Association of Serum Ferritin Level with Severity of Dengue Fever

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Abstract

Introduction - Dengue is arboviral disease which has Aedes mosquitoes as vector. Causative agent is dengue virus of family Flaviviridae. Dengue fever is classified as dengue fever, dengue haemorrhagic fever and dengue shock syndrome. These has complications of capillary permeability, a decrease in platelet count, disordered blood clotting, severe bleeding, and for DSS alongside systemic shock leading to organ failure. The aim of our study was to find a correlation between thrombocytopenia & hospital stay with serum ferritin level in dengue fever.

Material & methods- This prospective observational study was conducted on 100 patients of dengue fever (diagnosed by NS1 antigen/IgM/ ELISA) admitted in wards of Department of Medicine, RNT Medical College, Udaipur during the period September 2018 to September 2020 after getting institutional ethical committee clearance. In our study Clinical features, haematological and biochemical parameters was noted. serum ferritin was measured. Standard statistical methods were used to analyse the data. Patient's characteristics were expressed as mean ± SD for continuous variables and they were compared using Chi square test.

Observations & results - Dengue fever was more common in male than females, more common in age group 20-40 years. There was almost equal incidence of dengue fever in urban and rural areas. Maximum patients had platelet count range of 0.5-1.5 lac. Duration of hospital stay depends on levels of serum ferritin on day 1 of admission (p value = 0.9) and thrombocytopenia level (p value = 0.1).

Conclusion – Serum ferritin had a linear correlation with severity of dengue fever & drop in platelet counts.

Keywords: NIL

Introduction

Dengue is one of the most significant arboviral diseases of humans worldwide. It is predominantly distributed in tropical and subtropical regions that are the natural home for its vector, mosquitoes of the genus Aedes.[1] The aetiological agent is the Flavivirus genus of family Flaviviridae, otherwise called dengue virus (DENV). Infection with DENV may be subclinical or symptomatic. Dengue fever clinical illness is classified, in order of increasing severity, as either dengue fever (DF), dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). More recently, the WHO proposed a revised classification of clinical infection: dengue; dengue with warning signs; and severe dengue.[1] DF is due to primary infection with any of the serotypes and is typically mild and self-limiting. Recovery from infection is generally complete and confers lifelong homotypic immunity. DF manifests as a fever for 2–10 days, headache, retroorbital pain, joint and muscle pain with skin rashes.[2] Secondary infection with another serotype generates cross-reactive antibodies, which increases the potential risk of antibody-dependent enhancement of disease, a form of immunopathology. Hence, recurrent infection is the major risk factor for

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the serious, often fatal, complications of DHF and the rarer DSS. These are marked by problems of capillary permeability, a decrease in platelet count, disordered blood clotting, severe bleeding, and for DSS alongside systemic shock leading to organ failure.[3]

Increased serum ferritin has been associated with severe dengue in children. Hyperferritinemia in dengue infected subjects is associated with intense immune activation and coagulation disturbances as noted in Aruba Dengue outbreak. An Indian study had shown that serum ferritin levels are significantly elevated in dengue infected cases compared to the controls; On group analysis, cases with severe dengue had higher ferritin levels than milder forms which was noted both during the febrile and defervescence stages of the illness.[4] Objective of this study is correlation of Serum Ferritin Levels with thrombocytopenia level and dengue fever severity.

Materials And Methods

This prospective observational study was conducted on patients admitted in wards of Department of Medicine, RNT Medical College, Udaipur during the period September 2018 to September 2020.

Inclusion Criteria: All positive patients for NS1 antigen/IgM/ ELISA for dengue along with platelets counts less than 150000/ µl were included in the study.

Exclusion Criteria: Patients with underlying malignancy, haematological disorder, septicaemia, or use of any drug which may cause thrombocytopenia. Patients with dengue NS 1 Positive or dengue IgM Positive with other disease (malaria, typhoid, scrub typhus).

Patients were divided into four groups according to Total platelet count:

Group 1: Platelet count less than 1.50 Lakhs

Group 2: Platelet count between 50000 - 1.00 Lakh

Group 3: Platelet between 20000-50000 counts

Group 4: Platelet count less than 20000

Clinical features, haematological and biochemical parameters were noted. serum ferritin was measured. Single donor platelets (SDP) transfusion was done if patient is actively bleeding or if platelets level were less than 10000/µl. According to serum ferritin level patients were divided into three groups: serum ferritin < 22 ng/ml, 22-322 ng/ml and > 322 ng/ml.

Sample Size:

Total 100 cases of dengue were included in the study.

