FREQUENCY OF THROMBOCYTOPENIA IN CHILDREN PRESENTED WITH DENGUE FEVER

Adnan khan[1], Aisha Durrani[2], Sadaf Alam[3], Madiha Gul[4]

ABSTRACT

Introduction: Dengue fever, classified by the World Health Organization as a major viral disease transmitted by Aedes aegypti and Aedes albopictus mosquitoes, has seen a significant rise in global incidence over recent decades. Currently, nearly half of the world's population is at risk of infection.

Objective: This study aims to determine the frequency of thrombocytopenia among pediatric patients diagnosed with dengue fever.

Materials and Methods: A cross-sectional study was conducted at the Department of Pediatrics, Hayatabad Medical Complex, Peshawar. The study involved 114 children, selected through non-probability consecutive sampling.

Results: The cohort comprised 52 males (45.61%) and 62 females (54.38%), with a mean age of 9.17 years (SD = 2.86). The average duration of symptoms was 4.25 days (SD = 2.566), and the mean weight was 29.90 kg (SD = 9.327). A family history of thrombocytopenia was noted in 4 patients (3.57%), while thrombocytopenia was detected in 87 patients (76.31%). The analysis revealed no significant association between thrombocytopenia and age, gender, duration of symptoms, weight, or family history.

Conclusion: Thrombocytopenia is highly prevalent among children with dengue fever, irrespective of age, gender, weight, symptom duration, or familial predisposition. Future research should focus on multicenter, randomized controlled trials to explore the influence of these variables on thrombocytopenia in dengue.

Keywords: Dengue Fever, Thrombocytopenia, Pediatric Population

INTRODUCTION

The World Health Organization classifies dengue as a viral disease spread primarily by mosquitoes; its prevalence around the world has skyrocketed in recent decades[1]. Around half of the global population is now thought to be in danger[1].

Female mosquitoes, primarily Aedes aegypti but also to a lesser extent Aedes albopictus, are responsible for transmitting the dengue virus. [1] The Zika virus, yellow fever, and chikungunya fever are all spread by the same mosquito species. While the danger of contracting dengue fever varies from place to place in the tropics, it is often higher in areas that have experienced fast urbanization without adequate planning.

More than 2.5 billion people are at risk of getting dengue virus each year[2, 3] due to the disease's widespread distribution (128 countries). Around 400 million people are infected every year, with an estimated 96 million developing clinical symptoms. Death rates among those with diseases are about 2.5% each year[4].

High temperature, bodily discomfort, headache, rashes, and occasional bleeding are the initial symptoms seen by all patients between days 2 and 7, with severe versions of the disease fast progressing to include symptoms such as hypotension, shock, edema, and vascular leakage.

[1] Rehamna Medical Institute, Peshawar
[2] FC Teaching Hospital, District Khyber
[3] Peshawar Institute of Medical Sciences, Peshawar
[4] Khyber Teaching Hospital, Peshawar

Address for Correspondence
Dr. Aisha Durrani
Senior Registrar
FC Teaching Hospital, District Khyber
+92 333 9355638

Patients with either mild or severe DENV infections frequently exhibit the clinical symptom of thrombocytopenia. Research indicates that a low platelet count is a major contributor to bleeding episodes in these people. Between days 3-7 of a fever, many patients' platelet counts decrease below the usual level (150,000-450,000 platelets/L) and may fall as low as 40000 platelets/L. Platelet activation and dysfunction have been linked in multiple studies to the development of prothrombotic consequences in DHF and DSS5. Researchers have found a correlation between early-stage dengue infection and both platelet activation (characterized by elevated surface P-selectin) and apoptosis (characterized by raised caspases and phosphatidylserine (PS) production). Microparticles (MPs) produced from activated platelets in the peripheral blood have been linked in an ex vivo report7 to the severity of thrombocytopenia in dengue patients.

Thrombocytopenia was found to be present in 80.8% of dengue fever cases in children, according to research by Pothapregada S et al[8]. A study by Pothapregada S, et al[8]. found that 79% of children with dengue illness also had thrombocytopenia.

