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Original Research Article

Effectiveness of platelet transfusion in dengue fever: Rangpur community medical college and hospital experience at Rangpur, Bangladesh

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ABSTRACT

Background: Dengue fever, caused by the dengue virus and transmitted by mosquitoes, is a global health concern, causing mild to severe illness. Severe cases lead to thrombocytopenia, a low platelet count that can cause bleeding. Platelet transfusion is debated as a treatment strategy; some studies support its use to prevent bleeding, while others raise concerns about side effects. The aim of the study is to see the effectiveness of platelet transfusion in dengue patients who has a very low platelet count.
Methods: This single-center study was conducted at The Department of Medicine, Rangpur Community Medical College and Hospital, Bangladesh. A total of 52 patients were enrolled and analyzed in this study from March to August 2023.
Results: Most cases are Dengue Fever (86.54%), followed by Dengue Hemorrhagic Fever Grade 1 (7.69%) and Dengue Shock Syndrome (5.77%). Bleeding occurred in 15.38% of enrollment. Common symptoms include fever (78.85%), headache (57.69%), cough (67.31%), and myalgia (55.77%). Health parameters include blood pressure (110/70 mm Hg), pulse rate (86.5±12.8 bpm), and temperature (100.5±2.8°F). Investigation findings show S. bilirubin (0.61 mg/dl), S. creatinine (0.94 mg/dl), RBS (120.5 mg/dl), HB% (13.78 g/dl), and PCV (39.75). Platelet counts varied in different conditions, with most responders to platelet transfusion (94.23%) showing no deaths but adverse outcomes related to transfusion reactions (5.77%).
Conclusions: The prevalence of dengue fever in Bangladesh necessitates a comprehensive understanding of effective treatment modalities. By examining the outcomes and implications of platelet transfusion in this context, the research seeks to shed light on its effectiveness, thereby informing evidence-based medical practices and improving patient care.

Keywords: Effectiveness, Platelet transfusion, Dengue fever

INTRODUCTION

Dengue fever, caused by the dengue virus and transmitted primarily by Aedes mosquitoes, is a significant global health concern, particularly in tropical and subtropical regions. Dengue is the viral illness transmitted by mosquitoes, impacting 50 million individuals annually.[1] Characterized by a spectrum of clinical manifestations ranging from mild febrile illness to severe hemorrhagic fever and shock, dengue poses a substantial burden on

healthcare systems and public health resources. One of the critical complications of severe dengue is thrombocytopenia, a condition characterized by a decrease in platelet count, which can lead to bleeding tendencies and other complications.[2] Platelet transfusion has been widely employed as a therapeutic intervention for severe thrombocytopenia in dengue patients. However, severe thrombocytopenia can be seen in both dengue fever and dengue hemorrhagic fever. There is a significant negative co-relation between disease severity and platelet count.[3] Although low platelet counts and reduced fibrinogen levels stand out as the primary hemostatic issues causing bleeding during dengue infection, it is worth noting that thrombocytopenia and coagulation irregularities do not consistently serve as reliable indicators for bleeding in such cases.[4-6] Thrombocytopenia can develop from bone marrow suppression or platelet destruction, with immune complex-mediated platelet destruction likely playing a pivotal role in causing thrombocytopenia during dengue infection.[4] Platelet transfusion as a therapeutic strategy in dengue management has been a subject of conflicting opinions in the medical community. Some studies have advocated for its early and judicious use in severe dengue cases to prevent bleeding complications, while others have raised concerns about potential adverse effects such as transfusion-related reactions and fluid overload. Moreover, the World Health Organization (WHO) guidelines for dengue management do not universally recommend platelet transfusion and suggest a case-by-case assessment based on clinical and laboratory parameters.[7] Dengue fever is a vector-borne disease with a substantial impact on global health systems. In Bangladesh, the disease burden has escalated over the years, with recurring outbreaks affecting thousands annually.[8] Dengue first emerged swiftly in the 1960s in Bangladesh, predominantly afflicting the capital city, Dhaka, with the highest prevalence of infections.[9] The present outbreak of dengue, originating in Dhaka, has exhibited a rapid expansion into the surrounding districts. This expansion can be attributed to a significant migration of individuals from the capital to various districts. As of the beginning of 2023, medical facilities outside Dhaka are attending to more dengue cases than previous year. The prevalence of severe dengue cases has led to varying medical interventions, including platelet transfusion, to manage thrombocytopenia and prevent hemorrhagic complications. The evaluation of platelet transfusions efficacy in such cases remains a subject of scientific inquiry. In recent years, several research studies have attempted to address the gap in understanding the true effectiveness of platelet transfusion in dengue management. For instance, a study by Thomas et al conducted in a tertiary care hospital in India found that platelet transfusion was associated with reduced bleeding complications and mortality in severe dengue cases.[10] In contrast, a study by Li et al in a different geographical context highlighted that while platelet transfusion did increase platelet counts, it did not significantly alter the overall clinical outcomes of dengue patients.[11] The aim of the study is to see the effectiveness of platelet transfusion in dengue patients who has a very low platelet count.