Statistical Analysis

Standard statistical methods used to analyse the data. Patients' characteristics was expressed as mean ± SD for continuous variables and they were compared using Chi square test and P value < 0.05 was considered significant.

Result

Table no. 1 Platelet count distribution among study group

Platelet count (on day 1)	Male (n=60)	Female (n=40)	Total
Normal (>1.5lac)	14	7	21
Below normal:			
1-1.5 lac	17	10	27
0.5-1 lac	13	15	28
0.2-0.5 lac	10	6	16
<0.2 lac	6	2	8

Total	60	40	100

In this study 28% patients admitted with platelets counts in range of 0.5 lac - 1 lac, 27% patients admitted with platelet count in range of 1 - 1.5 lac, 21% patients admitted with platelet count more than 1.5 Lac (normal), 16% patients admitted with platelet count in range of 0.2 – 0.5 lac and 8% patients admitted with platelet count less than 0.2 lac

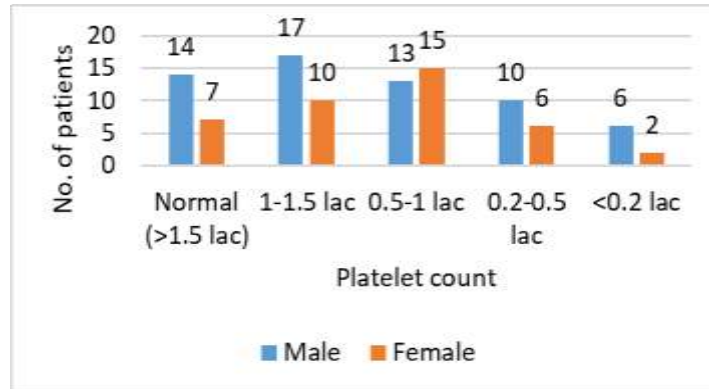### Platelet count distribution among study group

Table no. 2 Serum ferritin level among study group

Serum ferritin (ng/ml)	Male (n=60)	Female (n=40)	Total
Below normal <22	0	1	1
Normal (22-322	20	13	33
Above normal:			
(a)322-600	4	7	11
(b)>600-900	3	1	4
(c)> 900	33	18	51
Total	60	40	100

In this study 51% patients admitted with serum ferritin level more than 900 ng/ml, 33% patients admitted with serum ferritin level 22-322 ng/ml, 11% patients admitted with serum ferritin 322 – 600 ng/ml, 4% patients admitted with serum ferritin 600 – 900 ng/ml, 1% patients admitted with serum ferritin less than 22 ng/ml.

P value < 0.001   r = 0.3

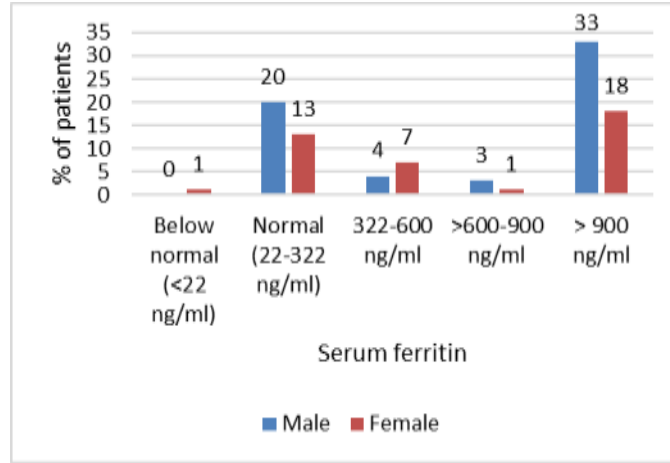**Fig: Serum ferritin level among study group**

Table no. 3 Serum ferritin level v/s Platelet count

Serum ferritin (ng/ml) (on day 1)	No. of patients					Total
	<0.2lac	**0.2-0.5lac**	**0.5-1.0lac**	**1.0-1.5lac**	**>1.5 lac**	
Below normal (<22)	0	0	0	0	1	1
Normal (22-322)	0	4	6	9	14	33
Above normal (>322)	8	14	21	17	6	66
Total	8	18	27	26	21	100

Serum ferritin level (ng/ml) v/s platelet count (lac)

In this study 66% patients had serum ferritin level above normal (more than 322 ng/ml) and platelet count of 21% patients were 0.5- 1 lac, platelet count of 17% patients were 1- 1.5 lac, platelet count of 14% were 0.2- 0.5 lac, platelet count of 8% patients were less than 0.2 lac, platelet count of 6% patients were more than 1.5 lac.

