

To assess the Relationship Between Platelet Count and Outcome of The Disease

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Abstract:

Fever is identified as a manifestation of diseases since old time, as written by former scholars like Hippocrates. Which was found as a disease but later as an accompaniment to varied diseases, fever is easily noted and a reliable marker of diseases. Normal body temperature is 37.0 °C or 98.6°F. The exact range is sort of wide, being littered with site of measurement, diurnal changes, vigorous exercise, hormonal and menstrual status, variation of individual, and surrounding factors. A patient's vital sign is usually estimated by measurements taken within the mouth. For reasons of convenience, but oral temperatures will be littered with mouth-breathing, by the rate of respiration, and by recent drinking of hot or cold liquids.

Keywords: Acute Febrile, Thrombocytopenia.

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Introduction

Commencing the study of the very important group of diseases to which human kind is facing.

In various historical statements, Medicine presents most common epidemics, which is fever, which occurs in all ages of every race and people.

In words of Sydenham, statement given by a great observer, except deaths because of violence, fever make nearly two thirds of all diseases by which humans are facing annually. And it is thought that, statement made hardly in any way regarded as an exaggeration for the day. It is not perhaps in the generation of humans that pass silently away by disease, as attacks homes of poor year after year, that it effects terribly and manifests strikingly.

The ancient hallmark of disease is fever. From Greek "pyretus" meaning fire, from this origin, fever is thought as pyrexia. within the same way, Febrile is from the Latin word Febris, which implies fever [1].

Fever is identified as a manifestation of diseases since old time, as written by former scholars like Hippocrates. Which was found as a disease but later as an accompaniment to varied diseases, fever is easily noted and a reliable marker of diseases [2].

Normal body temperature is 37.0 °C or 98.6°F. The exact range is sort of wide, being littered with site of measurement, diurnal changes, vigorous exercise, hormonal and menstrual status, variation of individual, and surrounding factors. A patient's vital

sign is usually estimated by measurements taken within the mouth. For reasons of convenience, but oral temperatures will be littered with mouth-breathing, by the rate of respiration, and by recent drinking of hot or cold liquids.

Many modern thermometry instruments take readings from the auditory canal, in order that the temperature is not littered with these factors. The core vital sign is more closely reflected by rectal measurements, which are usually 0.3-0.6 °C over oral measurements.

Within the recent period there's an upsurge within the amount of patients with fever and thrombocytopenia. This will be due to several emerging and re-emerging infections within the recent period^{Error! Reference source not found.}. Fever with thrombocytopenia could be a distinct clinical entity and refers to a discount in platelet count less than 1,50,000/μl in association with fever.

Fever along with thrombocytopenia tapers the medical diagnosis of the clinical entity. Febrile thrombocytopenia is commonly the results of infections like dandy fever, rickettsial infections, viral fever, septicemia, leptospirosis, malaria and enteric fever [3].

In developing countries acute infections remain the most common cause of acute febrile illness with thrombocytopenia, low socio-economic status is directly related to increased prevalence and severity of these acute infections. Knowledge of various symp-

toms and differentiating clinical signs and examination finding helps us to make correct diagnoses. By appropriate lab investigations, etiological diagnosis can be made, which will help to plan and select correct treatment protocols.

Material and Methods

This is an analytical cross-sectional study conducted at pediatric ward, pediatric intensive care unit at Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli, over a period of 18 months, among children in the age group 1 month to 18 years.

Study design: Analytical Cross-sectional Study.

Place of study: Pediatric ward, Pediatric Intensive Care Unit and at Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Sangli.

Study duration: 18 months.

Study Population: Children of age from 1 month to 18 years.

Study subjects: Children admitted in Pediatric ward, PICU of age from 1 month to 18 years.

Inclusion Criteria:

1. Children age 1 month – 18 years
2. Presenting with fever (temperature $>38^{\circ}\text{C}$) for >24 hours and <7 days
3. Thrombocytopenia (Platelet < 1.5 lakhs/cu.mm)

Exclusion Criteria:

1. Patients with hematological disorders causing thrombocytopenia.
2. Patients on drugs causing thrombocytopenia.
3. Diagnosed cases of platelet disorders causing thrombocytopenia

Sample size: Children of age from 1 month to 18 years with Acute febrile illness with thrombocytopenia admitted in pediatric ward from October 2018 to April 2020 Total number of cases who fulfill the above criteria over period of 1 year of data collection.

