



Epidemiological Analysis Of Acute Febrile Illness Patients With Thrombocytopenia: A Longitudinal Study

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Abstract: Identifying clinical outcome of Febrile thrombocytopenia from acute febrile illness. Acute fever with thrombocytopenia is a common problem with increased mortality and morbidity if not diagnosed and treated properly in time. Usually in conditions commonly caused by infection like malaria, dengue, enteric fever and septicaemia. It is necessary to know the cause, which will be useful to give proper treatment to patients.

Aims and Objective: To study the clinical outcome of acute febrile illness with thrombocytopenia.

Methods: This is Hospital based Longitudinal study was conducted on 438 patients who present acute febrile illness with thrombocytopenia and were admitted in Tertiary care hospital Mumbai from June 2012 to May 2013.

Result: acute febrile illness with thrombocytopenia affected all age groups but majority of 161 patients in the age group 25 - 40 years. Malaria was the commonest cause (34.9%) as compared to dengue (8.4%).

Conclusion: Outcome depends on the underlying cause of fever, early diagnosis and treatment.

Keywords: Acute Febrile Illness, Fever, Thrombocytopenia, Malaria, Dengue.

Introduction:

Fever is an elevation of body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in the hypothalamic set point (e.g., from 37°C to 39°C). This shift of the set point from "normothermic" to febrile levels very much resembles the resetting of the home thermostat to a higher level in order to raise the ambient temperature in a room. Once the hypothalamic set point is raised, neurons in the vasomotor centre are activated and vasoconstriction commences. The individual first notices vasoconstriction in the hands and feet. Shunting of blood away from the periphery to the

internal organs essentially decreases heat loss from the skin, and the person feels cold. For most fevers, body temperature increases by 1°–2°C. Shivering, which increases heat production from the muscles, may begin at this time; however, shivering is not required if heat conservation mechanisms raise blood temperature sufficiently. Non-shivering heat production from the liver also contributes to increasing core temperature. In humans, behavioural adjustments (e.g. Attention must be paid to the chronology of events and to other signs and symptoms preceding the fever. The temperature may be taken orally or rectally, but the site used should be consistent, putting on more clothing or bedding) helps raise body temperature by decreasing heat loss ¹.

Malaria is a significant and serious health problem in urban area of Maharashtra state and particularly in Mumbai & its surrounding areas. In the recent years there has been a sharp rise in the incidence of malaria & other vector borne diseases in this region due to rapid growth and urbanisation, which has led to construction boom. This represents a major challenge for public health in urban areas. There is an increase in the number of malaria cases with the onset of rainy season and so is the incidence of *P. falciparum* in the recent years, which is a matter of grave concern. Over-treatment with antimalarial drugs in non-malarial acute undifferentiated fever is a significant problem in India. This rampant use of antimalarials pose problems like adverse side effects of drugs, drug resistance and increased cost ². Serious consideration of other aetiologies may not occur unless there is no clinical response to antimalarial treatment.

Dengue infection is the most common arthropod-borne infection in the tropics where it carries significant morbidity, mortality and immense economic burden to the countries affected ³. Early diagnosis of dengue infection is important in order to minimise mortality ⁴. Diagnosis of dengue infection is supported if there is thrombocytopenia, the presence of which often signifies a more serious type of dengue infection ⁴. All these point to the importance of detecting thrombocytopenia in suspected dengue patients. It is difficult to differentiate dengue infection from other viral infections due to the overlap in the symptoms ⁵⁻¹⁰.

Several studies have shown that arboviral infections like dengue fever, chikungunya, kyananur forest diseases and scrub typhus and leptospirosis and malaria, military tuberculosis typhoid and Human immunodeficiency causes fever and thrombocytopenia ^{11,12}.

There is seasonal variation in the epidemic of fever. At times non-infective causes and drugs can also cause thrombocytopenia and fever. The mortality is very high when there is severe thrombocytopenia and mortality increases due to hemorrhagic manifestations. So, it is imperative that there should be regional studies to assess the aetiology of fever with thrombocytopenia. Though there are frequent epidemics of several arrival infections in our area, there are only few studies which focus the thrombocytopenia in patients with fever. Therefore, a well-structured systematic approach that is conducted with an awareness of different causes of fever with thrombocytopenia streamlines the differential diagnosis and determines the aetiology.

Thrombocytopenia is defined as platelet count below the normal range which is 150, 000–450, 000/ mm ¹³. Thrombocytopenia results from four processes: deficient platelet production, accelerated platelet destruction, abnormal distribution and artifactual thrombocytopenia. There is no absolute limit below which thrombocytopenia can lead to spontaneous bleeding. If the patient is hemostatically stable, platelet count more than 30000 will not lead to spontaneous bleeding. Bleeding may occur at higher platelet count if associated with severe anaemia, sepsis, fever etc.

