Original article

Malaria: change in a variety of clinical manifestations in Eastern India

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Abstract:

Objective: We had undertaken this study to find out the change in variety of clinical presentations in which a patient suffering from malaria could present. ***Materials and methods:*** In a retrospective, cross-sectional and observational study first 100 admitted malaria patients were taken in a tertiary hospital cum medical college at Kolkata, India from August 2009 to July 2011. Their clinical profile were noted and analysed. ***Results:*** A variety of clinical pattern was noted in various combinations, starting from fever, chill, and rigor to even hematemesis and rash. Change was noted in pattern of fever and other manifestations. ***Conclusion:*** Each patient suffering from malaria could present with a variety of clinical features with some specific patterns in specific cases as discussed. Treatment of malaria in Eastern India was efficacious but costly.

Key words: India, clinical, fever, vivax, falciparum

DOI: http://dx.doi.org/10.3329/bjms.v13i2.18298
Bangladesh Journal of Medical Science Vol.13(2) 2014 p.150-154

Introduction:

On 4th of July, 1898, a malaria researcher, working in Calcutta (now Kolkata), India, had made an astonishing discovery. After working for several years trying to discover the way in which the malaria plasmodium parasite was transferred from humans to other humans, Dr. Ronald Ross, a British military doctor, discovered that the mosquito's bite had transmitted the most devastating disease known to mankind and received the Nobel Prize for his discovery.[1]

The ancient Hindu text the Atharva-veda contained a number of references to malaria. The Atharva-veda specifically detailed the fact that fevers were particularly common after excessive rains (marhavasha) or when there was a great deal of grass cover (mujavanta). Other ancient writings also made references to malaria or malarial-type fevers in India. The Charaka Samhita, one of the ancient texts on Ayurvedic medicine, which was written in approximately 300BC and the Susruta Samhita written about 100BC; both had referred to diseases where fever was the main symptom. The Charaka Samhita classified the fevers into five different categories, namely continuous fevers (samatah), remittent fevers (satatah), quotidian fevers (anyedyuskah), tertian fevers (trtiyakah) and quartan fevers (caturthakah)[1].

Malaria was mostly caused by four distinct species of the Plasmodium parasite namely, P. vivax, P. falciparum, P. malariae, and P. ovale. P. vivax had the widest geographic distribution throughout the world. In India, about 70% infections were due to P. vivax, 20-30% infections were due to P. falciparum, 4-8% was due to mixed (both vivax and falciparum) infection. Rest of the two species had 1% incidence in total[2].

Literature stated that, malaria presents as high grade intermittent fever with chill and rigor. But recently patients were presenting with myriads of symptoms,

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from gastro-intestinal to neurological, even the pattern of fever being different. So we took up this study to find the pattern of involvement of organ-systems with malaria.

Malaria had continued to pose a major public health threat in India, particularly due to P. falciparum which was prone to complications. In India 27% population lived in high transmission areas (>= 1 case/1000 population) and about 58% in low transmission areas (0-1 case/1000 population) [3].

Materials and methods

This study was conducted in a tertiary hospital cum medical college at Kolkata, India during the period August 2009 to July 2011, including first hundred indoor cases (both from urban and rural areas, both adults and children of both genders) where malaria was detected using microscopy and/or rapid antigen method. Patients usually had come here from areas of unstable transmission, which included the city of Kolkata and the surrounding districts of West Bengal, India. Outdoor malaria patients were excluded.

The patients were observed from the day of admission till the day of discharge, death or referral. Each patient's name, age, sex, residential address, hospital serial number and type of malaria were recorded from hospital record sheet. Patient's complaints, past history, co-morbidities and clinical examination findings were noted from each patient's case file. Persistence of symptoms during treatment, duration of hospitalisation and cost of treatment were also recorded retrospectively from hospital record sheet. The study was observational, retrospective and cross-sectional. No sampling method was applied. High grade fever was taken as oral temperature > 102 degree Fahrenheit.

