

Severity of Dengue Fever and Serum Ferritin Levels- A Correlative Study in a Rural Tertiary Care Medical College and Hospital in Tamil Nadu (South India)

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ABSTRACT

Introduction: The commonly used investigations to identify the dengue virus infection are NS1 ANTIGEN (non structural protein 1), IgM and IgG by MAC-ELISA/RAPID KIT TEST. Viral culture and RT-PCR is also done in selective cases. Derangement in LFT (AST, ALT rise) is also noted. Apart from these investigations, serum ferritin level is also high in dengue fever. A raised serum ferritin level has been observed to have a linear correlation with severity of dengue fever infection. **Aim:** To study serum ferritin level in dengue fever and its correlation with severity of dengue virus infection. **Methods:** This study was done at Rajah Muthiah Medical College, a 1260 bedded rural tertiary care institution, Annamalai University. 147 cases of dengue fever confirmed with history, clinical examination and positive NS1 antigen and positive IgG and IgM antibodies were included in the study. Seasonal distribution was also included in the study. **Results:** The results were tabulated based on the observation of ferritin level during admission. There is a strong correlation between the ferritin levels and the severity of the disease. **Conclusion:** From the study it can be concluded that the ferritin levels of the patients can be taken as a biomarker to predict the severity of the dengue fever infection.

Keywords: Dengue, serum ferritin levels, severity, febrile, blood transfusion, hospital stay.

INTRODUCTION

An important cause of acute febrile illness especially in tropics and subtropics in the world is dengue fever.^[1] It is approximated that one million dengue cases are reported to WHO from these regions.^[2] The dengue virus which has four serotypes is transmitted to humans by Aedes mosquitoes especially Aedes aegypti. Tamilnadu is one of the leading geographical areas for dengue fever in India. Around 700 cases across the state were reported daily during the peak seasons of September to December in 2017. The four serotypes of dengue virus cause anywhere from asymptomatic infection to severe dengue.^[3] The illness is divided into 3 distinct phases. 1. An early febrile phase was lasting from day 1 to day 7. 2. A critical phase from day 3 to day 8. 3. Convalescent-phase. The dengue illness can proceed to potential complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), both defined as severe dengue by WHO. The commonly used investigations to identify

the illness are NS1 ANTIGEN (non-structural protein 1), IgM and IgG by MAC-ELISA/RAPID KIT TEST.^[4,5] Derangement in LFT (AST, ALT rise) is also noted.^[4,5] Viral culture and RT-PCR is also done in particular cases.^[6] Apart from these investigations, serum ferritin level is also high in dengue fever.^[7] Ferritin is an acute phase reactant released by the reticuloendothelial cells. Hyperferritinemia is associated with immune activation and coagulation disturbances.^[8] A rise in serum ferritin level has been observed to have a linear correlation with severity of dengue fever.^[9] Hence we got the idea that serum ferritin may serve as a good predictor in assessing the severity of dengue illness.

Aim

To study serum ferritin level in dengue fever and its correlation with severity of dengue virus infection in a tertiary medical college.

MATERIALS AND METHODS

This prospective observational study was done at Rajah Muthiah Medical College, a 1260 bedded rural tertiary care institution, Annamalai University, Cuddalore district, Tamil Nadu, India. The study was done for a period of 1 year from Jan 2017 to Dec 2017, approved by the ethical

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committee of the institution. 147 cases of dengue fever confirmed with history, clinical examination and positive NS1 antigen and positive IgG and IgM antibodies were included in the study. Seasonal distribution was also involved in the study. Exclusion criteria: Patients with pregnancy, patients with known hematological disorders, patients with qualitative and quantitative platelet disorders, patients who had other febrile illness and mixed infections, patients on heparin, radiotherapy, chemotherapy and immunosuppressive patients were excluded from the study. These patients were admitted to our institution and were intensively monitored and treated as per their clinical condition and were managed according to the standard protocol for dengue fever management. Serum ferritin levels of all these patients were sent to our lab and were measured in micrograms per decilitre. The normal levels of serum ferritin were defined as micrograms per decilitre. Out of these 147 patients. Patients were closely monitored and were followed for development of plasma leak and signs and symptoms of severe dengue. The endpoint of the study was taken as discharge from the hospital as per standard protocol. The statistics were calculated for Age, Gender, Similar illness at home/neighbourhood in the recent past, past dengue illness, Geographical distribution and dengue severity and along with its attendant complications. The Karl Pearson's correlation coefficient was calculated for the severity of the disease based on the serum ferritin levels and the number of male and female patients. It was found to be 0.999 was taken as significant.