As Mumbai is the economic capital of India, there are lakhs of commuters moving in & out of Mumbai. There are problems of sanitation which might have an impact on incidence of vector borne as well as water borne diseases. So study was done to assess epidemiological factors & its impact on clinical

outcome in acute febrile illness with special reference to Malaria patients in tertiary care hospital of Mumbai city.

Objectives of the Study:

1. To identify the various causes of fever with thrombocytopenia.
2. To assess the complication associated with fever with thrombocytopenia.

Methods:

This Hospital based longitudinal study was undertaken in the department of community medicine at Tertiary Care of hospital, Mumbai from June 2011 to April 2014.

Inclusion criteria: All acute febrile illness patients admitted in Medicine wards above 14 years of age with fever ($>37.5^{\circ}\text{C}$) and thrombocytopenia ($<1, 50000/\text{mm}$).

Exclusion Criteria: a) Patients not presenting clinically with fever.
b) Patients not admitted in wards or treated at outpatient departments.
c) Patients of less than 14 years of age will be excluded from the study.

Sample Size: A total of 438 patients admitted in the department of medicine were included based on the above inclusion and exclusion criteria.

Protocol

Informed written consent was taken from all patients. Their clinical features were recorded using a standard data collection sheet for all patients. An interview based semi-structured questionnaire was developed under expert guidance after review of literature was used to collect data.

The data collection sheet also asked for demographic data of patients, days of fever, presenting symptoms (headache, myalgia, nausea and vomiting, arthralgia, retro-orbital pain and rash).

We analysed the data using SPSS version 20.0 For non-categorical and normally distributed data, Student's t-test was used. For categorical data, χ^2 tests were used and odds ratios were calculated accordingly for each of the presenting symptoms. Significant level of difference was defined as $p < 0.05$. Universal sampling, i.e all patients meeting the inclusion criteria were enrolled in the study. Institutional Ethical Committee approval was obtained before the start of the study.

Results:

The present hospital based Longitudinal Study was carried out during June 2012 to May 2013, to assess epidemiological factors & clinical outcome in acute febrile illness patients in a tertiary care hospital, Mumbai. The total numbers of study subjects were 1860 in the study.

A total of 438 patients admitted over a period of one year in this Hospital were studied. Among the total 438 cases 126 were male and 312 were female. Commonest age group affected in most of this infection was 161 patients who were in the age group of 25 - 40 years & 119 patients were in the age group of 14 - 24 years. Mean age of the patients in this study was 36.45 years (range 14-89, $\text{SD} \pm 16.01$).

Table No.1. Relationship between Age and Sex in Acute Febrile Illness with Thrombocytopenia.

age group	sex		Total
	Female	Male	
14 - 24	82	37	119
25 - 40	121	40	161
41 - 60	80	37	117
61 - 90	29	12	41
Total	312	126	438

Table No. 2. Clinical feature in patients with acute febrile illness thrombocytopenia.

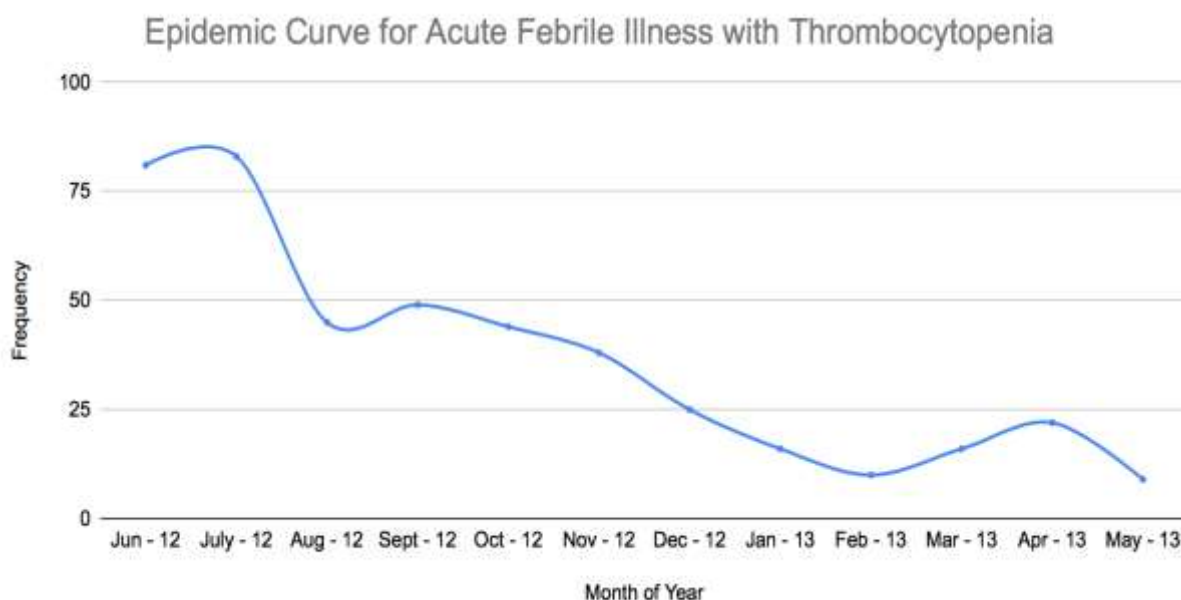
Signs & Symptoms	No. Of Cases (%)
Fever	438 (100.0%)
Vomiting	185 (42.2%)
Abdominal Pain	78 (17.8%)
Chest Pain	17 (3.9%)
Cough	76 (17.4%)
Breathlessness	51 (11.6%)
Hemoptysis	12 (2.7%)
Loose Motion	45 (10.3%)
Headache & Bodyache	206 (47.0%)
Arthralgia	80 (18.3%)
Bleeding tendency	16 (3.7%)
Anemia	184 (42.0%)
Pallor	207 (47.3%)
Icterus	73 (16.7%)
Oedema	16 (3.7%)
Lymphadenopathy	9 (2.1%)

