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# Clinical Profile of Fever with Thrombocytopenia in Tertiary Hospital, Nellore

**(Original Research Article)**

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**Abstract**

**Objective:** *Infection is the commonest cause of thrombocytopenia. Definite diagnosis helps to manage the patients effectively. The objective was to determine possible infective etiology for fever with thrombocytopenia and to study the presentation and complications of thrombocytopenia.*

**Methodology:** *This prospective study was conducted in Narayana Medical College and Hospital, Nellore between May 2015 – June 2016. 150 patients aged 15 years and above with fever and thrombocytopenia were included for this study. A detailed history, general and systemic examination was done and recorded.*

**Results:** *Out of 150 cases of fever with thrombocytopenia, 88(58.7%) were males and 62(41.3%) were females and the most common age group was between 15-30 years 67(44.7%). The most common presentation was fever 150(100%), followed by myalgia 52(34.7%),headache 46(30.7%),cough 24(16%), hepatomegaly 35(23.3%), splenomegaly 26(17.3%) and bleeding manifestations in 18(12%).45(30%) patients had bleeding manifestations of which malena in 18 (40%) was the commonest followed by petechiae/ purpura/ecchymosis in 13(28.8%), hematuria 5(11.1%), epistaxis 3(6.7%),gum bleed 3(6.7%) and hematemesis in 3 (6.7%). Common range of platelet count at the time of admission was in the range of 50000 – 1Lakh/cumm in 72(48%).Infection was the commonest cause of thrombocytopenia and the commonest infection was dengue 68 (45.3%), followed by viral fever other than dengue 22(14.7%), septicemia 19 (12.7%), malaria 17(11.3%), undiagnosed 13(8.7%), enteric fever 9(6%) and leptospirosis 2(1.3%). 140(93.3%) of them had good recovery and 10(6.7%) patients have expired. Of those 10 mortality cases, 6 died due to septicemia,3 due to dengue and 1 had malaria.*

**Conclusion:** *Infections, particularly dengue fever was the commonest cause of fever with thrombocytopenia. Majority of the patients with thrombocytopenia are asymptomatic but in significant number of cases there were bleeding manifestations also. Malena was the common bleeding manifestations. On treating the specific cause drastic improvement in platelet count was noted.*

**Keywords:** *Fever, Thrombocytopenia, Dengue, Malaria, Platelet count, Mortality.*

## Introduction

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". Carl Reinhold August Wunderlich (1815 - 1877), in his book, Das Verhalten der Eigenwarme in Krankenheiten (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 established 100.4°F (38°C) as the upper limit of the normal range and gave the first 4 quantitative definition of fever. Wunderlich is generally regarded as the father of clinical thermometry[1]. 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. 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[2]. 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 AM temperature of >37.2°C (98.9°F) or a P.M. temperature of > 37.7°C (99.9°F) would define fever[3]

Thrombocytopenia is defined as a reduction in the peripheral blood platelet count below the lower normal limit of 150,000/µl. Because platelet count are prone to error, a single platelet count that is lower than normal should be confirmed by a second count. It should also be confirmed by inspecting the blood film[4,5]. The life span of platelets once they enter the circulation is about 8-10 days. About 10% of the population is destroyed each day[5]. Thrombocytopenia may result from impaired platelet production, accelerated platelet destruction, or dilution/splenic sequestration[4,5]. Of these infections being the commonest cause of thrombocytopenia [4,6]

**Table 1:** Thrombocytopenia Associated With Infection

| Cause | Mechanism |
|---|---|
| 1.Viral:- Dengue,CMV,HIV etc[5] | a.Impaired platelet production<br>b.Accelerated destruction by forming Ag-Ab complex[5] |
| 2. Bacterial : Gram +ve and gram -ve septicemia, miliary tuberculosis, leptospirosis, typhoid , mycoplasma pneumonia, etc[5,7] | a.May be caused by disseminated intravascular coagulation (DIC)<br>b.Increased clearance of platelets[5,7] |
| 3. Protozoal : Malaria,Brucella[5] | Immune mediated destruction |
| 4.Others :- Lymphomas, Leukemias[5] | Marrow infiltration – Impaired production |

