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Original Research Article

Incidence, Severity & Therapeutic Response of Thrombocytopenia in Vector-Borne Diseases among Paediatric Age Group in Southern Rajasthan

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Abstract:

Background: Vector-borne diseases are a major cause of morbidity and mortality in developing countries like India. There is a relative lack of data on children of South Rajasthan regarding the incidence of thrombocytopenia, its severity, clinical manifestations, and response to treatment.

Methodology: The current study was conducted in a tertiary care hospital in southern Rajasthan over a period of 3 months. It included 127 children under 18 years of age admitted and diagnosed with vector borne diseases by specific laboratory investigations. All necessary data was collected according to the medical records observation technique.

Observations: In the current study, it was found that there is significant association between thrombocytopenia and vector borne diseases. Out of a total of 127 patients with vector-borne diseases in the study period, thrombocytopenia was observed in 88 (69.1 %) patients. This association was most frequently observed between malaria (81.5 %) followed by Dengue fever (76.4%) and Scrub Typhus (68.9 %). Minority of patients even required platelet transfusions for correction of thrombocytopenia.

Conclusion: Thrombocytopenia in a febrile child in endemic zone should alert the physician towards the possibility of malaria. Moreover, even in cases of severe thrombocytopenia, one should not panic and should give anti-malarial and appropriate supportive therapy as bleeding manifestations are rare and response to therapy is good.

Keywords: Epidemiology, thrombocytopenia, Vector, Paediatric.

Introduction

Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 700,000 deaths annually. Either parasites, bacteria, or viruses can cause them. Malaria is caused by intracellular Plasmodium protozoa transmitted in humans by female Anopheles mosquitoes. It is an acute illness characterized by paroxysms of fever, chills, sweats, fatigue, and splenomegaly. It causes an estimated 219 million cases globally, and results in more than 400,000 deaths every year. Most of the deaths occur in children under the age of 5 years. [1]

According to National Vector Borne Disease Control Program, in 2022, 0.18 million cases of malaria were reported in India; Out of which, 0.10 million cases were of Plasmodium falciparum malaria. The PF% was 57.26 and AFI was 0.13. In 2022, there were 83 confirmed deaths due to malaria. [2]

Dengue fever is a widespread viral infection caused by the Dengue virus and is transmitted to humans through the bites of infected female mosquitoes, primarily the Aedes aegypti mosquito. More than 3.9 billion people in over 129 countries are at risk of contracting dengue, with an estimated 96 million symptomatic cases and an estimated 40,000 deaths every year. As per data collected by the National Centre for Vector Borne Disease Control, 233251 cases of dengue were reported in India in the year 2022 and 303 deaths were reported. [1,2]

Scrub typhus is a rickettsia infection spread by Orientia tsutsugamushi via chigger (larval trobiculid mite) bites. Different studies from North India reported an incidence of 28% in the age group of 0-60 years, while different studies from Rajasthan reported an incidence of 23%-25%. While data is available on infection in adults, there is a lack of data regarding the clinical profile of

scrub typhus in the pediatric population from the northwest region of India. [3-5]

As there is a paucity of data about the incidence, severity of thrombocytopenia, and outcome of treatment in the patients living in the tribal areas of Southern Rajasthan, this study was conducted in this region.

Methodology

This prospective observational study was conducted at the Pacific Institute of Medical Sciences, Umarda, Udaipur from 1 June 2023 to 31 August 2023.

Inclusion Criteria: All children aged between 0 to 18 years admitted with high-grade fever and diagnosed with either malaria, dengue, or scrub typhus were included in the study.

Exclusion Criteria: All known cases of bleeding disorders, hematologic malignancies, immune thrombocytopenic purpura, and chronic liver disease were excluded from the study.