Ethical Considerations and Permission: The study proposal was approved by the Institutional Ethical Committee, as stated in a letter from the chairman, institutional ethical Committee (IEC) dated on 6/12/2017 with reference no (2017-18/237). While conducting this study, all the guidelines and instructions of the ethical committee were diligently carried out. Requisite permissions were taken from the authors, authorities and related personnel for the use of their intellectual material, screening tools etc., in this dissertation. Written authorization was acquired from the Head of the institute for conducting this study. Written consent/assent was taken from every guardian of the children included in this study.

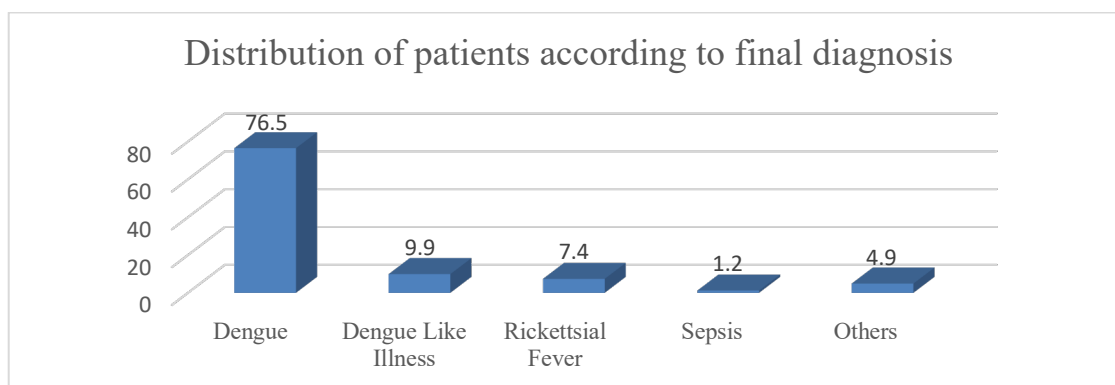
Results and Observations

Table 1: Distribution of patients according to their final diagnosis.

Diagnosis	Total=81	Percentage (%)
Dengue	62	76.5
Dengue Like Illness	8	9.9
Rickettsial Fever	6	7.4
Sepsis	1	1.2
Others	4	4.9

Final diagnosis was of dengue in 76.5% of the patients included in the study. Dengue like illness was present in 9.9%, Rickettsial Fever was

diagnosed in 7.4% and sepsis was diagnosed in 1.2% of the patients. Rest 4.9% of the patients were labelled as others.



Graph 1: Distribution of patients according to final diagnosis

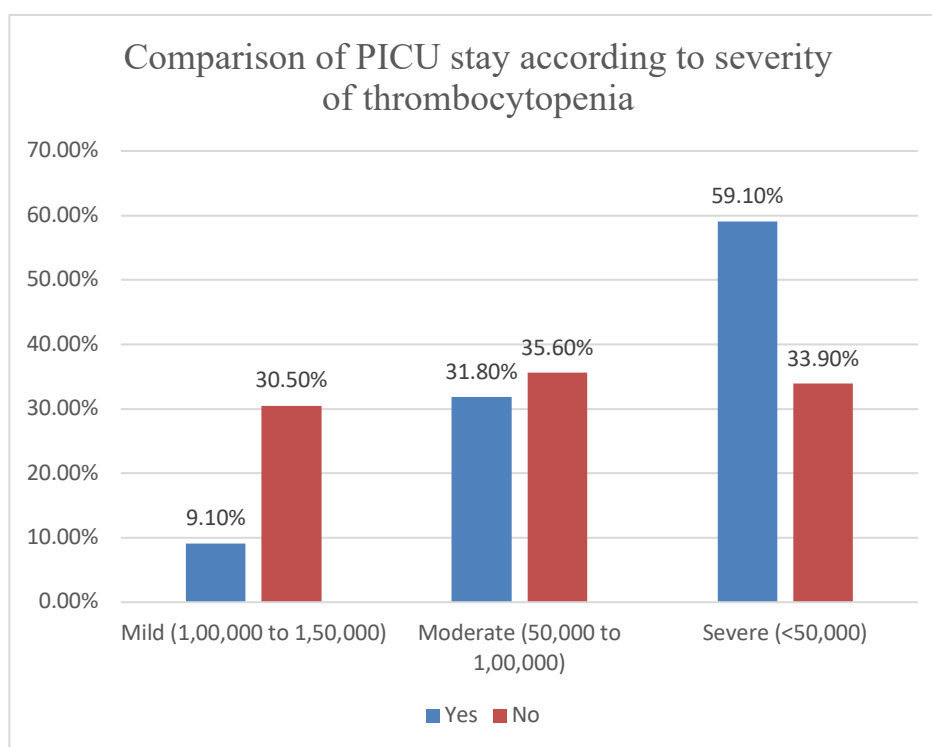
Table 2: Association of platelet count with PICU stay.

