Original Article

A study of severity of malaria with reference to thrombocytopenia

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Abstract

Introduction: Malarial infection reported as early as 1570 BC from Egypt still at times poses a diagnostic and therapeutic challenge in this modern anti- microbial era . All over the world fever has traditionally been recognized as a cardinal sign of illness and has had negative connotations for patient well-being **Aims and Objectives:** To Study Severity Of malaria with Reference to thrombocytopenia **Methodology:** After approval from institutional ethical committee, The present study was cross sectional study was carried out at tertiary care hospital in the urban setting. During The study period was 1 year. Total 105 Patients were included into study. Z-test (Standard Error of Difference Between two Proportion) used for statistical analysis. **Result:** Among 105 cases 81 (77.14%) cases had thrombocytopenia and 24 (22.86%) cases had normal platelet count. By Fisher's Exact test, $p < 0.001$, Among 105 cases 81 (77.14%) cases had thrombocytopenia and 24 (22.86%) cases had normal platelet count. By Fisher's Exact test, $p < 0.001$, Significant. All 46 cases of severe malaria had thrombocytopenia and 35 cases of uncomplicated malaria had thrombocytopenia. Out of 26 cases of mild thrombocytopenia 12 (14.16%) cases belongs to severe malaria while uncomplicated malaria consisted of 14 (53.84%) cases. Among 29 cases of moderate thrombocytopenia 14 (48.28%) cases had severe malaria while 15 (51.72%) cases had uncomplicated malaria. Out of 26 cases of severe thrombocytopenia 20 (76.92%) cases had severe malaria while only 6 (23.08%) of uncomplicated malaria had severe thrombocytopenia. Significantly more numbers of cases severe malaria have severe thrombocytopenia as compared to uncomplicated malaria. **Conclusion:** Severe thrombocytopenia is more commonly associated with severe malaria cases.
Keywords: Thrombocytopenia, Severity Of malaria.

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INTRODUCTION

Malarial infection reported as early as 1570 BC from Egypt still at times poses a diagnostic and therapeutic challenge in this modern anti- microbial era.[1] All over the world fever has traditionally been recognized as a cardinal sign of illness and has had negative connotations for patient well-being. The new knowledge has shifted the perception of fever as part of the acute-phase response to one of an adaptive nature. With the discovery of antipyretic drugs in the late 19th century, their use was advocated to treat fever [2]. In the developing world, the underlying causes for acute febrile illness (AFI) includes potentially significant illnesses such as malaria, dengue fever, enteric fever, leptospirosis, respiratory tract infections, urinary tract infection etc. So clinically at the time of admission it is difficult to diagnose cause of the fever[36]. The clinical symptoms of malaria are primarily due to schizont rupture and destruction of erythrocytes. Malaria can have a gradual or a fulminant course with nonspecific symptoms. The presentation of malaria often resembles those of common viral infections; this may lead to a delay in diagnosis[7]. The majority of patients experience fever (>92% of cases), chills (79%), headaches (70%), and diaphoresis (64%).[8] Other common symptoms include dizziness, malaise, myalgia, abdominal pain, nausea, vomiting, mild diarrhoea, and dry cough. Physical signs include fever, tachycardia, jaundice, pallor, orthostatic hypotension, hepatomegaly, and splenomegaly. Clinical examination in non-immune persons may be completely unremarkable, even without fever. The last decade has witnessed a changing pattern of

