# Etiology, treatment and outcome of pediatric thrombocytopenia due to infection: A prospective study

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## Abstract
**Introduction:** Thrombocytopenia is defined as decrease in the peripheral platelet count or low level of platelets in peripheral blood. Platelets are derived from megakaryocytes in the bone marrow. Platelets help in stoppage of bleeding.
**Objective:** To evaluate the causes, treatment required for infections associated with thrombocytopenia and their outcome.
**Materials and Methods:** This study was a prospective study over a period of 2 years between 2006 and 2007; total of 101 pediatric patients were included in this study between the ages 1 month and 15 years. Children with platelet count below 1, 50,000 /cu.mm were included.
**Results:** The male to female ratio was 2:1. A seasonal pattern was observed, 25.7 % of cases were in June and 52.4 % of the cases were between June and September. History of fever was present in all cases followed by vomiting and rash. The outcome was good and 93.6 % of the cases were improved and discharged after full recovery.
**Conclusion:** Dengue fever was the most common infection to causing thrombocytopenia followed by Non specific viral hemorrhagic fever and others. All the patients require good supportive treatment and specific treatment of etiology in case of other causes.

**Keywords:**Thrombocytopenia, Dengue fever, Platelet count, Rash, Petechiae.

## Introduction
Thrombocytopenia is defined as a platelet count below the normal range for the population (+ 2 standard deviations). In most laboratories, a normal platelet count is between 1, 50,000 to 4, 50,000/cu. Mm3.Thrombocytopenia can be inherited or acquired. Abnormally low platelets may be caused by dehydration, vitamin B12 or folic acid deficiency, leukemia, viral and bacterial infections, sepsis etc.Thrombocytopenia in children is the second most common hematological problem after anemia. Infection can produce thrombocytopenia through immune destruction, disseminated intravascular coagulation, hypersplenism, excessive consumption, marrow suppression, and medications. Common infections associated with thrombocytopenia are malaria, enteric fever, dengue fever, bacterial sepsis, Human Immunodeficiency Virus infection, Cytomegalovirus and Epstein-Barr viruses. The clinical features include features of the infection and the features of platelet deficiency. Treatment options include treating the infection, supportive treatment and platelet transfusion. Treatment to raise the platelet count, even when profoundly low is not always required.

## Aims and objectives of the study
To evaluate the causes, treatment required for infections associated with thrombocytopenia and their outcome.

## Materials and Methods
This study was a prospective study conducted over a period of 2 years 2006-2007, in Children's Medical Centre (Pediatric Ward), Krishna Institute of Medical Sciences, Secunderabad. Children from the age of 1 month to 15 years admitted with features of infection and found to have thrombocytopenia(platelet count <1,50,000/cu.mm) were included in the study.

### Inclusion Criteria
Children with features of infections and associated thrombocytopenia (platelets<1, 50,000/cu.mm)

### Exclusion Criteria
Children with thrombocytopenia due to other causes like Idiopathic Thrombocytopenic Purpura, drug induced thrombocytopenia, and malignancies etc. were excluded.

Children admitted in Children's Medical Centre (pediatric ward), Krishna institute of medical sciences, Secunderabad with features of infections like acute onset of fever were evaluated. Children found to have thrombocytopenia on complete blood picture; platelet count was confirmed by peripheral blood smear examination. They were further investigated for the possible cause of infection if not evaluated at the time of admission. Blood culture and chest radiograph were performed on infants with high grade fever without a focus of infection. Older infants with high grade fever without focus of infection were subjected to blood culture if fever is less than 7 days and Widal test if fever is 7-14 days duration. Parasite F/V or Smear for Malaria parasite was also performed.

Children with fever with rash or Petechiae or bleeding through orifices were subjected to Parasite Plasmodium Falciparum/Vivax and Dengue serology if the fever is more than 5 days duration. Children, who were in shock and those with disseminated intravascular coagulation, were subjected to blood culture, parasite F/V and Dengue serology if the fever is more than 5 days duration. They were commenced on treatment based on the etiology of fever. Drugs known to cause thrombocytopenia were avoided. Treatment of malaria

and dengue fever was based on WHO guidelines. Transfusion of platelets was done based on Red Cross guidelines.