Malaria detection was done with microscopy and/or rapid antigen detection methods. Microscopy demonstrated asexual forms of parasite in stained peripheral blood smear. We had used Giemsa stain at pH 7.2. Both thin and thick films were examined. The thin blood smear was rapidly air-dried, fixed in anhydrous methanol, and stained; the RBCs in the tail of the film were then examined under oil immersion (x1000 magnification). Uneven thickness thick blood film was dried thoroughly and stained without fixing. Both parasites and white blood cells (WBCs) were counted, and the number of parasites per unit volume was calculated from the total leukocyte count. 100–200 fields were examined under oil immersion, before a thick smear was judged to be negative. Thin blood films were more helpful in diagnosis of species of Plasmodium. Rapid antigen test was done using SD BIOLINE Malaria Antigen P.f. /P.v. test kit. The test is one step, rapid, qualitative and differential test for the detection of HRP-II (Histidine-rich protein II) specific to Plasmodium falciparum and pLDH (Plasmodium lactate dehydrogenase) specific to Plasmodium vivax in human blood sample.

The data were entered in MS-Excel software and the mean/median value and standard deviation were measured. Pie chart and Bar charts were created using MS-excel software. GraphPad Instat software was used for data analysis. Unpaired t test was used for parametric comparisons. Proportions were examined using Fisher's exact test and two sided p value was calculated. $p < 0.05$ was taken as the cut-off for significance.

Results:

In our study, Plasmodium vivax malaria was accounted for 57, Plasmodium falciparum for 32 and Mixed infection for 11 cases. Different parameters, which had been studied for different malaria patients, had been depicted in various tables and graphical representations had been made for easy viewing. P. vivax and P. falciparum cases were compared in table 1. It was found that median age was higher in P. vivax patients than P. falciparum patients (28 years vs. 26 years, $p = 0.62$). Higher numbers of male patients were suffering from malaria than their female counterparts (66% vs. 34%). Patients suffering from P. vivax malaria had more male preponderance than patients suffering from P. falciparum malaria (66.7% vs. 62.5%, $p = 0.81$). Median duration of symptoms before admission in patients suffering from vivax and falciparum was 4 days. Those differences were not statistically significant.

Symptoms:

In our study, patients had presented with myriads of gastro-intestinal symptoms like nausea & vomiting (48%), pain abdomen (7%), loose motion (6%), loss of appetite (5%), constipation (2%) and hematemesis (1%). There were also symptoms of cough (11%), shortness of breath (8%), chest pain (3%) and expectoration (2%) indicating respiratory system involvement. Drowsiness (11%), weakness (6%), vertigo (3%) and convulsion (2%) similarly showed nervous system involvement. Genitourinary system involvement was noted with complaints of burning sensation in micturition (8%), pain abdomen (7%), menstrual irregularity (2%) and retention or incontinence

of urine (2%). Although many patients had presented with general symptoms like headache (44%), body ache (26%), weakness (6%) and rash (1%), almost all of the patients had presented with multiple system involvement.

