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International Journal of Current Research
Vol. 10, Issue, 02, pp.65036-65041, February, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

A PROSPECTIVE STUDY OF CLINICAL ASSESSMENT OF FEVER WITH THROMBOCYTOPENIA

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ARTICLE INFO

Article History:
Received 28th November, 2017
Received in revised form
23rd December, 2017
Accepted 08th January, 2018
Published online 18th February, 2018

Key words:

Thrombocytopenia,
Dengue,
Leptospirosis,
Septicemia,
Petechiae.

ABSTRACT

Fever is defined as elevation of normal body temperature above the normal circadian variation[3]. Thrombocytopenia is defined as platelet count <1,50,000/microliter. Infection is the most common cause. Fever with thrombocytopenia narrows the differential diagnosis of the clinical entity. A well organised systemic approach is carried out with an awareness of cause of fever with thrombocytopenia to shorten the duration of investigation and bring out diagnosis.

Aims and objectives:

1. To study incidence of various etiological agents for patients getting admitted for fever with thrombocytopenia.
2. To analyse epidemiological data, clinical features, investigations, incidence of complications and outcome of patients.

Material and Methods: This is a prospective study done in patients admitted for fever with thrombocytopenia in NRI Institute of medical sciences, Sangivalasa, Visakhapatnam, India, over a period of one year from Jan 2017 to Dec 2017. 100 patients are selected based on inclusion and exclusion criteria. Based on symptoms, signs and investigations etiological factors were analysed and diagnoses were done..

Results: 100 cases were admitted with fever with thrombocytopenia. Out of this 100 cases, 70 cases were male and 30 cases were female with male female ratio of 2.3:1. Most of the cases admitted between age 26 to 35. The mean age for male and female cases was 33.76 and 33.1 respectively. The most common cause is infectious, of which dengue is most common (42%) followed by malaria (21%). Petechiae is common bleeding manifestation. Blood transfusion is not needed for all the cases even when platelet is below 20,000. Acute renal failure is the common complication. Mortality is 8%.

Conclusion: Fever with thrombocytopenia is one of the most challenging problems in field of medicine. Infection is the most common cause. Dengue, malaria, leptospirosis still present clinically in atypical and occult form, making diagnosis more difficult. So specific tests like rapid spot test, IgM ELISA for dengue, IgM ELISA leptospirosis antibodies, widal test etc are required for correct diagnosis. Spontaneous bleeding was noted in patients with platelet count <20,000. Platelet transfusion is not needed for all the cases. Overall mortality for fever with thrombocytopenia is 8%.

Citation: Salla Surya Prakasarao, Ram Prasad Kadiyala, Suma Pusapati, Kartheek Pyla and Srikanth Gummadi, 2018. "A prospective study of clinical assessment of fever with thrombocytopenia", *International Journal of Current Research*, 10, (02), 65036-65041.

INTRODUCTION

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholarslike Hippocrates (Larson, 1970). 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 (Nolan, 1987). 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 (Woodward, 1997). Most cases of prolonged fevers are instances of well-known diseases manifesting them typically. 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

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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 inthe thermoregulatory center located in the anterior hypothalamus. An AM temperature of >37.2°C (98.9°F) or a PM. temperature of >37.7°C(99.9°F) would define fever (Woodward, 1997). Though thrombocytopenia is encountered in various diseases, it is for sure that potentially fatal bleeding due tothrombocytopenia is rare. The causes of thrombocytopenia are impaired platelet production, accelerated platelet destruction or dilution and or splenic sequestration (Levine, 1993). Even though there is no absolute relation between platelet counts and bleeding, Certain broad generalizations can be made, with counts less than 10,000/µL, bleeding is usual and may be severe (Colman, 1982). Thrombocytopenia is characterized by bleeding most often from small vessels. This can manifest as petechiae over theskin, hemorrhages from mucosa of gastrointestinal and genitourinary tract. Intracranial hemorrhage is a dangerous consequence in thrombocytopenic patients. Thrombocytopenia is defined as platelet count <1,50,000/µL. This is due to decreased production, increased destruction (immunogenic and non-immunogenic), and increased sequestration in spleen. Of these infections being the commonest cause of thrombocytopenia (Firkin, 1990; George, 2001). Infections like dengue, leptospirosis, malaria, typhoid, military TB, HIV, septicemia are some of the common causesof 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 fataloutcomes. Hence a need for study to know the clinical profile and complications of fever with thrombocytopenia.

