

A Study of Acute Febrile Illness with Thrombocytopenia from Tertiary Care Centre of Uttarakhand.

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Received: February 2018

Accepted: February 2018

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ABSTRACT

Background: Acute febrile illness with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infection is a common cause of thrombocytopenia. Infections like Malaria, Dengue, Typhoid and septicaemia are some of them. The present study is intended to know the various clinical presentation, laboratory studies, aetiology, clinical complications, relationship between platelet count and severity of disease and prognosis associated with acute febrile illness and thrombocytopenia. **Material and Methods:** Total 200 patients of age more than 12 years with acute febrile illness with thrombocytopenia attending medicine department were enrolled and studied for demographic details, clinical presentation and complications. **Results:** Majority of patients were aged <40 years (66.0%) with males (72%) preponderance. Out of total 200 cases enrolled in this study, 82 cases (41%) were diagnosed as dengue fever, 60 cases (30%) were of malaria, 36 cases (n=36;18%) were of scrub typhus, 6 cases (3%) were of Septicemia, 5 cases (n=5;2.5%) were of typhoid fever and 11 cases(5.5%) remain undiagnosed. **Conclusion:** Dengue was the commonest cause of fever with thrombocytopenia. Common Bleeding manifestations were petechiae /purpura and gum bleeding. Thorough clinical and laboratory evaluation would be helpful to evaluate different causes of fever with thrombocytopenia.

Keywords: Infection, Dengue, Septicaemia, Petechiae/purpura, Mortality.

INTRODUCTION

Acute febrile illness (AFI) is a common cause of patients seeking healthcare in India, especially between June and September.^[1] The aetiologies of acute febrile illness can be diverse and may be dependent on geographic location.^[3-5] The infectious causes and epidemiology of acute febrile illness (AFI), defined as illness of < 1 week duration with no identified source, remain poorly characterized in many parts of the world.^[6,7]

In Asian countries, infectious diseases like influenza, dengue, chikungunya, typhoid fever and Japanese encephalitis virus dominate as the aetiologies of acute fever.^[8] In India too, infectious aetiologies have dominated the scene with dengue, malaria and typhoid being the major etiologies.^[9,10]

Thrombocytopenia if associated with fever helps to narrow differential diagnosis and management of fever. Platelet is important element in the blood for blood coagulation. The normal platelet count is 150000-450000/mm³.

In the recent years, acute febrile illness with thrombocytopenia has become a common clinical presentation in tertiary-care hospitals. Established infective causes such as dengue are well known for fever with thrombocytopenia. Thrombocytopenia is not a disease but is condition caused by the underlying illness, hence it is important to acquire details regarding the underlying etiology. Detailed examination and laboratory tests should be done, which are related to etiology. This calls for a detailed history taking for new drugs or drugs that are only taken intermittently, recent infection, previously diagnosed hematologic disease, nonhematologic diseases known to decrease platelet counts [e.g., eclampsia, sepsis, disseminated intravascular coagulation (DIC), anaphylactic shock, hypothermia, massive transfusions], positive family history of bleeding and/or thrombocytopenia, recent live virus vaccination, pregnancy, history pertaining to alcohol consumption, and human immunodeficiency virus (HIV). Risk factors should be assessed which might contribute to occurrence of thrombocytopenia among patients with acute fever. Overall, few studies have been done in the context in the past, and till date no such detailed, methodical and planned study has been done from Kumaon region of Uttarakhand that is geographically different from other parts of

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the country and moreover there is a paucity of literature in this matter from this area.

Keeping in view of these considerations, it is essential that the spectrum of underlying etiologies along with detailed clinical profile and associated complications in patients with acute fever with thrombocytopenia should be studied. Hence, the present study was planned with an aim to study the clinical profile and complications of acute fever with thrombocytopenia.