## Results

Total numbers of patients studied were 101. Out of 101 patients studied 68 patients were male (67.3 %) and 33 patients were female (32.7 %). The youngest child admitted was a month and the total number of infants was 12.

| Age Group | Number of the Child |
|---|---|
| 1 Month -1 Year | 12 |
| 1-5 years | 37 |
| >5 years | 52 |
| **Total** | **101** |

In this study, maximum number of children was admitted in the month of June-26(25.7%) and average number of days of stay- 5.7 days

**Table 1:**

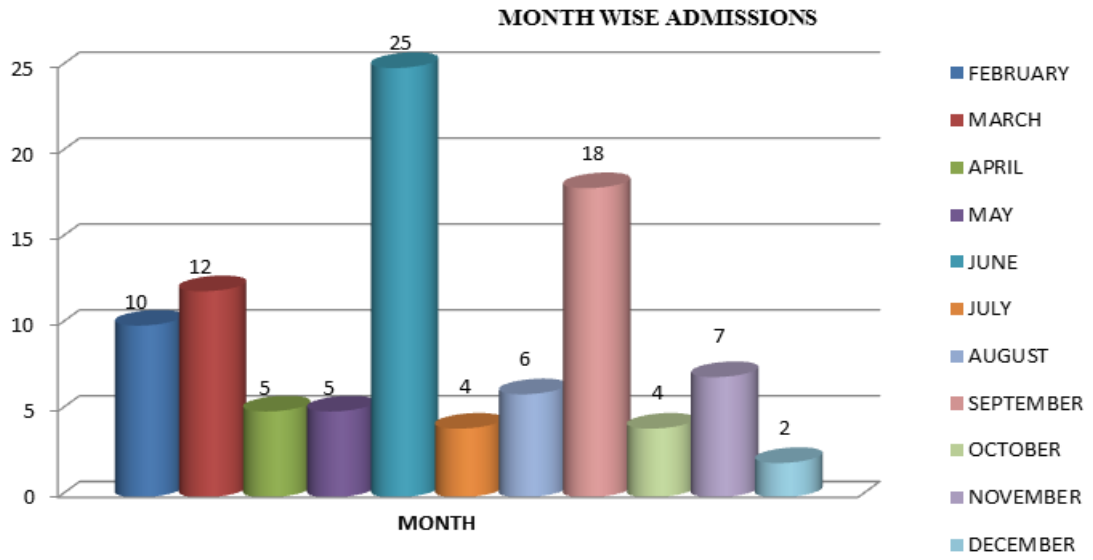


**Fig. 1:**

In this study, all the patients presented with fever followed by vomiting and rash, least common clinical feature was cough. Pattern of bleeding manifestations were predominantly petechiae followed by positive HESS test and least common was ecchymosis. When the diagnoses of these cases were made and the most common cause for fever with thrombocytopenia dengue fever followed by viral hemorrhagic fever and least common was malaria and streptococcal pharyngitis.

**Table 2:**

| Diagnosis | Number of patients |
|---|---|
| Viral hemorrhagic fever | 23 |
| Meningococcal septicemia | 3 |
| Falciparum Malaria | 8 |
| Vivax Malaria | 1 |
| Enteric fever | 9 |
| Dengue fever | 44 |
| Acute bronchopneumonia with septicemia | 2 |
| Acinetobacter septicemia | 2 |
| Acute viral hepatitis A | 3 |
| Chikungunya | 5 |
| Streptococcal pharyngitis | 1 |

In this study, when severity was estimated, most of the cases showed grade 1 thrombocytopenia (67 %) - platelet count between 75,000 and 1, 50,000 /cu.mm. 10 % showed grade 2 thrombocytopenia – platelet count between 50,000 and 75,000 /cu.mm. 12 % of the cases showed grade 3 thrombocytopenia- platelet count between 25,000 and 50,000/cu.mm and 11 % of the cases had grade 4 thrombocytopenia – platelet count below 25,000 /cu.mm.

In the study, the outcome was good and 93.6 % of the cases were improved and discharged after full recovery. 1.9 % of the cases Left against Medical Advice (LAMA) and remaining 4.9 % of the cases expired due to bleeding manifestations.

## Discussion

Thrombocytopenia is a condition characterized by abnormally low levels of thrombocytes or platelets in the blood. A normal human platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. Thrombocytopenia may be due to decreased production or increased destruction. Some of the causes for decreased production include dehydration, deficiency of folic acid and vitamin B12, leukemia and my elodysplastic syndromes, aplastic anemia, decreased production of thrombopoietin by liver due to liver disorders or liver failure, various infections such as bacterial, viral and leptospirosis. Immune and non-immune conditions lead to increased destruction of platelets as in cases of Immune thrombocytopenic purpura,

thrombotic thrombocytopenia purpura, and hemolytic uremic syndrome, disseminated intravascular coagulation, anti-phospholipid syndrome, dengue fever, zika virus fever and systemic lupus erythematosus. Thrombocytopenia can be drug induced due to medications such as valproic acid, methotrexate, carboplatin etc. Laboratory investigations for low platelet count include complete blood picture, liver and renal function tests, vitamin B12 and folic acid levels and peripheral blood smear examination. If the cause for thrombocytopenia is still unclear then a bone marrow biopsy is usually recommended.

