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## Assessment of Clinical Profile and Management of Viral Fever with Thrombocytopenia in Paediatric Patients



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### ABSTRACT

**INTRODUCTION:** Viral fevers with thrombocytopenia is common especially during monsoon season. Viral fevers can cause thrombocytopenia. It is a major challenge to public health especially in South East Asia. We have done an observational study of viral fevers with thrombocytopenia in which we have studied the clinical profile and management pattern of viral fevers with thrombocytopenia. **AIMS AND OBJECTIVES:** An observational study was carried out in pediatric patients. Data was collected by intensive care record review. Patients of age group 1-14 years of both gender diagnosed of viral fever with thrombocytopenia were included. Clinical parameters and prescribing pattern in children presenting at various stages of viral fever with thrombocytopenia was analyzed. **RESULTS:** A total of 130 patients diagnosed with viral fever with thrombocytopenia with one or more warning signs were admitted during the study period. Most of the cases admitted are between 7-12 years (42%). Most admitted Gender is male 75(58%). Most common sign and symptom is fever 130(100%). Most of the cases have platelet count less than 1 lakh cu.mm (65%). PCV increased in 64 cases (49%). 20% cases had hepatomegaly. In management IV fluids given was DNS 110(85%), followed by ringer lactate and other. Most common Antibiotics prescribed was Ceftriaxone+sulbactam 65(50%), followed by Piperacillin+Tazobactam 45(34%), and other symptomatic treatment was given consist of Paracetamol 130(100%), H2 Blocker(ranitidine) 130(100%), corticosteroids 130(100%), and Anti-emetics(Ondansetron) 61 (47%). Platelet transfusion done to 11 (8.5%). **CONCLUSION:** Viral fevers like Dengue are the commonest cause for thrombocytopenia. Antibiotics though not a part of standard World Health Organization was seen to be an important part of management. Supportive care with judicious fluid management during the critical and recovery period with continuous monitoring is required for all patients.

## INTRODUCTION

Viral fever like dengue that causes thrombocytopenia is a self-limiting acute mosquito borne disease characterized by fever, headache, muscle and joint pains, rash, nausea and vomiting. It is caused by an arbovirus and spread by *Aedes* mosquitoes. Some infections result in hemorrhagic manifestations and in its severe form is known as dengue shock or severe dengue, which can threaten the patient's life primarily through increased vascular permeability and hypertensive shock. Time and again dengue has given rise to pandemics all over the world. Dengue has a wide spectrum of clinical presentations, often with unpredictable clinical evolution and outcome. A small proportion progress to severe disease characterized by plasma leakage with or without hemorrhage. World Health Organization (WHO) has conferred it as a notifiable disease and since 2005 dengue is considered as a public health emergency of international concern. <sup>[1]</sup> WHO statistics have also shown that dengue burden from children in South East Asian Region (SEAR) countries is increasing.

The first evidence of occurrence of dengue fever in India was reported during 1956. Every year during the period of July to November there is an upsurge in the cases of dengue /DHF. <sup>[2]</sup>

Children are at higher risk of acquiring severe dengue. Epidemiological studies conducted in India during 2001 dengue epidemic have shown that DHF has been predominantly restricted to children. <sup>[3-5]</sup> Reports from other studies have shown that deaths due to dengue are potentially avoidable, and morbidity can be reduced to a great extent with appropriate measures. <sup>[6]</sup> A broad-angled evaluation with integration of clinical and laboratory parameters would direct the disease process as well as the on-going treatment and outcome of the disease.

### **Epidemiology:**

Dengue is one of the most important emerging viral diseases of humans in the world afflicting humanity in terms of morbidity and mortality. Currently, the disease is endemic in all continents except Europe. The Epidemiology of dengue is a complex phenomenon that mainly depends upon an intricate relationship between the 3 epidemiological factors: the host (man and mosquito), the agent (virus) and the environment (a biotic and biotic factor). The complexity of relationship among these factors eventually determines the level of endemicity in an area.

### Agent Factor:

The dengue viruses are the members of the genus flavivirus. These small (50nm) viruses contain single stranded RNA. There are four virus serotypes, which are designated as DEN-1, DEN-2, DEN-3 and DEN-4. Although all four serotypes are antigenically similar, they are different enough to elicit cross-protection only for a few months after infection by any one of them. Infection with any one serotype confers lifelong immunity to the virus serotype. Man and mosquito are reservoirs of infection. Transovarian transmission (infection carried over to next progeny of mosquitoes through eggs) has made the control more complicated.

- At present DEN1 and DEN2 serotypes are widespread in India.

### Vector Dengue:

Viruses are transmitted by the bite of female *Aedes* (Ae) mosquitoes. *Aegypti* is the most potential vector but other species such as *Aealbopictus*, *Ae. Polynesiensis* and *Ae. Niveus* have also been incriminated as secondary vectors. In India *Ae. Aegypti* is the main vector in most urban areas; however, *Aealbopictus* is also found as vector in few areas of southern India.

- Dengue is transmitted by the bite of female *Aedes* mosquito.

Female *Aedes* mosquito deposits eggs singly on damp surfaces just above the water line. Under optimal conditions the life cycle of aquatic stage of *Ae. aegypti* (the time taken from hatching to adult emergence) can be as short as seven days. The eggs can survive one year without water. At low temperature, however, it may take several weeks to emerge. *Ae. aegypti* has an average adult survival of fifteen days. During the rainy season, when survival is longer, the risk of virus transmission is greater. It is a day time feeder and can fly up to a limited distance of 400 meters. To get one full blood means the mosquito has to feed on several persons, infecting all of them. A female *Ae. aegypti* mosquito.

### Environmental Factors:

The population of *Ae. aegypti* fluctuates with rainfall and water storage. Its life span is influenced by temperature and humidity, survives best between 16°-30° C and a relative humidity of 60-80%. *Ae. aegypti* breeds in the containers, in and around the houses. Altitude is an important factor in limiting the distribution of *Ae. Aegypti*, it is distributed between sea level and 1000 ft above sea level. *Ae. Aegypti* is highly anthropophilic and rests in cool shady

places. The rural spread of *Ae. aegypti* is a relatively recent occurrence associated with the development of rural water supply schemes, improved transport systems, scarcity of water and like style changes. *Ae. aegypti* breeds almost entirely in domestic man-made water receptacles found in and around households, construction sites and factories; natural larval habitats are tree holes, leaf axils and coconut shells. In hot and dry regions, overhead tanks and groundwater storage tanks become primary habitats. Unused tyres, flower pots and desert coolers are among the most common domestic breeding sites of *Ae. aegypti*.

**Host Factor:** Dengue virus infects humans and several species of lower primates but in India man is the only natural reservoir of infection. All ages and both sexes are susceptible to dengue fever. Secondary dengue infection is a risk factor for DHF including passively acquired antibodies in infants. Travel to dengue endemic area is an important risk factor, if the patient develops fever more than 2 weeks after travel, dengue is unlikely. Migration of patient during viremia to a non endemic area may introduce it into the area.

**Transmission cycle:** The female *Ae. Aegypti* usually becomes infected with dengue virus when it takes blood meal from a person during the acute febrile (viraemia) phase of dengue illness. After an extrinsic incubation period of 8 to 10 days, the mosquito becomes infected and virus is transmitted when the infective mosquito bites and injects the saliva into the wound of the person. There is evidence that vertical transmission of dengue virus from infected female mosquitoes to the next generation occurs through eggs, which is known as transovarian transmission.