**Table 2:-** Clinical Complications of Thrombocytopenia

| Platelet Count | Symptoms | Bleeding time |
|---|---|---|
| 1. >1 Lakh | Assymptomatic | Normal[4] |
| 2. 50000-1 lakh | Bleeding after severe trauma | Mild increase[4] |
| 3. <50000 | Easy bruising, Purpura after minor trauma | Increase[4,5] |
| 4. <20000 | Spontaneous bleeding, Petechiae, Internal or Intracranial bleed | Increase[4,5] |

Nair P S conducted study of fever with thrombocytopenia and concluded that septicemia was the commonest cause [8]. Serial monitoring of platelet count has prognostic value. All fever cases should be investigated for platelet count whether they have bleeding manifestations or not. This highlights the importance of thrombocytop-enia in various febrile disease [9].

## Methodology

**Method of Study:** This was a prospective study done on 150 patients with fever and thrombocytopenia, who were admitted in Narayana Medical College, Nellore during the period of May 2015 to June 2016.

**Inclusion criteria**

- The patients of both sexes aged > 14 years.
- Patients admitted with fever and found to have thrombocytopenia are included in the study.

**Exclusion criteria**

- Patients <14 years are excluded.
- Patients with fever and no thrombocytop-enia are not included or vice versa.
- Previously diagnosed conditions which can lead to thrombocytopenia such as ITP,

cirrhosis, chronic liver disease, patients on drugs (aminosalicylic acid, Linezolid, Amiodarone Carbamazepine, Captopril, Methyldopa) causing thrombocytopenia were excluded.

Once the patients admitted with fever and those who had thrombocytopenia, a careful history was recorded, general physical examination was done. Detailed examination of various systems was done In whom a final definite diagnosis was reached, were treated for the disease and platelet count was repeated at the time of discharge in all patients and no effort treatment was given specifically made to gather follow-up information, if the patient was not followed up in our institution. If diagnosis was made, patients were treated specifically for the disease. Platelet transfusion was advised if patient had any bleeding manifest-ations or if platelet count was <10000/cumm.

**Laboratory Investigations**

Routine investigation was done; the specific and special investigations were done as and when indicated. Hemoglobin, total and differential leucocyte counts, platelet count with coagulation profile (PT, aPTT), hematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen. Platelet counts were monitored periodically. Dengue serological confirmatory test was performed using Immunochromatographic test (J. Mitra, India)for NS1,IgM and IgG, Leptospira serology IgM and IgG, MP(QBC) for malaria, Blood culture (3 samples sent).

**Results**

A total number of 150 patients were admitted over a period of one year in our hospital in the age group of 15- 72 years. Majority of these cases reported to our hospital coinciding with rainy season, showing the breeding of mosquitoes during the said period. Out of 150 cases of fever with thrombocytopenia, 88(58.7%) were males and 62(41.3%) were females and the most common age group was between 15-30 years 67(44.7%). The duration of hospitalization varied between 3 days to 21 days. The average duration of hospitalization was 6 days. The most common presentation was fever 150(100%), followed by myalgia 52(34.7%), headache 46 (30.7%), cough 24(16%), hepatomegaly 35(23.3%), splenomegaly 26 (17.3%) and bleeding manifestations in 18 (12%).On admission only 18(12%) of the patients presented with bleeding tendency where as other 27 patients developed during their course in the hospital. On the whole 45(30%) patients had bleeding manifestations of which malena in 18 (40%) was the commonest followed by petechiae/ purpura/ecchymosis in 13(28.8%),hematuria 5(11.1%), epistaxis 3(6.7%),gum bleed 3(6.7%) and hematemesis in 3 (6.7%). In our study 20(13.3%) of the patients had platelet count of less than 20000, 33 (22%) in the range of 20,000 - 50,000, followed by 72(48%) in the range of 50,000 – 1 Lakh and 25(16.7%) in 1 Lakh – 1.5 Lakh range. Common range of platelet count at the time of admission was in the range of 50000 – 1Lakh/cumm in 72(48%). 45(30%) of the patients developed the clinical manifestations of thrombocytopenia and 105(70%) of patients didn't show any bleeding tendency. Out of 150 patients of fever with thrombocytopenia, the commonest cause was dengue 68 (45.3%), followed by viral fever other than dengue 22 (14.7%), septicemia 19(12.7%), malaria 17 (11.3%), undiagnosed 13(8.7%),enteric fever 9 (6%) and leptospirosis 2(1.3%). In malaria, vivax malaria 11(64.7%) was commonest followed by falciparum malaria 6 (35.3%). Out of 150 patients, 140 of them had good recovery and 10 patients have expired. Of those 10 mortality cases, 6 died due to septicemia, 3 due to dengue and 1 had malaria. In these non survivors platelet range of 3 patients was in the range of 10-20000 cells/cumm which was the majority.140 patients who had good recovery, nearly 100 cases were followed up after 10 days and platelet count were within normal limits at that point of time.

