

# Serum ferritin as an early predictor of the severity of dengue infection in children

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#### Abstract

The study was conducted to evaluate whether the severity of dengue fever can be predicted by serum ferritin level or not. This prospective observational study was conducted during the endemic period of dengue fever in 2019. A total of 30 diagnosed cases of dengue fever who presented with bicytopenia during febrile phase of the disease were enrolled in this study. Pearson's correlation coefficient was calculated to compare ferritin levels with lowest platelet count and highest hematocrit level and it showed that there was significant correlation. There was no difference between lowest total count of white blood cell and serum ferritin level. The severity of dengue fever can be predicted by raised level of serum ferritin.

Keywords: Dengue fever; Ferritin

## Background

Dengue fever is a dynamic febrile illness which can manifest as a mild self-limiting or severe life threatening situation following hemorrhage, plasma leakage, or multiple organ failure [1-3]. Now-adays, it is endemic in more than 100 countries in Western Pacific, Latin America, Southeast Asia, Eastern Mediterranean regions and Africa. It is estimated that although annually worldwide 96 million human beings have clinical manifestation of dengue fever, 390 million people suffer from dengue infections [4-7]. The severity of dengue fever depends on the interactions between virus and host's immune response [8]. Now-a-days, many hematological parameters have been suggested to evaluate the severity of the disease including decreased platelet count, raised hematocrit level, prolonged prothombin time and activated partial thromboplastin time, liver transaminases, muscular enzymes, cytokines such as IL-6 and IL-10 [9-15] but there is paucity of researches which can predict bad outcome in dengue fever. Studies conducted by Zhang et al. (2014) [16] at the Caribbean island Aruba; Chaiyaratana et al. (2008) [17] at Thailand concluded that elevated ferritin level in serum is a distinguishing feature of dengue fever. Thanachartwet et al. (2015) [18] and Chaloemwong et al. (2018) [19] concluded that high hematocrit, thrombocytopenia and leukopenia were associated with severity of the disease. One of the effects of inappropriate activation of tissue macrophages is macrophage activation syndrome and could be responsible for morbidity and mortality in dengue fever. Serum ferritin, an acute phase reactant protein, is a surrogate marker of macrophage activation [20]. Elevated level of serum ferritin during the febrile phase of dengue fever might predict the severity of dengue fever during critical phase which would help physicians to prepare for the prevention and treatment of extended dengue fever. Thus, it can reduce the morbidity and mortality in dengue fever [20]. During the endemic period of dengue outbreak in Bangladesh, it was rational to conduct this study to early pickup of lethal cases which was helpful for the prevention of mortality and morbidity. In this study, we assessed the relationship of serum ferritin

concentration with the highest hematocrit, lowest platelet and total WBC count.

## Materials and Methods

This study was conducted from June to August, 2019 at the department of paediatrics at Marks Medical College Hospital, Mirpur 14, Dhaka, Bangladesh. Total 30 diagnosed cases of dengue fever (Dengue NS 1 positive) who developed bicytopenia during febrile phase of the illness [7,8] were included for the study. All participants later developed features of volume overloads in the form bilateral pleural effusions and ascites which resolved at variable period of time. The serum ferritin level was measured during the febrile phase of the illness (by electrochemiluminescence immunoassay-COBAS e411). On a daily basis, disease progression and complete blood count were monitored carefully. The patients were classified as having non-severe and severe infection as per National guideline of dengue fever [21].

#### Statistical analysis

The chi-squared test was done to compare the values of serum ferritin concentration with other parameters of the blood. Additionally Two-tailed, unpaired student's t test was done to compare the means of different variables Proportions were compared by means of the twotailed, Fisher's exact test. Correlations between the variables were analyzed by Pearson correlation.

#### Results

Figure 1 shows the positive correlation of serum ferritin and high haematocrit value. Pearson correlation value was 0.661. The result was statically significant (p=0.000).



Figure 1: Correlation of serum ferritin with serum Haematocrit (Hct.) level.

Figure 2 shows the negative correlation of serum ferritin and lowest platelet count. Pearson correlation value was -0.348. The result was statically significant (p=0.05).



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Figure 3 shows negative correlation of serum feritin and lowest total count of white blood cell count. Pearson correlation value was -0.132. The result was not statically significant (p=0.486).



**Figure 3:** Correlation of serum ferritin with lowest total count of WBC.

### Discussion

In the present study, we found that higher serum ferritin level during febrile phase, significantly associated with lower platelet count and higher hematocrit level during critical period of dengue fever which ultimately correlate with the severity of the disease. Similar findings were noted in other studies as well. In South India, Soundravally et al. (2015) [22] conducted a research work on 96 febrile patients equally divided into dengue and non-dengue groups. The plasma ferritin levels were monitored on 4th and 8th day of the onset of fever. Ferritin levels were significantly raised in severe dengue fever both in febrile and afebrile phases with a specificity and sensitivity 83.3 and 76.9% respectively. The current study also revealed similar results. Recently published another study by Petchiappan et al. (2019) [23] at Tamilnadu, India also described similar finding on 119 patients with dengue fever. Evalda et al. (2017) [24] at Indonesia described the association of high serum ferritin level with dengue shock syndrome in children. Another recent study in Brazil, authors described thrombocytopenia as the hallmark of dengue fever and found significant thrombocytopenia associated with hypofibrinogenemia [25]. On the other hand, in a study at South India, Visalakshy et al. (2018) found absence of any statistical difference between the mean ferritin levels, platelet and haematocrit counts of both groups (received or not received treatment with steroid suggesting that the levels of cytokine activation due to macrophage activation is similar in both groups [26].

### Conclusion

High serum ferritin level significantly associated with severe dengue fever.

## Authors' Contribution

All authors listed have contributed sufficiently in management of the patients, data collection and writing of the article.

**Informed Consent:** The study utilized data of hospital laboratories after obtaining written informed consent from parents of each patient

**Ethical Approval:** The study obtained ethics approval from Institutional Ethics Committee of The Marks Medical College Hospital, Dhaka, Bangladesh

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