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presentations and complications across the country [9]. The factors responsible for an increase in the proportion of deaths have not been ascertained, although there are a large number Any of such complications can develop rapidly and progress to death within hours or days. In many patients; several of such complications exist together or evolve in rapid succession within a few hours. In clinical practice, patients must be assessed for any signs or symptoms that suggest an increased risk for developing complications and must be treated immediately. In various studies risk factors for severe malaria and death include age greater than 65 years, female sex (especially when associated with pregnancy), non-immune status, coexisting medical conditions, no antimalarial prophylaxis, delay in treatment, and severity of the illness at admission (coma, acute renal failure, shock, pulmonary oedema, coagulation disorders)[10,11]. In tropical countries with a high transmission of malaria (hyperendemic areas), severe malaria is predominantly a disease of young children (1 month to 5 years of age). In industrialized countries, most life-threatening complications occur in non-immune travellers returning from endemic areas. Severe malaria accounts for approximately 5% of imported malaria cases (range 1–38%)[8].The case fatality rate in returning travellers with falciparum malaria varies from 0.6% to 3.8% and for severe malaria it may exceed 20%, even when managed in intensive care units (ICUs). Thrombocytopenia: The frequency of thrombocytopenia in malaria ranges from 24-94% in literature, despite low occurrence of bleeding, even in severe malaria. The clinical management of malarial thrombocytopenia is expectant and the level of evidence for platelet transfusion is insufficient to recommend this practice. It is not clear whether platelets are diminished during acute malarial infection as a consequence of the immune response to the parasite present or whether platelets are actually involved int he generation of severe malaria [12]. Gerardin P *et al*[13]studied cases of severe malaria matching with World Health Organization definition of severe malaria and found an association between thrombocytopenia and either severity or prognosis in childhood falciparum malaria. Thrombocytopenia and anemia are the most frequently malaria associated haematological complications of malaria. In endemic areas, malaria has been reported as the major cause of low platelet counts. This is so characteristic of malaria, that in some places, it is used as an indicator of malaria in patients presenting with fever [15].

MATERIAL AND METHODS

After approval from institutional ethical committee, The present study was cross sectional study was carried out at tertiary care hospital in the urban setting. During The study period was 1 year. Study population consisted of patient diagnosed as case of malaria and admitted at tertiary care hospital during period of one year, Patient admitted in inpatient department (Both wards and intensive care unit), Patient both male and female above the age of 12 years are included in, study group, Patient with smear positive for malaria parasite were included into study while Smear negative malaria parasite with fever and chills, rigors although with, clinical suspicion with malaria are excluded from study group, Thrombocytopenia of any other cause E.g. Aplastic anemia and viral fever-like Dengue, Chikungunya, HIV positive patients, Pregnant females, Patients not willing to participate in study excluded from the study. By this way Total 105 Patients were included into study.

RESULT

Table 1: Distribution of malaria cases according to thrombocytopenia

Sr. No.	Thrombocytopenia	No. of Cases	Percentage
1	No Thrombocytopenia	24	22.86%
2	Thrombocytopenia	81	77.14%
	Total	**105**	**100%**

Among 105 cases 81 (77.14%) cases had thrombocytopenia and 24 (22.86%) cases had normal platelet count.

Table 2: Prevalence of all malaria cases according to thrombocytopenia

Sr. No.	Thrombocytopenia	P.Vivax	P.falciparum	Mixed	Total
1	Normal Platelet Count	24 (41.38)	00(0.00)	00(0.00)	24(22.86)
2	Mild Thrombocytopenia	12(20.69)	09(21.09)	05(100)	26(24.76)
3	Moderate Thrombocytopenia	15(25.86)	14(33.33)	00(0.00)	29(27.62)
4	Severe Thrombocytopenia	07(12.07)	19(45.24)	00(0.00)	26(24.76)
	Total	**58(100)**	**42(100)**	**05(100)**	**105(100)**

By Fisher's Exact test, $p < 0.001$, Significant. Rows 2, 3, 4 are pooled together. Interpretation: - Thrombocytopenia is significantly more common in P. falciparum than P. vivax Among 105 patients mild thrombocytopenia was present in 26 (24.76%), moderatethrombocytopenia in 29 (27.62%) and severe thrombocytopenia in 26 (24.76%

cases. All cases 42 of P.falciparum had thrombocytopenia while 34 cases of P.vivaxhad thrombocytopenia.

Table 3: Distribution of malaria cases according to thrombocytopenia and severity

Sr. No	Thrombocytopenia	Un-complicated malaria	Severe malaria	Total	'Z' Score	'p' value	Significance
1	Normal platelet count	24 (100%)	00 (0.00%)	24 (100%)	NA	NA	NA
2	Mild thrombocytopenia (150,000 to >50,000/c.mm)	14 (53.84%)	12 (46.16%)	26 (100%)	0.28	> 0.05	NS
3	Moderate thrombocytopenia (50,000 to > 20,000/c.mm)	15 (51.72%)	14 (48.28%)	29 (100%)	0.57	> 0.05	NS
4	Severe thrombocytopenia (less than 20,000/c.mm)	06 (23.08%)	20 (76.92%)	26 (100%)	3.92	<0.001	S
	Total	**59**	**46**	**105**			

