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A Prospective Observational Study to Assess Clinical Profile and Outcome of Febrile Thrombocytopenia In a Tertiary Care Hospital

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Abstract: ***Background*: Febrile thrombocytopenia is a common clinical presentation in tropical regions, often associated with infections like dengue, malaria, leptospirosis, and septicemia. The presence of thrombocytopenia in febrile illness increases the risk of complications such as bleeding and multiorgan dysfunction. Understanding the clinical profile and outcomes of such cases is essential for timely diagnosis and management. *Methods*: This prospective observational study was conducted from January 2019 to December 2020 at a tertiary care hospital. A total of 200 patients aged over 12 years with fever and platelet count <150,000/cu mm were enrolled. After informed consent, clinical evaluations, targeted investigations, and outcome assessments were performed. Etiologies such as dengue, malaria, typhoid, and sepsis were confirmed through standard diagnostic tests. Data were analyzed using SPSS v21.0, and statistical significance was set at p<0.05. *Results*: Among the 200 patients, 67.5% were male with a mean age of 31.96 years. Fever (100%), chills (64%), and myalgia (63.5%) were the predominant symptoms. Clinical signs like dehydration (34.5%), altered sensorium (10%), and dyspnea (13.5%) were noted. Common complications included hepatomegaly, splenomegaly, and pleural effusion. Dengue was the leading cause followed by malaria and septicemia. Bleeding manifestations occurred in 20.5% of cases, and mortality was 6%, predominantly from septicemia. *Conclusion*: Infective etiologies dominate febrile thrombocytopenia cases, with dengue being most common. Most cases recover with supportive treatment, but severe forms, especially due to sepsis, require aggressive management. Prompt diagnosis and appropriate intervention improve prognosis.***

Keywords: thrombocytopenia, dengue, bleeding manifestation, tropical fever

1. Introduction

Fever has long been recognized as a key indicator of illness, with historical references from scholars like Hippocrates. Though once seen as a disease itself, it is now understood as a manifestation of various pathological conditions. Thrombocytopenia—defined as a platelet count less than 1,50,000/µL—is a frequent but often overlooked complication in febrile illnesses. Its causes include decreased platelet production, increased destruction, and splenic sequestration, with infections being the most common cause. Infectious diseases such as dengue, malaria, leptospirosis, typhoid, miliary tuberculosis, HIV, and septicemia are common etiologies. Mechanisms of thrombocytopenia in these illnesses include immune-mediated destruction, direct marrow suppression, hemophagocytosis, and toxin-induced platelet damage (1). In septicemia, disseminated intravascular coagulation (DIC) and increased platelet-associated IgG also contribute to low platelet counts (2). Malaria and dengue show particularly high rates of thrombocytopenia, which can lead to bleeding complications ranging from petechiae and mucosal bleeds to life-threatening intracranial hemorrhage. Serial monitoring of platelet counts is crucial, as thrombocytopenia correlates with increased morbidity and mortality in febrile conditions (3). A systematic diagnostic approach can aid in identifying the underlying etiology, allowing for timely intervention. Platelet transfusions may be needed in severe cases to prevent fatal outcomes. This study was undertaken to evaluate the clinical profile, underlying causes, and complications associated with fever and thrombocytopenia, emphasizing the need for early diagnosis and appropriate management.

2. Methodology

This single-center prospective observational study was conducted in the Department of General Medicine at a tertiary care hospital between January 2019 and December 2020. The study enrolled 200 patients aged above 12 years who presented with fever (defined as a 6 a.m. temperature >98.9°F or a 4 p.m. temperature >99.9°F) and thrombocytopenia (platelet count <150,000/cu mm). Patients with isolated fever or thrombocytopenia, hematological malignancies, those on chemotherapy or immunosuppressants, patients with known platelet disorders, chronic liver disease, or unwillingness to consent were excluded. Following ethical approval, informed consent was obtained from all participants. Clinical history and examination were recorded systematically. Diagnostic investigations included a complete blood count, peripheral smear, liver and renal function tests, blood and urine cultures, chest X-ray, and abdominal ultrasonography. Specific tests such as rapid diagnostic tests for malaria and dengue, Widal test, ELISA for Leptospira and HIV, and bone marrow examination were performed based on clinical suspicion. Data were analyzed using SPSS version 21.0. Categorical variables were expressed as percentages, while continuous variables were summarized as mean ± standard deviation. Normality of data was assessed using the Kolmogorov-Smirnov test. Statistical significance was determined using

the chi-square test or t-test as appropriate, with a p-value of <0.05 considered significant.