Common sign and symptom in this study was fever(100%), vomiting(42.2%), abdominal pain(17.8%), Chest pain (3.9%), Cough (17.4%), Breathlessness (11.6%), Hemoptysis (2.7%), Loose motion (10.3%), headache & body-ache (47.0%), Arthralgia (18.3%), Bleeding tendency (3.7%), Anaemia (42.0%), Pallor (47.3%), Icterus (16.7%), Oedema (3.7%) & Lymphadenopathy (2.1%).

Table No. 3. Comparison of causes of Acute Febrile Illness with thrombocytopenia.

Diagnosis	Thrombocytopenia
Malaria	153 (34.9%)
Dengue	37 (8.4%)
Leptospirosis	5 (1.1%)
Typhoid	5 (1.1%)
Hepatitis	7 (1.7%)
AFI RTAMAB	108 (24.7%)
Mixed Infection	5 (1.1%)
UD AFI	20 (4.6%)
LRTI	13 (3.0%)
UTI	13 (3.0%)
Tuberculosis	31 (7.1%)
PCP	5 (1.1%)
Septicaemia	31 (7.1%)
Encephalitis	5 (1.1%)
Total	438 (100.0%)

In the above table the relationship between thrombocytopenia in AFI patients & diagnosis has been examined. Thrombocytopenia was more commonly associated with malaria (34.9%), dengue (8.4%) & AFI responded to antimalarials & antibiotics (24.7%). The cure rate was amongst those present with thrombocytopenia 352 (80.3%). The death rate of patients presenting with thrombocytopenia 86 (19.5%).

Figure No. 1: Epidemic Curve for Acute Febrile Illness with Thrombocytopenia.

Discussion:

This study was conducted on 438 patients of acute febrile illness of fever with thrombocytopenia in Tertiary Care hospital in Mumbai during the study period from June 2012 to May 2013.

In our study, out of which 438 were 126 were males and 312 were females. Majority of patients 36.8% were in the age group of 25 - 40 years constituting Mean \pm S.D. was 30.92 ± 4.56 . Majority of patients 68.3% were in Hindu, followed by 27.9% were Muslim & 3.9% were Other religion.

In our study fever (100.0%) was the commonest symptom followed by vomiting(42.2%), abdominal pain(17.8%), Chest pain (3.9%), Cough (17.4%), Breathlessness (11.6%), Hemoptysis (2.7%), Loose motion (10.3%), headache & body-ache (47.0%), Arthralgia (18.3%), Bleeding tendency (3.7%), Anaemia (42.0%). In study by Gondhali M P et al ¹⁴ 90% had headache, 92% had bodyache, 43% nausea, 24% abdominal pain, 15% altered sensorium.

The commonest sign after fever was pallor in 47.3% and other signs seen in our study were icterus (16.7%), Oedema (3.7%) & Lymphadenopathy (2.1%). In study by Gondhali M P et al ¹⁴ 22% had pallor, 28% had icterus, 12% had hepatomegaly, 19% had splenomegaly.

In our study malaria fever was the commonest cause of febrile thrombocytopenia. Dengue fever was the commonest cause of febrile thrombocytopenia in studies by Gandhi A A et al 26.7% ¹⁵, Modi T et al 55.97% ¹⁶, Fawas M n et al 54.5% ¹⁷.

In our study the cure rate was amongst those present with thrombocytopenia 352 (80.3%). The death rate of patients presenting with thrombocytopenia 86 (19.5%) in studies by Yadav B S et. al.¹⁸ Overall mortality rate was 19.84%, where 29.54%, 22.22% & 14.96% cases died with severe, moderate and mild thrombocytopenia respectively.

Conclusion:

Fever with thrombocytopenia is one of the most challenging problems in the field of medicine. Among the patients of acute febrile illness with thrombocytopenia, the most common cause is malaria followed by AFI RT AMAB, Dengue, Tuberculosis & Septicaemia. A well organised systemic approach needs to be carried out with an awareness of different causes of fever with thrombocytopenia which can help to diagnose the case early and this will reduce the cost.

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