

To Study Acute Febrile Illness with Thrombocytopenia in Children**Shivani C. Rampure¹, Sneha Patil²**¹Assistant Professor, Dept. of General Surgery, Mahadevappa Rampure Medical College, Kalaburgi²Dept. of Pediatrics

Received: 09-01-2026 / Revised: 11-02-2026 / Accepted: 19-03-2026

Corresponding Author: Dr. Sneha Patil

Conflict of interest: Nil

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 an 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.**DOI:** 10.25258/ijpqa.17.3.59

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Commencing the study of the very important group of diseases to which humankind 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 an 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 symptoms 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.

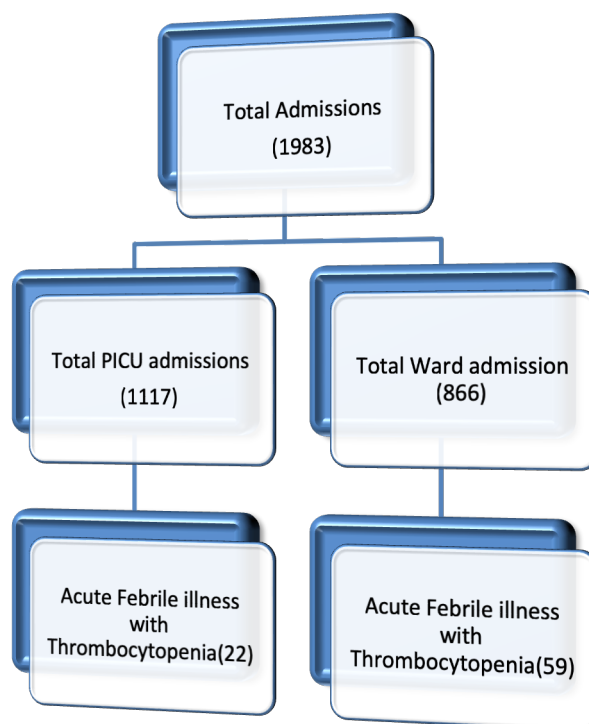
2. Patients on drugs causing thrombocytopenia.
3. Diagnosed cases of platelet disorders causing thrombocytopenia

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

Flow chart showing frequency of study cases, among total admissions occurred in paediatric ward and PICU in the time duration from October 2018 to April 2020.



Total frequency of study cases of acute febrile illness with thrombocytopenia admitted in paediatric ward and PICU among 1983 patients, admitted in

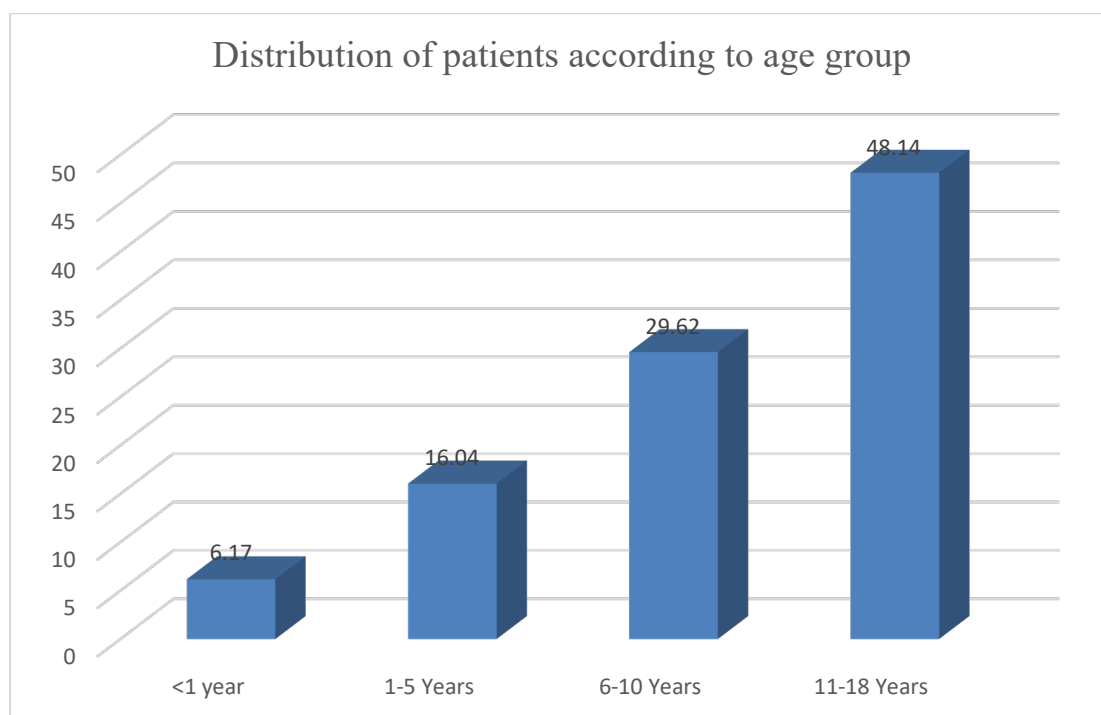
the duration of 18 months in Bharati Vidyapeeth (Deemed to be University), Medical College & Hospital, Sangli = 4%

