

## Diagnostic value of ferritin for the severity of dengue infection in children

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### Article Info

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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 level with lowest platelet count and highest hematocrit level and it showed that there was significant correlation. There was no difference between the 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.

### Introduction

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.<sup>1-3</sup> Now-a-days, 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 millions human beings have clinical manifestation of dengue fever, 390 millions people suffer from dengue infections.<sup>4,5</sup>

The severity of dengue fever depends on the interactions between virus and host's immune response.<sup>6</sup>

Now-a-days, many hematological parameters have been suggested to evaluate the severity of dengue fever including decreased platelet count, raised hematocrit level, prolonged prothrombin time and activated partial thromboplastin time, liver transaminases, muscular enzymes, cytokines such as IL-6 and IL-10,<sup>7-15</sup> but there is paucity of researches which can predict bad outcome in dengue fever. Studies conducted by Zhang et al. (2014)<sup>16</sup> at the Caribbean island Aruba; Chaiyaratana et al. (2008)<sup>17</sup> at Thailand concluded that elevated ferritin level in serum is a distinguishing feature of dengue fever. Thanachartwet et al. (2015)<sup>18</sup> and Chaloeuwong et al. (2018)<sup>19</sup> 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.<sup>20</sup> 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.<sup>20</sup>

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 white blood cell count.

### Materials and Methods

This study was conducted from June to August, 2019. In total 30 diagnosed cases of dengue fever (Dengue NS 1 positive) who developed bicytopenia during febrile phase of the illness<sup>2,8</sup> 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 from 1 mL venous blood sample during the 4<sup>th</sup> or 5<sup>th</sup> day of onset of 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.<sup>21</sup>

### 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 two-tailed, Fisher's exact test. Correlations between the variables were analyzed by Pearson correlation.

## Results

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

Figure 1B shows the negative correlation of serum ferritin and lowest platelet count. Pearson correlation value was  $-0.348$ . The result was statically significant ( $p=0.05$ ).

Figure 1C shows negative correlation of serum ferritin and lowest total count of white blood cell count. Pearson correlation value was  $-0.172$ . the result was not statically significant ( $p=0.05$ ).

## 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)<sup>22</sup> 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 level was significantly raised in severe dengue fever both in febrile and afebrile phases ( $p$  value 0.000). In the current study, although we did not compare serum ferritin level between the severe and nonsevere dengue fever, we found that higher the level of serum ferritin, lower the level of platelet count ( $p$  value 0.000). Recently published another study by Petchiappan et al. (2019)<sup>23</sup> at Tamilnaru, India also described similar finding on 119 patients with dengue fever. Evalda et al. (2017)<sup>24</sup> at Indonesia described the association of high serum

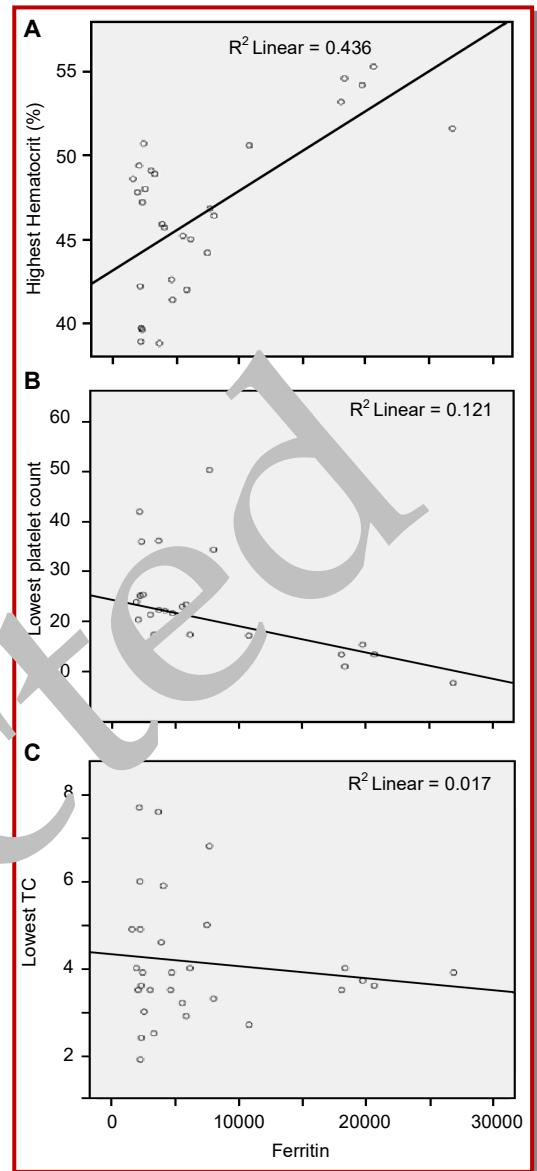


Figure 1: Correlation of serum ferritin level with serum haematocrit level (A), lowest platelet count (B) and lowest total count of white blood cell (C)

ferritin level with dengue shock syndrome in children.

## Conclusion

High serum ferritin level significantly associated with severe dengue fever.

## Ethical Issue

The research protocol was approved by the ethical committee of the United Hospital LTD, Dhaka, Bangladesh.

### Conflict of Interest

There is no conflict of interest.