In this study 33% patients had serum ferritin level normal range (22-322 ng/ml) and out of 33% platelet count of 14% patients were more than 1.5 lac, platelet count of 9% patients were 1 – 1.5 lac, platelet count of 6% patients were 0.5 - 1 lac, platelet count of 4% patients were 0.2- 0.5 lac.

In this study 1% patients had serum ferritin level less than 22 ng/ml which had platelet count > 1.5 lac.

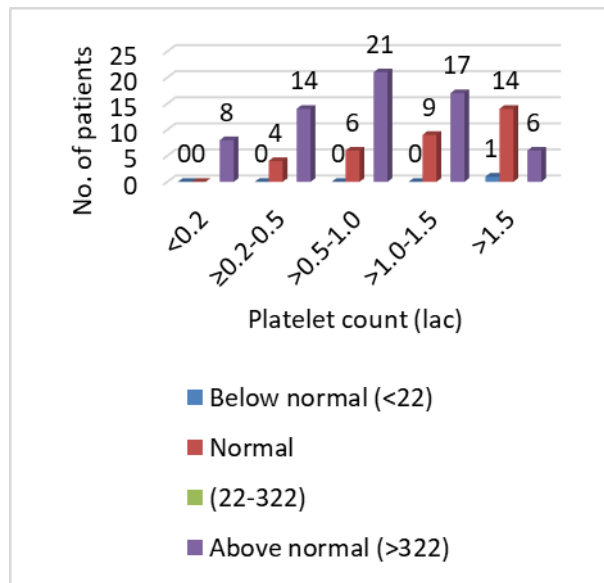In this study p value < 0.001 and coefficient of correlation (r) 0.37 and chi square test used.

Table No. 4 Serum ferritin v/s Platelet count

Serum ferritin (on day 1)	No. of patients	Mean platelet count (lac/mm^3)
Below normal (<22 ng/ml)	1	1.8
Normal (22-322 ng/ml)	33	1.33±0.64
Above normal:		
(a) >322-600 ng/ml	11	1.44±0.93
(b) >600-900 ng/ml	4	0.92±1.40
(c) > 900 ng/ml	51	0.76±0.52
Total	100	

In this study serum ferritin level of 51% patients were more than 900 ng/ml and mean platelet count were 0.76±0.52, serum ferritin level of 33% patients were normal 22 – 322 ng/ml and mean platelet count were 1.33±0.64, serum ferritin level of 11% patients were 322- 600 ng/ml and mean platelet count were 1.44±0.93, serum ferritin level of 4% patients were 600-900 ng/ml and mean platelet count were 0.92±1.40, serum ferritin level of 1% patients were less than 22 ng/ml and mean platelet count were 1.8.

Table no. 5 Hospital Stay

Hospital Stay (days)	Male (n=60)	Female (n=40)	Total
Less than 3 days	9	2	11
3-5 days	42	32	74
More than 5 days	9	6	15
TOTAL	60	40	100

In this study 74% patients stayed in hospital for 3–5 days, out of these, 42% patients were male and 32% patients were female,

15% patients stayed in hospital for more than 5 days, out of these patients, 9% patients were male and 6% patients were female.

11% patients stayed in hospital for less than 3 days, out of these patients, 9% patients were male and 6% patients were female.

Table no. 6 Hospital Stay

Hospital Stay	Serum ferritin (ng/ml)	Platelet count (lacs)
Less than 3 days	942.90±670.42	1.13±0.32
3-5 days	964.57±775.30	1.06±0.78
More than 5 days	987.81±699.58	0.89±0.57
P value	0.9064	0.01

Hospital Stay with serum ferritin
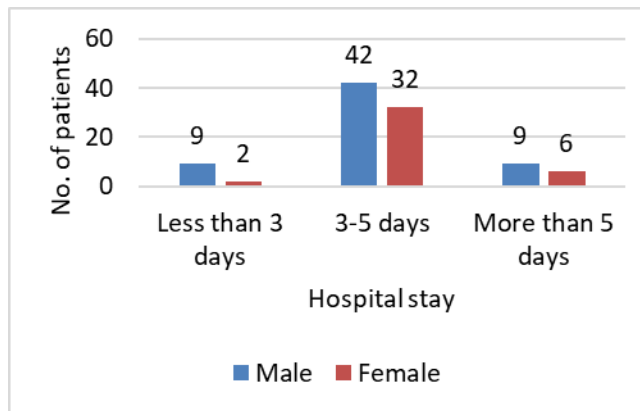
The patients admitted in the hospital less than 3 days had serum ferritin level 942.90±670.42 and patients admitted for 3-5 days had serum ferritin level 964.57±775.30 and more than >5 days had serum ferritin level 987.81±699.58 which indicate the severity of infection and mean serum ferritin increases with the staying time in hospital. The p value = 0.9.