MATERIALS AND METHODS

We enrolled 200 cases of acute febrile illness with thrombocytopenia in the present study. Patients of age more than 12 years with fever of less than one week duration and Platelet count less than 1,00,000 /cumm attending the medicine OPD & IPD from September 2015 to April 2017 were included. Detailed clinical examination was done in every case with special emphasis for search of rashes, eschar, splenomegaly, hepatomegaly, lymphadenopathy, signs of meningeal irritation, signs of respiratory system dysfunction and renal dysfunction and were subjected to complete routine hematological, biochemical investigations, peripheral blood smear examination and other special investigations relevant to our study like chest X-Ray, ultrasonography abdomen. Once the specific diagnosis was reached, patients were treated for it symptomatically and specifically. Platelet transfusions was done if platelet count was less than 20,000/cumm and/or in the presence of bleeding manifestations.

RESULTS

The present study was a prospective observational study was carried out in which a total of 200 patients falling in sampling frame were enrolled.

Table 1: Showing age wise distribution of patients.

(1) Age group	No. of cases	Percentage(%)
<20 Years	38	19
21-30 Years	48	24
31-40 Years	46	23
41-50 Years	36	18
51-60 Years	16	8
61-70 Years	10	5
71-80 Years	6	3
(2) Gender		
Male	144	72
Female	56	28
(3) Place of residence		
Hilly Region	64	32
Tarai or Plains	136	68

Demographic Profile of Patients

In our study, maximum number of patients (n=48; 24%) were between the age group of 21 to 30 years. Majority of patients (n=132; 66%) were having age less than 40 years. Mean age of patients was 36.31±15.31 years [Table 1 & Figure 1]. In our

study, out of total 200 cases, 144 (72%) were male and 56(28%) were female patients. Male to female ratio was 2.57. In our study, 136 (68%) patients were from tarai or plains region and remaining 64 (32%) patients were from hilly region. [Table 1]

Seasonal incidence

In our study, maximum number of cases were seen in the months of August-November (n=169; 84.5%). These are the months of monsoon when the vector borne diseases are supposed to be high. Only 31 cases (15.5%) were registered in the months of December to July. Minimum incidence were reported in months of March and June when only 2 (1%) cases were registered [Figure 1].

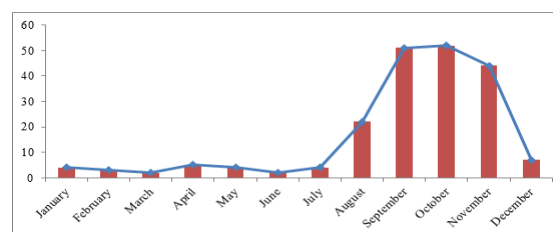


Figure 1: Showing month wise incidence of cases.

Aetiological spectrum of patients

Out of total 200 cases, 82 cases (n=82;41%) were diagnosed as dengue fever, 60 cases (n=60;30%) were of malaria, 36 cases (n=36;18%) were of scrub typhus, 6 cases (n=6;3%) were of septicemia, 5 cases (n=5;2.5%) were of typhoid fever and 11 cases(n=11;5.5%) remain Undiagnosed [Figure 2].

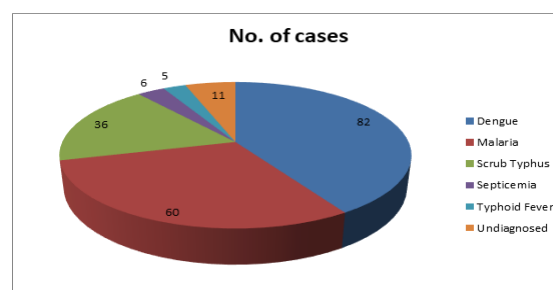


Figure 2: Showing distribution of cases according to aetiology.

Table 2: Showing pattern of presenting complaints in patients.