METHODS

The research involved a prospective analysis within a single center, utilizing a parallel-assignment design. This study focused on patients afflicted with dengue infection who underwent platelet transfusion therapy, with the analysis being non-blinded. The primary objective was to investigate the changes in platelet counts resulting from this therapeutic approach. The study was conducted at the Department of Medicine, Rangpur Community Medical College and Hospital at Rangpur, Bangladesh. A total of 52 patients were enrolled and analyzed in this study during six months period from March to August 2023.

Inclusion criteria

Inclusion criteria were; All adult dengue patients and Dengue patients confirmed by NS-1antigen and Dengue IgG and IgM antibody test with typical presentation.

Exclusion criteria

Exclusion criteria were; dengue patients who were less than 12 years of age.

Procedure

Patient demographics, historical backgrounds, and examination results were meticulously documented. Additionally, blood samples were procured to gauge platelet counts. These blood samples were collected using EDTA anticoagulant vials and analyzed using an automated counting apparatus for platelet counts. To counteract potential inaccuracies from platelet clumping induced by EDTA, citrated samples were utilized for a repeat platelet count whenever such clumping was observed. Platelet counts were assessed at three-time points: baseline (P0), 24 hours post-baseline (P24), and 72 hours post-baseline (P72) for all patients. The main parameter of interest was Platelet Plug Index (PPI) evaluated at 1-hour post-treatment initiation for the treatment group and at 24 and 72 hours for both groups. Supplementary outcome measures encompassed the progression to severe bleeding, occurrences of new-onset bleeding, time taken for bleeding to cease, and any untoward incidents, including fatalities.

Data analysis

Data were subjected to thorough analysis, with appropriate presentation in tables or graphs as per their nature. A clear explanation was provided for each table and graph to facilitate comprehension. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software on the Windows platform. Continuous parameters were expressed as mean±standard

deviation (SD), whereas categorical parameters were represented in terms of frequency and percentage. Between-group comparisons for continuous parameters were executed utilizing Student's t test. A significance level denoted by a p value of less than 0.05 indicated statistical significance.

RESULTS

In this prospective study, a total of 52 patients were enrolled and analyzed. The (Table 1) shows the baseline characteristics of the study population.

Table 1: Baseline characteristics of the study population (n=52).

Characteristics	N	%
Age range (years)		
21-30	27	51.92
31-40	13	25.00
41-50	7	13.46
51-60	5	9.62
Mean±SD	31.13±16.83	
Male:Female	9:4	
Diagnosis		
DF	45	86.54
DHF1	4	7.69
DHF2	0	0.00
DSS	3	5.77
Bleeding at the time of enrolment		
Yes	8	15.38
No	44	84.62
Site of bleeding (N=8)		
Oral and nasal	4	7.69
Gastrointestinal	1	1.92
Genitorinary	2	3.85
Pulmonary	1	1.92
Baseline platelet count/µl	**Median**	**Range**
	113269	180000-19000

Regarding age, most patients fall within the 21-30 age range, constituting 51.92% of the group, followed by those aged 31-40 at 25.00% and 8 patients under 12 years, respectively.

Table 2: Clinical Features of study population.

Signs and symptoms	N	%
Fever	41	78.85
Headache	30	57.69
Cough	35	67.31
Myalgia	29	55.77
Abdominal pain	21	40.38
Athralgia	18	34.62
Vomiting	15	28.85
Retro-orbital pain	8	15.38
Skin rash	7	13.46
Lethargy	5	9.62
Itching	5	9.62
Respiratory distress	3	5.77
Painful hepatomegaly	1	1.92
Black tarry stool	9	17.31
BP	110/70 mmHg	
Pulse rate	86.5±12.8 beat/min	
Temp.	100.5±2.8°F	

Table 3: Investigation finding of study population.