### **Immuno-pathogenesis**

Primary or first infection in non-immune persons usually causes Dengue fever. Subsequent dengue infection by different serotype causes more severe illness like DHF/DSS. The key manifestations of the DHF/DSS are sudden onset of shock, capillary leakage, haemorrhagic diathesis/ thrombocytopenia occurring at the time of defervescence of fever. Pathogenesis is not well defined but it is suggested that it is mediated through soluble mediators, compliment activation and cytokines that are responsible for various manifestations. <sup>[4]</sup>

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates. Seen first as a disease but later recognized as an accompaniment to a variety of disease entities, fever is an easily noted and reliable marker of illness.

Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is such a common manifestation of illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history. Most cases of prolonged fevers are instances of well-known diseases manifesting them atypically.<sup>[7]</sup>

The actual pattern of graphic recording of fever is variable that it is not helpful in pointing to specific diagnosis at all times an aggressive diagnostic effort is usually justified because curative or palliative measures can so often brought into use once the diagnosis has been achieved.

Fever is defined as an elevation of the body temperature above the normal circadian range as the result of a change in the thermoregulatory center located in the anterior hypothalamus.

An Ante Meridiem (AM) temperature of  $>37.2^{\circ}\text{C}$  ( $98.9^{\circ}\text{F}$ ) or a Post Meridiem (P.M) temperature of  $>37.7^{\circ}\text{C}$  ( $99.9^{\circ}\text{F}$ ) would define fever.<sup>[7]</sup>

### **Definitions of Febrile Patterns:**

The types of febrile patterns have been traditionally grouped according to the definitions listed below. Often, within these groups, specific infectious diseases may occur.<sup>[8]</sup>

**1. Continuous (sustained):** Fever does not fluctuate more than about ( $1.5^{\circ}\text{F}$ ) during 24 hours, but at no time touches the normal.

e.g.: Pneumonia, Rickettsial diseases, Typhoid fever central nervous system disorders, Tularemia, and Falciparum (malignant tertian malaria).<sup>[7]</sup>

**2. Intermittent fever:** When fever is present only for several hours during the day, it is called intermittent fever.

When a paroxysm of intermittent fever occurs daily, the fever is described as Quotidian, when on alternate days, it is tertian, when two days intervene between consecutive attacks, is quartan.<sup>[7]</sup>

E.g.: Localized pyrogenic infections and bacterial endocarditis; Malaria (commonly with leucopenia) may present as quotidian (daily spike), tertian (spike every third day), or quartan (spike every fourth day) types.

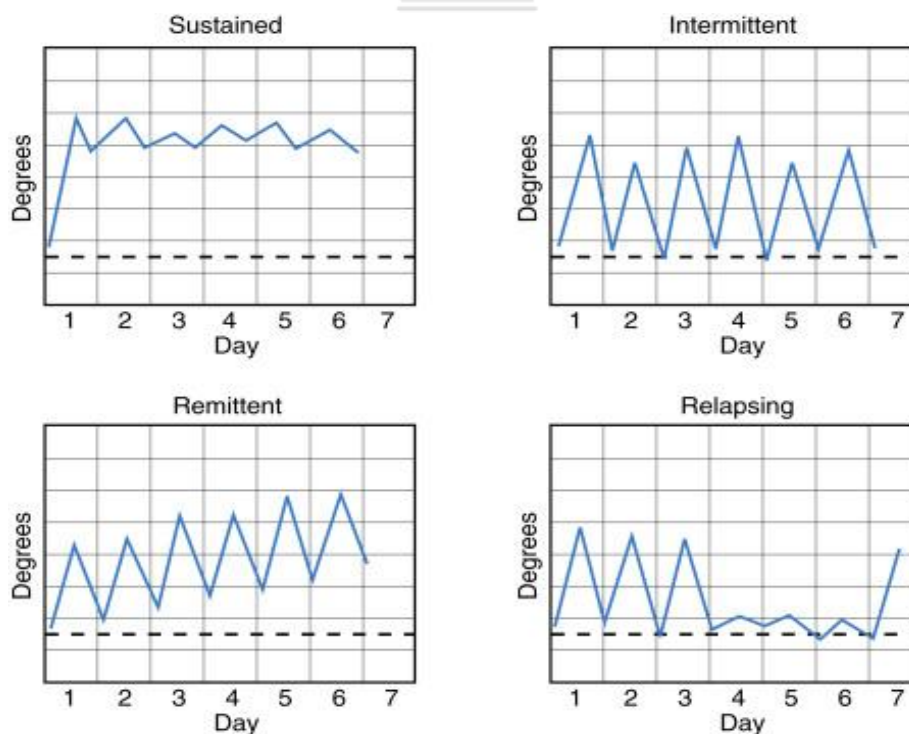
A double quotidian pattern with two daily spikes occurs sufficiently often to be helpful in salmonellosis, miliary tuberculosis, double malarial infections, and gonococcal and meningococcal endocarditis.

**3. Remittent Fever:** Fever with daily fluctuation exceeding  $2^{\circ}\text{C}$  in 24 hours without touching the baseline.

**4. Relapsing fever:** Short febrile periods punctuating one or several days of normal temperature. E.g.: Pel-Ebstein fever - Hodgkin's disease, brucellosis of the Brucella melitensis type, Rat-bite fever, Dengue fever, Yellow fever, etc.

**5. Saddleback (biphasic fever):** With several days of fever, a gap of reduced fever of about 1 day, and then several additional days of fever. This type characterizes dengue and yellow fever, Colorado tick fever. Rift Valley fever and viral infections such as influenza, poliomyelitis, and lymphocytic choriomeningitis.

Fever should be regarded as a reliable clinical sign and with the fever pattern mentioned above, it is possible to suggest a diagnosis within the group of disease and this can lead to specific therapy and ultimate cure.



**Figure No. 1: TYPES OF FEBRILE PATTERNS**

## PLATELETS AND THROMBOPOIESIS:

Platelets are small, a nucleate cell, they are formed in the bone marrow by megakaryocytes and subsequently released in to vascular compartment where they play an essential role in hemostasis. Platelets are the terminal stage of development of megakaryocyte series.

The most immature is the megakaryoblast which accounts for less than 8% of megakaryocyte population. The megakaryocyte population in total forms less than 1 % of Bone marrow cells.

Next stage is promegakaryocyte; these make up 25% of megakaryocyte population. These cells are nucleated and have basophilic cytoplasm.

Next stage is the mature megakaryocytes which range from 30-90  $\mu\text{m}$  in diameter and contain 4-16 nuclear lobes. Platelets appear to be formed by protrusion in to the bone marrow sinusoids of pseudopods of megakaryocyte cytoplasm.

### Morphology of Platelets:

- A mature platelet is 2-4 micrometer in diameter. Volume is  $7.06+4.85 \text{ micro m}^3$ .
- Thickness is  $0.9 +_0.3 \mu\text{m}$ .
- The normal life span is 8-12 days.
- In the stored blood life span is 1-2 days.
- Platelet turnover is  $1.2-1.5 \times 10^{11} / \text{day}$ .

Once released from the marrow platelets are trapped in the marrow for 36 hours. 60-75% of the circulating platelets are in the blood. The remainder is in the spleen.

Normal values for platelet numbers in peripheral blood vary with the method used for their estimation.

Normal range is 1.5-4.5 lakhs/ $\mu\text{L}$ . Thrombocytopenia may be defined as subnormal.

## FUNCTIONS OF PLATELETS

1. Hemostasis: Following vascular injury, immediate reaction is vasospasm. Next reaction is formation of platelet plug.



Following endothelial injury, platelets come in contact with subendothelial collagen, proteoglycans and vWF in the vessel wall.

- They exhibit 3 general reactions

a. Adhesion,

b. Secretion and activation. The activated platelets change shape, put out pseudopodia and discharge their granules.

c. Aggregation. The activated platelets stick to one another which is called aggregation. Aggregation is also fostered by platelet activating factor. Primary platelet plug gets formed which gets reinforced by fibrin to form stable platelet plug.