**Figure 1:-** Age Distribution

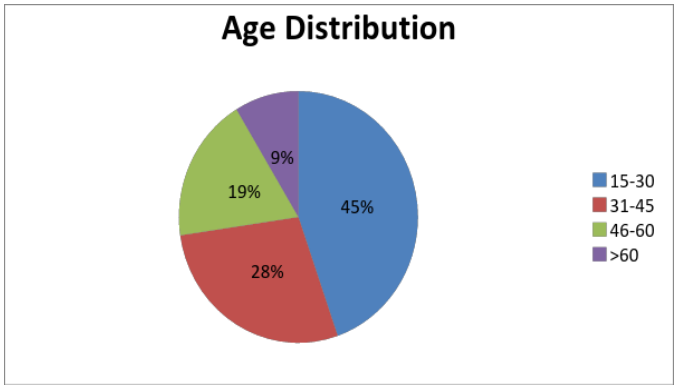



**Figure 2 :-** Sex Distribution

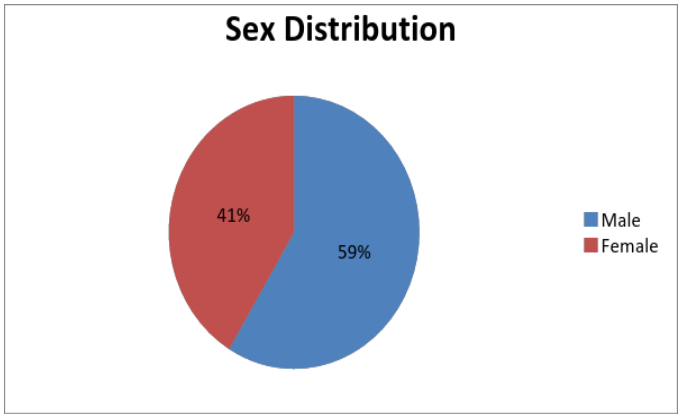



**Table 3 :-** Clinical Presentation

| Clinical Features | No.of patients | Percentage (%) |
|---|---|---|
| 1.Fever | 150 | 100% |
| 2.Myalgia | 52 | 34.7% |
| 3.Headache | 46 | 30.7% |
| 4.Cough | 24 | 16% |
| 5.Bleeding manifestation | 18 | 12% |
| 6.Hepatomegaly | 35 | 23.3% |
| 7.Splenomegaly | 26 | 17.3% |