Table 1: Distribution of patients according to their age

Age	Total (n=81) %
<1 year	05 (6.17%)
1-5 Years	13 (16.04%)
6-10 Years	24 (29.62%)
11-18 Years	39(48.14)

In the present study, 81 patients were included. Patients aged less than 1 year comprised of 6.17% of

the patients, 1 to 5 years were 16.04%, 6 to 10 years were 29.62% and 11 to 18 years were 48.14%.

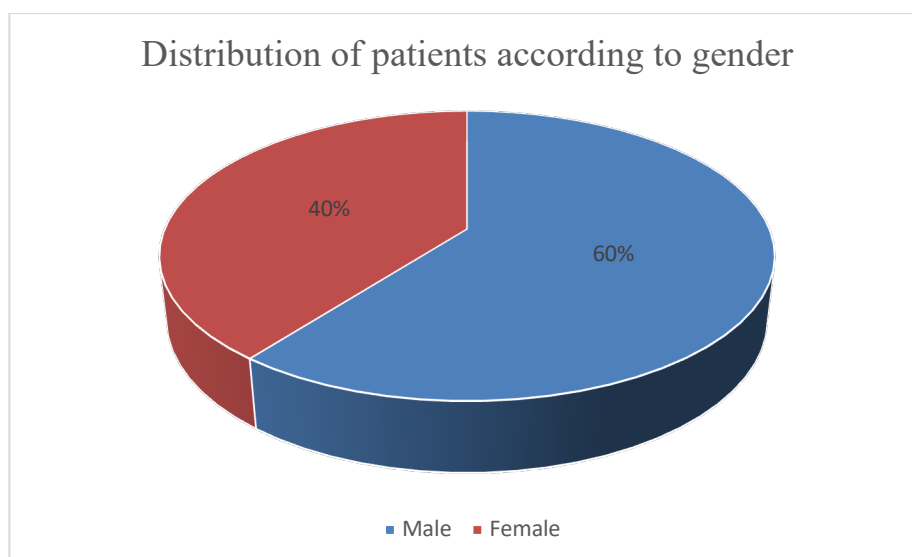


Graph 1: Distribution of patients according to age group

Table 2: Distribution of patients according to their gender

Sex	Total (n=81) %
Male	49 (60.49%)
Female	32 (39.50%)

In the present study, 39.5% of the patients were females (n=32) and rest being males (60.49%, n=49).