Variables	Mean	Range
S. bilirubin	0.61	0.1 to 1.2 mg/dl
S. creatinine	0.94	0.7 to 1.3 mg/dl
RBS	120.5	110-140 mg/dl
HB%	13.78	14 to 18 g/dl
PCV	39.75	25-51.5

The mean (SD) age was 31.13±16.83 years. The male-to-female ratio is 9:4. According to diagnosis, most individuals have DF (Dengue Fever), accounting for 86.54% of cases.

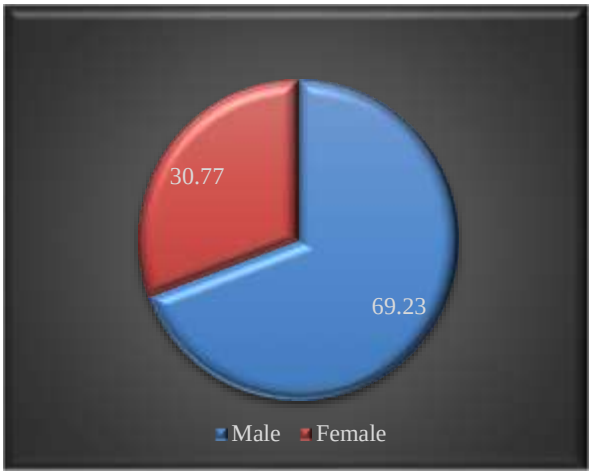

Figure 1: Gender distribution of the study population (n=52).

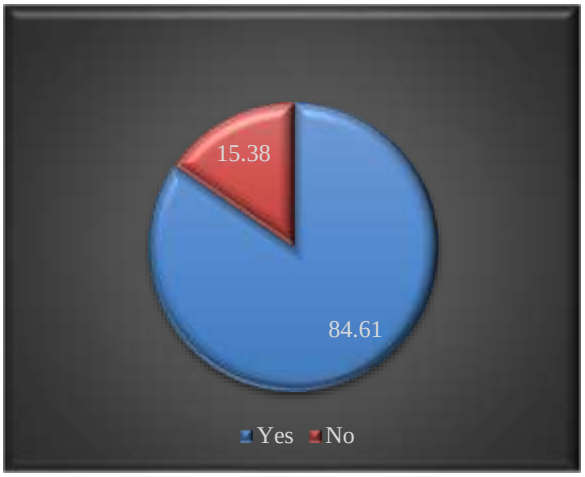

Figure 2: Patients traveling history before admission.

Table 4: PPI in treatment.

Platelets/µl	Mean±SD	Median	Range
PI24	34,780±43,820	22,000	12,000-45,750
PI72	75,430±69,465	53,500	31,750-89,250
Spontaneous increment at 24 h	4,525±38,080	1,500	5,750 to 10,000

Table 5: Comparison of PPI amongst responders, non-responders.

Parameter	Responders	Non-responders	P value
P0 (platelets/µl)			
Mean±SD	14,315±7,265	9,710±4,410	
Median	14,000	9,000	0.384
Interquartile range	10,000-20,000	7,500-11,500	
PI24 (platelets/µl)			
Mean±SD	53,310±56,760	18,770±16,800	
Median	38,000	16,000	<0.001
Interquartile range	18,000-81,000	9,000-31,000	
PI72 (platelets/µl)			
Mean±SD	103,440±72,950	51,430±58,660	
Median	72,000	34,000	<0.001
Interquartile range	52,000-130,000	18,000-65,500	
Spontaneous increment at 24 h			
Mean±SD	5,050±53,680	4,050±15,275	
Median	1,500	2,000	0.258
Interquartile range	33,000 to 11,000	5,000 to 11,500	

DHF1 (Dengue Hemorrhagic Fever Grade 1) is seen in 7.69% of cases, while DSS (Dengue Shock Syndrome) accounts for 5.77%, and there are no cases of DHF2 (Dengue Hemorrhagic Fever Grade 2).

Table 6: Clinical outcomes.