Platelet count		PICU Stay		Total
		Yes	No	
Mild (1,00,000 to 1,50,000)	N	2	18	20
	%	9.10%	30.50%	24.70%
Moderate (50,000 to 1,00,000)	N	7	21	28
	%	31.80%	35.60%	34.60%
Severe (<50,000)	N	13	20	33
	%	59.10%	33.90%	40.70%
Total	N	22	59	81
	%	100.00%	100.00%	100.00%
		p value* < 0.05		

*Analysed by chi-square

We observed that the severity of thrombocytopenia was significantly associated with PICU stay (p value < 0.05). We found that among mild thrombocytopenia cases, only 9.1% had PICU stay,

while among moderate thrombocytopenia cases 31.8% had to be admitted to PICU, while among severe thrombocytopenia, 59.1% had to be admitted to PICU.

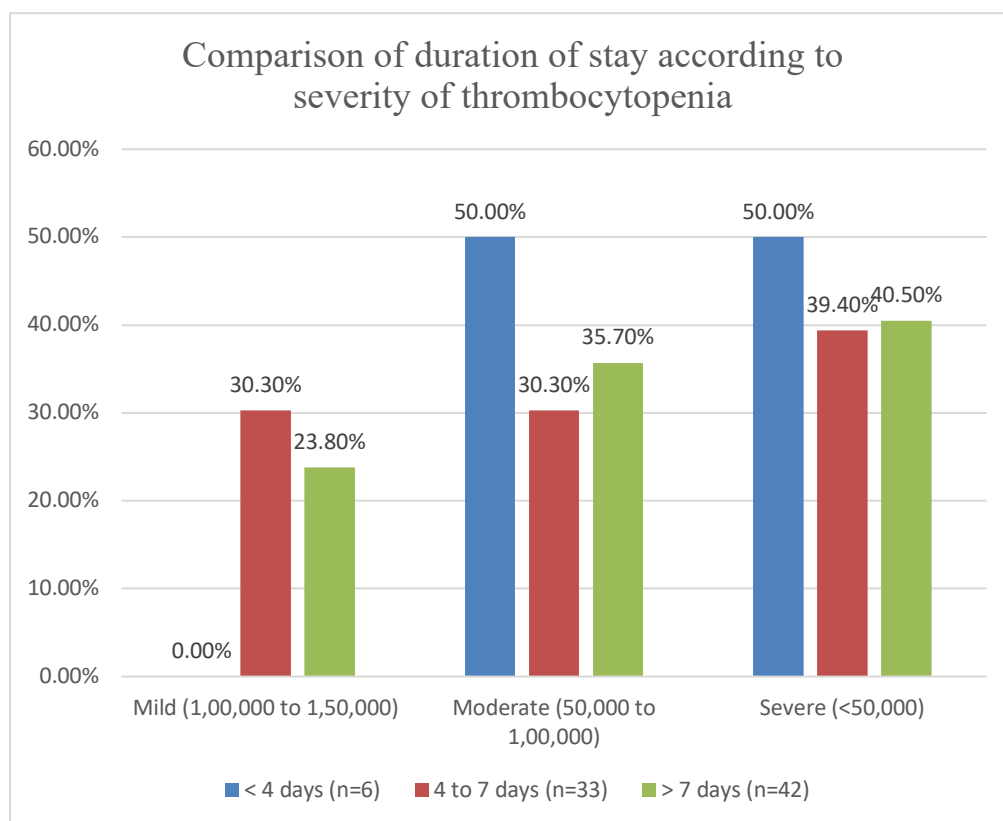
**Graph 2: Comparison of PICU stay according to severity of thrombocytopenia****Table 3: Association of platelet count with duration of hospital stay.**