**Figure 3** :- Platelet Count

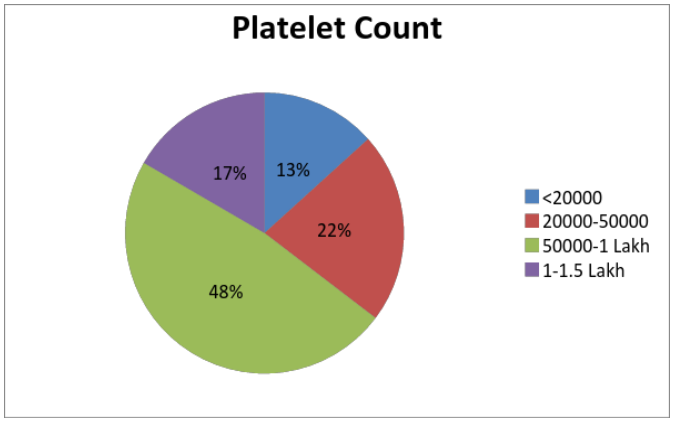



**Figure 4 :-** Bleeding Manifestations

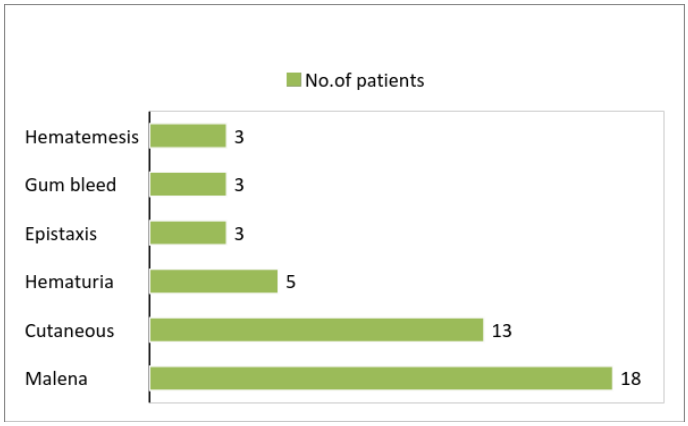



**Figure 5:-** Cause of Thrombocytopenia

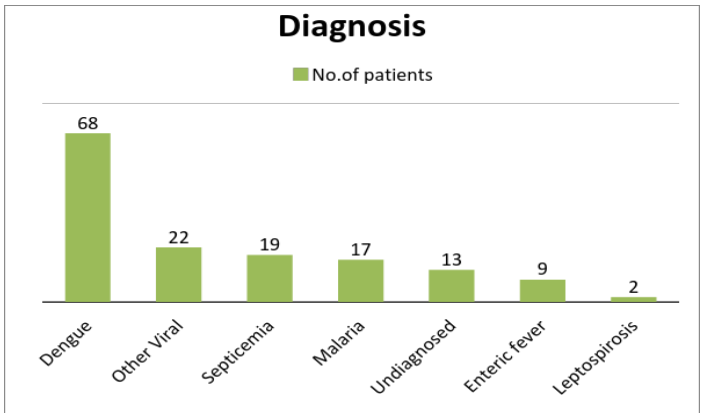



**Figure 6:-** Mortality

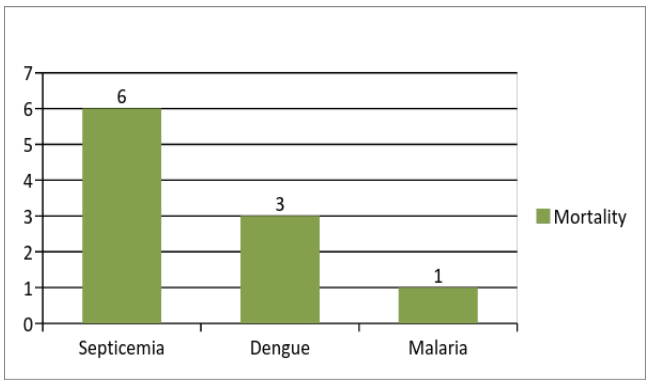
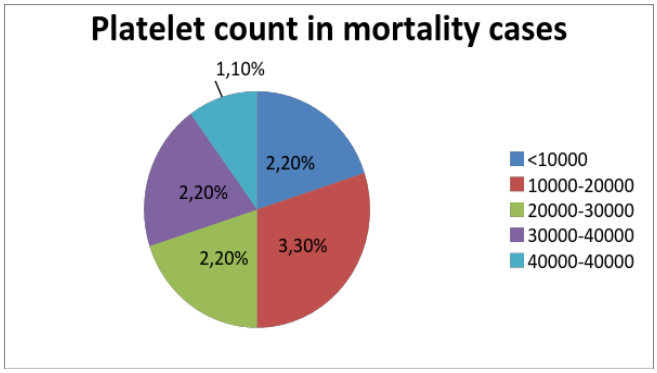