Procedures

Dengue was diagnosed by the identification of NS1 antigen in the patient's serum. Scrub typhus was diagnosed by PCR from a blood serum sample. The diagnosis and severity of malaria was made by identification of trophozoites or schizonts of different species of malaria on peripheral blood smear. This is the gold standard technique for the diagnosis of malaria. Platelet counts were estimated from an automated cell counter machine. (Table 1)

Table 1: Severity Grading of Malaria

Platelet count	Grades of Severity *(Platelets per µl)*
Normal	>150,000
Mild	101,000–150,000
Moderate	51,000–100,000
Severe	< 50,000

Improvement in platelet count was labelled when two consecutive samples showed an increase in platelet count 24 hours apart.

Based on platelet count, patients were divided into four groups. Patients with a platelet count of more than 1.5 lacs were normal, counts between 1.5 to 1 lac was mild, counts between 50,000 to 1 lac were moderate and platelet counts below 50,000 were labelled to have severe thrombocytopenia. Data were analyzed using SPSS Version 16. Patients were treated with chloroquine/Artemisinin combined therapy as per standard protocol based on their clinical condition and the parasite species involved. Platelet counts were taken at the time of admission and then every other day till day ten.

Observations: During the study period, a total of 127 patients were found positive for vector-borne diseases like malaria, scrub typhus, and Dengue fever. Out of these patients 88 (69.3 %) patients had thrombocytopenia i.e., platelet counts less than 1.5 lacs per mm^3, hence included in study. The rest of the patients with vector-borne disease were found to have normal platelet counts.

The age and gender-wise distribution of these patients were as follows:

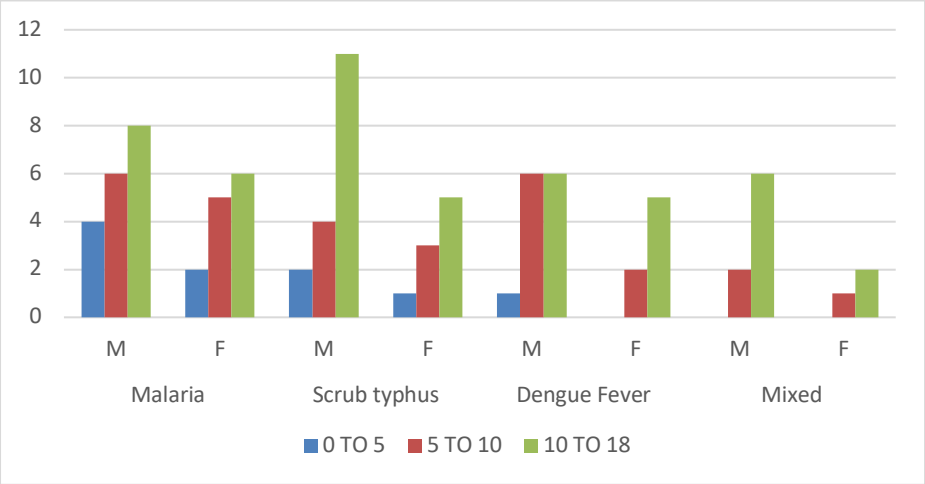

Figure 1: Demographic characteristics of the participants (n=88)

The highest prevalence of vector-borne diseases is seen in adolescents aged 10-18 years (55.6%). The prevalence is higher in males for malaria (20.4%), scrub typhus (10.2%) & dengue fever (7.9%) as compared to females.(Fig 1)

Table 2: Gender wise distribution of patients (n=127)

Disease	Male	Female	Total
Malaria	27	19	46
Dengue Fever	24	13	37
Scrub Typhus	18	10	28
Mixed Infections	10	6	16
Total	79 (62.2 %)	48 (37.8 %)	127

Table 3: Distribution of thrombocytopenia in vector-borne diseases (n=127)

Disease	Platelet normal	Thrombocytopenia	Total	P value
Malaria	7 (18.4 %)	31(81.5 %)	38 (29.9 %)	0.1546
Dengue Fever	8 (23.5 %)	26 (76.4 %)	34 (26.7 %)	0.5255
Scrub Typhus	9 (31 %)	20 (68.9 %)	29 (22.8 %)	1.0000
Mixed Infections	15 (57.6 %)	11 (42.3 %)	26 (20.4 %)	0.0127
Total	39 (30.7 %)	88 (69.2 %)	127	

Out of a total of 127 patients with vector-borne diseases in the study period, thrombocytopenia was observed in 88 (69.1 %) patients. This association was most frequently observed between malaria (81.5 %) followed by Dengue fever (76.4%) and Scrub Typhus (68.9 %). However, mixed infection shows lesser chance of having thrombocytopenia as compared to single entity, which is statistically significant (p< 0.0127).