3. Results and Discussion

This observational study evaluated the clinical profile and outcome of 200 patients with fever and thrombocytopenia admitted to a tertiary care hospital. Infections like dengue, leptospirosis, malaria, and HIV are common causes of this condition, and timely recognition and treatment, including platelet transfusions, are crucial to prevent fatal outcomes. The study aimed to understand the clinical profile and complications of fever with thrombocytopenia, highlighting the importance of prompt diagnosis and management. The average age of patients enrolled in our study was 31.96 ± 10.68 years with most patients in the age group of 20 to 40 years followed by those in the age group of 30 to 40 years. Male predominance (67.5%) was seen in our study population with male to female ratio of 2.07:1(table 1). Thus, young age males were more affected in our study. Since febrile illnesses in India are more associated with arthropod borne infection, the age and gender seen in our study correlated well with it. The age group between 20 to 40 years is the economically productive period during which they have a high chance of having contact with contaminated environments. Mosquito bites are more common in men due to their higher exposure to mosquitoes and mites. Men often work in environments where these insects are prevalent, especially during peak biting times or when migrating in endemic areas. Additionally, men tend to sleep outdoors, increasing their risk of exposure. In some societies, the male-dominated nature means that women often seek permission from men for basic healthcare needs, further contributing to the higher ratio of male patients. The above results can be well correlated with study conducted by Kakanale M et al (4) in India where male preponderance 60% compared to females and similar to study by Sujata S. Kumbhar et al, (5) where 59% males had fever with thrombocytopenia. Nikalje Anand et al,(6) in their study found that highest number of cases was seen in the age group of 18 - 40 years (75%) followed by 40 - 60 years (16%) and then above 60 years were 9% and similarly in study conducted by Kakanale M et al (4) where majority of patients were in the age group of 18-30 years (48.38%) followed by those in 30 to 60 years (46.67%) (table 1).

Table 1: Demographic and clinical profile of patients (N=200)

Variables	Category	No of patients	Percentage
Gender	Male	135	67.5
	Female	65	32.5
Age (years)	<20	24	12
	20-30	85	47.5
	31-40	57	28.5
	41-50	22	11
	>50	12	6
Mean age (years)	31.96 ± 10.68		
Duration (days)	<5	48	24
	5-10	111	55.5
	11-15	23	11.5
	>15	18	9
Mean duration (days)	9.44 ± 8.89		

The average duration of fever among our study population was 9.44 ± 8.89 days with the majority (79.55%) of patients presented within 10 days of fever onset. This can be compared to study conducted by Kakanale M et al (4) where the average duration of fever at presentation was 4.46±2.86 days. The duration of fever in the study conducted at Visakhapatnam, India, (7) ranged from 1-20 days with mean duration of 6.05 days (SD=3 days). In 92% of the cases the duration was < 10 days. Both the studies highlighted patients presented comparatively earlier than our study population. This may be because ours a tertiary care hospital and majority of the patients referred here have already taken primary care from outside and hence caused delay in the presentation. Since presence of fever was our inclusion criteria, all patients presented with fever, which was commonly associated with chills, rigors, body ache or myalgia.

Other associated symptoms include vomiting, abdominal pain, and gum bleeding and petechiae. Since tropical diseases like malaria, dengue, leptospirosis, enteric fever is more common in India, the presentation of patients enrolled in our study correlates well with these diseases. In the study conducted by Lakshmi M et.al, (7) fever was seen in 100% of the cases (table 2). Other than fever, headache was the most common symptom seen in 32 (32%) cases, followed by myalgias (31%), vomiting (27%), pain abdomen (6%), bleeding manifestations (3%), and altered sensorium (1%) cases. In a study conducted by Nair et.al. (8), other than fever most patients had headache (61.11%), body ache (66.67%) and joint pains (51.11%). Similar results were seen in Khan‟s study, (9) which showed chills and rigors in 80%, myalgia in 70%, vomiting in 60%, headache in 50% and rash in 25%. In the study by Lakum N et al (10) fever was the presenting complaint in all cases, weakness in 40% of cases, weight loss in 10% of cases and bleeding was the presenting complaint in 10% of cases. Dehydration (34.5%) was the most common reported feature among enrolled patients. Other common presentations seen were dyspnoea (13.5%), altered sensorium (10%), pallor (11%) and jaundice (9.5%). Hypotension was present in 10.5% patients. Systemic examination showed hepatomegaly was seen in 9% patients, whereas splenomegaly and pleural effusion in 8.5% each. In the study by Lakshmi M et.al, (7) most commonly detected signs were splenomegaly (24%), hepatomegaly (21%), jaundice (17%), and petechiae (16%). Other signs included pallor (7%) and conjunctival hemorrhage (4%). In the study by Lakum N et al (10) most common finding was pallor and was seen in 70% of cases, followed by splenomegaly in 45% of cases, hepatomegaly in 35% of cases and lymphadenopathy was seen in 10% of cases (table 2).