MATERIALS AND METHODS

The present study was done in patients admitted to NRI medical college, Visakhapatnam in between jan 2017 to dec 2017. The studywas approved by the Ethical and Research Committee of Nri Medical College, Visakhapatnam-531162, India. During the study period, all the patients presenting with Fever and Thrombocytopenia were screened for eligibility and Informed consent was obtained.

Selection Criteria

All patients more than 12years of age with fever (temperature >99.9°F and platelet count less than 1,50,000 cells/cu.mm.

No of patients selected: 100

Exclusion Criteria

- All patients less than 12years of age.
- All patients with thrombocytopenia without fever.
- Diagnosed cases of platelet disorders and dysfunction.
- Patients on treatment with antiplatelet drugs and other drugs causing thrombocytopenia.

Period of Study

All patients were age of ≥12 years who were admitted as in-patients between jan 2017 to dec 2017 in the medicine department in NRI Institute of Medical Sciences for fever with thrombocytopenia.

Study Design: Prospective study.

METHODS

All patients admitted with fever and thrombocytopenia were evaluated. History was taken regarding duration of fever, occupation, history of travel. Symptoms other than fever, headache, nausea, vomiting, abdominal pain, diarrhea, cough, anorexia, myalgia, gum bleeding, hemetemesis, conjunctival suffusion, oliguria, hematuria, loss of weight, etc., were noted. Signs like rashes, signs of dehydration, petechiae, jaundice, lymphadenopaty, hepatomegaly, spleenomegaly, anemia, abdominal tenderness, added sounds in lungs, altered sensorium, etc., were also noted. Investigations like complete hemogram, ESR, liver function tests, routine urinary examination, urine for bile salts and bile pigments, renal parameters like blood urea, serum creatinine, serum electrolytes, peripheral smear, X-ray chest, USG abdomen were done on admission. Other special investigations like peripheral smear for MP, dengue serology, widal study, IgMantibodiy for leptospirosis, sputum AFB, ELISA for HIV1 and HIV2, blood culture and urine culture, bone marrow aspiration. During the hospital stay all the patients were subjected to repeat CBC once in 2 days. The renal function tests were every 3rd day unless the patient developed ARF, for whom the test was done daily. Follow up of all patients regarding treatment and outcome were done during the hospital stay.

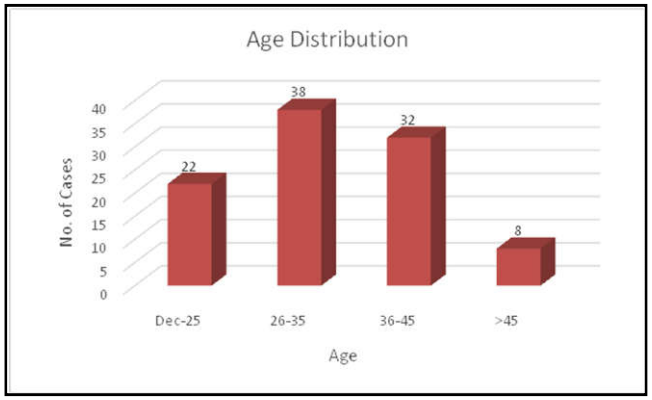
RESULTS AND ANALYSIS

Analysis of clinical symptoms, laboratory profile and complication of 100 patients presented with fever with thrombocytopenia admitted at NRI Medical College and Hospital, between January 2017 to december 2017, who met the inclusion criteria was done. Total number of cases admitted with fever with thrombocytopenia is 100. Out of this 100 cases, 70 cases were male and 30 cases were female with male, female ratio is 2:3:1. Most of the cases admitted between 26 to 35. The mean age for male and female cases was 33.76 and 33.1 respectively. The age and sex distribution is given below Fig 1, 2, and 3.

Age wise distribution of cases

Table 2.