SN	Characteristic	No. of cases	Percentage (%)
1.	Bodyache	96	48
2.	Joint pain	62	31
3.	Headache	88	44
4.	Muscular pain	94	47
5.	Maculopapular rash	56	28
6.	Lymphadenopathy	4	2
7.	Pruritus	26	13
8.	Pain/redness in eyes	12	6
9.	Photophobia	2	1
10.	Blurred vision/diplopia	0	0
11.	Bleeding manifestations	72	36
12.	Others (Abdominal pain, diarrhea, resp. distress, vomiting)	38	19

Presenting Complaints

Most common presenting complaint was bodyache(n=96;48%) followed by muscular pain(n=94;47%),headache (n=88;44%)bleeding manifestations (n=72;36%), joint pain(n=62;31%), maculopapular rashes (n=56;28%), pruritus (n=26;13%), pain in eyes (n=12;6%) lymphadenopathy (n=4;2%) [Table 2].

On physical examination

Most common general examination finding was pallor (n=92;46%) followed by icterus(n=32;16%) and lymphadenopathy(n=4;2%) [Table 12 & Figure 12]. Splenomegaly was found in 48(24%) patients, hepatomegaly was found in 12(6%) patients and hepatosplenomegaly was found in 8(4%) patients.

Pattern of bleeding manifestations

Out of 200 cases of febrile thrombocytopenia, 72(36%) patients had bleeding manifestations and rest of the 128(64%) patients did not have any bleeding manifestations [Figure 3].

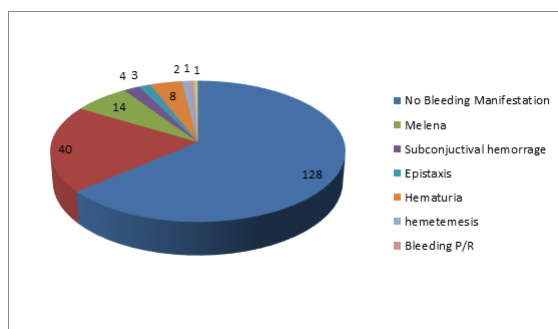


Figure 3: Showing distribution of bleeding manifestations among patients.

Among 72 patients who had bleeding manifestations, petechiae/ purpura was the most common presentation with 40(20%) patients followed by melena in 14(7%) patients, hematuria in 8(4%) patients, subconjunctival haemorrhage in 4(2%) patients, epistaxis in 3(1.5%) patients, hematemesis in 2(1%) patients, and bleeding per rectum in 1(0.5%) patient.

Correlation between etiology of fever and pattern of bleeding manifestations

Bleeding manifestations were present in 46(56%) out of 82 cases of dengue, 20(33.3%) out of 60 cases of malaria, 4(11.1%) out of 36 cases of scrub typhus and only 2(18.2%) out of 11 undiagnosed cases.

Hepatorenal dysfunction

In our study, derangement of liver function tests SGPT, SGOT and S. bilirubin was observed in 94(47%), 86 (43%) and 30(15%) patients respectively, and derangement of renal function tests serum creatinine and urea was observed in 48 (24%) and 32(16%) patients respectively.

Correlation between etiological profile and platelet transfusion

In present study, out of total 82 cases of dengue fever, 46(56.09%) patients required platelet transfusion. Platelet transfusion was done in 20(33.33%) out of 60 cases of malaria, 4(11.11%) out of 36 cases of scrub typhus and 2(18.18%) out of 11 undiagnosed cases. None of the patients of septicemia and typhoid fever required platelet transfusion [Figure 4].

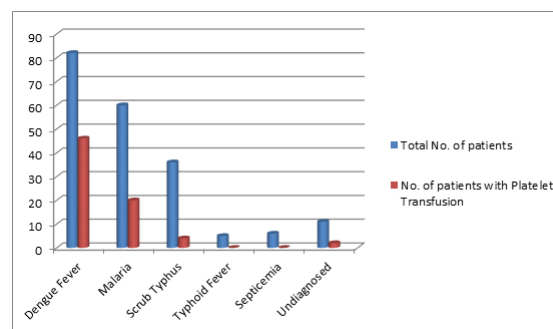


Figure 4: Showing correlation between etiological profile and platelet transfusion.