RESULTS

Out of 147 patients 87 patients were male 59.19 % (n=87), and 60 were female 40.81 % (n= 60). It is observed that in the age group of 20 -30 years the number of patients were very high 29.93% (n=44). Mean hospital stay duration was 5 ±2 days. In 20.44 % (n=30) patients serum ferritin level was found to be in the range of 200-300 ng/dl. In 33.33% of patients (n=49), serum ferritin level was in the range of 300- 400 ng/dl. In 42.17% of patients (n=62) the serum ferritin level was in the range 400-500 ng/dl. Only in 4.06% of the patients (n=6) the serum ferritin level was in the range 500-600. Out of 12 patients out of 30 with ferritin levels 200-300ng/dl developed severe dengue, whereas 30 patients out of 49 patients developed severe dengue with ferritin levels 300– 400ng/dl and 46 out of 62 patients developed severe dengue with ferritin levels 400– 500ng/dl and 6 patients who had ferritin levels 500–600ng/dl had severe dengue. It is observed that higher the ferritin levels the longer was the duration of hospital stay and the number of blood transfusion was also higher.

Mean ferritin levels were much higher in patients who required multiple blood transfusions (350±400 ng/dl)

Table 1: Sex ratio

	Number	%
Male	87	59.20
Female	60	40.80

Table 2: Age distribution

AGE	<12 YEARS	12 – 20	20 - 40	- 60	>60
MALE	17	10	27	17	16
FEMALE	17	8	17	10	8
TOTAL	34	18	44	27	24
%	23.12	12.24	29.93	18.36	16.32

Table 3: Duration of hospital stay

	3-5 DAYS	5-7 DAYS	>7 DAYS
MALE	27	58	2
FEMALE	22	37	1
TOTAL	49	95	3
%	33.33	64.62	2.04

Table 4: Comparison of ferritin levels with severity with respect to male and female patients

Ferritin Level Ng / Dl	No Of Male Patients	No Of Female Patients	Total	% Male	% Female	Total %
200 – 300	19	11	30	12.96	7.48	20.44
300 – 400	31	18	49	21.09	12.24	33.33
400 – 500	33	29	62	22.45	19.72	42.17
500 – 600	4	2	6	2.7	1.36	4.06
Total	87	60	147	59.20	40.80	100

DISCUSSION

In our study, the majority of patients belonged to the male gender 59.19 % (n = 87). A study conducted in Singapore revealed that all PCR positive patients with dengue fever were male (71%).^[6] In a Lahore based study, regarding dengue fever, the majority of the patient were also male.^[10] The clinical presentation and duration of hospital stay and seasonal variation in our study was comparable with similar studies.^[7] The dengue fever cases in our study had no mortality. Further, 6 cases 4 male patients and 2 female patients had gone for severe dengue in the form of dengue hemorrhagic fever and dengue shock syndrome. The highest number of hospital duration in our study was 12 days, 11 days and 10 days in these cases. One case of dengue hemorrhagic fever required 17 blood transfusions over a period of 12 days. All these severe dengue patients had substantially raised serum ferritin levels upon admission to the hospital. (> 500 ng /dl). This

prompted us and helped us in keeping these patients under critical hemodynamic monitoring and surveillance from day 1 of admission to our institution. Only two patients with serum ferritin levels of >500 ng/dl did not go in for severe dengue manifestations. Hence the serum ferritin levels in our study correlated well with the presently available national and international studies. In our study, the Karl Pearson correlation coefficient of serum ferritin levels was calculated and was found to be 0.999. This implies that there is a strong correlation between the serum ferritin levels and the severity of the dengue fever infection. 2 female patients in our study had menorrhagia at the time of admission, and this was noted to be one of the occult bleeding manifestations of dengue fever. It should be noted that the obvious findings of fever, retro-orbital pain, headache, skin rashes, myalgia, arthralgia, clinical manifestations of rapid and weak pulse and narrow pulse pressure (<20 mm/Hg), hypotension, cold clammy extremities, positive tourniquet test, persistent lethargy, fluid accumulation in the form of ascites, pleural effusion, liver enlargement of more than 4 cms are usually noted. Investigatory features of low hemoglobin raised PCV, thrombocytopenia apart from LFT and electrolyte disturbances is noted in classical dengue cases. Apart from these, patients who are going in for severe dengue may have severe plasma leakage leading to fluid accumulation with respiratory distress. High serum ferritin level was noted at the time of admission itself which correlated well with the disease severity, which means that patients who required multiple blood transfusions and critical monitoring and treatment had expressed high serum ferritin levels at the time of admission to the hospital itself.

These results were comparable to the available different national and international studies. The study conducted by soundaravalli R et al.^[7] has concluded that ferritin may serve as a potential biomarker for an early prediction of disease severity in dengue.

CONCLUSION

In confirmed cases of dengue fever requiring admission in an institution, serum ferritin levels taken on admission can serve as a reliable and cost-effective biomarker in the assessment and in predicting the severity of dengue fever. The Serum ferritin levels can also help as an adjunct investigation in delineating the spectrum of dengue suspected patients. Serum ferritin levels may help in identifying an uncomplicated dengue illness, from that of patients who may require inpatient admission / intensive critical care with or without telltale signs upon the time of presentation to the hospital to the outpatient department itself. There is scope for

further study with serum ferritin level in the form of assessment of serial ferritin level measurements in other illnesses, Identifying high-risk patients in endemic areas. The study revealed another fact that due to acute shortage of water, the people stored water in containers without lids which became the breeding place for Aedes mosquitoes. Hence, we conclude that serum ferritin level may be used to monitor and predict the severity and outcome of dengue fever.

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