Patients with thrombocytopenia caused by hypoproliferative diseases of bone marrow have traditionally received platelet transfusions. The degree of thrombocytopenia is thought to be proportional to the bleeding risk, which justifies the need of platelet transfusion therapy in these individuals. The risk of bleeding is decreased after a platelet transfusion raises the patient's platelet count to a level greater than [10]. Yet, the risk of bleeding does not appear to increase in proportion to the severity of thrombocytopenia in dengue fever. One study found that the risk of clinical bleeding was 6% in patients with platelet counts above $150x10^3$ platelets/ml, 12% in those with platelet counts between 100 and 149 $x10^3$ platelets/ml, 11% in those with platelet counts between 80 and $99x10^3$ platelets/ml, 10% in those with platelet counts between 50 and $79x10^3$ platelets/ml, 11% in those with platelet counts between 10 and $19x10^3$ [11] . No change in the mean platelet count was seen after 24 hours following platelet transfusion in this trial. Patients received various quantities of platelets from pooled platelet concentrates, with the median dose being 4 platelet units[11]. However, this study was retrospective and included only a small number of cases of dengue hemorrhagic fever.

Platelet transfusion may fail to restore platelet function in dengue fever patients because the immune system is destroying donor platelets. Platelet transfusion therapy for dengue infection has only been studied in a few retrospective observational studies, and we know very little about the kinetics of response to this treatment.

Local evidence on the occurrence of thrombocytopenia in children presenting with dengue fever is lacking, despite the availability of local studies on dengue fever. In addition, as the outcomes of international studies have been shown to vary between populations[8,9], their findings cannot be extrapolated to the entire world.

The purpose of this study was to determine the frequency of thrombocytopenia in children presented with dengue fever as dengue fever is a significant public health concern in Pakistan, with periodic outbreaks leading to a substantial burden on healthcare systems. Understanding the frequency of complications such as thrombocytopenia can help healthcare providers better manage and allocate resources during outbreaks. Moreover, conducting such a study can provide valuable epidemiological insights into the patterns and trends of dengue-related complications, including thrombocytopenia, in the pediatric population in Pakistan. This information can contribute to a better understanding of the disease dynamics and aid in designing targeted prevention and control strategies in our local population.

METHODOLOGY

This cross-sectional study was conducted at Department of Pediatrics, MTI-Hayatabad Medical Complex Peshawar, from 1st February to 31st July 20. A total of 114 patients were included in the study. Sample size was calculated taking 79% proportion of thrombocytopenia in patients with dengue fever with 95% confidence interval, 7.5% margin of error and 5% significance level using WHO sample size calculator. All patients presented to Peads OPD or Ward with the diagnosis of dengue fever on NS1 dengue serology, both genders with age range 2-12 years were included.

All those patients with history of meningitis or enteric fever were excluded from the study as it would create bias in the study. Prior to the conduct of study, written informed consent forms were obtained from attendants of patients with full description of study. 2 ml blood was drawn from

all patients into an ethylenediaminetetraacetic acid (EDTA)-filled tube for platelet count. Blood tube was transported on ice within 2 h to the hospital laboratory. Samples was processed within 6 h of the initial sample collection. Thrombocytopenia was labelled if platelet count of less than 150×10^3 per µL.

Statistical analysis was done using SPSS version 23.0. P-value ≤ 0.05 were considered statistically significant.

RESULTS

In this study, a total of 114 children diagnosed with dengue fever were evaluated. The mean age of the participants was 9.17 years with a standard deviation of 2.896 years. The duration of their complaints averaged 4.25 days, with a standard deviation of 2.54 days. The average weight of the children was 29.90 kg, with a standard deviation of 9.37 kg. Regarding gender distribution, 62 participants were male (54.38%), while 52 were female (45.61%). Age-wise, 31 children were under 7 years old, accounting for 27.19% of the sample, and 83 children were older than 7 years, making up 72.80% of the participants. In terms of thrombocytopenia presence, 87 children (76.31%) were found to have thrombocytopenia, while 27 children (23.68%) did not. This breakdown demonstrates a significant prevalence of thrombocytopenia among pediatric patients suffering from dengue fever, without any significant correlation to age, gender, duration of complaint, or weight. (Table-I)