2. Platelets secrete growth factors which cause vascular endothelial cells, vascular smooth muscle cells and fibroblasts to multiply and grow that helps repair damaged vascular walls. They maintain capillary integrity. This is evident by the fact that in thrombocytopenia due to any cause endothelium thins out with development of more fenestrations.

The major components of the hemostatic system, which function in concert, are

- (1) Platelets and other formed elements of blood, such as monocytes and red cells;
- (2) Plasma proteins (the coagulation and fibrinolytic factors and inhibitors); and
- (3) The vessel wall itself.

### **Platelet Plug Formation:**

On vascular injury, platelets adhere to the site of injury, usually the denuded vascular intima surface. Platelet adhesion is mediated primarily by von Willebrand factor (vWF), a large multimeric protein present in both plasma and in the extracellular matrix of the subendothelial vessel wall, which serves as the primary "molecular glue," providing sufficient strength to withstand the high levels of shear stress that would tend to detach them with the flow of blood. Platelet adhesion is also facilitated by direct binding to subendothelial collagen through specific platelet membrane collagen receptors.

Platelet adhesion results in subsequent platelet activation and aggregation. This process is enhanced and amplified by humoral mediators in plasma (e.g., epinephrine, thrombin);



mediators released from activated platelets (e.g., adenosine diphosphate, serotonin); and vessel wall extracellular matrix constituents that come in contact with adherent platelets (e.g., collagen, vWF). Activated platelets undergo the release reaction, during which they secrete contents that further promote aggregation and inhibit the naturally anticoagulant endothelial cell factors. During platelet aggregation (platelet-platelet interaction), additional platelets are recruited from the circulation to the site of vascular injury, leading to the formation of an occlusive platelet thrombus. The platelet plug is anchored and stabilized by the developing fibrin mesh.

### **Fibrin Clot Formation:**

Plasma coagulation proteins (clotting factors) normally circulate in plasma in their inactive forms. The sequence of coagulation protein reactions that culminate in the formation of fibrin was originally described as a waterfall or a cascade. Two pathways of blood coagulation have been described in the past: the so-called extrinsic, or tissue factor, pathway and the so called intrinsic, or contact activation, pathway.

Coagulation is normally initiated through tissue factor (TF) exposure and activation through the classic extrinsic pathway, but with critically important amplification through elements of the classic intrinsic pathway. These reactions take place on phospholipids surfaces, usually the activated platelet surface. Coagulation testing in the laboratory can reflect other influences due to the artificial nature of the in vitro systems used.

### **Thrombocytopenia:**

Thrombocytopenia is defined as reduction in the peripheral blood platelet count below the lower normal limit of 1, 50,000 lakh. Because platelet count are prone to error, a single platelet count that is lower should be confirmed by a second count. It should also be confirmed by inspecting the blood film.<sup>[9,10]</sup>

Thrombocytes are involved in both thrombotic and bleeding disorders, abnormalities of platelet production might lead to either dysfunction. The life span of platelets once they enter the circulation is about 8-10 days.

Thrombocytopenia may result from impaired platelet production, accelerated platelet destruction, or dilution/splenic sequestration.<sup>[9,10]</sup>

**Table No. 1: CAUSES OF THROMBOCYTOPENIA**

Decreased marrow production	<ul style="list-style-type: none"> <li>● Marrow infiltration with tumor, fibrosis</li> <li>● Marrow failure-aplastic, hypoplastic anemia's, drug effect</li> </ul>
Splenic sequestration of circulating platelets	<ul style="list-style-type: none"> <li>● Splenic enlargement due to tumor infiltration</li> <li>● Splenic congestion due to portal hypertension</li> </ul>
Increased destruction of circulating platelets	<ul style="list-style-type: none"> <li>● Nonimmune destruction                             <ul style="list-style-type: none"> <li>➤ Vascular prostheses, cardiac valves</li> <li>➤ Disseminated intravascular</li> <li>➤ Coagulation</li> <li>➤ Sepsis</li> <li>➤ Vasculitis</li> </ul> </li> </ul>
	<ul style="list-style-type: none"> <li>● Immune destruction                             <ul style="list-style-type: none"> <li>➤ Autoantibodies to platelet antigens</li> <li>➤ Drug associated antibodies</li> <li>➤ Circulating immune system complexes (systemic lupus erythematosus, viral agents, bacterial sepsis)</li> </ul> </li> </ul>

Despite the number and diversity of disorders associated with thrombocytopenia,

Thrombocytopenia results from 4 processes.

1. Accelerated platelet destruction
2. Deficient platelet production
3. Abnormal distribution or pooling of platelets within the body.
4. Art factual Thrombocytopenia

A single platelet count that is lower than normal should always be confirmed by a second count. Thrombocytopenia should also be confirmed by the examination of blood film. The electronic particle counters now widely employed gives accurate results.

### **PATHOPHYSIOLOGIC CLASSIFICATION OF THROMBOCYTOPENIA**

- A. Artifactual Thrombocytopenia
- B. Increased platelet destruction
  - i. Immunologic process

ii. Non immunologic process

C. Decreased platelet production

D. Abnormal platelet pooling.

Viral fever Infections like dengue is some of the common monsoon seasonal causes of fever with thrombocytopenia. Therefore a well-organized systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity and brings out diagnosis. Timely recognition and treatment of the underlying condition, platelet transfusions are required to prevent fatal outcomes. Hence a need for study to know the clinical profile, complications and management of viral fever with thrombocytopenia.

### **AIMS OF THE STUDY**

1. To assess clinical profile of viral fever with thrombocytopenia in pediatric patients.
2. To assess the clinical complication associated with fever and thrombocytopenia.
3. To study the pattern of management of viral fever with thrombocytopenia in pediatric patients.

### **REVIEW OF LITERATURE**

#### **HISTORY OF FEVER:**

Depicted in the Sumerian pictographs as flaming brazier, fever was recognized as a cardinal feature of disease. Sir William Osler stated “Humanity has three great enemies: Fever, famine and war; of these, by far the greatest, by far the most terrible is fever”. Like Osler, physicians since antiquity have viewed fever as an entity worthy of unremitting attention.

Hippocrates mentioned that “Heat is the immortal substance of life endowed with intelligence, hence, heat must also be refrigerated by respiration and kept within bounds if the source or principle of life is to persist; for if refrigeration is not provided, the heat will consume itself” The writing of Hippocrates provided the detailed description of febrile disease. Although Galileo in the 16th century and Santori S in the 17th century constructed devices to measure

body temperature, an effective thermometer was not developed until beginning of the 18th century by Dutch instrument maker Gariel Daniel Fahrenheit.

Wonderlich in 1868 clearly established that abnormality of temperature was a cardinal sign of diseases and normality a sign of health. Since then physicians have used fever as a reliable guide to the presence of disease and the response of disease to therapy. It is in the diagnosis of febrile illness that the science and art of medicine come together.

Celsius, of the early Roman Empire first suggested the possible relationship between fever and the cardinal manifestations of inflammation – heat, swelling, redness and pain.

Carl Reinhold August Wunderlich (1815 –1877), in his book, *Das Verhaltender Eigen warm in Krankheiten* (the course of temperature in diseases) gave 98.6°F(37°C) its special significance Vis-à-vis the normal temperature. He described the normal diurnal variation of the body temperature.

He described the normal diurnal variation of the body temperature, established 100.4°F (38°C) as the upper limit of the normal range and gave the first quantitative definition of fever. Wunderlich is generally regarded as the father of clinical thermometry.

He also wrote that “Fever can give more certainly than anything else information as to the grade of disease”. Because of his work, fever, which has previously been viewed as a disease, came to be recognized more appropriately as a clinical sign.

The mercury thermometer had been perfected in Holland in the early 18th century by Gabriel Daniel Fahrenheit. The work “thermometer” surfaced in the literature of Leurechon’s “Recreation Mathematique” (1624) which mentioned the use instrument “to test the intensity of fever”.