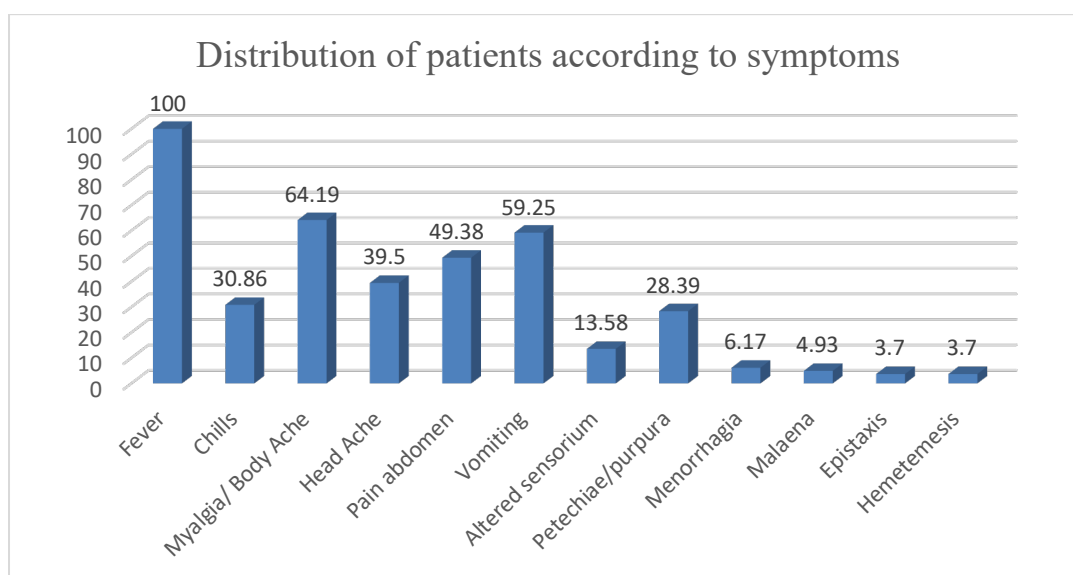
Graph 2: Distribution of patients according to gender

Table 3: Distribution of patients according to their symptoms

Symptoms	Total (n=81) %
Fever	81 (100%)
Chills	25 (30.86%)
Myalgia/ Body Ache	52 (64.19%)
Head Ache	32 (39.50%)
Pain abdomen	40 (49.38%)
Vomiting	48 (59.25%)
Altered sensorium	11 (13.58%)
Petechiae/Purpura	23 (28.39%)
Menorrhagia	05 (6.17%)
Malaena	04 (4.93%)
Epistaxis	03 (3.70%)
Hemetemesis	03 (3.7%)

It was observed that fever was observed in all the patients (100%). Myalgia/body ache was present in 64.19% of the patients, vomiting in 59.25%, pain in abdomen in 49.38%, chills in 30.86% and altered

sensorium in 13.58%, Petechiae/purpura in 28.39%, Menorrhagia in 6.17%, Malaena in 4.93%, Epistaxis in 3.7% and Hemetemesis in 3.7% as well.



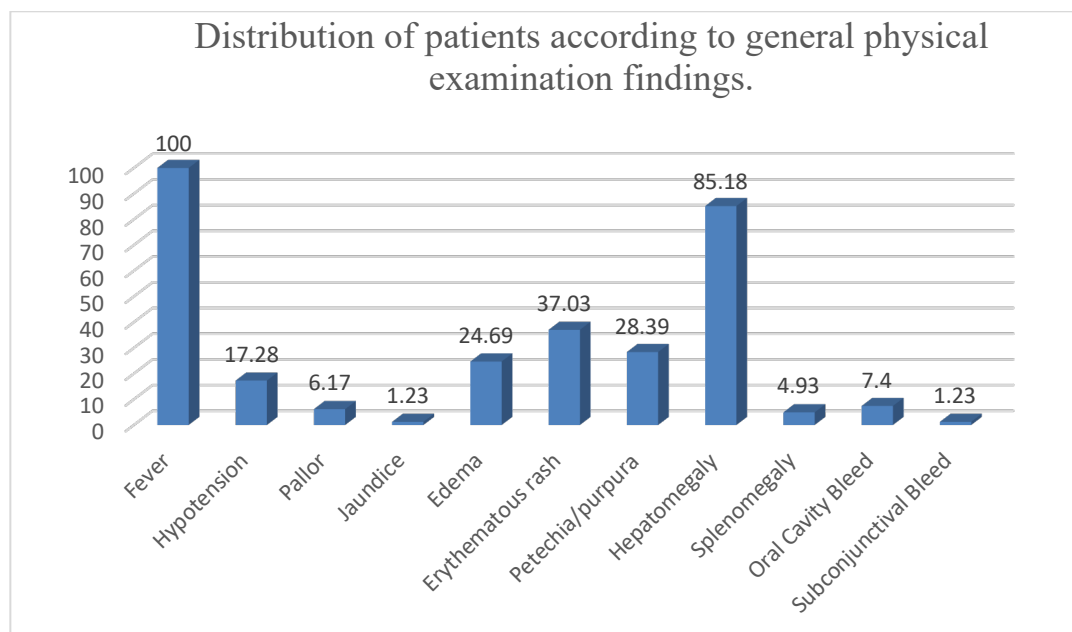
Graph 3: Distribution of patients according to symptoms