Variables	N	%
Response to platelet transfusion		
Responders	49	94.23
Non-responders	3	5.77
Adverse outcome (N=3)		
Transfusion reactions	3	100.00
Death	0	0.00

Regarding bleeding incidents, 15.38% of individuals experienced bleeding at enrollment, while the remaining 84.62% did not. Among those who bled, 7.69% experienced bleeding in the oral and nasal areas, 1.92% in the gastrointestinal tract, 3.85% in the genitourinary system, and 1.92% in the pulmonary region. The median baseline platelet count is 113,269/µl, from 18,000 to 190,000/µl. The (Table 2) presents the clinical features of the study population. The data highlights the prevalence of symptoms among individuals. Fever is the most common symptom, reported in 78.85% of cases, followed by headache (57.69%), cough (67.31%), and myalgia (55.77%). Other symptoms include abdominal pain (40.38%), athralgia (34.62%), vomiting (28.85%), retro-orbital pain (15.38%), skin rash (13.46%), lethargy (9.62%), itching (9.62%), and respiratory distress (5.77%). Less frequently reported symptoms include painful hepatomegaly (1.92%) and black tarry stool (17.31%). Additional health parameters such as blood pressure, with a reading of 110/70 mm Hg, pulse rate averaging 86.5±12.8 beats per minute, and temperature averaging 100.5±2.8°F, provide a more comprehensive clinical picture. The investigation finding of the study is shown in (Table 3), where the mean values for these variables are as follows: S. bilirubin at 0.61 mg/dl, S. creatinine at 0.94 mg/dl, RBS at 120.5 mg/dl, HB% at 13.78 g/dl, and PCV at 39.75. The ranges within which these values typically fluctuate are also provided: S. bilirubin ranges from 0.1 to 1.2 mg/dl, S. creatinine ranges from 0.7 to 1.3 mg/dl, RBS varies between 110 and 140 mg/dl, HB% falls within the range of 14 to 18 g/dl, and PCV spans from 25 to 51.5. Most 84.61% of patients had a traveling history before admission, and the rest (15.35%) had none (Figure 2). The (Table 4) presents data regarding platelet counts in different conditions, expressed in platelets per microliter (µl). For the parameter PI24, the mean platelet count is approximately 34,780 platelets/µl with a standard deviation of ±43,820. The median platelet count for this condition is 22,000 platelets/µl, while the range spans from 12,000 to 45,750 platelets/µl. Moving to the PI72 condition, the mean platelet count notably increases to around 75,430 platelets/µl, accompanied by a standard deviation of ±69,465. The median count for PI72 is 53,500 platelets/µl, and the range of values fluctuates between 31,750 and 89,250 platelets/µl. Additionally, the table provides information about the spontaneous increment in platelet count observed at 24 hours. The mean increment

is 4,525 platelets/µl, with a mean deviation of ±38,080. The median increment stands at 1,500 platelets/µl, and the range spans from 5,750 to 10,000 platelets/µl. The comparison of PPI amongst responders and no-responders is shown in (Table 5). Regarding the response to platelet transfusion, 49(94.23%) patients responded to the platelet transfusion, and 3(5.77%) patients were not. According to the adverse outcomes involving 3 cases, all (100%) are associated with transfusion reactions. At the same time, there have been no reported instances of death from platelet transfusions (Table 6).

DISCUSSION

The exact mechanisms behind thrombocytopenia in dengue infection remain incompletely understood and likely involve multiple factors. The destruction of platelets through immune-mediated processes stands out as a significant contributor. For instance, a study found antibodies targeting the dengue virus non-structural protein 1 (NS1), which exhibited cross-reactivity with human platelets and endothelial cells. This cross-reactivity led to damage and inflammation in platelets and endothelial cells.[13] In most cases, the bone marrow responds to the loss of platelets by increasing production. Eventually, the immune-mediated destruction of platelets subsides, and spontaneous recovery in platelet counts occurs for nearly all patients. The degree of thrombocytopenia can vary during dengue infection, and in a small subset of patients, platelet counts may become extremely low. In our investigation, the age group most affected was 21-30 years, aligning with findings from a study conducted in Kolkata, where most cases fell within the 11-30-year age range.[14] Our study showed a higher occurrence among males, unlike findings by Gupta and Bansal, as well as Karoli et al. in North India.[14,15] Similarly, trends were consistent with a study in Karnataka by Kumar et al. and Ukey et al in central India.[16,17] Our study encompassed the full spectrum of Dengue infection, including 86.54% with Dengue Fever (DF), 7.69% with Dengue Hemorrhagic Fever grade 1 (DHF1), and 5.77% with Dengue Shock Syndrome (DSS). A Taiwan study observed DHF in 46.2% of cases, with DSS in 15.4%.[18] Bleeding was noted in 15.38% of patients upon enrollment, akin to a study by Jain et al which reported bleeding manifestations in various forms in 22.8% of patients.[19]

