

ORIGINAL ARTICLE

Association of Serum Ferritin and Crp with Disease Severity in Dengue Fever

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ABSTRACT

Background: Dengue fever is one of the major public health issues and clinical identification of patient who may develop severe dengue is still a challenge.

Objective: to determine the association of serum ferritin and CRP with disease severity in dengue fever.

Material and Methods: The current prospective observational study was carried out at the department of Medicine, Khalifa Gul Nawaz teaching Hospital / Bannu Medical College, Bannu. The duration of our study was six months from April 2023 to September, 2023. Based on the WHO sample size calculator the sample size in our study was 120 patients. A pre-designed proforma was used to record demographic information's, co-morbid conditions, hematological and biochemical parameters and inflammatory biomarkers. SPSS version 16 was used to analyze the data. Categorical variables in our study were presented as frequency and percentages while continuous variables were presented as means ($\pm$ SD).

Results: In our study, a total of 120 patients were enrolled. The severe cases in our study were 24 (20%) and non-severe dengue cases were 96 (80%). The major co-morbid condition in patients of both the groups was hypothyroidism, diabetes and hypertension. By using pearson correlation coefficient method, a significant positive correlation was observed between CRP and ferritin.

Conclusion: Our study concludes that ferritin can serve as another biomarker apart from CRP for hospitalization of patients infected by dengue and may assist in predicting the severity of the disease in the initial phase.

Keywords: Serum ferritin; CRP; disease severity; dengue fever

INTRODUCTION

Dengue is one of the rapidly expanding viral diseases carried by the mosquitoes and between 100-400 million cases of dengue infections are registered each year in the tropics and subtropics^{1,2}. The clinical manifestations are broad, ranging from a non-symptomatic infection to the severe form of dengue with plasma leaking, hemorrhages and organ dysfunction³. The ability to detect at-risk patients in a timely manner is vital, particularly in the constrained setting whereby the impact of timely triage on morbidity and mortality could be deleterious⁴. Numerous biomarkers have been identified for disease severity prediction purposes, but the majority are costly, insensitive, or unavailable on a regular basis in different health care systems⁵.

Ferritin is an intracellular protein involved in iron storage and also acts as an acute-phase reactant that has gained increasing attention as a potential marker of hyperinflammation in diseases caused by viruses and immune system⁶. Elevated serum ferritin levels, considered to reflect activated macrophages, excessive cytokines, and oxidative stress, have been shown to reflect pathophysiologic processes in severe dengue infection⁷. Various studies have shown that there is a significant rise in the levels of ferritin in patients with severe dengue when compared with those without severe dengue infection, however, the findings vary greatly among various populations and experimental conditions^{8,9}. Additionally, there is lack of a consensus definition of the cut-off levels of ferritin within the literature. Also, little research has been done to systematically assess its predictive value in different settings of health care resources. This inconsistency points towards an important gap in terms of the practicality of using ferritin as a risk-stratifying marker for dengue¹⁰.

C-reactive protein (CRP) is an acute phase protein which is produced by the liver after six hours of inflammation and tissue damage¹¹. Therefore, CRP is termed an inflammatory biomarker and is applied in clinical setting to determine whether the patient is suffering from viral infection or bacterial infection or even differentiate between malaria and DF¹². There have been very few research studies carried out to check the use of CRP test

for differentiation between mild and severe dengue patients. The current was carried out to determine the association of serum ferritin and crp with disease severity in dengue fever.