Table 4: Distribution of patients according to their general physical examination findings

Findings	Total (n=81) %
Fever	81(100%)
Hypotension	14(17.28%)
Pallor	05 (6.17%)
Jaundice	01 (1.23%)
Edema	20 (24.69%)
Erythematous Rash	30 (37.03%)
Petechiae /Purpura	23 (28.39%)
Hepatomegaly	69 (85.18%)
Splenomegaly	4 (4.93%)
Oral cavity bleed	06 (7.4%)
Subconjunctival haemorrhage	01 (1.23%)

On examination, we observed that high body temperature was present in all the patients (100%), as it was our inclusion criteria for the study. Hepatomegaly was present in 85.18% of the patients. Erythematous Rash was present in 37.03%, Petechiae or purpura were present in 28.39%, edema

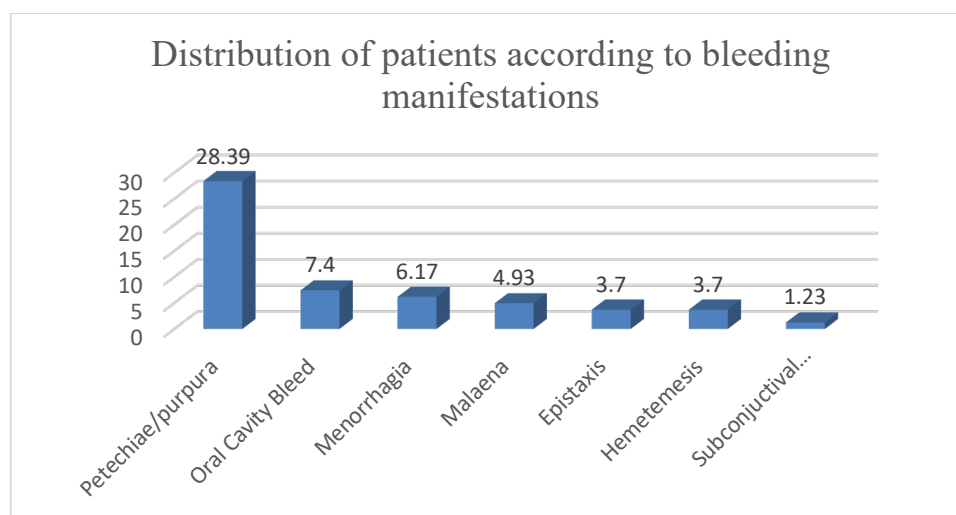
in 24.69%, hypotension in 17.28%, pallor in 6.17%, splenomegaly in 4.93% and jaundice was present in 1.23% of the patients. Oral cavity bleed was present in 7.4% and subconjunctival hemorrhage was present in only one patient.

**Graph 4: Distribution of patients according to general physical examination findings.****Table 5: Distribution of patients according to their bleeding manifestations**

Bleeding Manifestations	Total (n=81) %
Petechiae/purpura	23 (28.39%)
Oral Cavity Bleed	06 (7.40%)
Menorrhagia	05 (6.17%)
Melaena	04 (4.93%)
Epistaxis	03(3.70)
Hematemesis	03 (3.7%)
Subconjunctival Hemorrhage	01(1.23%)

We observed that the most common bleeding manifestation was petechia/purpura seen in 28.39% of the patients. Next most common bleeding manifestation was oral cavity bleed, seen in 7.4%,

menorrhagia was present in 6.17%, melaena in 4.93%, epistaxis in 3.7%, hematemesis in 3.7% and subconjunctival hemorrhage in 1.23%.



