Serum Ferritin: An Indicator of Disease Severity in Patients with Dengue Infection

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Abstract

Background: Serum ferritin levels are usually raised in dengue virus infection. This study was conducted to see the association of raised serum ferritin levels on the day of admission with the disease severity.

Methods: In this cross-sectional observational study, patients admitted with the diagnosis of dengue fever were included. Serum ferritin levels of all the patients were measured by ELISA on the day of admission. Patients were divided into two groups on the basis of ferritin levels. Group A comprised those with normal ferritin level; those having raised level were included in group B. Patients were followed up during their hospital stay for development of severe dengue. Chi-square test was used as test of significance.

Results: Out of 104 patients 63.5% (n=66) patients were male and 36.5% (n=38) were female. Mean patient age was 30.7 ± 13.8 years. Mean duration of hospital stay was 3.7 ± 1.02 days. In 70% serum ferritin level was found >100 µg/dl, whereas 30% had ferritin level ≤ 100µg/dl. Out of 31 with normal ferritin level only 2 (6.45%) developed severe dengue, whereas 35 (47.94%) out of 73 developed severe dengue with ferritin level >100 µg/dl (p Value <0.005).

Conclusion: Serum ferritin levels on the day of admission may serve as biomarker for an early prediction of disease severity in dengue virus infection.

Key Words: Dengue fever, Severe Dengue, Serum Ferritin

Introduction

Dengue fever is an important cause of febrile illness in the tropical and subtropical areas and approximately one million cases of dengue fever are reported to WHO per year from these regions.1 It is a mosquito borne viral disease and is transmitted to humans by infected Aedes mosquitoes, mainly Aedes aegypti.2 Dengue virus has four serotypes, all four cause similar illness ranging from asymptomatic infection to severe dengue.3 Early laboratory diagnosis of dengue fever is important to provide appropriate treatment to the patients and to prevent potential complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), both defined as severe dengue by WHO.4 Commonly used investigations include detection of dengue-specific IgG or IgM by MAC-ELISA and rapid kit test to detect dengue virus non-structural protein 1 (NS1) antigen.5 Other tests include virus isolation by culture and detection of viral nucleic acid by RT-PCR. Liver biochemistry is also deranged commonly in dengue fever; especially AST and ALT are raised.6 Apart from other lab findings in dengue fever, serum ferritin level is also high 7. Ferritin is acute phase reactant and it is expressed by cells of reticuloendothelial system in response of infection or inflammation. Hyperferritinemia was found to be associated with severity of the dengue fever in children.8 Level of ferritin was also found to be associated with viral load in adult patients.9 These observations gave the idea that serum ferritin level may be used as an early predictor of dengue fever severity in adult patients also.

Patients and Methods

This cross-sectional observational study was conducted at Department of Medicine, District Headquarter Hospital Rawalpindi from August 2014 to December 2014. Patients admitted with the diagnosis of Dengue fever on the basis of history, clinical examination and positive non structural protein 1 (NS 1) antigen or positive IgM antibodies against Dengue were included consecutively. Patients having microcytic anemia, presenting with DHF or DSS were excluded. Every patient was managed according to the standard protocols for Dengue fever and severe Dengue i.e. careful fluid management, acetaminophen, ICU admission with platelets and FFPs transfusion, and other measures depending upon the severity of the disease. Serum ferritin level of all the
patients was sent to pathology department and was measured by ELISA on the day of admission. Patients were divided into two groups on the basis of ferritin levels. Group A comprised those with normal ferritin level; those having raised level were included in group B. Normal levels were defined as serum ferritin level up to 100µg/dl. Patients were followed up during their hospital stay for development of severe dengue. Severe dengue was defined as patients having warning signs like mucosal bleeding, increasing hematocrit, decreasing platelet count, fluid accumulation, abdominal pain etc, or those with severe plasma leakage, severe bleeding and organ failure.\(^9\) Discharge from the hospital without complications or developing severe dengue during the hospital stay was the end point of study.

Means and standard deviations were calculated for age, duration of fever at the time of presentation, duration of hospital stay and serum ferritin levels. Frequency and percentage was calculated for qualitative data like gender, dengue severity. Chi square test was used to compare categorical variables and to determine the relationship of serum ferritin with outcome of dengue fever. P value less than 0.05 was considered as significant.

**Results**

Out of 104 patients 63.5% (n=66) were male and 36.5% (n=38) were female. Mean patient age was 30.7 ± 13.8 years. Fever was the common presenting symptom and mean duration of fever was 5.6 ± 1.3 days. Mean duration of hospital stay was 3.7 ± 1.02 days. In 70% (n=73) patients serum ferritin level was found >100 µg/dl, whereas only 30% (n=31) had ferritin level ≤ 100µg/dl.

### Table I: Relationship between serum ferritin level and Dengue severity i.e Dengue hemorrhagic fever and Dengue shock syndrome

<table>
<thead>
<tr>
<th>Serum ferritin level</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤100µg/dl</td>
<td>&gt;100 µg/dl</td>
</tr>
<tr>
<td>Severe Dengue</td>
<td>No 29</td>
</tr>
<tr>
<td></td>
<td>Yes 2</td>
</tr>
<tr>
<td></td>
<td>35</td>
</tr>
</tbody>
</table>

Out of 31 with normal ferritin level only 2 patients developed severe dengue, whereas 35 patients out of 73 developed severe dengue with ferritin level >100 µg/dl. Mean ferritin levels were much higher in patients with severe dengue i.e 317.54 ± 109.52 as compared to the patients with uncomplicated dengue fever i.e 168.69 ± 130.7 (Table I).

**Discussion**

In present study, high serum ferritin level at the time of admission was found significantly associated with severe dengue fever. Mean serum ferritin was found significantly higher in patients with dengue shock syndrome and dengue hemorrhagic fever as compared to dengue fever.

Majority of our patients were male. This is in accordance with previous studies. A study conducted in Singapore showed that among all PCR positive dengue fever cases 71% were male.\(^1\) In another study done at Services Institute of Medical Sciences and Fatima Memorial Hospital Lahore 69.4 % patients were male.\(^2\)

Duration of fever at presentation and duration of hospital stay was also comparable with other studies. A study conducted by Ahmed A et al. showed that mean duration of fever at presentation was 5.49 ± 2.65 days and mean duration of hospital stay in dengue fever was 2.73 ± 1.41 days.\(^3\)

Significant association was found between raised serum ferritin levels on the day of admission and development of severe dengue during hospital stay in our study. Same was shown by different international studies. Study conducted by Soundravally R et al. concluded that raised ferritin levels could predict the dengue severity with sensitivity of 76.9 % and specificity of 83.3% on the day of admission.\(^4\) Another study conducted in Aruba and Brazil showed that increased levels of ferritin were significantly associated with the disease severity in dengue virus infection.\(^5\)

**Conclusion**

1. Raised serum ferritin levels are significantly associated with severe dengue. Mean ferritin levels are also high in patients with severe dengue as compared to dengue fever.

2. Serum ferritin levels on the day of admission may serve as biomarker for an early prediction of disease severity in dengue virus infection.

**References**
