



1. Postgraduate
Department of Medicine
Liaquat University of Medical and
Health Sciences
Jamshoro, Sindh, Pakistan
(LUMHS)
2. FCPS
Assistant Professor
Department of Otorhinolaryngology
Liaquat University of Medical and
Health Sciences
Jamshoro, Sindh, Pakistan
(LUMHS)
3. FCPS, Dip.card
Assistant Professor
Department of Medicine
Liaquat University of Medical and
Health Sciences
Jamshoro, Sindh, Pakistan
(LUMHS)
4. Department of Medicine
Liaquat University Hospital
Hyderabad
5. Department of Medicine
Liaquat University Hospital
Hyderabad
6. Postgraduate
Department of Medicine
Liaquat University Hospital
Hyderabad

Correspondence Address:
Dr. Syed Zulfiqar Ali Shah
House No: 279, Doctor's Colony
Hirabad, Hyderabad, Sindh, Pakistan
zulfikar229@hotmail.com

Article received on:

29/10/2014

Accepted for publication :

23/12/2014

Received after proof reading :

06/05/2015

INTRODUCTION

Malaria remains the most important human parasitic disease globally, causing over 170; million clinical cases annually, of which over a million die, mostly in Africa.¹ It has had large effects on the course of history and settlement in tropical regions, and it is currently responsible for the loss of 35 million disability-adjusted life years each year, about 2.6 per cent of the total disease burden of the world.² In recent years malaria has been subject to massive control efforts, with varying degrees of success, and the disease has been resurgent for the last two decades. The recent history of health care in the Third World can only be understood in the light of malaria eradication programmes.³ The nomination of malaria as the pre-eminent tropical disease is thus well deserved, and the problems of both

VIVAX MALARIA; FREQUENCY, SEVERITY OF THROMBOCYTOPENIA AND VARIATION IN RED CELL DISTRIBUTION WIDTH (RDW)

Dr. Ghulam Mustafa Mangrio¹, Dr. Mushtaq Ali Memon², Dr. Mumtaz Ali Shaikh³, Dr. Hamid Nawaz Ali Memon⁴, Dr. Suneel Arwani⁵, Dr. Syed Zulfiqar Ali Shah⁶

ABSTRACT... Objective: To determine the frequency and severity of thrombocytopenia and to evaluate the variation of red cell distribution width (RDW) in patients with acute vivax malaria. **Study Deign:** Cross sectional descriptive case series study. **Period:** Six months. **Setting:** Liaquat University Hospital. **Methods:** All the patients with acute vivax malaria were evaluated for thrombocytopenia its severity and RDW. The data was analyzed in SPSS 10 and the frequency and percentage was calculated. **Results:** Total 126 patients with acute vivax malaria were recruited, of which 88 were males and 38 were females. The mean age \pm SD for male and female subjects was 44.76 ± 6.83 and 40.83 ± 7.42 . The common features observed were fever 31%, rigor 15% and combined features 14% ($p=0.05$). The thrombocytopenia was identified in 86 patients of which 65 were males and 21 were females ($p=0.04$). The increased RDW was observed in 75 patients of which 57 were males and 18 were females ($p=0.05$). The bleeding was detected in 56 and dyspnea and heart failure was found in 30 thrombocytopenic subjects ($p=0.02$). Regarding outcome 82 subjects were recovered while the 04 patients were expired ($p=0.05$). Regarding severity of thrombocytopenia majority 48.8% were in moderate category with male predominance ($p=0.02$). **Conclusion:** The thrombocytopenia and increased RDW was observed in patients with acute vivax malaria.

Key words: Malaria, Vivax, Thrombocytopenia, RDW, Bleeding and outcome

Article Citation : Mangrio GM, Memon MA, Shaikh MA, Memon HNA, Arwani S, Shah SZA. Vivax malaria; frequency, severity of thrombocytopenia and variation in red cell distribution width (rdw). Professional Med J 2015;22(5):559-564.

treatment and control today are more complex and intractable then ever before.