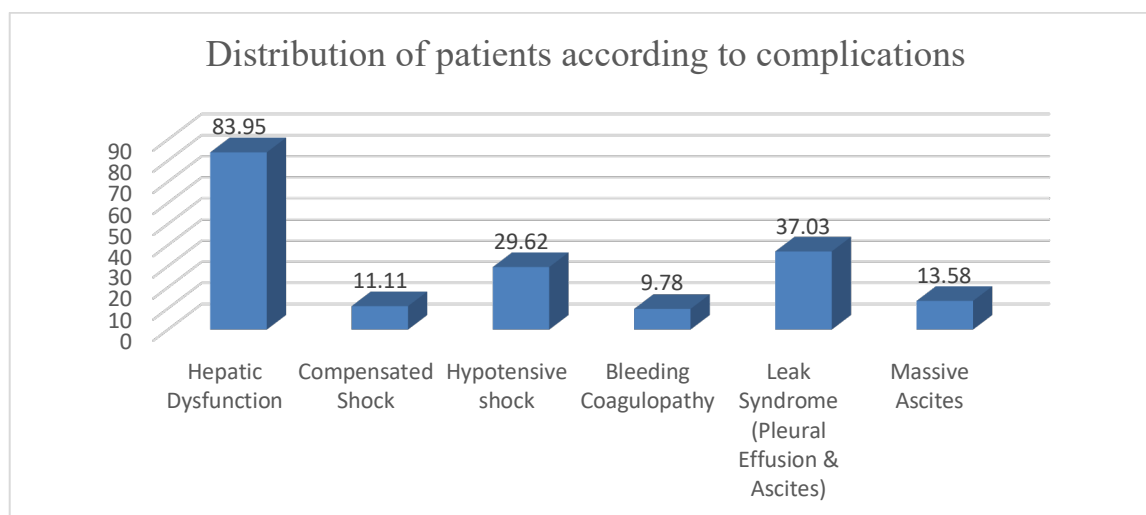
Graph 5: Distribution of patients according to bleeding manifestations

Table 6: Distribution of patients according to their complications.

Complications	Total (n=81) %
Hepatic Dysfunction	68 (83.95%)
Compensated Shock	09 (11.11%)
Hypotensive shock	24 (29.62%)
Bleeding Coagulopathy (DIC)	08 (9.87%)
Leak Syndrome (Pleural Effusion & Ascites)	30 (37.03%)
Massive Ascites	11 (13.58%)

The most common complication observed in our study population was hepatic dysfunction, seen in 83.95% of the patients. Hepatic dysfunction in the present study is defined on the basis of raised SGOT/SGPT, deranged coagulation profile, tender hepatomegaly, ascites, hypoalbuminemia, and also

Ascitis and hepatomegaly on USG reports. Bleeding coagulopathy (DIC) were present in 9.87%, leak syndrome was present in 37.03%, hypotensive shock was present in 29.62%, massive ascites was present in 13.58% and compensated shock was present in 11.1%.



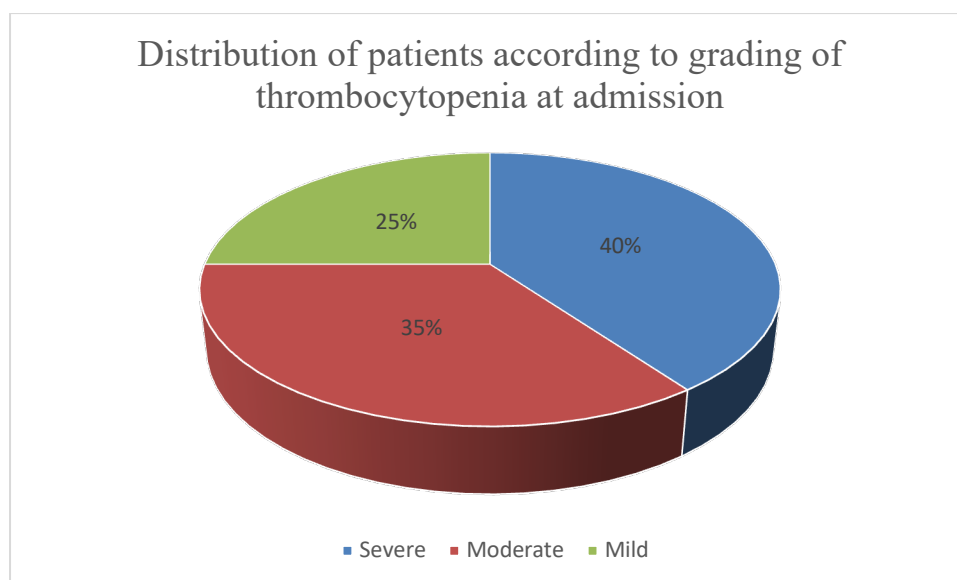
Graph 6: Distribution of patients according to complications

Table 7: Distribution of patients according to the Grading of thrombocytopenia at admission.