Age	No.Of Cases	Percentage
12-25	22	22%
36-35	38	38%
35-45	32	32%
>45	8	8



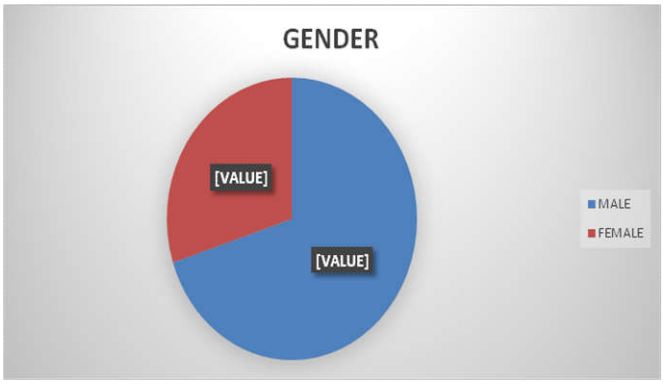
Graph 1.

Sex Wise Distribution

Table 3.

Sex	No Of Cases	Percentage
Male	70	70%
Female	30	30%

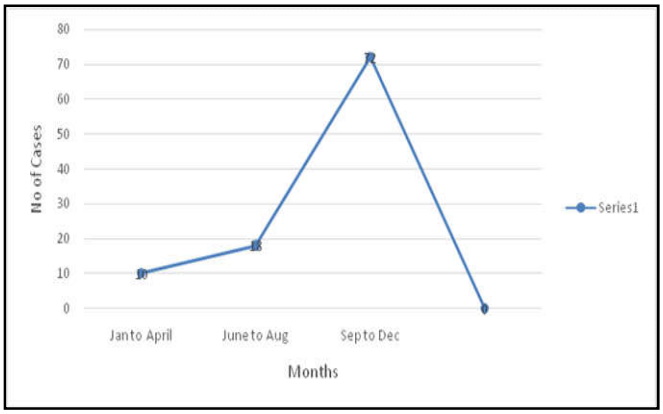
Graph 2.



Seasonal Variaton

Out of 100 cases, 50 of fever with thrombocytopenia admitted between September and November month. The seasonal variation distribution is given below.

Graph – 3

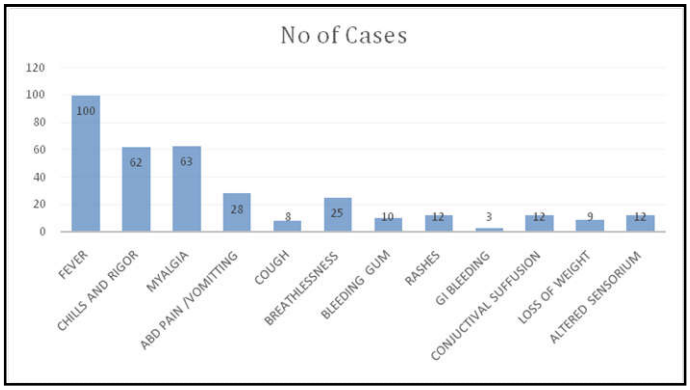


Distribution of Symptoms

Most common presenting symptoms is fever with chills and rigor, myalgia followed by abdominal pain and vomiting.

Table 4.

Si.No.	Symptoms	No.of Cases	Percentage
1	Fever	100	100%
2	Chills And Rigor	62	62%
3	Myalgia	63	63%
4	Abd Pain /Vomitting	28	28%
5	Cough	8	8%
6	Breathlessness	25	25%
7	Bleeding Gum	10	10%
8	Rashes	12	12%
9	Gi Bleeding	3	3%
10	Conjuctival Suffusion	12	12%
11	Loss Of Weight	9	9%
12	Altered Sensorium	12	12%



Graph 4.

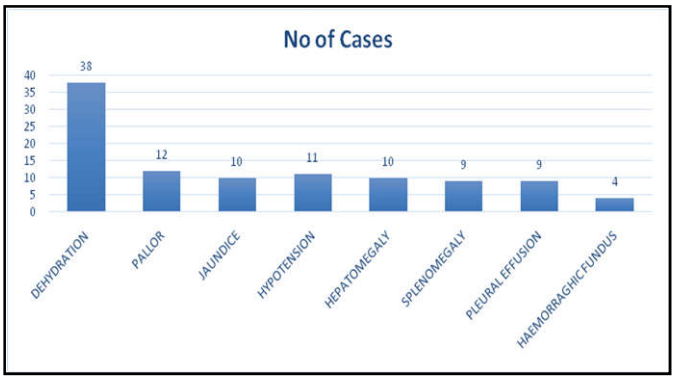
Districation of Signs

Table 5.