LFT parameters were normal in majority of the patients but elevated in minority of patients. Among deranged patients, the average total bilirubin was 2.26 ± 2.23 mg/dl and SGOT and SGPT was 84.91 ± 63.31 U/L and 86.06 ± 47.13 U/L respectively (figure 1). Similarly, RFT parameters were deranged in less than half of the patients. Serum urea was normal in 55% patients and abnormal in 45%. Among deranged patients, the average serum urea was 40.27 ± 30.72 mg/dL and serum creatinine were 1.92 ± 1.03 mg/dL (figure 2). Similar to our study, Lakshmi et.al. (7) reported LFT normal in majority of patients, the total bilirubin level was abnormal in 26.47% of viral fever cases, 58.62% of dengue fever cases and 76.92% of leptospirosis cases and 30% of malaria cases in the present study. The abnormal SGOT was

seen in 38.24% of viral fever cases, 65.52% of enteric cases, 84.62% of leptospirosis and 30% of malaria cases in the present study. The abnormal SGPT was seen 32.35% of viral fever cases, 68.97% of dengue fever cases, 84.62% of leptospirosis and 20% of malaria cases in the present study. This shows that abnormal liver function test was more prevalent in leptospirosis and dengue fever because of dengue hepatitis and hepatitis in leptospirosis. Whereas in a study conducted by Bindu Nair (8) RFT was abnormal in 10.8% patients with dengue, 45.45% of sepsis, 50% of malaria and 6.25% of scrub typhus. (table 3).

Table 2: Clinical Features

Parameters	Variable	No of patients	Percentage
Symptoms	Fever	200	100
	Chills / Rigors	128	64
	Myalgia	127	63.5
	Abdominal pain	49	24.5
	Vomiting	45	22.5
	Gum bleeding	16	8
	Petechiae	21	10.5
	GI bleed	4	2
	Weight loss	19	9.5
Signs	Altered sensorium	20	10
	Dehydration	69	34.5
	Dyspnoea	27	13.5
	Pallor	22	11
	Jaundice	19	9.5
Systemic and Imaging examination	Hypotension	21	10.5
	Hepatomegaly	18	9
	Splenomegaly	17	8.5
	Pleural effusion	17	8.5

Table 3: Laboratory Profile

		Average value
CBC	Hb (gm%)	11.99 ± 169
	TC (Cells/ml/µl)	8.02 ± 4.47
	Platelet (/ul)	52344.5 ± 30461.3
	Hematocrit (%)	34.68 ± 9.48
LFT	Total Bilirubin (mg/dl)	2.26 ± 2.23
	SGOT (U/L)	84.91 ± 63.31
	SGPT (U/L)	86.06 ± 47.13
RFT	Urea (mg/dL)	40.27 ± 30.72
	Serum Creatinine (mg/dL)	1.92 ± 1.03