Platelet Count	Grade of Thrombocytopenia	Total (n=81) %
<50,000	Severe	33 (40%)
50,000- <1,00,000	Moderate	28 (35%)
1,00,000- <1,50,000	Mild	20 (25%)

Of the 81 patients, severe thrombocytopenia was present in 40% of the patients. Moderate

thrombocytopenia was present in 35% and 25% had mild thrombocytopenia.



Graph 7: Distribution of patients according to grading of thrombocytopenia at admission

Table 8: Description of patients according to their hematological and liver parameters

Laboratory parameters	Minimum	Maximum	Mean $\pm$ SD
Hemoglobin (gm%)	7.1	19	12.85 $\pm$ 2.07
PCV	22	57	39.18 $\pm$ 6.19
TLC (per cumm)	1000	23700	5550.62 $\pm$ 4242
Polymorphs (per microL)	19	93	59.47 $\pm$ 17.85
Lymphocytes (per microL)	4	77	31.95 $\pm$ 17.68
Platelet Count ((per mL)	13000	144000	68827.16 $\pm$ 38504
SGOT (IU/L)	20	4466	214.53 $\pm$ 47.23
SGPT (IU/L)	10	2651	111.06 $\pm$ 12.42

The above table describes the hematological parameters of the patients included in the study. 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 found to be 68827.16 per ml. We found that mean SGOT and SGPT levels were 214.53 and 111.06 IU/L respectively.

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%

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%

In the present study, 81 patients were included, patients aged less than 1 year comprised of 6.17% of the patients, 1 to 5 years were 16.04%, 6 to 10 years were 29.62% and 11 to 18 years were 48.14%. So, 11 to 18 years was the most common age group. Age group of 11 to 18 years is the one with increased outdoor activity and thereby increased risk of exposure to mosquito vectors as compared to pre-schoolers. In the present study, 39.5% of the patients were females (n=32) and rest being males (60.49%, n=49).

In a similar study, Gutthi et al evaluated the clinical profile and assessed clinical outcomes of children with febrile thrombocytopenia. [1] Of the 100 patients of fever with thrombocytopenia, 54% were males and rest were females. The authors observed that 41% of the cases were aged 6 to 10 years. Gowd et al performed a study to elicit the causes of febrile thrombocytopenia among children presenting to the hospital. [4] The authors observed that 40% of the patients in five years of age and 45% of the sample size comprised of male children. Nair et al evaluated the clinical profile of children presenting with fever and thrombocytopenia and evaluated the association between severity of thrombocytopenia and their clinical presentation. [5] They included children up to 18 years of age. The authors observed thrombocytopenia to be more common among male children as compare to female patients (52.22% vs 47.78%) In another study, Rambhatta et al assessed the underlying causes of thrombocytopenia in children presenting with fever. [6] The study group consisted of 306 children with febrile thrombocytopenia. One hundred and fifty-five (50.7%) children were more than 10 years of age, 101 (33%) in the 6-10 years age group, 43 (14.4 %) in the 1-5 year age group and 7 (2.3%) were infants. Of the children, 184 (60%) were males. Shewale et al evaluated the clinical profile and clinical outcomes in children diagnosed with dengue. [7] The authors included 95 patients who presented with warning signs of dengue or features suggestive of severe dengue. Out of 95, 68(71.5%) were male and 27(28.4%) were female. Seventy children (73.68%) patient were aged above 8 year while 26.3% were less than 8year of age.