Si.No	Sign	No of Cases	Percentage
1	Dehydration	38	38%
2	Pallor	12	12%
3	Jaundice	10	10%
4	Hypotension	11	11%
5	Hepatomegaly	10	10%
6	Splenomegaly	9	9%
7	Pleural Effusion	9	9%
8	Haemorraghic Fundus	4	4%

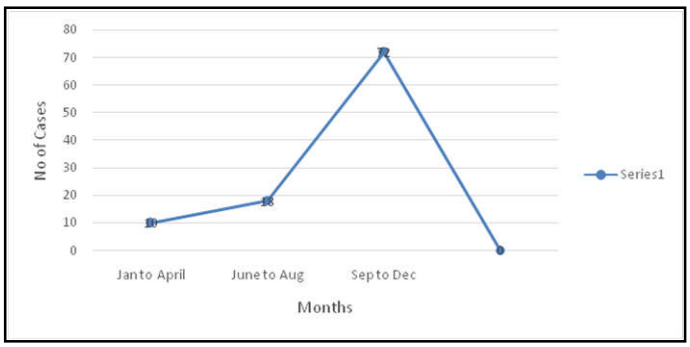
Signs Distribution

Graph 5.



Distribution of Etiological Agents

Out of 100 cases, most common causes for fever with thrombocytopenia is dengue fever (42), followed by malaria (21) and leptospirosis (11). Etiological distribution is given below.



Graph 5.

Analysis of Lab Investigation

Complete Hemogram:

- Mean hemoglobin value was 11.8 gm%
- Range 5.5 – 14.4gm%.

Platelet Count

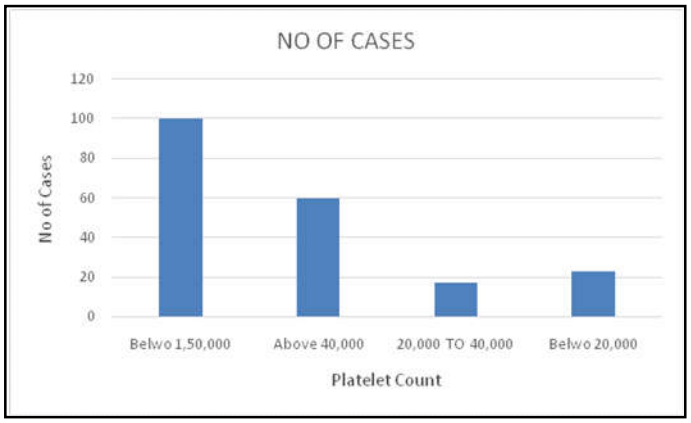
- Mean platelet count was 52,175.00 / µ L
- Ranges from 5,500 /µ L
- Out of 100 cases with thrombocytopenia (<1,50,000), 60 cases were above 40,000. 17 cases were between 20,000 to 40,000. But 23 cases were below 20,000

Platelet Count

Table 6.

Si.No	Platelet Count	NO of Cases	Percentage
1	<1,50,000	100	100%
2	>40,000	60	60%
3	20,000 TO 40,000	17	17%
4	< 20,000	23	23%

Platelet Count



Graph 6.

Haematocrit

- Mean haematocrit value was 32.05
- The value ranges from 21 to 55

Renal Function Test

Out of 100 cases, 12 cases had elevated renal parameter. Out of this 12 cases, 8 patients renal parameter improved with rehydration alone. Only 4 cases who needed nephrologist's intervention and dialysis.

Table 7.

Si.No	Blood urea	No of cases
1	<40	88
2	40-60	5
3	60-100	2
4	>100	5

Liver Function Test

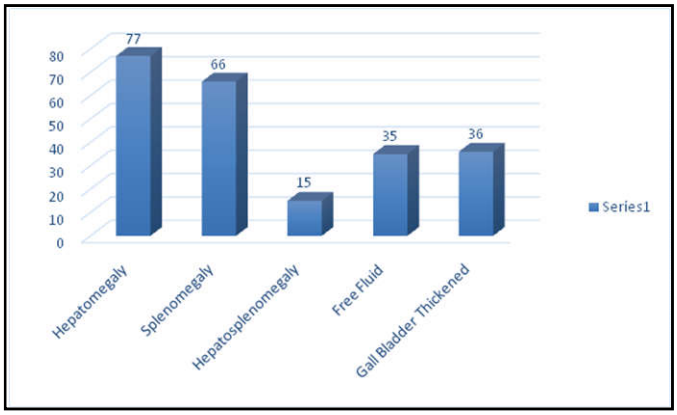
Out of 100 cases, 13 cases had elevated liver function test. Out of this 13 cases, 6 patient had bilirubin level > 5.0 mg/dl. Out of this 6 cases, 3 patients were died.