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### References

- Islam QT. Changing epidemiological and clinical pattern of dengue in Bangladesh 2018. *J Med.* 2019; 20: 1-3.
- Shamsuzzaman AKM. Dengue virus and Aedes mosquitoes: Ecological relationship. *J Curr Adv Med Res.* 2019; 6: 67-68.
- Azad MAK, Mohammad H, Alam MB, Saha AK, Ahmed T. Clinical presentation of dengue in 150 admitted cases in Dhaka Medical College Hospital. *J Med.* 2006; 7: 3-9.
- Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Lounibos AG, Sankoh O, Myers MF, George DB, Jansen T, Wint GR, Simmons CP, Scott TW, Farrar JJ, Hay SI. The global distribution and burden of dengue. *Nature* 2013; 496: 504-07.
- Pervin M, Tabassum S, Islam MN. Isolation and serotyping of dengue viruses by mosquito inoculation technique from clinically suspected cases of dengue fever. *Bangladesh Medical Counc Bull.* 2002; 2: 100-11.
- Alam ABMS, Sifat SA, Swapan Z, Ahmed AU, Karim MN, Paul MC, Zaman S. Clinical profile of dengue fever in children. *Bangladesh J Child Health.* 2009; 33: 55-58.
- Fahmina R, Ayatof KF, Khanum H, Akter T. Prevalence of dengue fever among the patients of different economic status attended at local hospital in Dhaka. *Bangladesh J Zool.* 2014; 42: 161-68.
- Prusty BSK, Momin MAB. Dengue fever with pulmonary alveolar haemorrhage- Common infection with uncommon association: Rare case report. *Bangladesh J Med.* 2019; 30: 38-40.
- Ribeiro E, Kassab S, Pistone T, Receveur MC, Fialon P, Malvy D. Primary dengue fever associated with hemophagocytic syndrome: A report of three imported cases, Bordeaux, France. *Intern Med.* 2014; 53: 899-902.
- Rajjee S, Ashok I, Manwani N, Rajkumar J, Gowrishankar K, Subbiah E. Profile of hemo-phagocytic lymphohistiocytosis: Efficacy of intravenous immunoglobulin therapy. *Indian J Pediatr.* 2014; 81: 1337-41.
- Ray S, Kundu S, Saha M, Chakrabarti P. Hemophagocytic syndrome in classic dengue fever. *J Glob Infect Dis.* 2011; 3: 399-401.
- Lehmberg K, Ehl S. Diagnostic evaluation of patients with suspected haemophagocytic lymphohistiocytosis. *Br J Haematol.* 2013; 160: 275-87.
- Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J, Janka G. Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer.* 2007; 48: 124-31.
- Ergonul O, Tuncbilek S, Baykam N, Celikbas A, Dokuzoguz B. Evaluation of serum levels of interleukin (IL)-6, IL-10 and tumor necrosis factor-alpha in patients with Crimean-Congo hemorrhagic fever. *J Infect Dis.* 2006; 193: 41-44.
- Papa A, Bino S, Gelo E, Haxhiu A, Kota M, Antoniadis A. Cytokine levels in Crimean-Congo hemorrhagic fever. *J Clin Virol.* 2006; 36: 272-76.
- Zheng Y, Kramer CV. Corticosteroids for dengue infection. *Cochrane Database Syst Rev.* 2014; 2014.
- Chivaratana W, Chuansumrit A, Atamasirikul K, Tanjaratchakit K. Serum ferritin levels in children with dengue infection. *Southeast Asian J Trop Med Public Health.* 2008; 39: 832-36.
- Chanachartwet V, Oer-Areemitr N, Chamnanachant S, Sahassananda D, Jittmittraphap A, Suwanakudt P, Desakorn V, Wattanatham A. Identification of clinical factors associated with severe dengue among Thai adults: A prospective study. *BMC Infect Dis.* 2015; 15: 420.
- Chaloemwong J, Tantiworawit A, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Rattarittamrong E, Norasetthada L. Useful clinical features and haematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: A retrospective study. *BMC Hematol.* 2018; 18: 20.
- Petchiappan V, Hussain TM, Thangavelu S. Can serum ferritin levels predict the severity of dengue early?: An observational study. *Int J Res Med Sci.* 2019; 7: 876-81.
- National guidelines for clinical management of dengue syndrome. National malaria elimination and aedes transmitted disease control program disease control unit directorate general of health services. 4<sup>th</sup> ed. 2018.
- Soundravally R, Agieshkumar B, Daisy M, Sherin J, Cleetus CC. Ferritin levels predict severe dengue. *Infection* 2015; 43: 13-19.
- Petchiappan V, Hussain TM, Thangavelu S. Can serum ferritin levels predict the severity of dengue early: An observational study. *Int J Res Med Sci.*

- 2019; 7: 876-81.
24. Evalda P, Soebagyo B, Riza M. Serum ferritin as a predictor of shock in children with dengue infection. *Indonesian J Med.* 2017; 2: 154-60.
25. Van de Weg CAM, Huits RMHG, Pannuti CS, Brouns RM, van den Berg RWA, van den Ham HJ, Martina BEE, Osterhaus ADME, Netea MG, Meijers JCM, van gorp ECM, Kallas EG. Hyperferritinemia in dengue virus infected patients is associated with immune activation and coagulation disturbances. *PLoS Negl Trop Dis.* 2014; 8: e3214.
26. Visalakshy SJ, Saminathan SS, Surendran S, Pillai MGK. Hyperferritinemia in dengue fever-correlation between serum ferritin and thrombocytopenia. *J Clin Diag Res.* 2018; 12: OC07-OC09.
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