25%)	18(19%)
	Two or more complications	2(4%)	7(20.5%)	1(12.5%)	10(10.8%)

**P Value-between p vivax and p. falciparum <0.05

Deaths

In spite of best treatments, 3 patients with more than two complications especially-cerebral malaria, ARDS and severe hypotension succumbed.

Discussions

National Vector Borne Disease Control Program suggests 95% of country's population to be living in "malaria endemic areas"[4]. In the year 2014, 1.10 million cases of malaria reported with high mortality and morbidity rate[9,10]. This signifies the importance of the present evaluation of clinical profile so as to make early diagnosis and treatment. The burden of malaria in India is complex and the proportions of p. vivax and p. falciparum vary across India[11]. Present evaluation revealed that malaria in the Magadh zone of Bihar recorded 54% p. vivax, 37% p. falciparum and 9% mixed infection. Comparative analysis from Rourkela revealed increasing incidence of complicated malaria affecting 23.7% in 2000-2002. A general shift in the clinical profile has been observed and multiorgan dysfunction/failure is becoming more common feature[10]. P vivax considered to be benign reported to cause severe manifestations -jaundice(45.8%), severe anaemia 15.3%; ARDS 11.1%, Acute renal failure in 9.7%, cerebral malaria 8.6%, shock 6.9%. 38 Many cases presented with more than one of these complication[11]. The observation from present study showed that 31% suffered complicated malaria; 18% of p. vivax, 47% of p. falciparum and 50% of mixed infection suffered revealing the fact that p. falciparum including mixed infection is more dangerous form but p. vivax is also not so benign as is usually expected[14,15]. P. vivax patients also suffered although less frequently than p. falciparum from cerebral malaria, ARDS and severe hypotension. Nearly 11% has two or more than two complications especially the p. falciparum. Severe jaundice, acute renal failure, acidosis, severe anaemia and severe hypotension increases the morbidity including hospital stay and needs to be recognized earlier and manged promptly. 15% patients presented with warning signs(table1) which were recognized and accordingly managed resulting in better outcome emphasizing the importance of giving special attention to look for these clinical features in day to day management.

In India, mortality due to p.falciparum is reported to be 7.9% in Vellore[12], 25.6% and 30% in Jabalpur (Madhya Pradesh)[13] and Rourkela (Orissa)[11] respectively. In Jabalpur medical college 8.5% were reported to suffer from cerebral malariaof which 25.6% died, delayed diagnosis and comatose condition were the main determinants of death[13].

Early diagnosis is the key to prevent morbidity and mortality. So recognising the relatively uncommon misleading clinical features like cough, severe headache, severe myalgia, diarrhea, abdominal pain, severe arthralgia, oliguria, malena beside the common presentation is important. In

the present series a good number of patients presented with uncommon symptoms (table1)

In May 2015, the Global Technical Strategy for Malaria 2016-2030 (GTS) was adopted by the World Health Assembly to eliminate malaria[16] thus giving a hope to be free from malarial menace.

Conclusions

Malaria is a sustained menace, continues to kill and threaten millions around the world. Malarial clinical profile shows changing pattern with multiorgan involvement in p. falciparum and severe complications in p. vivax. Uncommon symptoms like cough, severe headache, vomiting , abdominal pain, malena, severe arthralgia are not unusual and requires high alertness for considering malaria in these situations. Severe thrombocytopenia, severe anaemia, jaundice, > 3 mg s creatinine were found to complicate malaria. Cerebral malaria, hypotension, ARDS appeared as important cause of mortality. Acknowledging local clinical pattern helps in speedy diagnosis and proper management; timely recognition of severe symptoms is essential for better outcome.

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