The concept of central set-point temperature was introduced by H.T.Hammel who proposed an original neuronal model to explain regulation of a set-point temperature, by preoptic. Heat production responses were shown to regulate near a set-point of 37°C by the respective effector neurons.

In 1961, Pittendrigh enumerated all of the characteristics required to explain temporal organization in living organism. He proposed that internal timekeeping is achieved by a self-sustained oscillator(s) with a temperature compensated period that can be entrained by the

external environment. These characteristics of circadian temporal organization were described in detail by a group of scientists meeting at the Cold Spring Harbor symposium (1960) on biological clocks.

The term “Circadian” (derived from circa or “about” and dies or “day”) was proposed by Dr. Franz Harberg in the late 1950s to denote these daily cycles.

In 1948, Kleitmann and Ramsaroop provided some of the first detailed information concerning endogenous and exogenous influences on the diurnal rhythm of core (oral) temperature. In most of their subjects, there was a 12 hours difference between the maximum and minimum observed temperatures.

The current concept of fever physiology is that host cell-derived molecules induce fever, which usually occurs in the context of an overall inflammatory response directed against pathogenic microbes. The host derived molecules responsible for fever used to be known as endogenous pyrogens, as first demonstrated by Paul Beeson in 1948. He described temperature-elevating effect of a substance obtained from polymorphonuclear leucocytes.

Patrick Murphy and late Barry Wood were the first to obtain a purified form of endogenous pyrogen from rabbit peritoneal exudates cells.

The late Phyllis Bodel described an intracellular form of Endogenous pyrogen (EP) and reported production of EP by both murine macrophages and human lymphoma cell.

In 1972, Gery and Waksman described the chemical nature of “Lymphocyte-activating factor” which showed striking similarity with endogenous pyrogens. Kluger and co-workers provided proof that endotoxin-induced fever is mediated by IL-1 B induction of IL-6, suggesting that IL-6 might be the final common pathway for such fever.

Milton and Wendlandt originally proposed that E-series prostaglandins (PGE) might mediate the febrile response to pyrogens. This consensus of opinion still favors the proposition that PGE<sub>2</sub>, the endogenous isoform of PGE, plays an essential role in production.

Rotondo et al. proposed that the PGE<sub>2</sub> involved in fever might be generated peripherally, transported to the Pre Optic/Anterior Hypothalamus (POAH) by the bloodstream, and then, being Lipophilic, either cross the BBB at this site or diffuse to the POAH through the Organum Vasculosum Laminae Terminalis (OVLT) to cause the induction of fever.

## **MATERIALS AND METHODS**

➤ The present study was done in pediatric patients admitted to a tertiary care hospital, Khammam over a period of 6 months. No. of patients selected: 130.

### **INCLUSION CRITERIA:**

➤ All pediatric patients of age between 0-16 years of age with viral fever (temperature >99F) with thrombocytopenia (<1,50,000 cells/cu.mm).

### **EXCLUSION CRITERIA:**

- All patients above 17 years of age.
- All patients without fever and thrombocytopenia.
- Diagnosed cases of platelet disorder and dysfunction.
- Patients on treatment with drugs that cause thrombocytopenia.
- Pregnant and lactating women.



### **PERIOD OF STUDY:**

6 months from September 2019 to February 2020

**STUDY DESIGN:** Prospective Observational study

## **METHODS**

All patients admitted in a tertiary care Pediatric Hospital with viral fever with thrombocytopenia were evaluated. History was taken regarding duration of fever from patient guardian. Symptoms like fever, headache, abdominal pain, vomiting, cough etc were noted.

Signs like rashes, dehydration, hepatomegaly, splenomegaly, pleural effusion, free fluid added sounds in lungs were also noted.

Investigations like complete hemogram, chest X-ray, liver function tests, serum electrolytes, USG abdomen were also done.

Other special investigations like dengue serology were done.

During hospital stay, all patients were subjected to repeat platelet count on daily basis. Follow up of all patients regarding treatment were done during hospital stay.

All the lab data and treatment written in the data collection during the hospital stay data collection form is in appendix.

## RESULTS

Statistical Analysis of clinical symptoms, laboratory profile and management of 130 patients presented with viral fever with thrombocytopenia admitted at a Tertiary care Hospital, between September to November 2019, who met the inclusion criteria was done.

A total of 130 patients of diagnosed with viral fever with thrombocytopenia were admitted during the study period.

The results are as follows:

The gender of patients was taken into consideration for the study. Out of 130 cases of viral fever with thrombocytopenia, 75 cases are male patients and 55 cases are female patients.

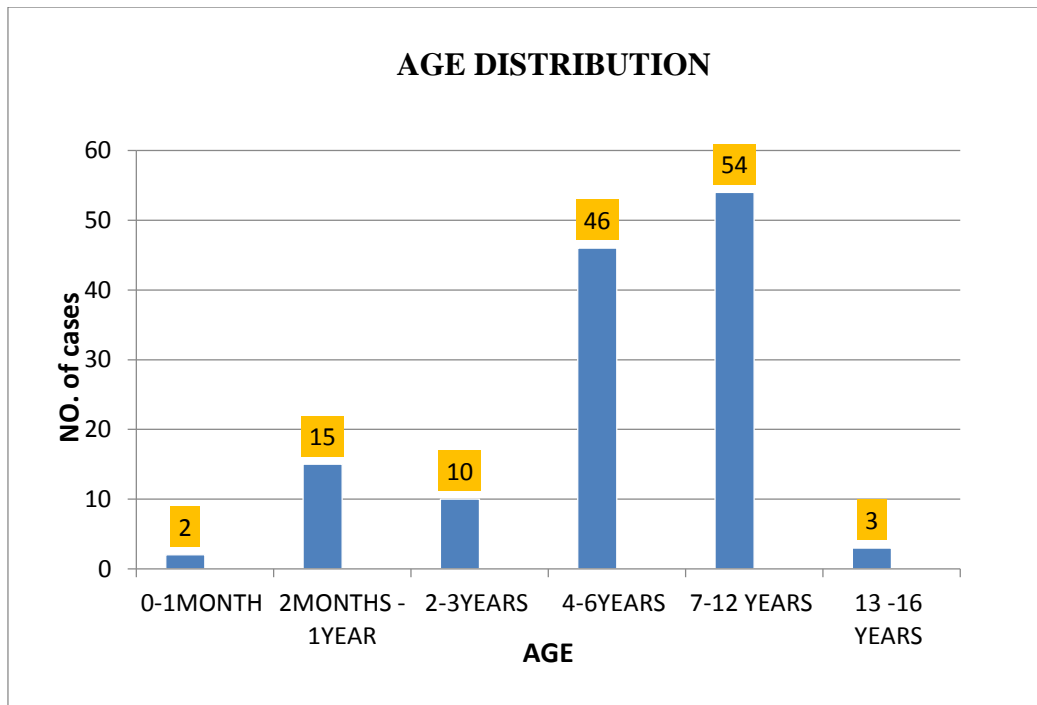
Most of the cases admitted between ages 7 to 12 years.