The average platelet count was 52344.5 ± 30461.3 / ul, with most patients in the range of 30001-50000 (25%) followed by those in 10000-30000 (24.5%) and 50001-70000 (22%) (table 5). Thus almost 50% of patients enrolled in our study had platelet count less than 50000. Like our study, Modi T et.al (11) reports 45.29% patients had platelet count >50000/mm3, 38.17% had platelet count in range of 20000-50000/mm3 ,11.19% had platelet counts in range of 10000-20000 and 5.34% had platelet count less than 10000/mm3. In study by Lakshmi M et.al. (7), platelet count of ≤40000/cumm was seen in 20% of patients and 18% of patients had platelet count of 40000- 60000/cumm. 27% patients had platelet count of 60000- 80000/cumm and 30% of patients had platelet count in the range of 80000 to 100000/cumm. In the study by Dash et al (12) majority of patients (26%) had platelet count in the range of 61000 – 80000/cu.mm, followed by 25% (21000 – 40000/cu.mm), 19% in the range of 81000- 100000/cu.mm, 17% of cases in the range of 0- 20000/ cu.mm, 13% of cases in the range of 41000 – 60000/cumm. Gum bleed (8%), petechiae (10.5%) and GI bleed (2%) were the bleeding manifestation seen in our study population. All the patients with reported manifestation had platelet count <70000/cumm. Majority of patients with above manifestation had platelet count between 10000 to 30000/ ul. The average platelet in patients presented with Gum bleed, petechiae and GI bleed was 25406.25 ±19003/cumm, 18476.19 ± 14882 /cumm and 13375 ± 5153.9/cumm respectively. This was similar to study conducted by Kakanale M et.al. (4) where 27 patients (10.18%) had petechiae which were the most common presentation followed by malena (17patients), bleeding gums (15 patients), epistaxis (12 patients), haematuria (6 patients), hematemesis (5 patients) and bleeding PV in 3 patients. Similar to our study, Tejas Modi (11) also reported petechiae as the major bleeding manifestation (67.23%) followed by spontaneous bleeding (32.77%) but prevalence was higher than our study.

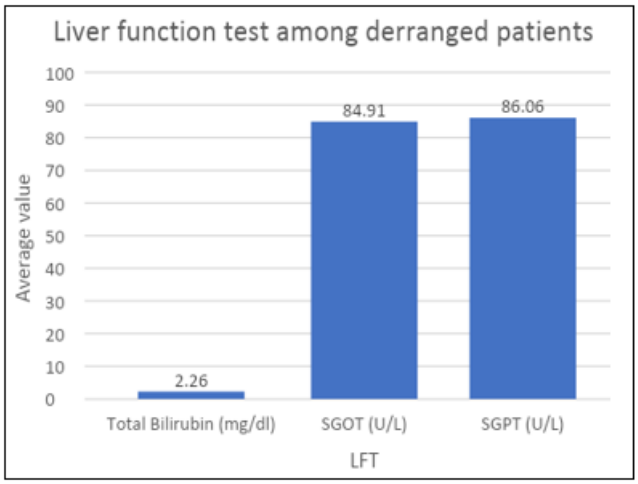

Figure 1: LFT among deranged patients

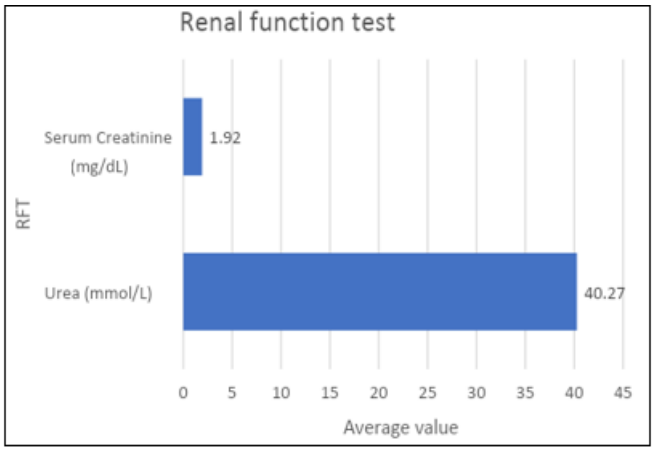

Figure 2: RFT parameter among deranged patients

The average platelet in his study among patients presenting with petechiae, gum bleeding, epistaxis, hematemesis, hemoptysis, bleeding per rectum, hematuria, abnormal bleeding per vaginum, melena, subconjunctival hemorrhage occurred was 32000/mm3, 15000/mm3, 22000/mm3, 21000/mm3, 35000/mm3, 31000/mm3, 23000/mm3, 37000/mm3, 37000/mm3, 44000/mm3 respectively. Significant negative correlation was seen between platelet count and bleeding manifestation in our study population, this implies that the risk of bleeding manifestation increases with decrease in platelet count (table 6). Similar inverse correlation was seen in study Lakshmi et al. (7) In contrast study by

Raikar et al (13) showed no correlation was seen between the platelet count and bleeding manifestations.