We observed that fever was observed in all the patients (100%). Myalgia was present in 64.19% of the patients, vomiting in 59.25%, pain in abdomen in 49.38%, chills in 30.86% and altered sensorium in 13.58%, Petechiae/purpura in 28.39%, Menorrhagia in 6.17%, Malaena in 4.93%, Epistaxis in 3.7% and Hemetemesi in 3.7% as well. On examination, we observed that high body temperature in all the patients (100%), hepatomegaly in 85.18%, erythematous rash in

37.03%, edema in 24.69%, hypotension in 17.28%, pallor in 6.17%, splenomegaly in 4.93% and jaundice was present in 1.23% of the patients. In addition, oral cavity bleed was present in 7.4% and subconjunctival hemorrhage was present in only one patient.

In a similar study, Gutthi et al observed that the most common presenting symptoms among these patients was abdominal pain (seen in 43% of the cases) and vomiting (seen in 38% of the cases). Other common complaints being headache bodyache and jaundice [1]. Furthermore, the authors observed that abdominal pain was the most common feature in patients diagnosed with dengue followed by vomiting, purpura, GI bleed and malena. On systemic examination hepatomegaly was a observed in 41%, large spleen was observed in 32% and 55% had both enlarged spleen and liver. Enlarged lymph nodes were present in only 5% of the patients.

In the study by Gowd et al, approximately half of all the children included in the study had presenting features of pain abdomen, decreased urine output and dark stools.[4] The authors observed that the presence of warning symptoms what is significantly associated with the clinical outcomes of these patients (p value <0.001). In addition 20% head shock 19% had warning symptoms 30% had respiratory distress and another 25% had distended abdomen. In another study, Nair et al observed that the most common clinical presentation was fever, myalgia, painful joints, headache, pain abdomen, nausea and vomiting [5] Only 5% of the cases had cough and dyspnoea. The authors reported 2 deaths in the study population which were due to dengue.

We observed that the most common bleeding manifestation was petechia/purpura seen in 28.39% of the patients. Next most common bleeding manifestation was oral cavity bleed, seen in 7.4%, menorrhagia was present in 6.17%, malena in 4.93%, epistaxis in 3.7%, hematemesis in 3.7% and subconjunctival hemorrhage in 1.23%. The most common complication in our patients was hepatic dysfunction, seen in 83.95% of the patients. Hepatic dysfunction in the present study was defined on the basis of raised SGOT/SGPT, deranged coagulation profile, tender hepatomegaly, ascites, hypoalbuminemia, and also Ascitis and hepatomegaly on USG reports. Leak syndrome was present in 37.03%, hypotensive shock was present in 29.62%, massive ascites was present in 13.58% and compensated shock was present in 11.1%, bleeding coagulopathy (DIC) was present in 9.87%. The reason high incidence of hepatic involvement in my study was because of high incidence of dengue fever with warning signs and severe dengue that is 76.5%. Dengue virus is a hepatotropic virus and hepatic dysfunction is caused by direct effect of dengue virus on liver cells and as a consequence of deranged post immune response against virus.

In a study by Iqtadar S, hepatic failure was observed in 38% of those diagnosed with dengue and 18% in those diagnosed with dengue haemorrhagic fever. [7] For the more India study 85% had elevated AST and 51% had raised ALT. Ahmed and colleagues reported AST levels two times that of ALT levels in such patients [8] Although bench research has not provided any concrete evidence as to the hepatotropic nature of dengue virus, the above mentioned evidence points towards the fact that hepatic failure is fairly common among patients diagnosed with dengue. More so, Parkash et al demonstrated high AST in 95% and high ALT in 86% of the patients. [9] This high percentage of liver involvement could be explained by the fact that patients diagnosed with only dengue haemorrhagic fever with included in the study. No third reported three deaths in patients who had severe hepatitis C, hypotension and acalculous cholecystitis.

In the study by Gutthi et al, bleeding manifestations were seen in 45% of the patients [1] GI bleed and malena was observed in Half of all patients with bleeding manifestations while petechia was present in 35% and bleeding from nose in 18%. Nair et al observed 19% of the patients to have bleeding manifestations, major bleeding features included skin and mucosal bleeds while approximately 4% had gum bleeding. Less common bleeding manifestations including haematemesis, malina, epistaxis, subconjunctival haemorrhage and intracranial bleed.