MATERIALS AND METHODS

The current prospective observational study was carried out at the department of Medicine, Khalifa Gul Nawaz teaching Hospital / Bannu Medical College, Bannu. The duration of our study was six months from April 2023 to September, 2023. The ethical approval of our study was obtained from the ethical committee of our hospital. Based on the WHO sample size calculator the sample size in our study was 120 patients. Informed consent for our study was obtained from all the enrolled subjects in our study. The criteria for inclusion in our study was all the adult hospitalized patients of both the gender diagnosed by antigen test for dengue by antigen test whereas the criteria for exclusion were all the patients with pre-existing autoimmune diseases based on history, culture positive secondary bacterial infections and patients not willing to participate in our study. A pre-designed proforma was used to record demographic information's, co-morbid conditions, hematological and biochemical parameters and inflammatory biomarkers. In our study, the enrolled patients were divided into dengue severe and non-severe dengue cases based on the WHO criteria revised in 2009⁶. SPSS version 16 was used to analyze the data. Categorical variables in our study were presented as frequency and percentages while continuous variables were presented as means ($\pm$ SD). The univariate analysis included the assessment of the independent variables, with comparison being done between the severe and non-severe categories. The correlation of the significant univariates was conducted using the Pearson correlation coefficient method. A P value less than 0.05 was statistically significant.

RESULTS

In our study, a total of 120 patients were enrolled. The severe cases in our study were 24 (20%) and non-severe dengue cases were 96 (80%) based on the criteria used by WHO for determining dengue severity. (Figure 1) The mean ($\pm$) age in our study in severe dengue cases was 38 ($\pm$ 9.36) years while in non-severe dengue cases the mean age was 39 ($\pm$ 11.22) years. The female patients in severe dengue cases were 13 (54.17%) and males

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were 11 (45.83%) whereas in non-severe cases males were 57 (59.38%) females were 39 (40.63%).(Figure 2) The major co-morbid condition in patients of both the groups was hypothyroidism, diabetes and hypertension. Fever, myalgia, vomiting, loose stools and headache were common in patients of both the groups. Rashes were observed in 4 (16.67%) patients in severe cases while rashes were observed in 6 (6.25%) patients in non-severe cases. (Table 1)

The mean ($\pm$ SD) C reactive protein level in severe dengue patients was 51.22 ($\pm$ 12.21) mg/L while in non-severe dengue patients it was 20.09 ($\pm$ 8.56) mg/L. The mean($\pm$ SD) ferritin level in severe dengue patients was 880 ($\pm$ 3.90) ng/mLwhile in non-severe dengue patients it was 850 ($\pm$ 4.1) ng/mL. (Table 2)

By using pearson correlation coefficient method, a significant positive correlation was observed between CRP and ferritin (R-value: 0.37/P 0.02). (Table 3)

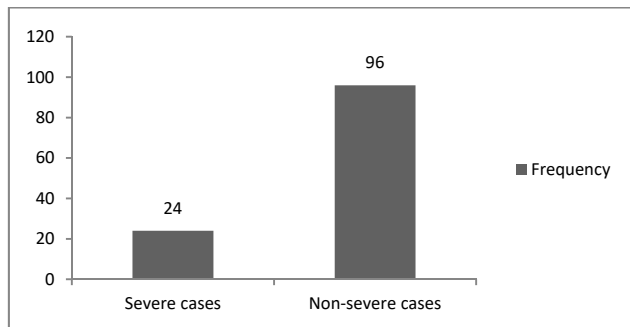


Figure 1: Frequency of patients in severe and non-severe group

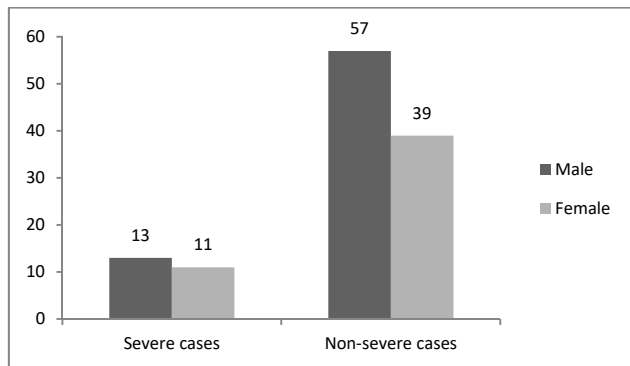


Figure 2: Gender wise distribution of patients

Table 1: Clinical features of enrolled patients in both the groups

Co-morbidities	Severe cases	Non-severe cases
diabetes	3 (12.5%)	17 (17.71%)
hypothyroidism	4 (16.67%)	6 (6.25%)
hypertension	6 (25%)	20 (20.83%)
Fever	24 (100%)	96 (100%)
myalgia	12 (50%)	61(63.54%)
vomiting	8 (33.33%)	30 (31.25%)
loose stools	6 (25%)	20 (20.83%)
headache	8 (33.33%)	34 (35.42%)
Rashes	4 (16.67%)	6 (6.25%)