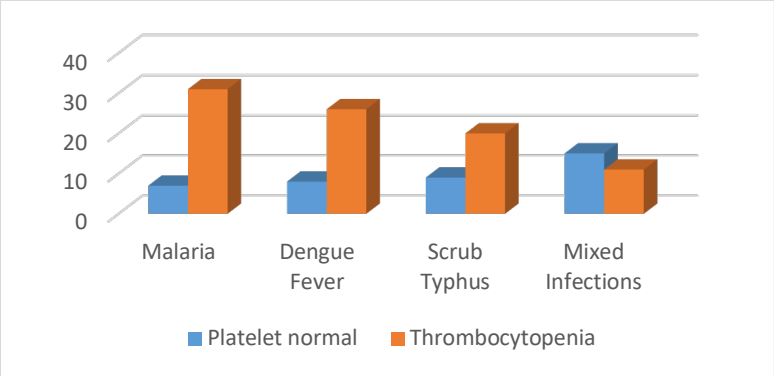

Figure 2: Distribution of thrombocytopenia in vector-borne diseases (n=127)

Table 4: Disease-wise distribution of severity of thrombocytopenia (n=88)

Disease	Mild (1,00,000-1,50,000/mm^3)	Moderate (50,000-1,00,000/ mm^3)	Severe (<50,000/ mm^3)	Total
Malaria	13 (14.7 %)	10(11.3 %)	8 (9 %)	31(35.2%)
Dengue Fever	11(12.5 %)	9(10.2 %)	6 (6.8 %)	26 (29.5%)
Scrub typhus	12 (13.6 %)	6(6.8 %)	2(2.2%)	20 (22.7%)
Mixed	7(7.9 %)	3(3.4 %)	1(1.1 %)	11 (12.5%)
Total	43 (48.8 %)	28 (31.2 %0	17 (19.2 %)	88

In the study, majority of patients had mild thrombocytopenia (48.8%). The prevalence of thrombocytopenia was highest in malaria (35.2%) followed by dengue fever (29.5%) & scrub typhus (22.7%).

Table 5: Response to treatment with time in vector-borne diseases (n=88)

Disease	< 48 Hrs.	P value	48-72 Hrs	Hrs	>96 Hrs	Total
Malaria	16(18.1 %)	0.6762	9(10.2%)	4(4.5 %)	2(2.2%)	31(35.2%)
Dengue fever	10(11.3 %)	0.6563	7 (7.9 %)	5(5.6 %)	4(4.5 %)	26(29.5%)
Scrub typhus	9(10.2 %)	1.0000	7(7.9 %)	3 (3.4 %)	1 (1.1 %)	20(22.7%)
Mixed infection	5 (5.6 %)	1.0000	4 (4.5 %)	2 (2.2%)	0 (0)	11(12.5%)
Total	40(45.4 %)	0.2643	27(30.6%)	14 (15.9 %)	7(7.9 %)	88

In the study, out of 88 patients, 40 (45.4%) responded to treatment within 48 hours; 7.9% of patients took longer than 96 hours to respond. The p value was not found significant ($p>0.05$) for malaria, dengue, scrub typhus & mixed infection.