Table 5: Platelet counts among enrolled patients and bleeding manifestation

Platelet (/ul)	No of patients	Percentage	Gum bleed	Petechiae	GIT bleed
<10000	3	1.5	1	2	1
10000-30000	49	24.5	10	16	3
30001-50000	50	25	3	2	0
50001-70000	44	22	2	1	0
70001-90000	35	17.5	0	0	0
90000-150000	19	9.5	0	0	0

Table 6: Correlation of mean platelet count, bleeding manifestation

Manifestations	Mean platelet count	Correlation coefficient	P value
Gum bleed	25406.25 ±19003	-0.27 (-0.4045 to - 0.1404)	<0.0001
Petechiae	18476.19 ± 14882	-0.42 (-0.5325 to - 0.2955)	<0.0001
GIT bleed	13375 ± 5153.9	-0.20 (-0.3346 to - 0.05741)	0.004

*Spearman Correlation

Various investigations were performed among our study population to determine the cause of febrile thrombocytopenia. Peripheral smear examination was normal in 2/3rd of the study population but showed malarial parasite in 15% patients. USG abdomen was normal in similar 2/3rd patients but showed presence of hepatomegaly/ splenomegaly or hepato-splenomegaly in the remaining patients. Chest x-ray was normal in almost 90% patients, B/L pleural effusion was the commonest manifestation among the rest. In few patients in whom other investigations did not give idea about the etiology, bone marrow examination was done.

18.5% patients underwent Bone marrow examination, it was normal in majority, few reported presences of AML, CML and NHL. Almost similar investigations were done is study conducted by Kakanale M et al. (4), among 83 out of 465 had Chest X ray changes, 56 patients had pleural effusion, 15 had non-homogenous opacities, 6 patients had cardiomegaly 2 had COPD changes and 2 patients had X ray features of ARDS. Among 336 patients had normal USG abdomen, 89 patients had ascites, 87 patients had thickened and oedematous gall bladder, 30 patients had splenomegaly, 22 patients had hepatomegaly, 2 patient had features of cholecystitis and 3 had gravid uterus. CT and MRI brain was done for patients in altered sensorium; no abnormalities were detected. 1 patient was diagnosed with dengue encephalitis.

Dengue was the most common (41%) diagnosis among our enrolled patients. This was followed by malaria (24%), leptospirosis (12%) and typhoid (7%) (table 7). Thus, infection was the commonest cause of fever with thrombocytopenia in our study, while septicemia was seen in 2% patients. Similar findings were reported in a study conducted by Kakanale M et.al. (4) where the most common cause for febrile thrombocytopenia was Dengue followed by sepsis, Malaria, Typhoid, Leptospira, Rickettsia and HIV. Similar results were reported in study conducted by Gondhali MP et.al. (14), where Dengue was the leading cause of fever associated with thrombocytopenia, but second common cause was Septicemia followed by Malaria, HIV, viral hepatitis, and enteric fever cases. This might be due to seasonal, regional variations and other multifactorial etiologies. Tejas Modi (11) in his study reported viremia (61.32%) as the most common etiology of febrile thrombocytopenia including dengue fever (55.98%) and other viral infection (5.34%) like H1N1 swine flu (novel) influenza, Human Immunodeficiency Virus infection and Crimean Congo Hemorrhagic fever. In contrast, a study conducted by Nair et.al. (8) reported septicemia as the leading cause of febrile thrombocytopenia followed by fever of unknown origin and hematological malignancies. Thus, our study and similar other study does highlight that dengue is the most common cause of febrile thrombocytopenia in India.

Table 7: Diagnosis among enrolled patients

Diagnosis	No of patients	Percentage
Dengue	82	41
Malaria	48	24
Typhoid	14	7
Leptospirosis	24	12
Malaria + leptospirosis	2	1
HIV	8	4
Septicemia	4	2
AML	2	1
CLL	1	0.5
CML	2	1
NHL	2	1
Unspecified	11	5.5

Mortality was reported in 20 (10%) patients enrolled in our study with dengue being the most common cause of mortality followed by leptospirosis and malaria-septicemia (figure 3). The mortality rate among the series of patients enrolled in the study conducted by Harsha N S(15) was 11% and septicemia accounted for 72% followed by malaria in 18%. Mortality was 1.11% (2 patients) in study conducted by Nair et.al. (8) and both were due to malaria. Almost similar result was seen in a study conducted by Kakale M et.al. (4) where mortality reported was 1.9%, with dengue being the cause in all patients. Gondhali MP et.al. (16) reported 6% mortality with septicemia being the most common cause followed by dengue. The increased mortality in our study can be explained by the fact that ours is a tertiary care center and most of the patients are referred from the primary center once failed on primary therapy or disease progression. Mortality depends on severity of disease, diagnosis made, available treatment and care, time of initiation of treatment and associated other medical illness. Mortality can be reduced by early and right diagnosis, timely and effective treatment and care. Significant negative correlation was seen between mortality and platelet

count among our study population also platelet count was significantly low among those patients who expired (table 8).