Immune mechanism causes destruction of platelets, spleen sequestration and disturbed thrombopoiesis are all responsible for the thrombocytopenia in malaria. The detection of low platelets along with fever should gives suspicion of the existence of malaria. Thrombocytopenia is seen in both complicated and uncomplicated malaria. In the study by Lacerda MV et al thrombocytopenia was present in as high as 90% of patients, Metanat M et al found thrombocytopenia in 85% of *P. falciparum* and 72% of *P. vivax* patients respectively.^{4,5} Thrombocytopenia is generally unrelated to clinical severity but the degree of thrombocytopenia co-related with the size of the spleen. Thrombocytopenia usually resolves

spontaneously once the infection subsides. The pathogenesis of thrombocytopenia is thought to be similar to that of anaemia and often co-exists. It has been shown that anaemia and thrombocytopenia occur simultaneously and subside gradually with therapy and clearance of parasitemia.

The factors involved in pathogenesis of thrombocytopenia include:

- 1) Hypersplenism and splenic pooling of parasites.
- 2) Hypersplasia of reticulo endothelial cells and increased phagocyte destruction.
- 3) Destruction of platelets bound by immune complexes by the reticulo endothelial system.
- 4) And rarely disseminated intra vascular coagulation.

Platelets are thought to be passively absorbed by the malarial antigen which then binds to Immunoglobulin molecules. These antibody coated platelets are then cleared by phagocytosis in the spleen. It is possible that platelet bound immunoglobulin is a qualitative recognition trigger for splenic removal of platelet that the threshold is lowered in patients with malaria.

The present study was conducted to determine the frequency and severity of thrombocytopenia and to evaluate the variation of red cell distribution width (RDW) in patients with acute vivax malaria.

PATIENTS AND METHODS

This case sectional descriptive case series of six months was conducted at Liaquat University Hospital Hyderabad. All the patients of age >12 years, presented with history of recurrent fever, chills, perspiration and duration is of less than 07 days with positive malarial parasites (plasmodium vivax) on blood film by thick and thin blood smear and of either gender were included in the study

while the exclusion criteria were, the subjects already on antimalarial therapy and other drugs, known case of idiopathic thrombocytopenic purpura, known case of malignancy. The detail history was taken and relevant clinical examination and investigation was performed. The positive plasmodium vivax subjects were assessed for their platelet count and RDW via complete blood count (CBC) by taking 3cc venous blood sample and sent to laboratory for analysis. The informed consent was taken from every patient and the data was collected on a structured proforma. The thrombocytopenia was considered when platelet count <150,000/l while the red cell distribution width (RDW) is a measurement of the variability of red blood cell size with the normal range is 11 - 15. The severity of thrombocytopenia was categorized as mild <150,000 to >50,000/l, moderate <50,000 to >20,000/l and severe <20,000/. In case of epistaxis the ENT specialist opinion was also taken as far as management strategy was concerned. The data analyzed in SPSS version 10.00 and the frequency and percentage (%) was calculated. The statistical significance was considered thru chi square test when p-value ≤ 0.05 .

RESULTS

During study period total 126 subjects evaluated for thrombocytopenia, RDW and outcome of which eighty eight were males and thirty eight were females. The mean age \pm SD for male and female subjects was 44.76 ± 6.83 and 40.83 ± 7.42 . Table-I-III shows the age distribution in context to gender, thrombocytopenia and RDW. Table 04-05 shows the sex distribution in context to thrombocytopenia and RDW. Table 06 displayed the thrombocytopenia in relation to RDW. The thrombocytopenia is identified in 86/126 (68%), out of which 65 were males and 21 were females. Table-VII displayed the severity of thrombocytopenia in context to sex distribution.