Table 2: Mean CRP and ferritin in enrolled patients of both the groups

Parameter	Severe cases	Non-severe cases
CRP mg/l	51.22 ($\pm$ 12.21)	20.09 ($\pm$ 8.56) mg/L
Ferritin ng/ml	880 ($\pm$ 3.90)	850 ($\pm$ 4.1)

Table 3: Correlation of CRP and ferritin in patients with dengue fever

Parameter	Correlation coefficient (R)	P value
CRP mg/l	0.37	0.02
Ferritin ng/ml		

DISCUSSION

In tropical and sub-tropical countries, dengue is one of the main health issues with very high mortality¹³. DF is a vector borne disease spread by two species of Aedes mosquitoes (Aedes aegypti and A albopictus). Four types of serotypes of DENV (DENV-1, DENV-2, DENV-3, and DENV-4) infect the body¹⁴. As per the WHO guidelines in 1997 to 2009, the clinical features of dengue are non-specific febrile illness, DF, dengue hemorrhagic fever, and dengue shock syndrome (DSS)¹⁵. From this the dengue patients are categorized as severe and non-severe (with and without warning signs)¹⁶.

In our study, a total of 120 patients were enrolled. The severe cases in our study were 20% and non-severe dengue cases were 80% based on the criteria used by WHO for determining dengue severity. The mean ($\pm$) age in our study in severe dengue cases was 38 ($\pm$ 9.36) years while in non-severe dengue cases the mean age was 39 ($\pm$ 11.22) years. The female patients in severe dengue cases were 54.17% and males were 45.83% whereas in non-severe cases males were 59.38% females were 40.63%. The results found by us coincide with those by another author regarding the fact that there is higher exposure to dengue virus among males than females¹⁷.

The major co-morbid condition in patients of both the groups was hypothyroidism, diabetes and hypertension. Fever, myalgia, vomiting, loose stools and headache were common in patients of both the groups. Rashes were observed in 16.67% patients in severe cases while rashes were observed in 6.25% patients in non-severe cases. Studies conducted in Singapore and Brazil with a large population have suggested that hypertension is a risk factor in dengue infection^{18,19}.

In our study, the mean ($\pm$ SD) C reactive protein level in severe dengue patients was 51.22 ($\pm$ 12.21) mg/L while in non-severe dengue patients it was 20.09 ($\pm$ 8.56) mg/L. The mean($\pm$ SD) ferritin level in severe dengue patients was 880 ($\pm$ 3.90) ng/mLwhile in non-severe dengue patients it was 850 ($\pm$ 4.1) ng/mL. By using pearson correlation coefficient method, a significant positive correlation was observed between CRP and ferritin (R-value: 0.37/P 0.02).

Various researches have revealed that ferritin acts as an important marker of DF. A research was done on 119 patients and it was observed that high level of ferritin was found in severe dengue cases and Petchiappan et al [20] have also found high levels of ferritin in dengue severe cases in the febrile stage²⁰. Previously it was found that there is a strong correlation between serum ferritin, CRP and platelet counts with severity and mortality of hemorrhagic fever²¹.

CONCLUSION

In our study it was observed that ferritin, and CRP levels are high in severe dengue patients compared to non-severe dengue patients. In our study there was a positive correlation between CRP and ferritin in patients with dengue fever. In conclusion, our study shows that ferritin can serve as another biomarker apart from CRP for hospitalization of patients infected by dengue and may assist in predicting the severity of the disease in the initial phase.

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