### AGE WISE DISTRIBUTION

Table No. 2: AGE WISE DISTRIBUTION

AGE	NO. OF CASES	PERCENTAGE
0-1(month)	2	1.5%
2months -1year	15	12%
2years -3years	10	8%
4years - 6years	46	35%
7years - 12years	54	42%
13years +	3	2%





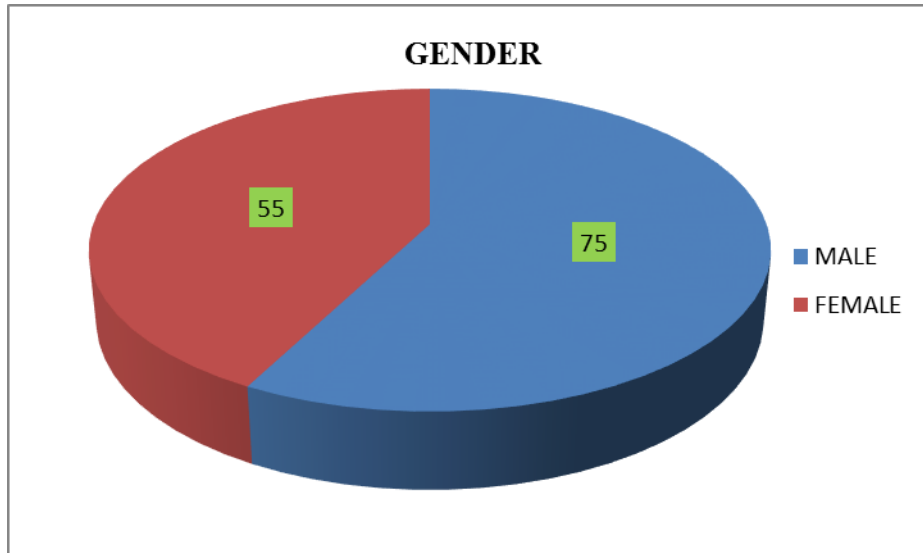
**Figure No. 2: AGE WISE DISTRIBUTION**

Out of 130 patients 54 (42%) patients were found between the age group of 7-12years, 46 (35%) patients were found between the age group of 4-6years, 15 (12%) patient were found between the age group of 2months – 1year, 10 (8%) patients were found between the age group of 2-3years, 3 (2%) patients were found between the age group of above 13years and 2 (1.5%) patients were found between the group of 0-1month.

**GENDER WISE DISTRIBUTION**

**Table No. 3: GENDER WISE DISTRIBUTION**

GENDER	NO. OF CASES	PERCENTAGE
Male	75	58%
Female	55	42%



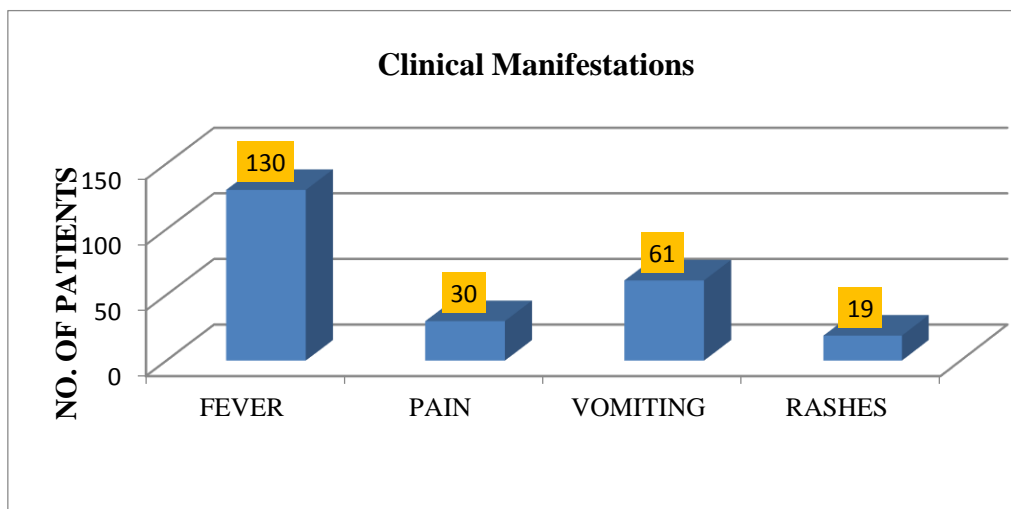
**Figure No. 3: GENDER WISE DISTRIBUTION**

Out of 130 patients, 75 patients (58%) are males and 55 patients (42%) are females.

**DISTRIBUTION OF SIGNS AND SYMPTOMS**

**Table No. 4: SIGNS AND SYMPTOMS WISE DISTRIBUTION**

S. NO.	SYMPTOMS	NO. OF CASES	PERCENTAGES (%)
1	FEVER	130	100
2	PAIN	30	23
3	VOMITING	61	47
4	RASHES	19	15



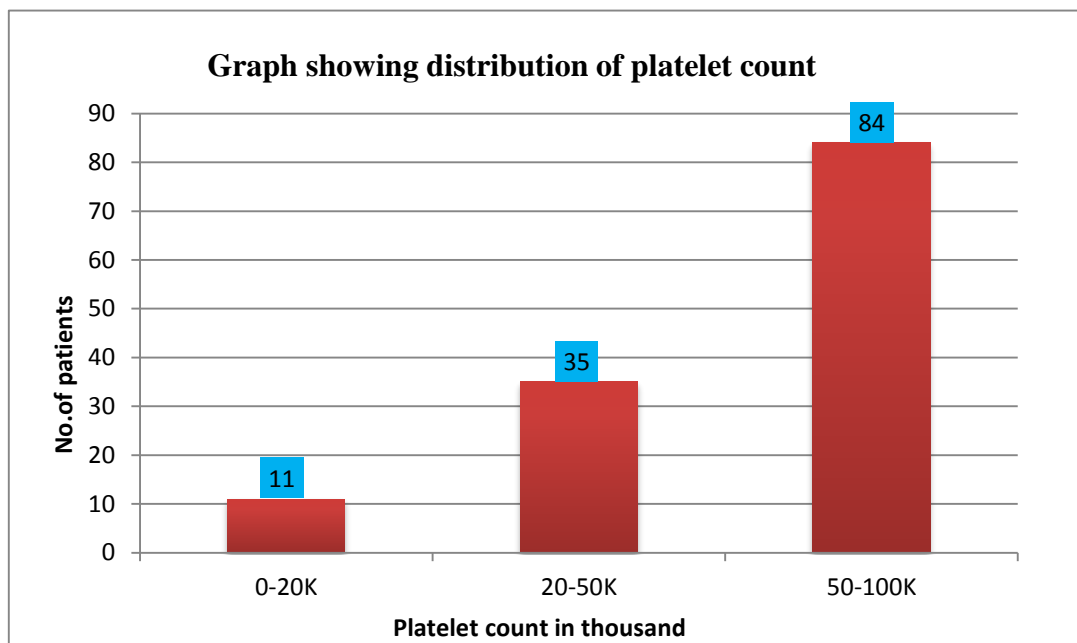
**Figure No. 4: SIGNS AND SYMPTOMS WISE DISTRIBUTION**

In our study out of 130 patients, 130 (100%) patients experienced fever and it is the most common sign. 61 patients (47%) have vomiting, 30 patients (23%) have experienced pain and 19 patients (15%) have rashes.