		GENDER		Total	P-value
		Male	Female		
AGE	12-19	13	3	16	0.02*
		14.8%	7.9%	12.7%	
	20-29	23	4	27	
		26.1%	10.5%	21.4%	
	30-39	20	9	29	
		22.7%	23.7%	23.0%	
	40-49	20	6	26	
		22.7%	15.8%	20.6%	
	50-59	6	8	14	
		6.8%	21.1%	11.1%	
	60-69	3	5	8	
		3.4%	13.2%	6.3%	
	70+	3	3	6	
		3.4%	7.9%	4.8%	
Total		88	38	126	
		100.0%	100.0%	100.0%	

Table-I. Age and gender stratification

**Statistically significant
Pearson Chi-square value = 14.47; df = 6*

		RDW		Total	P-value
		Increased	Normal		
AGE	12-19	14	2	16	<0.01*
		18.7%	3.9%	12.7%	
	20-29	15	12	27	
		20.0%	23.5%	21.4%	
	30-39	16	13	29	
		21.3%	25.5%	23.0%	
	40-49	20	6	26	
		26.7%	11.8%	20.6%	
	50-59	6	8	14	
		8.0%	15.7%	11.1%	
	60-69	1	7	8	
		1.3%	13.7%	6.3%	
	70+	3	3	6	
		4.0%	5.9%	4.8%	
Total		75	51	126	
		100.0%	100.0%	100.0%	

Table-III. The age in relation to RDW

**Statistically highly significant
Pearson Chi-square value = 18.05; df = 6*

		Thrombocytopenia		Total	P-value
		Yes	No		
AGE	12-19	14	2	16	0.03*
		16.3%	5.0%	12.7%	
	20-29	13	14	27	
		15.1%	35.0%	21.4%	
	30-39	17	12	29	
		19.8%	30.0%	23.0%	
	40-49	21	5	26	
		24.4%	12.5%	20.6%	
	50-59	11	3	14	
		12.8%	7.5%	11.1%	
	60-69	7	1	8	
		8.1%	2.5%	6.3%	
	70+	3	3	6	
		3.5%	7.5%	4.8%	
Total		86	40	126	
		100.0%	100.0%	100.0%	

Table-II. The stratification for age and thrombocytopenia

**Statistically significant
Pearson Chi-square value = 13.87; df = 6*

		Thrombocytopenia		Total	P-value
		Yes	No		
GENDER	Male	65	23	88	0.04*
		75.6%	57.5%	69.8%	
	Female	21	17	38	
		24.4%	42.5%	30.2%	
Total		86	40	126	
		100.0%	100.0%	100.0%	

Table-IV. The gender in relation to thrombocytopenia

**Statistically significant
Pearson Chi-square value = 4.23; df = 1*

		RDW		Total	P-value
		Increased	Normal		
GENDER	Male	57	31	88	0.05*
		76.0%	60.8%	69.8%	
	Female	18	20	38	
		24.0%	39.2%	30.2%	
Total		75	51	126	
		100.0%	100.0%	100.0%	

Table-V. The stratification for gender and RDW

**Statistically significant
Pearson Chi-square value = 3.37; df = 1*

		RDW		Total	P-value
		Increased	Normal		
Thrombocytopenia	Yes	72	14	86	<0.01*
		96.0%	27.5%	68.3%	
	No	3	37	40	
		4.0%	72.5%	31.7%	
Total		75	51	126	
		100.0%	100.0%	100.0%	

Table-VI. The stratification for thrombocytopenia and RDW

**Highly significant*
Pearson Chi-square value = 65.83; df = 1

		GENDER		Total	P-value
		Male	Female		
SEVERITY	Mild	25	2	27	0.02*
		38.5%	9.5%	31.4%	
	Moderate	27	15	42	
		41.5%	71.4%	48.8%	
	Severe	13	4	17	
		20.0%	19.0%	19.8%	
Total		65	21	86	
		100.0%	100.0%	100.0%	