Correlation between etiological profile and clinical outcome

In present study, out of 82 cases of dengue fever 80(97.56%) patients improved and 2(2.43%) patient expired, out of 60 cases of malaria 59(98.33%) patients improved and 1(1.66%) patient expired, out of 36 cases of scrub typhus 32(88.89%) patients improved and 4(11.11%) patient expired, out of 6 cases of septicemia, 5(83.33%) patients improved but 1(16.67%) patient expired and out of 11 undiagnosed cases 1patient (9.09%) expired.

DISCUSSION

Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like malaria, dengue, typhoid and septicemia are some of the common causes of fever with thrombocytopenia.

Demographic Profile

Age

In our study the maximum prevalence of fever with thrombocytopenia was in the age group of 21-30 years with about 48(24%) patients and the mean age was 36.31 years. These findings are consistent with the result of study done by Gondhali et al. (2016),^[11] in which maximum prevalence was in this age group only i.e. 26%. Similarly in study done by Nakhle et al. (2016),^[12] prevalence of febrile thrombocytopenia in the age group of 21-30 years was even higher (41.8%). Younger age group are the most active working group of population and hence are at increased risk of exposure to vector borne diseases like dengue, malaria and scrub typhus. In our study

the bulk of the patients were involved in farm or forestry operations.

Sex

In our study, there was male preponderance with 144 (72%) males and 56 (28%) females which is in concordance with studies conducted by Nair et al. (2003),^[13] Gondhali et al. (2016) and Modi et al. (2016),^[11,14] which had 76%, 56% and 70% males respectively. Male preponderance can be attributed to increased outdoor activities among men.

Topographic profile

In our study, 136(68%) patients were from tarai or plains region and remaining 64 (32%) patients were from hilly region. As our hospital drains patients from both hilly and plain/tarai regions.

Seasonal profile

In our study, maximum number of cases were seen in the months of August-November (n=169; 84.5%) which is in concordance with studies conducted by Modi et al. (2016),^[14] in which larger proportion of cases coincided mainly during rainy and early winter season(August to November) with 71%. Most of vector borne diseases exhibit a distinctive seasonal pattern and climatic factors such as rainfall, temperature and other weather variables affecting in many ways both the vector and the pathogen they transmit. Thereby, maximum number of cases are seen in rainy seasons because of water logging which acts as breeding ground for mosquitoes. Increased number of cases of scrub typhus in our study was probably due to increased farming activity during the months of August to September and intense growth of scrub vegetation in the monsoon and post monsoon period which lead to the proliferation of the mites.

Aetiologies of febrile thrombocytopenia

In our study dengue 82(41%) was the leading cause of fever associated with thrombocytopenia followed by malaria 60(30%), scrub typhus 36(18%), undiagnosed cases 11(5.5%), septicemia 6(3%) and typhoid fever 5(2.5%) cases respectively.

In study done by Gondhali et al. (2016),^[11] among 100 cases of fever with thrombocytopenia dengue fever 56 (56%) was the commonest cause followed by septicaemia 17 (17%), malaria 15(15%), HIV 5 (5%), Viral Hepatitis 4 (4%), Typhoid 3 (3%). In similar study done by Masamatti et al.(2016),^[4] commonest infectious etiology of febrile thrombocytopenia was dengue 48.2% followed by septicemia 19.8%, typhoid fever 15% and disseminated intravascular coagulation 5.7% respectively. In our study second most common cause of febrile thrombocytopenia was malaria but in studies done by Gondhali et al. (2016) and Masamatti et al.(2016) second most common cause was septicaemia.^[4,11]

In study done by Modi T et al.^[14] (2016) viremia constituted the commonest etiology of febrile thrombocytopenia of which 56% cases were of dengue fever and other viral fever followed by

malaria 26%, septicaemia 5.3%, megaloblastic anemia 2.8%, haematological malignancy 2% and enteric fever 1.6% respectively. In study done by Modi T et al.(2016),^[14] two most common etiologies were dengue fever and malaria which is in concordance with findings in our study. All of these studies were in concordance with our results having infection as the commonest cause of febrile thrombocytopenia and dengue being the commonest etiology among infections.