### ANALYSIS OF LAB INVESTIGATION

**Table No. 5: PLATELET COUNT DISTRIBUTION**

S. NO.	PLATELET COUNT	NO. OF CASES	PERCENTAGE
1.	<1,00,000	84	65%
2.	<50,000	35	27%
3.	<20,000	11	8%



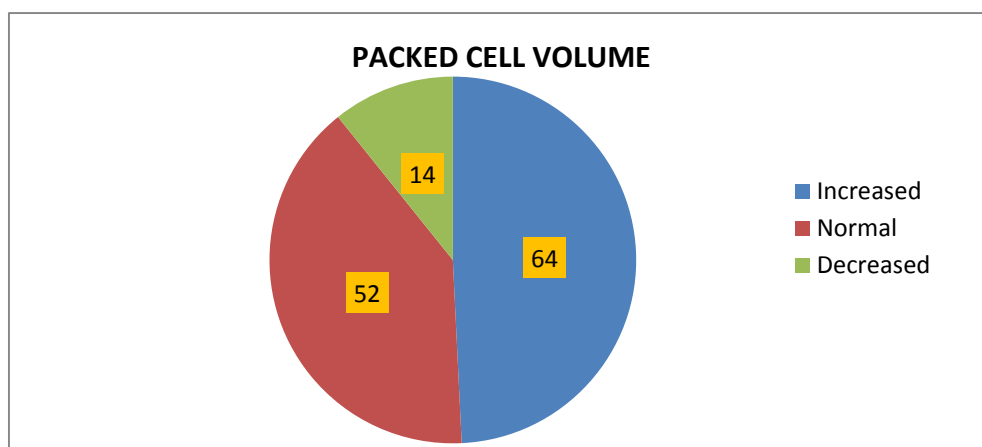
**Figure No. 5: PLATELET COUNT DISTRIBUTION**

Out of 130 cases of viral fever with thrombocytopenia (<1, 50,000>) in pediatrics, 84 cases were less than 1 lakh, 35 cases were less than 50,000. But 11 cases were below 20,000.

**PACKED CELL VOLUME:**

**Table No. 6: PACKED CELL VOLUME**

PACKED CELL VOLUME	NO. OF CASES	PERCENTAGE (%)
Increased	64	49
Normal	52	40
Decreased	14	11



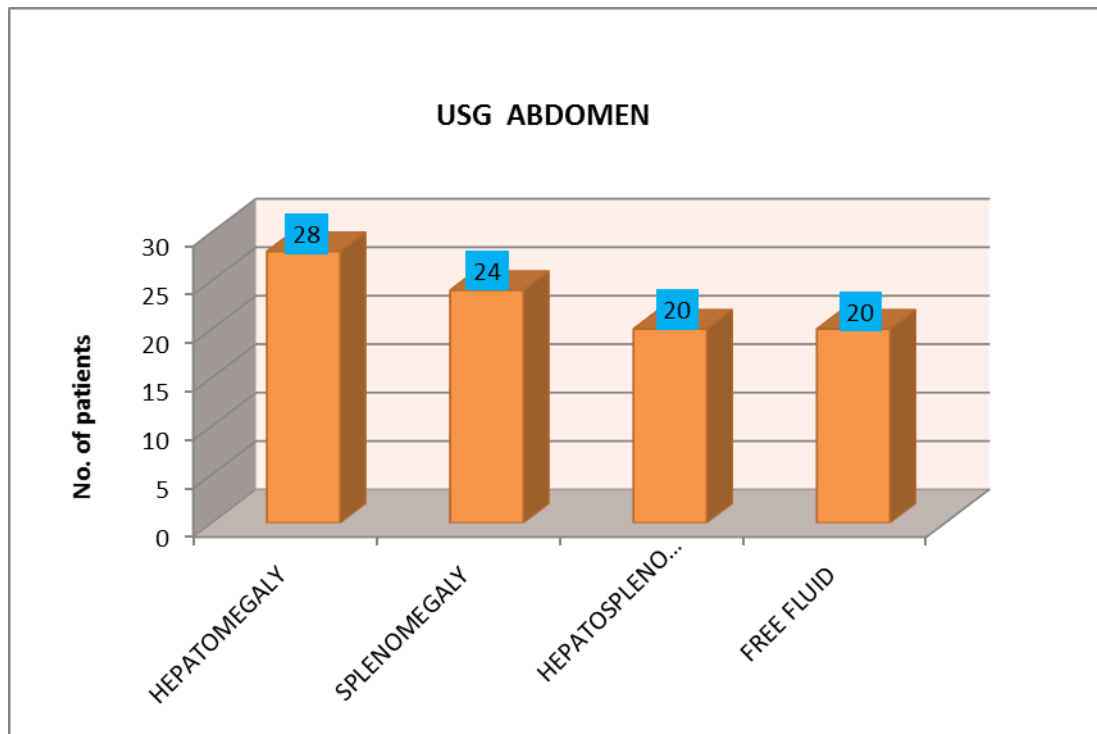
**Figure No. 6: PACKED CELL VOLUME**

Out of 130 cases, PCV increased in 64 cases, decreased in 52 cases and normal in 14 cases.

**USG ABDOMEN:**

**Table No. 7: USG ABDOMEN**

USG ABDOMEN	NO. OF CASES	PERCENTAGE (%)
Hepatomegaly	28	22
Splenomegaly	24	18.5
Hepatosplenomegaly	20	15
Free fluid	20	15



**Figure No. 7: USG ABDOMEN**

Out of 130 cases, 28 cases had hepatomegaly, 24 cases had splenomegaly, 20 cases had hepatosplenomegaly and 20 cases had free fluid.

**CHEST X-RAY:**

**Table No. 8: CHEST X-RAY**

PLEURAL EFFUSION	NO. OF CASES	PERCENTAGE (%)
Increased	32	24.6

Out of 130 cases 32 (24.6%) cases had pleural effusion.

**DENGUE SEROLOGY:**

24 cases were positive and 106 cases were negative.

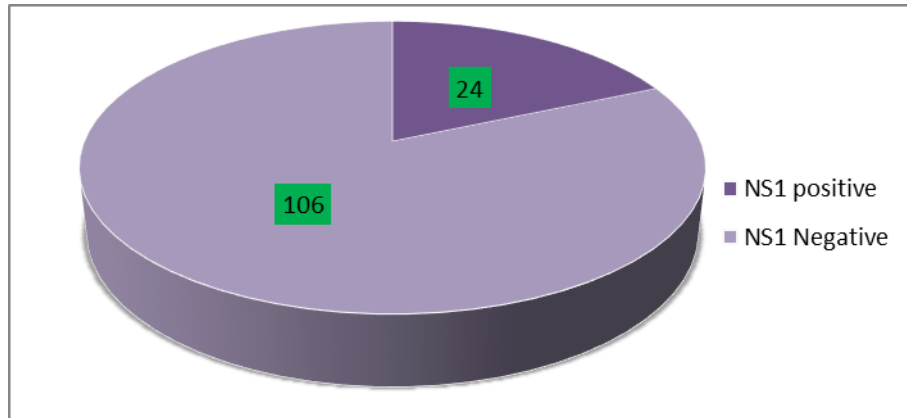


Figure No. 8: DENGUE SEROLOGY

**MANAGEMENT:**

**Table No. 9: TYPES OF TREATMENT GIVEN**

S. NO.	CATEGORY	NO. OF CASES	PERCENTAGE (%)
1.	IV fluids	130	100
2.	Antibiotics	130	100
3.	Analgesics	130	100
4.	H2 blocker	130	100
5.	Corticosteroids	130	100
6.	Anti-emetics	61	47