Platelet count		Duration of hospital stay			Total
		< 4 days (n=6)	4 to 7 days (n=33)	> 7 days (n=42)	
Mild (1,00,000 to 1,50,000)	N	0	10	10	20
	%	0.00%	30.30%	23.80%	24.70%
Moderate (50,000 to 1,00,000)	N	3	10	15	28
	%	50.00%	30.30%	35.70%	34.60%
Severe (<50,000)	N	3	13	17	33
	%	50.00%	39.40%	40.50%	40.70%
Total	N	6	33	42	81
	%	100.00%	100.00%	100.00%	100.00%
		p value* = 0.65			

*Analysed by chi-square.

We observed that 23.08% of the cases with mild thrombocytopenia had hospital stay of more than 7 days, while 35.7% of moderate thrombocytopenia cases had a hospital stay of more than 7 days.

Among cases with severe thrombocytopenia, 40.5% of the cases had a hospital stay of more than 7 days. Thus the duration of hospital stay was not found to be significantly associated with the severity of thrombocytopenia (p value = 0.65).



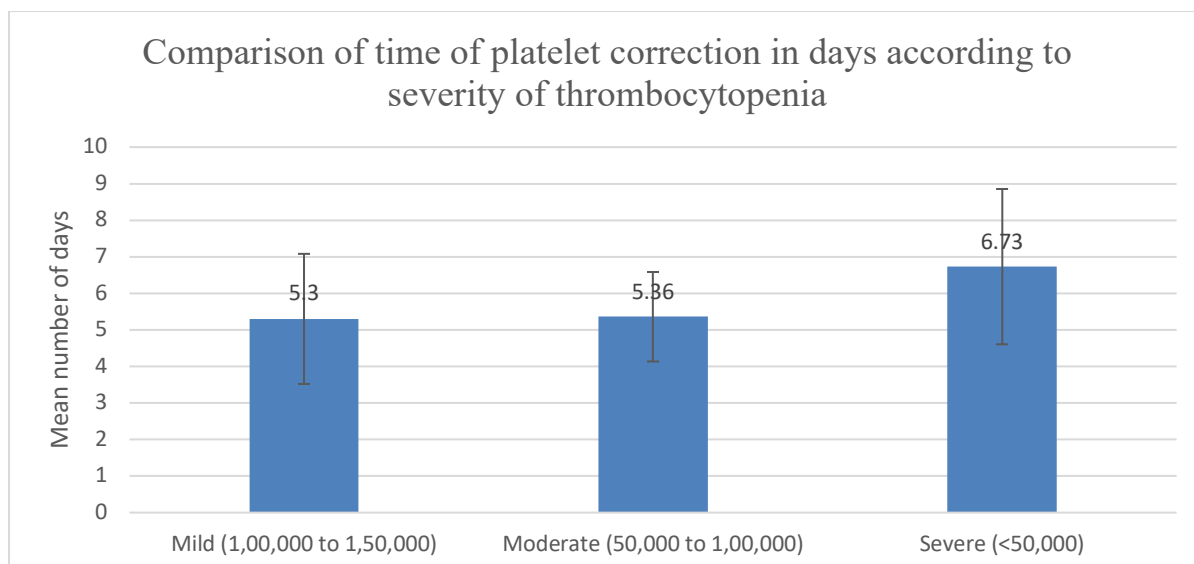
Graph 3: Comparison of duration of stay according to severity of thrombocytopenia

Table 4: Description of mean duration of time for normalization of platelet count.