Study done by Anjali S Raj et al, 10% of the patients had shock which was refractory to fluid therapy and blood products. Leak syndrome was found in 50.4%. [10] In the study done by Subramanian. V et al, shock was documented in 13.19% of patients, thus above mentioned results correlate with my study results.[11]

In another study, Ramabhatta et al reported that Eighty-seven (28.4%) children had bleeding symptoms. Among them, 55 (63%) had subcutaneous bleeding.[4] Mucosal bleeding, in the form of epistaxis, gum bleeding, haematuria, melaena, haematemesis and intracranial haemorrhage, was seen in 32 (37%) children.

Of the 81 patients in our study, severe thrombocytopenia was present in 40% of the patients. Moderate thrombocytopenia was present in 35% and 25% had mild thrombocytopenia. In our study 76.5% of the case studies were due to dengue infections, the reason for thrombocytopenia is due to increased peripheral destruction of antibody coated platelets, acute bone marrow suppression, mild DIC like presentation, adhesion of platelets to sticky vascular endothelium.[12]

In a similar study, Gutthi et al found mild, moderate and severe thrombocytopenia in 22% 39% and 39% of the cases respectively. [1] In another study from

Sri Lanka, Ramabhatta et al reported that the platelet count was between 100,000-150,000/mm³ in 107 (35%) children, 50,000-100,000/mm³ in 85 (28%), 20,000-50,000/mm³ in 88 (29%) and less than 20,000/mm³ in 26 (8%) children [4] In the study by Nair et al, platelet count was less than 10,000/ mm³ in 133.3%, 10,000 – 20,000 / mm³ in 16.6%, 20,000 – 50,000 / mm³ in 23.8% and more than 50,001 mm³ in 46.1% of the patients. [5]

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.

References

1. Lakshmi Prasanna Gutthi. Sunita Vegesna, Varanasi Pundarikaksha, swetha Kolla, Manasa Gundapaneni, Prudhvi Krishna Karimi. A study of clinical and lab profile of fever with Thrombocytopenia, International Journal of Contemporary medical Research 2017; 4(5):1057-1061.
2. Y Vijapura, Preeti shah, Mayank Jain. "Fever with thrombocytopenia current scenario". Journal of Evolution of Medical & Dental sciences 2015; 4(21): 3709-3714.
3. Linda S Nield and Deepak Kamnt, Fever, first south Asia Edition, Elsevier, 2015, 1277-1279
4. Ramabhatta S, Kariyappa P, Kondappa B, Rao U, Sanikam H. An aetiological profile of febrile thrombocytopenia in children. Sri Lanka Journal of Child Health. 2018 Jun 5;47(2):146-8
5. Ambruso DR, Hays T and Goldenberg N. Hematological disorders in current pediatric diagnosis and treatment 18th edition a Lange medical books/Mc Graw-Hill. 2007:860-862.
6. Shewale NS. Clinical profile and outcome of children admitted for dengue with warning

- signs and severe dengue. *MedPulse International Journal of Pediatrics*. July 2017; 3(1): 23-27
7. Iqtadar S, Akbar N, Naima H, Randhava FA. Profile of Hepatic Involvement in Dengue Infections in adult Pakistani population. *Pak J Med Sci* 2017; 33:963-967
 8. Parkash O, Almas A, Jafri SM, et al. Severity of acute hepatitis and its outcome in patients with dengue fever in a tertiary care hospital Karachi, Pakistan (south asia). *BMC Gastroenterol* 2010; 10:43-47
 9. Jawed Ahmed Badvi, Bahawaluddin Jamro, Aftab Ahmed Soomro, Shankar Lal, Saifullah Jamro. An experience of thrombocytopenia in children at tertiary care hospitals sukkur and larkana MC. 2012; 19:23-26
 10. Anjali S Raj, Sucheta Munshi, Bela H Shah. A study on clinical presentation of dengue fever in children. *International journal of Science and Research* 2016;5(4): 2272-2275.
 11. Dinarello CA, Cannon JG, Wolff SM. New concepts on the pathogenesis of fever. *Rev Infect Dis*. 1988 Jan-Feb;10(1):168-89
 12. Derek S Wheeler, Hector R Wong, Thomas P Shanley. *Paediatric Critical Care Medicine: Basic Science And Clinical Evidence* [internet] London: Springer Science + Business Media; 2007. Chapter 15, Molecular Biology in the Paediatric Intensive Care Unit.