Classic dengue fever is primarily a disease of older childrenand adults. It is characterized by the sudden onset of fever anda variety of nonspecific signs and symptoms, including frontalheadache, retro-orbital pain, body aches, nausea and vomiting, joint pains, weakness, and rash. Patientsmay become anorexic, can have altered taste sensorium, and have a mild to moderatesore throat and dryness of the mouth. Constipation, diarrheaand respiratory symptoms are infrequently reported and mostly due to concurrent infections. The initial temperature may rise to 102 to 105 degreesF, and fever may last for 2 to 7 days. The temperature may drop after a few days, only to rebound 12 to 24 h later (saddleback fever). A relativebradycardia may be noted despite the fever and lymphadenopathy is seen in few patients. Rash is variable but occurs in up to50% of patients as either early or late eruptions. Facial flushingor erythematous mottling may occur coincident with or slightlybefore onset of fever and disappears 1 to 2 days after onset of symptoms. A second rash, varying in form from scarlatiniform to maculopapular, may appear between days 2 and 6 of illness. The rash usually begins on the trunk and spreads to the faceand extremities. In some cases, an intense erythematous patternwith is lands of normal skin is observed. The average durationof the second rash is 2 to 3 days. Toward the end of the

Febrile phase of illness or after the temperature falls to orbelow normal, petechiae may appear; these may be scatteredor confluent. Intense pruritus followed by desquamation on thepalms of the hands and soles of the feet may occur.Hemorrhagic manifestations in dengue fever patients arenot uncommon and range from mild to severe. Skin hemorrhages, including petechiae and purpura, are the most common,along with gum bleeding, epistaxis, menorrhagia, and gastrointestinal(GI) hemorrhage. Hematuria occurs infrequently, and jaundice is rare.

Dengue fever is generally self-limiting and is sometimes fatal when proper treatment is not initiated at right time.The acute phase of illness lasts for 3 to 7 days, but the convalescent phase may be prolonged for weeks and may be associated with weakness and depression, especially in adults. No permanent sequelae are known to be associated with this infection.

In this study, there was a male preponderance in our study. The male to female ratio was 2:1 which is in tandem with the study conducted by Choudhury J et al.[1] A seasonal pattern was observed, 25.7 % of cases were in June and 52.4 % of the cases were between June and September, 12.8 % of cases were from October to December, 31.6 % of cases were from February to May. Highest incidence occurred during the monsoon and post monsoon season. Wongkoon S, et al have also described seasonal pattern of dengue which corresponded with the rainy season due to abundance of mosquito breeding in the season.[2]History of fever was present in all cases. Vomiting and Rash were the next common symptom in our study which is correlation with the study conducted by Agarwal, et al, in their study they have also noted fever, abdominal pain and vomiting as the commonest symptoms.[3] In a study done by Choudhury et al, fever was the first common symptom followed by abdominal pain.[1]In the studies done by KabilanL et al, Kamath SR et al, Tantawichien T et al, Choudhury et al, the commonest hemorrhagic manifestation was hematemesis and epistaxis but petechiae was common in this study.[4-6]Hemoconcentraion, thrombocytopenia, abnormal liver function tests, ultrasono graphic evidence of hepatomegaly along with ascites and/or pleural effusion and gall bladder wall edema were noted in few cases. NS1 antigen was found in 84% of cases. Dengue IgM antibodies in 46 % of cases and IgG in 31% of cases (with and without coexisting NS1 positivity). Previous studies have also reported similar findings.[7,8]There was a clear correlation between platelet counts and bleeding manifestations, grade 3and grade 4 thrombocytopenia cases showed bleeding manifestations which is against the findings reported by Choudhury et al.[1]

## Conclusion

Despite high incidence of infection associated thrombocytopenia especially in India with tropical infectious diseases contributing a lion's share of pediatric mortality, there is a paucity of studies in pediatric population. This study shows that most of dengue fever is the most common infection to cause thrombocytopenia followed by Nonspecific viral hemorrhagic fever and others. All the patients require good supportive treatment and specific treatment of etiology in case of other causes.

**Conflict of Interest:** None.

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