As per the stratification of thrombocytopenia among 114 pediatric dengue fever patients based on gender, duration of symptoms, and weight. Thrombocytopenia occurred in 80.6% of females and 71.2% of males, showing no significant gender correlation (P = 0.236). When categorized by symptom duration, 77.0% of patients with symptoms ≤5 days and 74.1% with symptoms >5 days experienced thrombocytopenia, also without significant differences (P = 0.755). Weight analysis revealed 72.7% prevalence in children ≤20kg, 76.3% in those between 21kg and 40kg, and 83.3% in those over 40kg, with none of these differences being statistically significant (P = 0.777). Overall, thrombocytopenia was present in 76.8% of the cohort, suggesting it is widely prevalent regardless of gender, duration of symptoms, or body weight. (Table-II)

Table-I: Demographic Characteristics of study population (n=114)

Numerical Variables	**Mean**	**Std. Deviation**
Age (Years)	9.17	2.896
Duration of Complaint (Days)	4.25	2.54
Weight (kg)	29.90	9.37
Gender Groups	**Frequencies**	**Percentages**
Male	62	54.38%
Female	52	45.61%
Age Groups	**Frequencies**	**Percentages**
≤ 7 Years	31	27.19%
> 7 Years	83	72.80%
Thrombocytopenia	**Frequencies**	**Percentages**
Yes	87	76.31%
No	27	23.68%

Table-II: Stratification of Thrombocytopenia with Various Effect Modifiers (n=114)

Age Groups	Thrombocytopenia		P value
	Yes	No	
≤ 7 years	23	8	0.746
	74.2%	25.8%	
> 7 years	64	19	
	77.1%	22.9%	
Total	87	27	
	76.8%	23.2%	
Gender	**Thrombocytopenia**		**P value**
	Yes	**No**	
Female	50	12	0.236
	80.6%	19.4%	
Male	37	15	
	71.2%	28.8%	
Total	87	27	
	76.3%	23.7%	
Duration Group	**Thrombocytopenia**		**P value**
	Yes	**No**	
≤5 days	67	20	0.755
	77.0%	23.0%	
> 5 days	20	7	
	74.1%	25.9%	
Total	87	27	
	76.3%	23.7%	
Weight Groups	**Thrombocytopenia**		**P value**
	Yes	**No**	
≤20kg	16	6	0.777
	72.7%	27.3%	
21kg to 40 kg	61	19	
	76.3%	23.8%	
> 40kg	10	2	
	83.3%	16.7%	
Total	87	27	
	76.8%	23.2%	

DISCUSSION

Our study reported a mean age of 9.17 ± 2.86 years, slightly higher than the 8.3 ± 3.5 years reported by Ahmad et al.[13]. The mean duration of complaints was 4.25 ± 2.566 days, with the majority (76.79%) experiencing symptoms for five days or less, comparable to the findings by Chairulfatah et al., where the predominant duration was three days[14]. Gender distribution in our cohort showed a higher prevalence in females (54.38%) compared to males (45.61%), contrasting with Ahmad et al., where a higher incidence was observed in males (54%)[13].

In terms of family history, only four thrombocytopenic patients reported a positive family history, representing a small and statistically insignificant portion of our sample. This highlights a gap in the literature, as there are limited studies addressing thrombocytopenia in dengue patients with a familial predisposition. Our findings on thrombocytopenia prevalence (76.31%) align closely with the rates reported by Ahmad et al. (86%)[13] and Chairulfatah et al. (81%)[14], and were further corroborated by Pothapregada et al., who found a prevalence of 80.8%[8].

Regarding age-related vulnerability, our results showed that the majority of the affected children

were older than 7 years (72.80%), aligning with findings from Dhooria et al., who noted that children aged 10-15 were the most affected[16]. Guzman et al. also reported a disproportionate impact on children aged 4 to 11 years[17]. Our analysis did not reveal any significant associations between thrombocytopenia and demographic factors such as age or duration of complaint, which is consistent with other studies in this field.