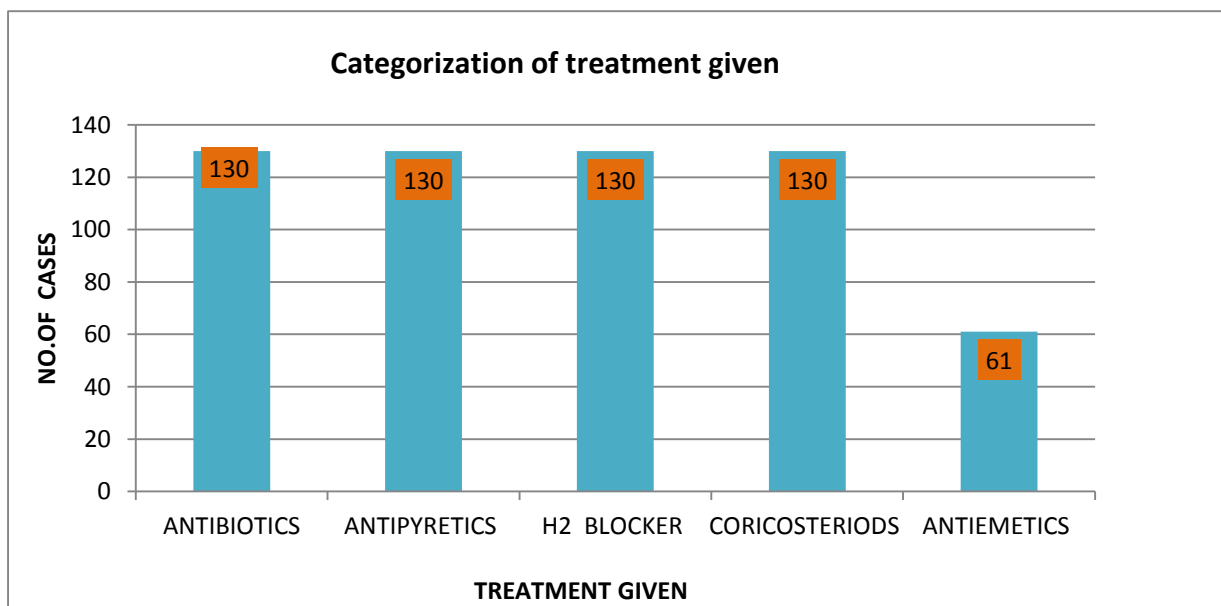


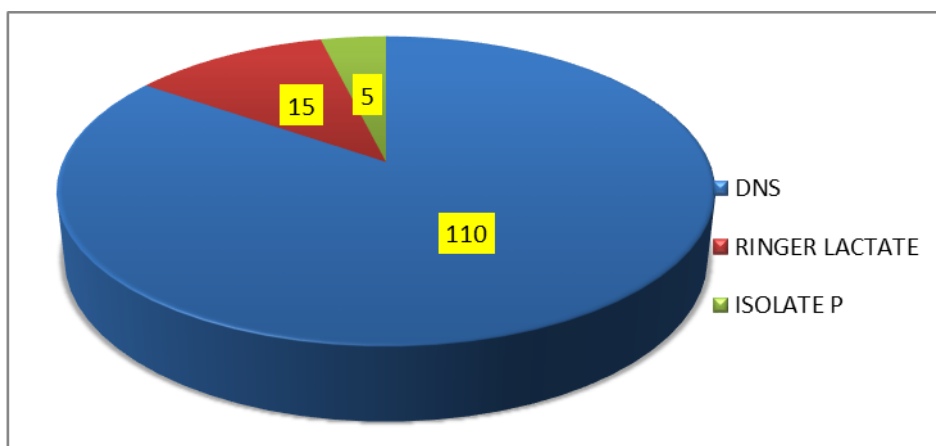
Figure No. 9: TYPES OF TREATMENT GIVEN

All patients received intravenous (IV) fluids, antibiotics, analgesics, H2 blockers, corticosteroids and anti-emetics.

**IV FLUIDS:**

**Table No. 10: TYPES OF IV INFUSION GIVEN**

S. NO.	TYPE OF IV FLUIDS	NO. OF CASES	PERCENTAGE (%)
1.	DNS	110	85
2.	Ringer lactate	15	11
3.	Isolate P	5	4



**Figure No. 10: TYPES OF IV INFUSION GIVEN**

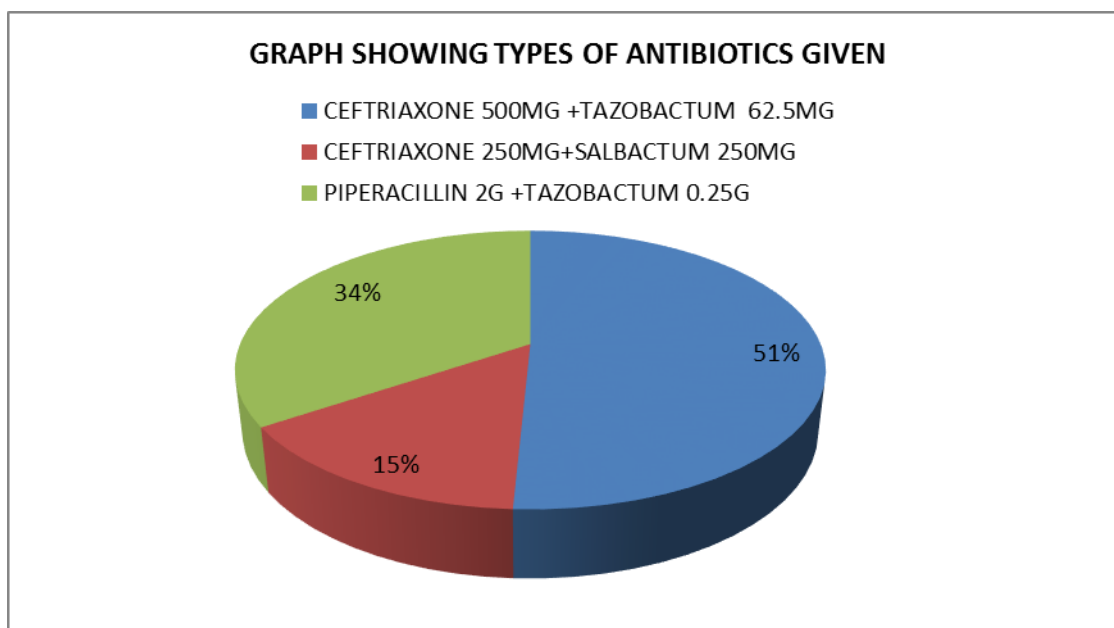
All patients received intravenous (IV) fluids, antibiotics and other supportive measures. The most common IV fluid prescribed was DNS 110 cases (85%) followed by ringer lactate 15 cases (11%) and isolate P 5 cases (4%).

**ANTIBIOTICS:**

**Table No. 11: TYPES OF ANTIBIOTICS GIVEN**

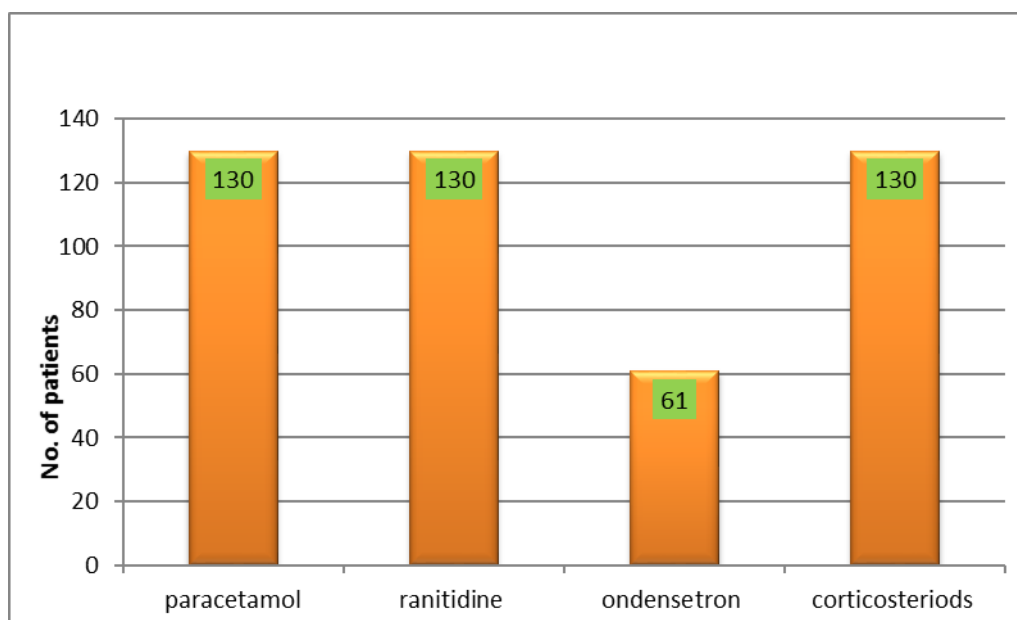
S. NO.	TYPE OF ANTIBIOTICS	NO. OF CASES	PERCENTAGE (%)
1.	Ceftriaxone 500mg + Tazobactam 62.5mg	20	15
2.	Ceftriaxone 250mg + Sulbactam 250mg	65	50
3.	Piperacillin 2g + Tazobactam 0.25g	45	34