**Figure 7:-** Distribution of platelets in mortality cases



## Discussion

Of 150 cases included in this study 88 (58.7%) were males and 62(41.3%) were females with 67 (30%) patients in the age group of 15-30 years. Slightly higher number of males is primarily because of the serving soldiers or staying outdoors most of the time. In a similar study done by Suresh et al showed similar results with male preponderance with males 54% and females 46% [10]. In another study conducted by Nair P S et al 76 were male and 33 were female patients [8] where as in another done by Rekha et al 162(49.4%) were males and 166(50.4%) were females [11]. The most common age group was between 15-30 years 67(44.7%) in our study where as Suresh et al showed 21-40 years was the common age group [10]. The most common presentation was fever 150(100%) and bleeding manifestation in 18(12%). Later 27 patients developed bleeding tendency after admission in the hospital making it a total of 45(30%). In study done by Rekha et al fever was seen in 116(35.4%) and bleeding manifestation was seen in 4 (1.2%)[11]. The most common bleeding manifesttation in our study was malena in 18 (40%) followed by petechiae/purpura/ecchymosis in 13(28.8%), hematuria 5(11.1%), epistaxis 3(6.7%), gum bleed 3(6.7%) and hematemesis in 3 (6.7%). Compared to study by P.S. Nair et al[8] spontaneous bleeding in 77.78% was a major manifestation followed by petechiae/purpura accounting for 22.22%. While in a similar study by Dr. Srinivas et al [12] purpura (63%) was the commonest bleeding manifestations followed by spontaneous bleeding (37%). In study done by Patil et al [13] petechiae was the major manifestation73.9% followed by spontaneous bleeding (26.9%). In our study, majority of patients had platelet count above 50000 cm/mm 97(64.7%) at the time of presentation, followed by 20000-50000 cm/mm in 33(22%) and <20000 cu/mm in 20 (13.3%). On serial platelet count monitoring, most of them presented with a falling trend whereas some showed improvement. Our study was compared with other studies [Table 4].

**Table 4:-** Fever with Thrombocytopenia: Platelet Count range in comparision with different studies:-

| Platelet Count | Present Study | Amita A Gandhi et al [14] | Nair et al[8] | Bhalara et al[15] |
|---|---|---|---|---|
| <20000 | 20(13.3%) | 64(57.14)) | 62(56.8) | 196(59.8) |
| 20000-50000 | 33(22%) | 33(29.47) | 28(25.7)) | 77(23.5) |
| >50000 | 97(64.7%) | 64(57.14)) | 62(56.8) | 196(59.8) |

In this study, the most common aetiology responsible for newly diagnosed thrombocytopenia in adult patients was found to be Dengue fever 68(45.3%). The two mechanisms probably involved in dengue-induced thrombocytopenia are impaired thrombopoiesis and peripheral platelet destruction [16]. Our study results compared to other studies [Table 5].

**Table 5:-** Comparision of causes of thrombocytopenia

| Diagnosis | Present study | Amita A Gandhi et al[12] | Nair et al[8] | Patil et al[13] | Dash et al[17] |
|---|---|---|---|---|---|
| Dengue | 68(45.3%) | 26.79% | 13.8% | 15% | 20% |
| Malaria | 17(12.7%) | 41.07% | 9.2% | 54% | 45% |
| Septicemia | 19(12.7%) | 4.46% | 26.6% | 4% | 21% |
| Enteric Fever | 9(6%) | 4.46% | 14.7% | 6% | 10% |
| Other Viral Fever | 22(14.7%) | 16.07% | 18.3% | 21% | 2% |

On specific diagnosis treatment was given accordingly. Platelet transfusions are not routinely recommended in the management of Dengue fever [18,19]. According to recent guidelines by the World health organization and National Vector-borne Diseases Control Programme prophylactic transfusion of platelets is not indicated unless the patient has bleeding or a count of less than 10000/cumm [20,21]. Mortality in our study was 10 (6.7%) and it was mainly due to septicemia 6(60%), followed by Dengue 3(30%) and Malaria 1 (10%).

## Conclusion

Infections, particularly dengue fever was the commonest cause of fever with thrombocytopenia. Majority of the patients with thrombocytopenia are asymptomatic but in significant number of

cases there were bleeding manifestations also. Malena was the common bleeding manifestations. On treating the specific cause drastic improvement in platelet count was noted. Platelet transfusion was done only if bleeding is present or platelet count was <10000 cu/mm.

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