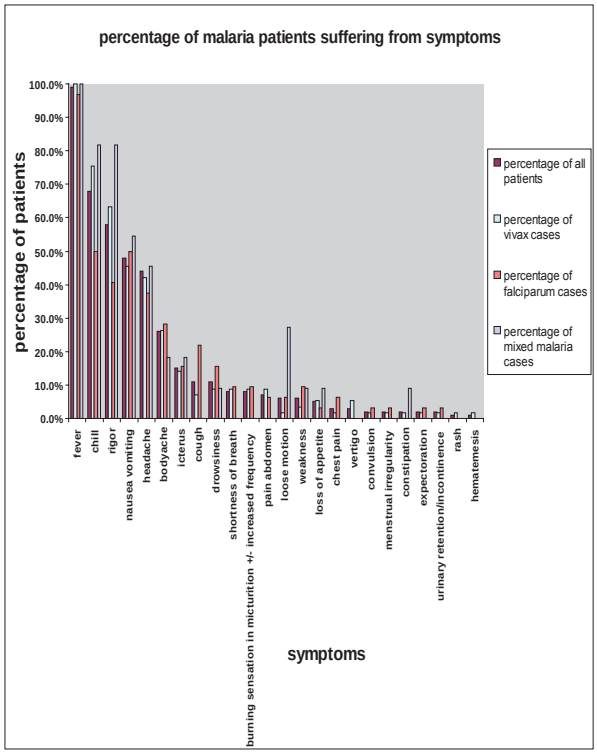

Fig 1. Different malaria patients suffering from different symptoms

Figure 1 had depicted the comparison between patients suffering from vivax (n=57), falciparum (n=32) and mixed (n=11) malaria as well as total study population (n=100) regarding presence of different symptoms/complaints. The figure 1 had shown that fever was the commonest complaints in all groups. Chill and rigor were more common in patients suffering from P. vivax malaria than patients suffering from P. falciparum malaria (75.4% vs. 50%, p = 0.02) and (63.2% vs. 40.6%, p = 0.048), respectively. Higher percentage of patients suffering from mixed malaria was found to have loose motion than their vivax counterparts (27.3% vs. 1.8%, p = 0.01) and falciparum counterparts (27.3% vs. 6.3%, p = 0.09). Moreover, greater proportion of patients suffering from mixed malaria were found to have rigor (81.8% vs. 40.6%, p = 0.03) and chill (81.8% vs. 50%, p = 0.08) in comparison to their falciparum counterparts. But there were no significant difference between patients suffering from vivax and mixed malaria in regard to chill (75.4% vs. 81.8%, p = 1) and rigor (63.2% vs. 81.8%, p = 0.31).

Female patients had higher incidence of shortness of breath than their male counterparts (6 vs. 2; 17.7% vs. 3.0%, p= 0.0175). Past history of malaria was higher in P. falciparum patients than P. vivax patients (12.5% vs. 0%, p= 0.015). Male patients had suffered from higher proportion of intermittent fever than females (66.7% vs. 47.1%, p=0.08) but not quite significant.

Signs:

Anemia was higher in females than males (88.2% vs. 62.1%, p= 0.0096). In falciparum malaria, females were more susceptible to suffer from anemia than male patients (35.3% vs. 18.2%, p= 0.0135). Median [SD] systolic blood pressure in females were significantly less than males (119 [16] vs. 110 [15.5], p= 0.0083) and significantly more in age group more than equal to 30 years than the group of less than 30 years age (120 [19] vs. 110 [12.7], p= 0.0039). Median [SD] arterial pulse was more in females than males (100 [10.7] vs. 96 [9.9], p= 0.07) and in falciparum malaria cases than vivax malaria cases (100 [10] vs. 96 [11], p= 0.09); both of the situations were statistically not quite significant. Median [SD] respiration was higher in males than females (22 [3] vs. 20.5 [4.2], p= 0.07), but not quite significant. High grade fever is more common in vivax malaria than falciparum malaria but not significant (47.4% vs. 31.2%, p= 0.18).

Higher incidence of malaria was found in younger age group (fig 3). Low grade and intermittent fever were more common in patients suffering from vivax, falciparum and mixed malaria.

Falciparum malaria patients had significantly higher duration of hospital stay than vivax malaria patients (6 ± 4.9 days vs. 4 ± 2.2 days, p= 0.035). Cost of treatment was found to be very high patients suffering from in all types of malaria among which investigation charges were found to be the highest.