The patients admitted in the hospital less than 3 days had platelet count 1.13±0.32 and patients admitted for 3-5 days had platelet count 1.06±0.78 and more than >5 days had platelet count 0.89±0.57. The p value = 0.01.

Discussion

In our study male patients were 60% and female patients were 40% out of total 100 patients which showed male pre dominance. This is similar with the study done by Afsar et al. which showed dengue fever had a higher incidence in males than females (34 male and 11 females out of 45).[5] Prakash GM et al. studied total of the 313 patients, out of 55% were males and 45% were females.[6] Tak et al studied on 40 patients, 21 was male and 19 was female.[7]

In our study 50% patients were in age group 20-40 years, 29% patients were in age group 41-60 years, 12% patients were in age group less than 20 years, and 9% patients were in age group more than 60 years. The highest incidence was seen in 20-40 year age group. As compared with study done by Afsar et al. which showed Dengue fever had a higher incidence in individuals younger than 30 years of age. An another study by Kularatne SA et al (2005) which showed mean age of 30 years.[8]

In this study 28% patients admitted with platelets counts in range of 0.5 lac - 1 lac, 27% patients admitted with platelet count in range of 1 - 1.5 lac,

21% patients admitted with platelet count more than 1.5 Lac (normal), 16% patients admitted with platelet count in range of 0.2 – 0.5 lac and 8% patients admitted with platelet count less than 0.2 lac. In our study 51% patients admitted with serum ferritin level more than 900 ng/ml, 33% patients admitted with serum ferritin level 22-322 ng/ml, 11% patients admitted with serum ferritin 322 – 600 ng/ml, 4% patients admitted with serum ferritin 600 – 900 ng/ml, 1% patients admitted with serum ferritin less than 22 ng/ml which showed higher percentage of patients with higher serum ferritin level is admitted.

In our study serum ferritin level of 51% patients were more than 900 ng/ml and mean platelet count were 0.76±0.52, serum ferritin level of 33% patients were normal 22 – 322 ng/ml and mean platelet count were 1.33±0.64, serum ferritin level of 11% patients were 322- 600 ng/ml and mean platelet count were 1.44±0.93, serum ferritin level of 4% patients were 600-900 ng/ml and mean platelet count were 0.92±1.40, serum ferritin level of 1% patients were less than 22 ng/ml and mean platelet count were 1.8 which showed patients admitted with higher degree of serum ferritin level had more severe thrombocytopenia.

In our study 74% patients stayed in hospital for 3 – 5 days, out of 74% patients 42% patients were male and 32% patients were female, 15% patients stayed in hospital for more than 5 days, out of 15% patients 9% patients were male and 6% patients were female. 11% patients stayed in hospital for less than 3 days, out of 11% patients 9% patients were male and 6% patients were female which showed mostly patients admitted for 3- 5 days for dengue fever in hospital.

The patients admitted in the hospital less than 3 days had serum ferritin level 942.90±670.42 and patients admitted for 3-5 days had serum ferritin level 964.57±775.30 and more than >5 days had serum ferritin level 987.81±699.58 which indicate the severity of infection increases with the staying time in hospital. (The p value = 0.9) which showed that patients with higher degree of serum ferritin level at admission time stayed more days in hospital. As compared with study done by S Jyothi Visalakshy et al (2018) had shown that that hyperferritinemia does not correlate with the severity of platelet drop,[9] as compared with study done by Selvamuthu kumaran S. et al (2018) which showed raised serum ferritin

level has been observed to have a linear correlation with severity of dengue fever infection.[10] As compared with study done by Velammal Petchiappan (2019) which showed that serum ferritin levels negatively correlated with the platelet count (r=-0.51, p<0.001). High ferritin levels in severe cases are noted from day 4 of clinical illness. Elevated serum ferritin levels can be used as a potential early prognostic marker to predict the severity of dengue infection in clinical practice. And as compared with study done by Gupta A et al. (2020) which showed strong correlation between the severity of the disease and serum ferritin levels[11]. It can be concluded that Serum ferritin levels can be taken as a significant marker for assessing the severity of Dengue Fever.

Conclusion:

According to our study dengue fever is more common among male than female, age group 20-40 years group. High ferritin level was found in severe thrombocytopenic patients. Patients with higher ferritin level and low platelets counts took more time to recover from dengue fever.

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