The possible explanation for scrub typhus being the third cause of febrile thrombocytopenia in our study is that our center drains patients from hilly regions of Kumaun too, where scrub typhus occurs frequently.

Clinical presentation

The common presenting symptoms and signs were analyzed and all the salient clinical features were evaluated in detail. It was observed that all patients experienced constitutional symptoms with generalized weakness (n=164;82) being the most common symptom followed by lassitude, arthralgia, myalgia, headache and bone pain. A similar type of clinical presentation was also present in study done by Bhatnagar et al. (2016),^[15] Nair et al (2003) and Modi T et al.^[13,14] (2016) with commonest constitutional presentation being generalized weakness followed by headache, bodyache, retroorbital pain, nausea and abdominal pain. Author does not find any reason for discrepancy in the clinical presentation.

In Our study, the most common general examination finding was pallor (n=92;46%) followed by icterus (n=32;16%) and lymphadenopathy(n=4;2%). The most common abdominal examination finding was splenomegaly (n= 48;24) followed by hepatomegaly (n=12;6%) and hepatosplenomegaly (n= 8;4%). The most common respiratory symptom was shortness of breath (n=24;12%) followed by chest pain and cough with expectoration. On CNS examination, altered sensorium was found in 12(6%) patients and seizures in 4(2%) patients. Our study findings are similar to the study done by Gondhali et al (2016),^[11] in which on general physical examination, 22% had Pallor, 28% Icterus, 12 % hepatomegaly, 19% splenomegaly. Malaria cases were most commonly associated with hepatosplenomegaly or splenomegaly alone.

Bleeding manifestations

In our study, out of 200 cases of febrile thrombocytopenia, 72(36%) patients had bleeding manifestations. In study done by Nair et al,^[13] Out of 109 patients 45(41.3%) patients had bleeding manifestations. In our study petechiae/ purpura was the most common bleeding manifestation with 40(20%) patients followed by melena 14(7%), hematuria 8(4%) , subconjunctival hemorrhage 4(2%), epistaxis 3(1.5%), hematemesis 2(1%) and bleeding per rectum 1(.5%) patients respectively.

Biochemical tests

In our study, derangement of liver function tests SGPT, SGOT and S. bilirubin was observed in 94(47%), 86 (43%) and 30 (15%) patients respectively. Most common aetiology associated with deranged liver function in our study was malaria(63.33%) followed by scrub typhus (55.55%), septicemia(50%), dengue(34.14%), undiagnosed cases (27.27%) and typhoid fever(20%).

In study done by Gondhali et al.(2016),^[11] out of 56 cases of dengue fever 3 cases had abnormal total bilirubin values, 17 cases had abnormal SGOT levels and 13 cases had abnormal SGPT levels, out of 15 cases of malaria, 11 cases had abnormal total bilirubin values, 7 cases had abnormal SGOT levels and 3 cases had abnormal SGPT levels, all cases of septicaemia and viral hepatitis had abnormal levels of total bilirubin, SGOT and SGPT. These findings are in contrast to our study where majority of the patients having deranged liver function tests were found in malaria followed by scrub typhus.

In our study, derangement of renal function tests serum creatinine and urea were observed in 48 cases (n=48;24%) and 32 cases(n=32;16%) respectively.

Most common aetiology associated with deranged renal function in our study was malaria(40%) followed by scrub typhus (38.88%), septicaemia (33.33%), undiagnosed cases (27.27%) and dengue fever(7%).

In study done by Gondhali et al (2016),^[11] 24% cases had abnormal renal function tests out of 100 cases majority of which were seen in septicaemia cases followed by dengue, malaria and viral hepatitis with 3,3 and 1 case respectively. These findings are in contrast to our study where majority of the patients having deranged renal function tests were found in malaria followed by scrub typhus.