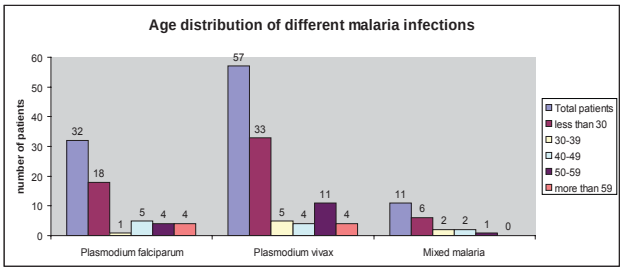

Fig 2: Age distribution in patients suffering from different malaria species

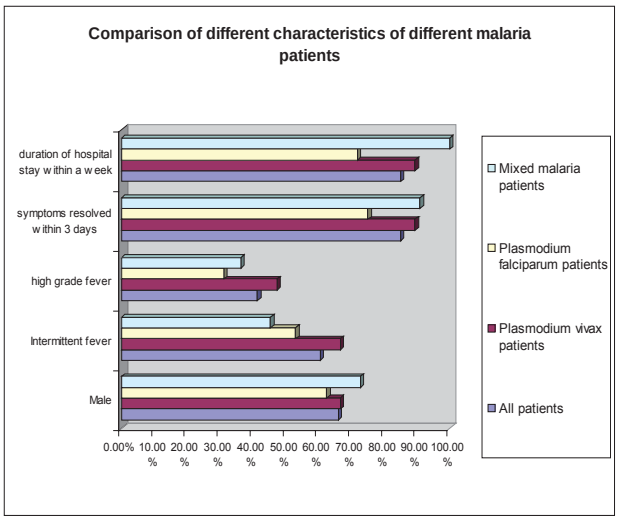

Fig 3: Comparison of different characteristics of different malaria patients

Table 1. Comparison between vivax and falciparum malaria cases		Plasmodium vivax malaria (n=57)	Plasmodium falciparum malaria (n=32)	p value
Parameters				
Age in years(SD)		28 (16.9)	26 (19.8)	0.62
Male (%)		38 (66.7)	20 (62.5)	0.81
Duration of symptoms median (SD) (days)		4 (7)	4 (8)	>0.99
Symptoms	Fever	57 (100)	31 (96.9)	0.36
	type of fever, intermittent (%)	38 (66.7)	17 (53.1)	0.36
	grade of fever, high (%)	27 (47.4)	10 (31.2)	0.18
	chill	43 (75.4)	16 (50)	**0.02**
	Rigor	36 (63.2)	13 (40.6)	**0.048**
	Nausea vomiting	26 (45.6)	16 (50)	0.82
	Headache	24 (42.1)	12 (37.5)	0.82
	Body ache	15 (26.3)	9 (28.1)	1.00
	Icterus	8 (14)	5 (15.6)	1.00
	Cough	4 (7)	7 (21.9)	0.05
	Drowsiness	5 (8.8)	5 (15.6)	0.49
	shortness of breath	5 (8.8)	3 (9.4)	1.00
	Burning sensation in micturition +/- increased frequency	5 (8.8)	3 (9.4)	1.00
	pain abdomen	5 (8.8)	2 (6.3)	1.00
	Loose motion	1 (1.8)	2 (6.3)	0.29
	Weakness	2 (3.5)	3 (9.4)	0.35
	loss of appetite	3 (5.3)	1 (3.1)	1.00
	chest pain	1 (1.8)	2 (6.3)	0.29
	Vertigo	3 (5.3)	0 (0)	0.56
	Convulsion	1 (1.8)	1 (3.1)	1.00
	menstrual irregularity	1 (1.8)	1 (3.1)	1.00
	Constipation	1 (1.8)	0 (0)	1.00
	Expectoration	1 (1.8)	1 (3.1)	1.00
	Urinary retention/incontinence	1 (1.8)	1 (3.1)	1.00
	Rash	1 (1.8)	0 (0)	1.00
	Hematemesis	1 (1.8)	0 (0)	1.00
Past history of malaria		0 (0)	4 (12.5)	**0.015**
Signs	General condition, alert (%)	51 (89.5)	27 (84.4)	0.52
	Arterial pulse (rate/minute)	96 (11)	100 (10)	0.09
	Systolic blood pressure (mm Hg)	110 (18)	114 (14)	0.28
	Diastolic blood pressure (mm Hg)	70 (12.3)	70 (9.3)	>0.99
	Temperature (degree F)	101 (1.4)	101 (1.6)	>0.99
	Respiration (rate/minute)	20 (4)	20 (3)	>0.99
	Anemia (total)	38 (66.7)	24 (75)	0.48
	Icterus	17 (29.8)	8 (25)	0.81
	Oedema	2 (3.5)	2 (6.3)	0.62
	Clubbing	0 (0)	0 (0)	
	Cyanosis	0 (0)	0 (0)	
	neck vein	0 (0)	0 (0)	
	Lymphadenopathy	1 (1.8)	1 (3.1)	
	weight (kg)	54 (14.2)	52 (15.4)	0.54