Platelet count	N	Mean (days)
Mild (1,00,000 to 1,50,000)	20	5.30 ± 1.78
Moderate (50,000 to 1,00,000)	28	5.36 ± 1.22
Severe (<50,000)	33	6.73 ± 2.13
Total	81	5.90 ± 1.88

Cases with mild thrombocytopenia had platelet normalization in mean 5.3 days, while for moderate thrombocytopenia a mean duration of 5.36 days was required for platelet count normalization. A mean of

6.73 days was taken by cases with severe thrombocytopenia for normalization of platelet count.



Graph 4: Comparison of time of platelet correction in days according to severity of thrombocytopenia

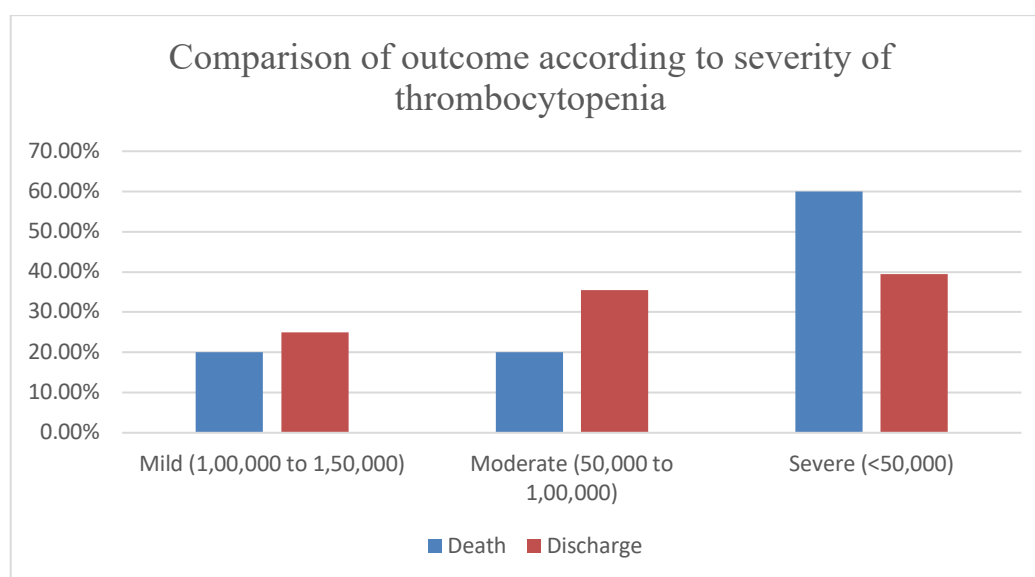
Table 5: Association of platelet count with the final outcome of the patients.

Platelet count		Outcome (Discharge/Death)		Total
		Death	Discharge	
Mild (1,00,000 to 1,50,000)	N	01	19	20
	%	20.00%	25.00%	24.70%
Moderate (50,000 to 1,00,000)	N	01	27	28
	%	20.00%	35.50%	34.60%
Severe (<50,000)	N	3	30	33
	%	60.00%	39.50%	40.70%
Total	N	5	76	81
	%	100.00%	100.00%	100.00%
		p value* = 0.65		

*Analysed by chi-square

There were a total of 5 deaths (6.17%). There was one case with mild thrombocytopenia and moderate thrombocytopenia each and three cases with severe

thrombocytopenia. The severity of thrombocytopenia was not found to be significantly associated with the final outcome of the patients (p value = 0.65).



Graph 5: Comparison of outcome according to severity of thrombocytopenia

Discussion

Acute Febrile Illness with Thrombocytopenia is an individual clinical presentation, which is fairly commonly observed in numerous infections. Several infections such as viral causes like, influenza infections, zika viral infection, dengue fever, chikungunya, HIV infection. In some situations bacterial causes like rickettsial infection, enteric fever, leptospirosis, and also fungal sepsis. Many times thrombocytopenia is diagnosed based on clinical presentation and maybe detected during testing for other diseases. Febrile thrombocytopenia is common in children as well however most of the paediatric cases are reactive in nature which is not the case among adult patients. While recovering from an infection it has been observed among children that thrombocytopenia is fairly common. Because of its non-specific presentation unexplained cases of thrombocytopenia need to be investigated thoroughly so that the specific disease can be diagnosed and the treatment be guided. It is also important to diagnose thrombocytopenia among paediatric age group for the reason that minority of the cases can bleed rapidly, progress to shock and die. This cross-sectional study was done to study the clinical profile of children who presented with acute febrile illness with thrombocytopenia and to find the association of severity of thrombocytopenia with various clinical outcomes. Frequency of study cases of acute febrile illness with thrombocytopenia admitted in paediatric ward and PICU among 1983 patients, admitted in the duration of 18 months in Bharati Vidyapeeth (Deemed to be University), Medical College & Hospital, Sangli = 4%.