Similarly, significant positive correlation was seen with duration of fever among our study population: also, the average duration of fever was significantly high among patients who expired (p=0.001) (table 9). This implies that mortality among our enrolled patients increases with decrease in platelet count and increases with duration of fever. Similar to our study Lakshmi M et.al. (7) reported thrombocytopenia correlates inversely with mortality and morbidity in various febrile illnesses. In contrast Tejas Modi (11) and Nair BT et.al. (8) in his study reported thrombocytopenia has no correlation to mortality.

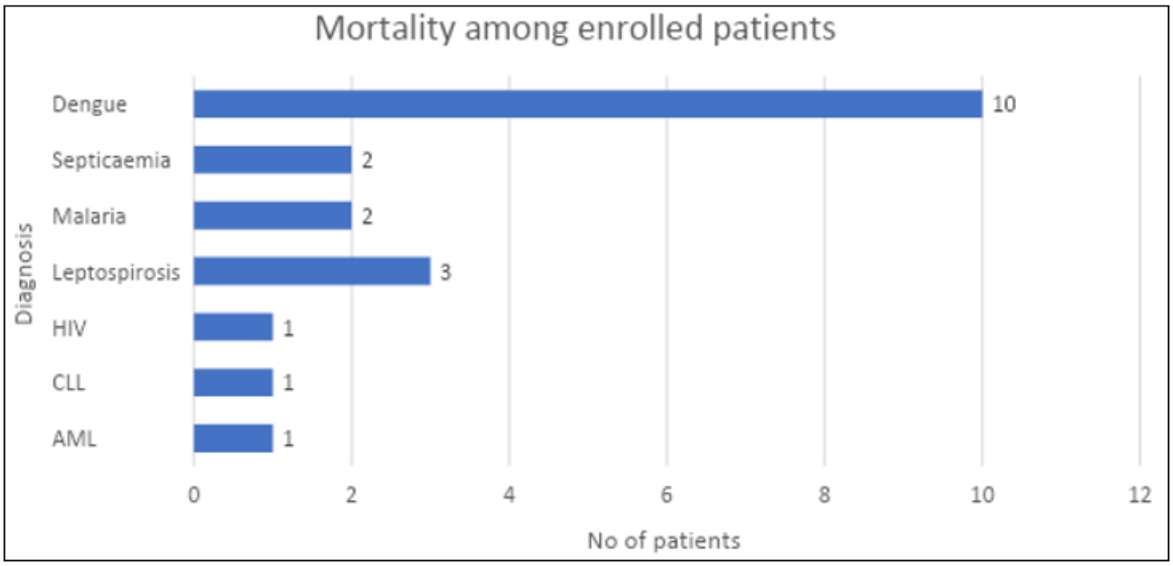

Figure 3: Diagnosis among expired(N=20)

Table 8: Outcome and platelet count

Outcome	No of patients and percentage	Mean platelet count
Cured	180(90%)	56113.33 ± 29445
Expired	20(10%)	18425 ±14299
P value	<0.0001	

Table 9: Duration of fever in cured and expired patient

Outcome	Average duration of fever(days)	P value
Cured	8.98 ± 8.484	0.001
Expired	13.6 ± 11.36	(Mann Whitney test)

Thus, the results of our study and similar other studies highlights the importance of thrombocytopenia in various febrile disorders and a completed diagnostic workup is needed in evaluating the cause of thrombocytopenia in febrile patients, since the cause is not limited to the infection.

4. Conclusion

Our study thus concludes,

- Dengue as the most common diagnosis among our study population, this was followed by malaria, leptospirosis and typhoid.
- Mortality was reported in 10% patients enrolled in our study.
- Dengue was the most common cause of mortality followed by leptospirosis and malaria-septicemia.

Conflict of Interest Statement:
None declared.

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