NA = Not Applicable, NS = Not Significant, S = Significant

All 46 cases of severe malaria had thrombocytopenia and 35 cases of uncomplicated malaria had thrombocytopenia. Out of 26 cases of mild thrombocytopenia 12 (14.16%) cases belongs to severe malaria while uncomplicated malaria consisted of 14 (53.84%) cases. Among 29 cases of moderate thrombocytopenia 14 (48.28%) cases had severe malaria while 15 (51.72%) cases had uncomplicated malaria. Out of 26 cases of severe thrombocytopenia 20 (76.92%) cases had severe malaria while only 6 (23.08%) of uncomplicated malaria had severe thrombocytopenia. Significantly more numbers of cases severe malaria have severe thrombocytopenia as compared to uncomplicated malaria.

DISCUSSION

The Relationship between Malaria and Thrombocytopenia: Few postulated mechanisms are[16]: (i) Increased levels of cytokines, macrophage activation leading to platelet destruction. (ii) Hyperplasia of reticuloendothelial cells and phagocyte destruction. (iii) Hypersplenism and splenic pooling of blood.(iv) Immunological destruction due to antiplatelet IgG, oxidative stress. (v) Shortened platelet life span in peripheral blood and sequestration in nonsplenic areas. (vi) Partly due to psuedothrombocytopenia due to clumping of platelets. Thrombopoietin (TPO) is the key growth factor for platelet production and is elevated in states of platelet depletion. TPO serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14-21 days of therapy. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves. Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyperactivity; this is followed by platelet hypoactivity. Platelet hyperactivity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells. The injured platelets undergo lysis intravascularly. The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypo-activity is seen following this phase and returns to normal in 1 to 2 weeks. In many studies undertaken, the significance of haemostatic abnormalities as a consequence of malaria has been difficult to assess as a result ofthe presence of various associated complications such as liver dysfunction, uraemia and treatment with low molecular weight dextran, dexamethasone and heparin [16]. Complicated malaria is commonly caused by P.falciparum and P.vivax. Though mild thrombocytopenia is more common with both falciparum and vivax infection, severe thrombocytopenia is reported usually in P.falciparum malaria and is less common in P.vivax infection**.** Horstman RD *et al* [17]study of malaria induced thrombocytopenia found thrombocytopenia in 85% of P.falciparum and 72% of P.vivax infection. Patel U *et al*[18] evaluated the role of platelet count for predicating malaria infections found the sensitivity of platelet count for diagnosing malaria as

100% and specificity as 70%.The negative predictive value was 100% and the positive predictive value was 86%. Koltas IS *et al* [19] study of supportive presumptive diagnosis of P.vivax malaria and thrombocytopenia and red cell distribution width findings indicated that routinely used laboratory findings such as low haemoglobin, leukocyte or platelet counts and especially high red cell distribution width values could present a more supportive clue in the diagnosis of vivax malaria in endemic areas. In Our study we have found that Among 105 cases 81 (77.14%) cases had thrombocytopenia and 24 (22.86%) cases had normal platelet count. By Fisher's Exact test, $p < 0.001$, Among 105 cases 81 (77.14%) cases had thrombocytopenia and 24 (22.86%) cases had normal platelet count. By Fisher's Exact test, $p < 0.001$, Significant. Rows 2, 3, 4 are pooled together. All 46 cases of severe malaria had thrombocytopenia and 35 cases of uncomplicated malaria had thrombocytopenia. Out of 26 cases of mild thrombocytopenia 12 (14.16%) cases belongs to severe malaria while uncomplicated malaria consisted of 14 (53.84%) cases. Among 29 cases of moderate thrombocytopenia 14 (48.28%) cases had severe malaria while 15 (51.72%) cases had uncomplicated malaria. Out of 26 cases of severe thrombocytopenia 20 (76.92%) cases had severe malaria while only 6 (23.08%) of uncomplicated malaria had severe thrombocytopenia. Significantly more numbers of cases severe malaria have severe thrombocytopenia as compared to uncomplicated malaria.

CONCLUSION

Severe thrombocytopenia is more commonly associated with severe malaria cases.

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