Comparison of outcome of patients

In our study, overall mortality was 9 patients (4.5%). Two patients (2.43%) out of 82 cases of dengue fever, 1 patient (1.66%) out of 60 cases of malaria, 4 patients (11.11%) out of 36 cases of scrub typhus, 1 patient (16.67%) out of 6 cases of septicemia and 1 patient (9.09%) out of 11 undiagnosed cases expired.

In study done by Gondhali et al. (2016),^[11] overall mortality was 6%, maximum in septicemia (5%) followed by dengue fever(1%). In study done by Patil et al. (2013),^[16] good outcome was seen in 95% patients, mortality was noticed in 5% of patients and major cause for mortality was septicemia in 60% patients followed by malaria and viral fever. In the study by Lohitashwa et al.^[17] (2009) septicemia accounted for 78% and dengue accounted for 22% of mortality.

Mortality in our study is similar to the study done by Gondhali et al.(2016) and Patil et al.^[11,16] (2013) but major cause of mortality was different. In our study major cause of mortality was scrub typhus whereas

in the studies done by Gondhali et al.(2016) Patil et al. (2013),^[11,16] major cause of mortality was septicemia. Possible explanation for this fact is that patients of septicemia in our study were less as compared to the studies done by Gondhali et al.(2016) and Patil et al. (2013),^[11,16] whereas scrub typhus was the third major cause of febrile thrombocytopenia in our study. Majority of the patients of scrub typhus were from hilly areas where primary health infrastructure is not in good shape and delay in arrival to the tertiary care center lead to lack of timely intervention, more complications and higher mortality in this group.

CONCLUSION

Mean age was 36.31±15.31 years. Majority were aged <40 years (66.0%). There was male (n=144;72%) preponderance out of total 200 patients. Majority of patients were from plain/tarai region (n=136;68%) and out of total 200 patients 78 (39%) patients were from Haldwani. A total of 169 (84.5%) patients presented during the months of August to November. All patients experienced constitutional symptoms with generalized weakness (n=164;82) as the most common symptom followed by lassitude, arthralgia, myalgia, headache and bone pain. Most common general examination finding was pallor(n=92;46%) followed by icterus(n=32;16%) and lymphadenopathy(n=4;2%). In this study, splenomegaly was found in 48(24%) patients, hepatomegaly in 12(6%) patients, and hepatosplenomegaly in 8(4%) patients. Out of 200 cases, 72(36%) patients had bleeding manifestations and the rest 128(64%) patients did not have any bleeding manifestation. Among 72 patients who had bleeding manifestations, petechiae/ purpura was the most common manifestation with 40(20%) patients followed by melena in 14(7%) patients, hematuria in 8(4%) patients, subconjunctival haemorrhage in 4(2%) patients, epistaxis in 3(1.5%) patients, hematemesis in 2(1%) patients, and bleeding per rectum in 1(0.5%) patient. Out of the 82 cases of dengue, 46(56%) cases had bleeding manifestations. Out of the 60 cases of malaria 20(33.3%) cases had bleeding manifestations. Out of the 36 cases of scrub typhus 4(11.1%) cases had bleeding manifestations. Derangement of liver function tests were observed in 94 patients(47%). Derangement of renal functions was observed in 48 cases(24%). Out of total 200 cases enrolled in this study, 82 cases (41%) were diagnosed as dengue fever, 60 cases (30%) were of malaria, 36 cases (n=36;18%) were of scrub typhus, 6 cases (3%) were of Septicemia, 5 cases (n=5;2.5%) were of typhoid fever and 11 cases(5.5%) remain undiagnosed. Thus dengue, malaria and scrub typhus were the major etiologies. As dengue and malaria were the most common infectious etiologies in this region, preventive measures such as avoidance of water pooling, spraying of insecticides and

larvicides, along with personal protective measures can be undertaken.

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How to cite this article: Negi A, Singh Y, Singh M, Saxena SR. A Study of Acute Febrile Illness with Thrombocytopenia from Tertiary Care Centre of Uttarakhand. *Ann. Int. Med. Den. Res.* 2018; 4(3):ME01-ME06.

Source of Support: Nil, **Conflict of Interest:** None declared