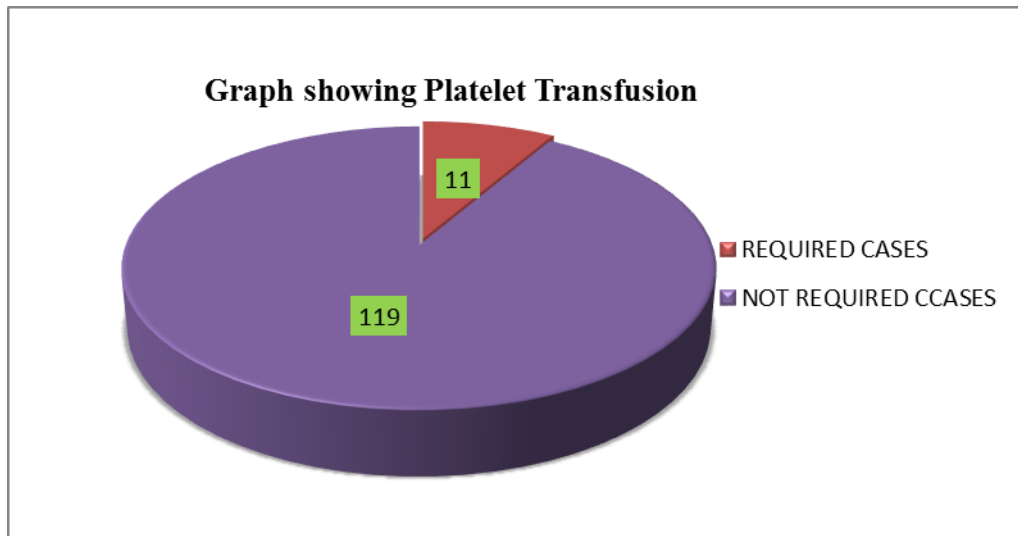
**Figure No. 11: TYPES OF ANTIBIOTICS GIVEN**

All pediatrics patients received antibiotics, the maximum number of patients received ceftriaxone 500mg + tazobactam 62.5 mg (15%) followed by piperacillin 2g + tazobactam 0.25g 45 cases (34%) and patients received ceftriaxone 250mg + sulbactam 250mg 65 (50%) .OTHER Symptomatic treatment consisted of Paracetamol, Ranitidine (injection rantac), Antiemetics (injection emeset) and Corticosteroids.



**Figure No. 12: SYMPTOMATIC TREATMENT**

**PLATELET TRANSFUSION:**



**Figure No. 13: PLATELET TRANSFUSION**

Platelet transfusion done to 11 cases. Platelet count <20000 thousand SDP transfusion was done.

**DISCUSSION**

In our study, there were more 75(58%) males with viral thrombocytopenia than females 55(42%).

This finding is similar to observation made by of Ghazala Z et al.<sup>[11]</sup>

Most admitted age group was found to be 7-12 years similar to the finding of Ghazala Z et al.<sup>[11]</sup>

Most common clinical manifestation is fever 130(100%), this finding is similar to Shubhankar Mishra et al.<sup>[12]</sup>

In our study, most of the patients have platelet count less than 1 lakh (100%).

This finding correlates to that of Kamath SR, Ranjit S.<sup>[13]</sup>

In our study packed cell volume increased by 49% and this finding is similar to that of Shamanth marg.<sup>[14]</sup>

In our study pleural effusion is about 24.6%, this finding is similar to the study of Shubhankar Mishra et al. [12]

In our study, hepatomegaly (22%), splenomegaly (18.5%), pleural effusion (24.6%) and ascites (15%). This finding is identical to Ghazala Z et al. [11]

In our study, all patients received treatment like IV fluids (100%) mostly used IV fluid are DNS, ringer lactate followed by isolate P. Antibiotics (100%) the most commonly used antibiotic is ceftriaxone, anti-acidity (100%) the only used anti-acidity drug is ranitidine and anti-emetics (47%) ondansetron are given.

This treatment is equivalent to World Health Organization. [15]

In our study corticosteroids given to 130(100%) patients. WHO guidelines for management of dengue do not recommend the use of corticosteroids.

This finding is parallel to Ghazala Z et al. [11]

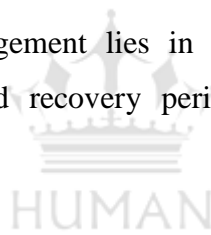
In our study, Platelet transfusion done to 11 cases, this finding is related to Shubhankar Mishra et al. [12]

In our study the obtained P value for clinical profile was found to be near to Jahnavi k et al. [16]

## CONCLUSION

- Viral fever with thrombocytopenia is one of the most challenging problems in the field of medicine.
- Viral fever with thrombocytopenia consists of occult presentation of common disease rather than rare disease.
- Virus like dengue is the commonest cause of viral fever with thrombocytopenia.
- Dengue virus still present clinically in atypical and occult forms, making diagnosis difficult and prolonged, so high index of clinical suspicion is needed.
- So investigated should be done with routine and specific test like rapid test IgM, ELISA for dengue. But dengue has no treatment only supportive care is given.

- In significant number of cases, thrombocytopenia lead to various bleeding manifestations and influenced the clinical profile of these febrile illness.
- Generally, spontaneous bleeding was noted in platelet count <20,000 but in some, it was seen in platelet count in range of 40,000 cell cu/mm also the reason of which is not known.
- Spontaneous bleeding patients should be evaluated for disseminated intravascular coagulation also.
- It has wide clinical spectrum that includes both severe and non-severe manifestations after incubation period, the illness begins abruptly and is followed by three phases febrile, critical and recovery. A high index of suspicion for early diagnosis, monitoring and prompt fluid management and supportive treatment as per WHO guidelines can reduce mortality in patients of sever viral fever like dengue.
- There is no specific treatment for viral fever like dengue as now.
- The only rationale of its management lies in supportive care with judicious fluid management during the critical and recovery period with continuous monitoring and assessment.



#### LIST OF ABBREVIATIONS USED

WHO	:	World Health Organisation
SEAR	:	South East Asian Region
Ae	:	Aedes
DHF	:	Dengue Hemorrhagic F ever
RNA	:	Ribo Nucleic Acid
DEN-1	:	Dengue -1
DEN-2	:	Dengue -2
DEN-3	:	Dengue -3
DEN-4	:	Dengue -4

DSS	:	Dengue Shock Syndrome
Ae	:	Aedes
AM	:	Ante Meridiem
PM	:	Post Meridiem
Vwf	:	Von Willebrand Factor
TF	:	Tissue Factor
EP	:	Endogenous Pyrogen
IL-1	:	Interleukin 1
IL-6	:	Interleukin 6
PGE	:	Prostaglandin
PGE 2	:	Prostaglandin E 2
POAH	:	Pre Optic Anterior Hypothalamus
BBB	:	Blood -Brain Barrier
OVLТ	:	Organum Vasculosum Laminae Terminalis
USG	:	Ultra Sono Graphy
IV	:	Intra Venous
H2 Blocker	:	Histamine 2 Blocker
DNS	:	Dextrose Normal Saline
SDP	:	Single Donor Platelet
IGM	:	Immuno-Globulin M
ELISA	:	Enzyme Linked Immunosorbent Assay

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