We found that mean hemoglobin was 12.85 gm%, mean PCV was 39.18, mean cell count was 5550.62 cells per cumm, mean polymorphs was 59.47 cells per microL and mean lymphocytes were 31.95 cells per microL. Mean platelet count was observed to be 68827.16 per ml. We found that mean SGOT and SGPT levels were 214.53 and 111.06 IU/L respectively.

In another study by Gowd et al, 52% children admitted with platelet count less than 1 lakh and 25% children admitted with PCV more than 40, 6% children had abnormal renal function, 15% children had elevated liver enzymes, 12% children admitted with abnormal coagulation profile and 72% children had ascites demonstrated by ultrasonogram abdomen.⁴ While eliciting the courses the authors found positive serology for dengue in 60% positive Vidal test in 12% while 8% had a positive urine culture.

In my study, dengue was common diagnosis, seen in 76.5% of the patients in the study. Dengue like illness was present in 9.9%, Rickettsial Fever was diagnosed in 7.4% and sepsis was diagnosed in 1.2%

of the patients. In last 4-6 years we are seeing increasing trend of dengue infection in our areas due to urbanization, and increasing population density and poor water storage facilities. At the same time there is a decreasing trend of malaria and enteric fever. Rickettsial Infection is also seen with increasing trend, in our area since last 4-6 years.

In the study by Gutthi et al malaria was a common cause of febrile thrombocytopenia which was observed in 35% of the patients. Next most common cause was dengue fever observed in 34% of the patients. Less common causes included sickle-cell anaemia (7%), typhoid fever (5%) and sepsis in 5%. [1] In addition to these, rare presentations like scrub typhus, acute lymphoblastic leukaemia, and viral hepatitis was also seen in the patients, while 6% of the patients remained undiagnosed. Other minor causes include scrub typhus in 3% of cases, ALL (Acute Lymphoblastic Leukemia) in 3% of cases, viral hepatitis in 2% of cases, undiagnosed in 6% of cases. In the study by Nair et al, the most common cause of low platelet count was viral fever except dengue and chikungunya which was observed in 27% of the patients. Dengue was diagnosed in 22% typhoid fever in 12% chikungunya in 11% malaria in 8.5% sepsis in 5% idiopathic thrombocytopenic purpura in 5% blood malignancies in 1.6% and vitamin B12 deficiency anaemia in another 1%. In another study, Ramabhatta et al made a definitive diagnosis in 280 (91.5%) children. Twenty-six (8.5%) children were diagnosed as probable viral fever after excluding other causes [6] Dengue fever was diagnosed in 83.0%, Viral fever in 8.5%, Enteric fever in 7.2%, Malaria 1% and Hepatitis A in 0.3%.

We observed that the severity of thrombocytopenia was significantly associated with PICU stay (p value < 0.05) and also longer duration of PICU stay. We found that among mild thrombocytopenia cases, only 9.1% had PICU stay, while among moderate thrombocytopenia cases 31.8% had to be admitted to PICU, while among severe thrombocytopenia, 59.1% had to be admitted to PICU.

Previous studies have shown that higher consumption of platelets among patients admitted in PICU caused due to DIC and haemolytic uremic syndrome syndrome is fairly common.[7] It has been observed that thrombocytopenia is diagnosed in 13% to 58% of the patients who are admitted to ICU use of various departments, The range of this prevalence varies according to the clinical presentation and the final diagnosis of the patient.[8] Numerous studies which evaluated the role of thrombocytopenia among ICU patients found and inverse association of the platelet count with the duration of ICU stay as well as death rate (mortality rate 31% to 46% vs 16%–20%).[9]

The various contributing factors for prolonged PICU stay in addition to severe thrombocytopenia were hepatic dysfunction, DIC and associated sepsis.