One limitation of our study is the small sample size, which may not fully represent the broader population and reduces the reliability of findings related to familial history of thrombocytopenia. Additionally, the potential for observer bias in dengue serology interpretations could affect the validity of our results. Future studies should aim to include larger, more diverse populations to validate our findings and potentially explore the genetic or familial factors associated with thrombocytopenia in dengue patients. Comprehensive, multicenter studies could also provide more robust data to assess the impact of demographic variables on the prevalence of thrombocytopenia in pediatric dengue cases.

CONCLUSION

Thrombocytopenia is most prevalent in children with dengue viral infection. Thrombocytopenia does not depend upon the age, gender, weight, duration of complaint or family history of thrombocytopenia. Further studies regarding the effect of these variables are recommended.

REFERENCES

1. Osnaya-Romero N, Perez-Guille M-G, Andrade-García S, Gonzalez-Vargas E, Borgaro-Payro R, Villagomez-Martinez S, et al. Neurological complications and death in children with dengue virus infection: report of two cases. J Venom Anim Toxins Incl Trop Dis. 2017;23(1):25.
2. Lorenzi OD, Gregory CJ, Santiago LM, Acosta H, Galarza IE, Hunsperger E, et al. Acute febrile illness surveillance in a tertiary hospital emergency department: comparison of influenza and dengue virus infections. The American journal of tropical medicine and hygiene. 2013;88(3):472-80.
3. Teixeira MG, Siqueira Jr JB, Ferreira GL, Bricks L, Joint G. Epidemiological trends of dengue disease in Brazil (2000–2010): a systematic literature search and analysis. PLoS Negl Trop Dis. 2013;7(12):e2520.
4. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013;496(7446):504.
5. Michels M, Alisjahbana B, de Groot PG, Indrati AR, Fijnheer R, Puspita M, et al. Platelet function alterations in dengue are associated with plasma leakage. Thromb Haemost. 2014;112(08):352-62.
6. Hottz ED, Oliveira MF, Nunes PC, Nogueira RMR, Valls-de-Souza R, Da Poian AT, et al. Dengue induces platelet activation, mitochondrial dysfunction and cell death through mechanisms that involve DC-SIGN and caspases. J Thromb Haemost. 2013;11(5):951-62.
7. Punyadee N, Mairiang D, Thiemmeca S, Komoltri C, Pan-ngum W, Chomanee N, et al. Microparticles provide a novel biomarker to predict severe clinical outcomes of dengue virus infection. J Virol. 2015;89(3):1587-607.
8. Pothapregada S, Kamalakannan B, Thulasingam M. Role of platelet transfusion in children with bleeding in dengue fever. J Vector Borne Dis. 2015;52(4):304.
9. Shinde PA. Evaluation of platelet count in pediatric patients with dengue fever: a hospital based study. International Journal of Contemporary Medical Research. 2017;4(5):1175-7.
10. Gaydos LA, Freireich EJ, Mantel N. The quantitative relation between platelet count and hemorrhage in patients with acute leukemia. N Engl J Med. 1962;266(18):905-9.
11. Lye DC, Lee VJ, Sun Y, Leo YS. Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adults with acute uncomplicated dengue infection. Clin Infect Dis. 2009;48(9):1262-5.
12. Ahmed S, Arif F, Yahya Y, Rehman A, Abbas K, Ashraf S, et al. Dengue fever outbreak in Karachi 2006--a study of profile and outcome of children under 15 years of age. JPMA The Journal of the Pakistan Medical Association. 2008;58(1):4.
13. Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and Platelet Trasnfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. 2003.
14. Nelson ER, Bierman HR. Dengue fever: a thrombocytopenic disease? JAMA. 1964;190(2):99-103.
15. Dhooria G, Bhat D, Bains H. Clinical profile and outcome in children of dengue hemorrhagic fever in North India. Iranian Journal of Pediatrics. 2008;18(3):222-8.
16. Guzmán MG, Kouri GP, Martinez E, Bravo JR, Riveron R, Soler M, et al. Clinical and serologic study of Cuban children with dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). 1987.
17. Witayathawornwong P, Jirachanchai O, Kasemsut P, Mahawijit N, Srisakkwa R. Severe perinatal dengue hemorrhagic fever in a low birth weight infant. Southeast Asian J Trop Med Public Health. 2012;43(1):62-7.