Discussion

In this hospital-based observational study of vector-borne diseases in children, most of the patients were male and of the adolescent age group. In a similar study conducted in Raichur district, India by Patel A. in 2018, a higher incidence of malaria was seen in adolescent males (38.1%) [6]. A cross-sectional study performed in Western parts of Uttar Pradesh showed a similar higher incidence of dengue fever among adolescent males [7]. Males accounted for 189 (64%) of the total cases while the remaining 106 (36%) were females. The means ± SD of age 12.85 ± 5 years were noted in all dengue seropositive cases. A similar study conducted in the eastern parts of India to study the prevalence of scrub typhus showed a male-to-female ratio of 1.68:1. The maximum number of cases were seen in the age group of 1 to 5 years with 86 cases (41.1%) which is in contrast to our study.

School-going children are seen to bear the brunt of disease due to a lack of awareness of protective measures in this age group. More involvement of adolescents can be explained by the diurnal adaptation of the *Aedes* mosquito in stored water. These children play in the open fields and it makes them prone to an attack from *Aedes* mosquitoes [8].

Understanding the burden of malaria among school-age children is essential to justify investment in school-based malaria control interventions and to identify delivery mechanisms to help control malaria in this underserved population.

In this study, malaria was the most common cause of thrombocytopenia among various vector-borne diseases. Similar results were observed by Gupta NK and Bansal Y in studies from Rajasthan, India. [9,10]

The exact mechanism of thrombocytopenia is not well understood however, immune-mediated lysis, sequestrating in the spleen has been documented. An abnormality in platelet structure and function has been described as a consequence of malaria parasites themselves. Decreased thrombopoiesis has been ruled out because platelet-forming megakaryocytes in the marrow are usually normal or increased. [10]

Reports of adequate or increased number of megakaryocytes in the bone marrow make decreased thrombopoiesis an unlikely cause of thrombocytopenia in malaria. Immune-mediated destruction of circulating platelets has been postulated as a cause of thrombocytopenia seen in malaria. Platelets have also been shown to mediate clumping of *P. falciparum-infected* erythrocytes. This could lead to pseudo-thrombocytopenia. Malaria-infected patients have elevated levels of specific IgG in their blood which binds to platelet-bound malaria antigens possibly leading to accelerated destruction.

Fajardo and Tallent demonstrated *P. vivax* within platelets and suggested a direct lytic effect of the parasite on the platelets. Both non-immunological destruction, as well as immune mechanisms involving specific platelet-associated IgG antibodies that bind directly to malarial antigens in the platelets, have been recently reported to play a role in the lysis of platelets [11]. Oxidative stress damage of platelets has also been implicated in etiopathogenesis based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation levels in malaria patients, when compared to those of healthy subjects. Decreased thrombopoiesis has been ruled out, because platelet forming megakaryocytes in the marrow are usually normal or increased [12]. A good tolerance of low platelet count is well-known in malaria. This could be explained by platelet activation and enhanced agreeability. The hyperactive platelets may enhance haemostatic responses and that is why bleeding episodes are very rare in acute malarial infections, despite significant thrombocytopenia [13].

The mechanisms involved in thrombocytopenia and bleeding during DENV infection are not fully understood. Several hypotheses have been suggested to elucidate the mechanism involved. In this context, DENV could directly or indirectly affect bone marrow progenitor cells by inhibiting their function to reduce the proliferative capacity of hematopoietic cells [14]. Indeed, there is evidence that DENV can induce bone marrow hypoplasia during the acute phase of the disease. Besides platelet counts, the functional disruption of these cells is associated with significant deregulation of the plasma kinin system and the immune pathogenesis of Dengue fever [15]. Scrub typhus is one of the differential diagnosis for fever and thrombocytopenia [16].

In most cases, thrombocytopenia is not associated with bleeding and requires no treatment, with the platelet count rapidly returning to normal after successful treatment of the malarial episode. In this study, it was observed that response to therapy, which is monitored with an increase in platelet counts seen most rapidly in cases of malaria.

Conclusion

This study can be of practical significance for medical practitioners as simple diagnostic methods

were used in the diagnosis of vector-borne diseases and monitoring the platelet counts of the patients.

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