Moreover 15 to 50% of the patients were admitted to ICU have been demonstrated to have low platelet count making it one of the most common haematological abnormalities in these patients.[10] High morbidity and mortality which is associated with thrombocytopenia stems from the fact that patients who are admitted in ICU can have spontaneous bleeds when suffering from thrombocytopenia which may require urgent interventions to save the patient.[11] Platelet count had been studied for being an independent prognostic risk factor in ICU patients and linked to increased mortality, morbidity, and length of stay, independent of severity of illness or the number of dysfunctional organs at baseline. [12] We observed that 23.08% of the cases with mild thrombocytopenia had hospital stay of more than 7 days, while 35.7% of moderate thrombocytopenia cases had more than seven days of hospital stay. Among cases with severe thrombocytopenia, 40.5% of the cases had a hospital stay of more than 7 days. Thus the duration of hospital stay was not found to be significantly associated with the severity of thrombocytopenia (p value = 0.65). None of the previous studies evaluating pediatric population assessed association between severity of thrombocytopenia and duration of hospital stay. However, it has been studied in adult populations. Ibrahim et al in their study found no significant association between platelet counts at the time of admission and use of interventions like fluids with the location of hospital stay.[13] Similar to this, Jayanthi and Tulasi also observed a significantly inverse correlation between platelet count and the length of hospital stay.[14]

Cases with mild thrombocytopenia had platelet normalization in mean 5.3 days, while for moderate thrombocytopenia a mean duration of 5.36 days was required for platelet count normalization. A mean of 6.73 days was taken by cases with severe thrombocytopenia for normalization of platelet count. In the study by Gutthi et al, patients took 2 to 8 days for the platelets to return to normal count and it was not dependent on whether they received single donor platelets or not.[1] In a study from Saudi Arabia, median symptom duration was eight days while that of total hospitalisation was four days.[15] In another study Lye et al reported, the mean length of hospital stay to be four days among adults admitted with dengue.[16] In their study older patients were more likely to receive a pressure transfusion however age was not significantly associated with a longer duration of hospital stay or mortality.

In our study 8 patients that is 10% of study cases required platelet transfusion who were having active

bleeding manifestations, due to hepatic dysfunction and DIC in addition to severe thrombocytopenia. Remaining patients with severe thrombocytopenia did not require platelets transfusion as they had no any active bleeding signs and hepatic dysfunctions. These patients responded to fluid therapy according to the WHO guidelines.

There were a total of 5 deaths (6.17%). There was one case with mild thrombocytopenia and moderate thrombocytopenia each and three cases with severe thrombocytopenia. Among all the 5 deaths, all were dengue patients with variable platelet counts but, all 5 had severe hepatic dysfunction, DIC and shock. One patient in addition had ARDS and the other in addition had acute dengue encephalopathy.

We observed that the severity of thrombocytopenia was not significantly associated with the final outcome of the patients (p value = 0.65). In the study by Gutthi et al, 94% of the patients had a good recovery and rest did not survive. Among the 6 deaths, three were due to sepsis, two were due to complicated malaria and one was due to underlying ALL. [1] In another study by Nair et al, mortality rate was 1.11%, both due to dengue. Shewale et al reported case fatality rate was 7.36% among children with dengue. [17] Mortality rate was significantly higher in cases diagnosed with severe dengue as compared with those patients who presented with one or more warning sign (21.4% vs 1.4%).

Conclusion

Based on the results of the present study, we conclude that:

1. Acute febrile illness with thrombocytopenia is one of the commonest causes of admissions in paediatric ward and PICU.
2. Petechia/purpura rash were the most common general examination finding and hepatomegaly was the most common finding on per abdomen examination.
3. Most of the patients admitted in PICU, not only had severe thrombocytopenia with fever, but also had other complications like shock, leak syndrome, hepatic dysfunction and DIC.
4. Dengue was the commonest cause of fever with thrombocytopenia followed by rickettsial fever then sepsis.
5. Low platelet count is not the only independent high risk factor for mortality.

Febrile thrombocytopenia is a challenging problem in clinical practice to diagnose and is usually caused by infections. Dengue was the most common cause of febrile thrombocytopenia in our study population and is endemic in India.

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