Table 8. Liver function test

LFT	MEAN	RANGE
Sr.Bilirubin	2.14 mg/dl	0.8 – 18.0 mg/dl
SGOT (U/L)	53.10	21-360
SGPT (U/L)	57.54	23-336
ALP (IU/L)	82.53	54-179

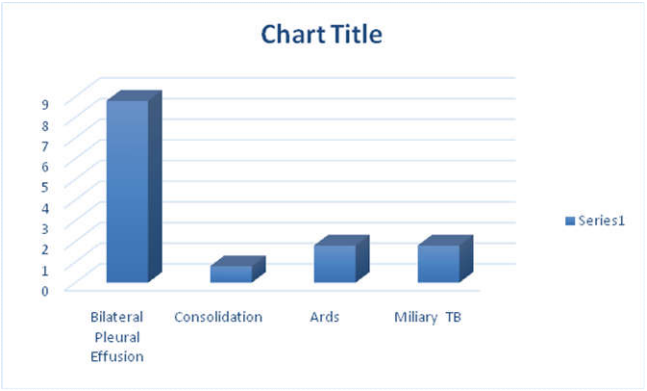
Usg Abdomen

Graph 7.



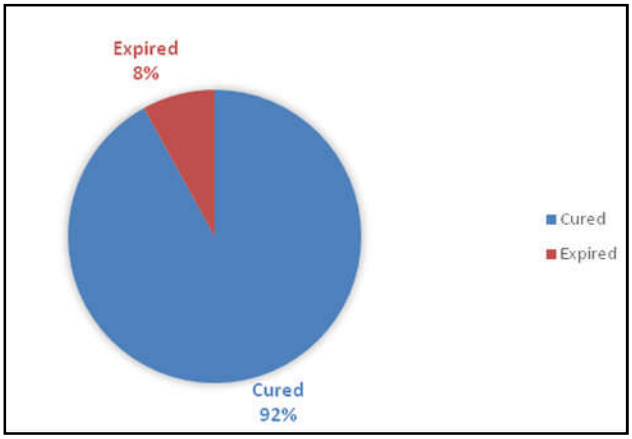
Graph 8.

X – Ray Chest Pa View



MORTALITY

- No. of patients expired is – 8.
- Mortality rate is - 8



Graph 9.

DISCUSSION

For a study of fever with thrombocytopenia, patient must satisfy above mentioned criteria's prospective case collection is necessary and careful follow up is warranted. The three conditions allow the delineation of standard study population. Out of 100 cases admitted with history of fever with thrombocytopenia, most common causes is infections. Out of this infections condition, dengue is the most common cause (42%), second most common cause is malaria 21%. Most of the patients were in the working group aged between 25 and 35 years. Further most of them were males (2:3:1). Further as far as the Seasonal Distribution of cases were concerned, most of the cases were admitted during the months of September, October and November during which the Northwest monsoon is active in Tamil Nadu though sporadic cases were also seen during other months of the year.Among symptoms other than fever, myalgia is most common 63%, followed by chills and rigor 62%. Among bleeding manifestation, purpura 12% is the most common followed by bleeding gum 10% and GI bleeding is least 3%. Out of 100 cases, 38% patients had dehydration at the time of admission. Among 38%, 11% patients had hypotension during admission. Most of the patients improved with treatment except few. Among 100 cases with reduced platelet count, 60% cases had platelet above 40,000. 17% case had platelet between 20,000 to 40,000. Remaining 23% cases had platelet below 20,000. Among 17 patient with platelet count between 20,000 and 40,000, 15 patients cured without blood transfusion. Only 2 patients needed blood transfusion.
Among 23 patient with <20000 platelet count, 12 patient improved without platelet transfusion. So only 11 patients actually need blood transfusion. Out of this 11 patients, 5 patients platelet count improved with FFB alone. So 6 out of 23 patients actually needed platelet transfusion.