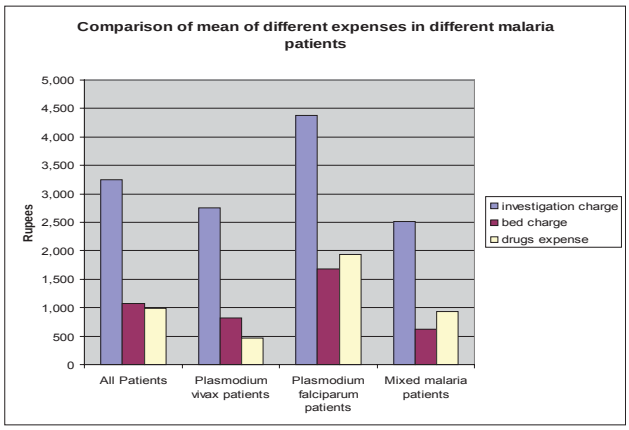

Fig 4: Treatment expenses in patients suffering from different types of malaria

Discussion:

Malaria had been a significant cause of morbidity and mortality in our country. Malaria was caused by commonly Plasmodium vivax and falciparum. This disease was rampant in both urban and rural India. We had undertaken a hospital-based study in Eastern India taking both urban and rural patients of all ages.

In our study, we had found that malaria caused by Plasmodium vivax was more common (57%) than malaria caused by Plasmodium falciparum (32%). Studies done by Kumar A et al[4], and Singh N et al[5], also indicated that Plasmodium vivax was the major cause of malaria in India.

We had also found mixed malaria infections in a good number of cases (11%). Mayxay et al[6], reported that careful clinical studies had detected around 30% of mixed infections and this rate was higher if PCR technique had been utilized for detection.

Gender-wise, in our study, males (66%) were seen to be more affected than females (34%). Some recent studies done by Kocher DK et al[7], and Erhart LM et al[8], had also shown this gender bias.

In our study, median age of patients suffering from vivax malaria were (28 ± 16.9) years and patients suffering from falciparum were (26 ± 19.8) years. Erhart LM et al[8], found mean age of patients to be 28 years (range 20-70 year) and Nand N et al[9], found mean age of patients to be (32.7 ± 14) years in their respective studies on malaria patients.

In our study, patients with malaria had presented with various clinical manifestations with fever being the commonest (99%) manifestation. Most common type of fever was of intermittent variety (60%). Low

grade fever was more common in both vivax (52.6%) and falciparum malaria (65.6%). Similar varied spectrum of presentations were also found in various studies done by Luxemburger C et al[10], Collins WE et al[11], Erhart LM et al[8], and Nand N et al[9], indicating that malaria could present as a multi-system disease. Chill and rigor was not common in falciparum malaria in comparison with vivax malaria, as shown in table 1.

Figure 3 had shown that, contrary to popular belief, majority of the patients having low grade fever; with barely half of the patients having intermittent type. With treatment, most of the patients became asymptomatic within 3 days and got discharged within 7 days.

One pregnant lady, on her second trimester, was admitted with uncomplicated vivax malaria. She was cured without any feto-maternal complication. Clinical findings from Thailand and India have shown that vivax malaria during pregnancy had caused maternal anemia and a significant reduction in mean birth weight (about 110gm) but that was about 60% of that observed with falciparum malaria[12-13].

Cost of treatment was found to be very high, being a big burden to a society. It should be curtailed down. Number of laboratory tests should be curtailed to basic minimum, as that was the biggest chunk in the total cost of treatment of patients suffering from malaria.

Conclusion:

Malaria had a varied clinical presentation. Different malaria patients could present with different combination of clinical features.

Fever in malaria was commonly low grade, intermittent.

Treatment of malaria was efficient in Kolkata, India; morbidity and mortality being low.

Cost of treatment of malaria patients was very high, posing economical burden to society.

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