Table-VII. Severity of thrombocytopenia in relation to gender

**Statistically significant*
Pearson Chi-square value = 7.14; df = 2

DISCUSSION

A total of 126 malaria cases were studied. The mean age \pm SD for male and female patients was 44.76 ± 6.83 and 40.83 ± 7.42 . Older age groups are susceptible to infection due to lack of immunity. This study includes 88 male and 38 female patients. In the present study males are commonly involved due to the fact that most of the patients had recent history of travel to endemic areas.⁶ The commonest clinical manifestation were fever with chills (31%) and rigors (15%), headache (7.9%), vomiting (7.1%). Commonest sign being splenomegaly (80%) followed by pallor (40%). A clinical spectrum of fever, splenomegaly and pallor is always associated with malaria.⁷

In this study 86(68%) subjects out of 126 malaria

cases had thrombocytopenia. Thrombocytopenia in a patient with febrile illness increases the possibility of malarial infection.⁸

Prevalence of *P. vivax* malaria is common in Pakistan, because of variation in climatic condition, breeding places of mosquito and resistance to parasite.⁹ In this study severity of thrombocytopenia was statistically significant; the mechanism of thrombocytopenia is uncertain reported by several studies.¹⁰⁻¹³ In this study 82 recovered with adequate medical therapy within 7 to 10 days. Four patients died of severe metabolic acidosis and multi organ dysfunction. Forty two cases of *P.vivax* malaria had moderate thrombocytopenia and seventeen had severe thrombocytopenia. In this study 04 patients developed acute renal failure, the renal impairment is common among adults with severe *P. vivax* malaria. Studies also suggested that *P.vivax* can also cause renal dysfunction.¹⁴ In this study all the four patients who developed ARF, their serum creatinine returned to normal by second week. Three patient required dialysis and was treated conservatively.

When thrombocytopenia is co-related with severity of thrombocytopenia, maximum thrombocytopenia occurred on third and fourth day of infection and gradually returned to normal by fifth to sixth day.¹⁵⁻²⁰ Those persisted to have severe thrombocytopenia beyond 6th day, their mortality and morbidity increased despite of adequate therapy.²¹ Patients who had severe thrombocytopenia at the time of admission are 8.5 times more prone to develop complications when compared to gradual increase of thrombocytopenia.²²

In present study the RDW was observed in 75(59.5%) subjects with *P.vivax* malaria and it is consistent with the study by Koltas IS, et al.²³ In current series the bleeding was identified in (%) subjects, Makkar et al reported cases of *P. vivax* presenting with bleeding gums, hamaturia and epistaxis.²⁴

Severe thrombocytopenia is a good predictor

of poor prognosis than mild and moderate thrombocytopenia the patients who present with severe thrombocytopenia are 8.5 times more prone to develop complications than mild and moderate thrombocytopenia. If severe thrombocytopenia persists for more than six days despite of adequate therapy, mortality rate increases.^{25, 26}

CONCLUSION

Thrombocytopenia was a common haematological finding in patient with Plasmodium infection particularly marked in vivax species infection. The identification of thrombocytopenia is of diagnostic help, as it raises the suspicion of malaria particularly in severely ill patients.

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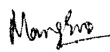


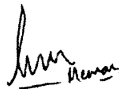
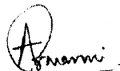
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Ghulam Mustafa Mangrio	Contribution to conception and design, acquisition of data, analysis and interpretation of data.	
2	Dr. Mushtaq Ali Memon	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript.	
3	Dr. Mumtaz Ali Shaikh	Contributed in conception and interpretation of data and give his expert view for manuscript designing.	
4	Dr. Hamid Nawaz Ali Memon	Analysis and interpretation of data, contributed in conception and shares its expert research opinion.	
5	Dr. Suneel Arwani	Drafting, interpreting and analyzing data.	
6	Dr. Syed Zulfiquar Ali Shah	Data collection and manipulation of data	