In conclusion our study of fever with thrombocytopenia reveals that. Infection is the most commonest cause, among infections, dengue is the common cause because of seasonal and regional variation. Second most common cause is malaria, in that p.vivax is more common. Petechiaeis common bleeding manifestation. Blood transfusion is not needed for all the cases even when platelet is below 20,000. Acute renal failure is the common complication.

Summary

A prospective study of 100 patients, who had fever and thrombocytopenia was done in our hospital. The inclusion and exclusion criteria were followed according to the criteria' mentioned in the material and methods of the study.

- The age range of the patient was 18-62 years, with male and female ration being 2.3:1
- Most of the cases admitted during September to December.
- Among symptoms other than fever, myalgia is most common 63%, followed by chills and rigor 62%.
- Among bleeding manifestation, purpura 12% is the most common followed by bleeding gum 10% and GI bleeding is least 3%.
- A definitive diagnosis was made in 95% of the case.
- Among the diagnosed case, dengue is most common cause of fever with thrombocytopenia (42%). Our of this 42 cases, 37 cases were dengue haemorrhagic fever. 5 cases were dengue haemorrhagic shock.
- Other cases diagnosed were malaria, leptospirosis, typhoid, septicaemia, HIV, miliary tuberculosis, haematological malignancy.

Platelet count	No of cases	No. of cases improved without bl. Transfusion	No of cases improved after bl. Transfusion
40,000 – 1,50,00	60	60	0
20,000 – 40,000	17	15	2
< 20,000	23	12	11

Comparison of nair study, srinivasstudy our study

Disease category	Nair study		srinivas study		Our study	
Septicaemia	29	26.6%	19	19%	2	2%
Dengue /VHF	15	14.7%	14	14%	42	42%
Malaria	10	9.2%	41	41%	21	21%
Haematological	17	15.6%	0	0%	5	5%
Others	20	18.3%	26	26%	30	30%

Distribution of platelet count	Nair study		Our study	
0 – 20,000	19	17.5%	23	23%
40,000 – 40,000	28	25%	17	17%
40 – 1,50,000	62	56.8%	60	60%

A Similar type of study conducted in India by Nair Ps, Jain A at St.Stephen's Hospital, New Delhi, for period of one and half year. A total study of 109 cases were studied with same criteria as in our study[13]. Septicaemia 29% was the leading cause of fever associated with thrombocytopenia. Second common cause was enteric fever followed by dengue, malaria. In Srinivas study [14] malaria with 41 cases was the leading cause of fever associated with thrombocytopenia. Second common cause was enteric fever followed by septicaemia, dengue, leptospirosis with 24, 19, 2 cases respectively.

- Out of 21 cases, 19 cases were P.vivax and 2 cases were P.falciparum.
- Among 100 cases, most of the patients with platelet count above 40,000, 17 cases between 20,000 to 40,000. 23 cases had platelet below 20,000.
- Clinical manifestation of the thrombocytopenia are present only in 12 cases out of 100 cases.
- Among 23 patients with < 20000 platelet count, 12 patients improved without platelet transfusion. So, only 11 patients actually need blood transfusion.

- Out of 100 cases, 12 cases had elevated renal parameter. Out of this 12 cases, 8 patients renal parameter improved with rehydration alone. Only 4 cases who needed nephrologist's intervention and dialysis.
- In general, 92 cases had recovered and 8 cases had expired.
- In 92 cases who had good recovery 45 cases followed up and platelet count reached normal at the time of discharge.

Conclusion

- Fever with thrombocytopenia is one of the most challenging problem in the field of medicine.
- Fever with thrombocytopenia consists of occult presentation of common disease rather than rare disease.
- Infection is the most common cause of fever with thrombocytopenia.
- Dengue, malaria, leptospirosis still present clinically in a typical and occult form, making diagnosis more difficult. So high index of clinical suspicion is needed.
- So other than routine investigation they should do specific test like rapid spot test, IgM ELISA for dengue, IgM ELISA leptospirosis antibodies, widal test etc for correct diagnosis.
- In majority of the patient, thrombocytopenia without bleeding manifestation.
- Generally, spontaneous bleeding was noted in platelet count <20,000, even some patients not have any bleeding manifestation with this platelet count. But due to qualitative defect it was seen in platelet count in the range of 40,000 cell cu/mm also.
- Even with platelet count less than 20,000 platelet transfusion is not needed for all the cases.
- Overall mortality for fever with thrombocytopenia is 8%.

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