Other symptoms included vomiting, arthralgia, abdominal pain, body ache, diarrhoea, giddiness, and convulsions. Fever emerged as the most common manifestation, consistent with other studies.[14,20,21] Cough was the second most common symptom in our study, followed by headaches in 89% of patients, in line with Deshwal et al findings.[14] This study offered insights into the platelet transfusion response in dengue infection. Ordinarily, platelet transfusion immediately increases platelet count, peaking around 10 minutes to 1-hour post-transfusion. Afterwards, the platelet count gradually decreases, typically returning to baseline after about 72 hours. A single donor platelet transfusion can raise the platelet count by roughly 30,000/µl one hour after infusion in an adult with a body surface area of 2.0 m². Poor response or refractoriness to platelet transfusions is considered when consecutive transfusions yield post-transfusion Corrected Count Increment (CCI) values of less than 5,000/µl at 10 minutes to 1 hour.[22] However, unlike prolonged hematological disorders, dengue-related thrombocytopenia tends to resolve relatively quickly, often not requiring repeated platelet transfusions. Thus, the term "refractoriness" was avoided, and recipients were classified as responders or non-responders based on the outcome of a single donor platelet transfusion. While immune-mediated platelet destruction in dengue fever may reduce the effectiveness of transfused platelets, this study revealed that around half of the patients displayed a post-transfusion platelet increase of *10,000/µl within 1 hour. Patients who received platelet transfusion exhibited higher platelet increments at 24 and 72 hours, independent of baseline platelet counts. Notably, 94.23% of patients responded positively. These findings suggest that immune-mediated destruction's contribution to thrombocytopenia in dengue infection can vary among patients. Even with similar degrees of thrombocytopenia, immune-mediated platelet destruction might be less severe in responders than non-responders. Non-responders generally had lower baseline platelet counts, and a more significant proportion had counts below 10,000/µl than responders. It is plausible that patients with lower platelet counts experience heightened immune-mediated platelet destruction, leading to inadequate responses to platelet transfusion. This implies that although patients with platelet counts below 10,000/µl are more likely to receive platelet transfusions, they might benefit less from such interventions. Similar scenarios are observed in other autoimmune thrombocytopenic conditions. For instance, patients with conditions like idiopathic thrombocytopenic purpura or drug-induced thrombocytopenia also harbour antibodies that expedite the destruction of transfused platelets.

Nonetheless, some of these patients experience acceptable increases in platelet counts following transfusion. For example, one report showed that 42% of platelet transfusions elevated platelet counts to over 20,000/µl, with sustained elevation seen in 5 of the 7 responders the next day.[22] This suggests that severe bleeding progression might not be averted even with higher baseline platelet counts and successful transfusions. Notably, platelet transfusions come with a risk of severe adverse reactions. One study noted severe adverse reactions in 5.77% of platelet transfusions.[24] Another study documented deaths attributed to platelet transfusion at a rate of 0.015% (20 out of 1,712 transfusions).[25] While the reasons for this study's higher frequency of severe reactions are unclear, hyperactive immune mechanisms could be involved. Although no deaths directly linked to Transfusion-Related Acute Lung Injury (TRALI) were recorded, the hospital's experience with 52 apheresis platelet transfusion recipients with dengue fever showed no deaths due to platelet transfusion.

Limitations

Every study conducted within a hospital setting has inherent limitations, and the current study is no different. This study's limitations are explicitly outlined below. They encompass a modest sample size, the potential for selection bias in the recruitment of patients, and a reliance on retrospective data. Furthermore, this study does not thoroughly investigate external factors that could influence platelet counts, such as variations in transfusion protocols, as well as should be presence of patient co-morbidities. These specific limitations collectively pose a challenge to extending the findings to a broader population and hinder the ability to establish a definitive causal link between platelet transfusion and treatment outcomes in cases of Dengue Fever.

CONCLUSION

In conclusion, this study sheds light on the effectiveness of platelet transfusion in the context of Dengue Fever, drawing insights from the Rangpur Community Medical College and Hospital. The findings emphasize the judicious utilization of platelet transfusion based on clinical parameters rather than platelet count alone.

Recommendations

It was recommended that medical practitioners exercise caution in resorting to platelet transfusion, ensuring alignment with evidence-based guidelines. Further research is warranted to refine transfusion protocols and explore alternative treatments for Dengue Fever, optimizing patient care and resource allocation. This study underscores the significance of tailored medical interventions in complex viral illnesses like dengue fever.

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