Section: Miscellaneous

Original Research Article

SERUM FERRITIN AN INFLAMMATORY MARKER, PREDICTING THE SEVERITY OF DENGUE

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ABSTRACT

Background: Dengue infection is a major health problem; early recognition is crucial to improve the survival in severe dengue. There are various biomarkers to predict the severity of dengue, we want to analyse whether serum ferritin, an inflammatory marker can be used to predict the severity at an earlier stage. The aim and objective are to analyse whether serum ferritin level in febrile phase of dengue illness, can predict and classify the severity. To analyse the correlation of serum ferritin with other parameters like Hb, PCV, platelets, WBC, SGOT, SGPT, serum albumin. **Materials and Methods:** We conducted a prospective observational study for a period of 10 months involving 65 cases, involving cases of primary and secondary dengue. At admission serum ferritin was sent along with other laboratory parameters sent routinely. Further dengue was further classified according to WHO(2021) into DF, DHF-1, DHF-2, DHF-3 and DHF-4. **Result:** Out of 65 patients, DF group had 6 cases, DHF-1, DHF-2 and DHF-3 had 32, 4 and 23 cases respectively in the age group of 1-14years. The ferritin level increased in groups as the severity increased, but statistical correlation could not be established (p-0.16). However there was a significant NEGATIVE correlation between serum ferritin and Platelets(p=0.0052), serum Albumin(p=0.0071) and a positive correlation between SGOT(p=0.0001), SGPT(p=0.0036), WBC(0.050) separately. **Conclusion:** The level of ferritin at admission wasnot useful to classify the severity of dengue. Statistically significant positive correlation was established between Ferritin with SGOT, SGPT, WBC and negative correlation was established between Ferritin with platelets and serum albumin.

INTRODUCTION

Dengue is one of the rapidly spreading mosquito-borne arboviral disease in the world. Dengue fever is transmitted by the bite of infected Aedes mosquitoe. Dengue virus is a small single-stranded RNA virus, belonging to Flavivirus, family Flaviviridae comprises four distinct serotypes (Dengue virus 1 to 4). Primary infection is thought to induce life long protective immunity to the infecting serotype.[1-5]

Dengue infection is a major health problem in tropical and subtropical countries. Efficient and accurate diagnosis of dengue is of primary importance for clinical care.[4]

The course of dengue illness is divided into febrile phase, where patients typically develop high grade fever in this phase which lasts usually for 2-7 days. Second phase is critical phase around the time of defervescence, ranges from 3-7 days of illness, an increase in capillary permeability in parallel with increasing haematocrit levels may occur. The period of clinically significant plasma leakage usually lasts 24-48 hours. After this period a gradual reabsorption of extravascular compartment fluid takes place in the following 48-72 hours. Patients who improve after defervescence are said to have non-severe dengue. This is marked by general well-being, gastrointestinal symptoms abade, appetite returns, haemodynamic status stabilizes and diuresis ensues.[4] Young children in particular may be less able than adults to compensate for capillary leakage and are consequently at a greater risk of dengue shock.[5]

Ferritin is an iron storage protein complex of isoferritins produced by reticuloendothelial (RE) system. The RE system plays a major role in iron metabolism by processing haemoglobin from senescent red blood cells. Acute inflammation and infection induce the blockade of iron release resulting in a decreased serum iron, a virulence factor for many microorganisms. Elevated levels of serum ferritin, an acute phase reactant, reflect the clinical response to deprive microorganisms of serum iron.[1]

In this study, we analysed whether the serum ferritin measured at the earliest, during febrile stage can be used as an early indicator of the severity of the

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disease which helps us to anticipate the course of the disease and manage appropriately.

MATERIALS AND METHODS

Inclusion Criteria

1. Primary dengue infection (Ns1 and IgM positive).
2. Secondary dengue (Ns1, IgG positive or Ns1,IgM, IgG,).
3. Age group 1-14y.
4. Febrile phase of dengue fever.

Exclusion Criteria

1. Age less than 1year or more than 14years.
2. Dengue serology negative.
3. Other co-existing infections.
4. Other co-existing chronic inflammatory disease.
5. Critical or recovery phase of dengue fever.

Diagnostic Criteria: The severity of DHF is classified into four grades.[2,4] The presence of thrombocytopenia with concurrent haemoconcentration differentiates Grade I and Grade II DHF from dengue fever. Grading the severity of the disease has been found clinically and epidemiologically useful in DHF epidemics in children in the South-East Asia, Western Pacific and America Regions of WHO.[5]

Dengue fever comprise of symptoms suggestive of dengue fever and laboratory parameters like leukopenia (WBC <5000cells/mm3), platelet count (<150000 cell/mm3). Rise in HCT by 5-10% and no evidence of plasma loss. Where as in dengue haemorrhagic group (DHF), thrombocytopenia <100000cells/mm3, HCT rise >20% was common in all 4 groups. In DHF- 1 Fever and haemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage was considered. In grade II (DHF-2) spontaneous bleeding was present. Grade III patients had circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness) in addition to features of Grade I or II. In grade IV features of Grade III plus profound shock with undetectable BP and pulse was considered.[5]

Materials and Methods.

We conducted a prospective observational study for a period of 10 months at SDM Medical College and Hospital, a tertiary care center in North Karnataka. Standard WHO definations were used to classify dengue cases as DF, DHF-1, DHF-2, DHF-3, DHF-4. Study included children between age group of 12months to 14 years. Data was collected and analysed from patients fulfilling the inclusion criteria, admitted in ward or PICU.

Patients were divided into DF, DHF (DHF-1, DHF-2, DHF-3, DHF-4) based on clinical presentation and laboratory parameters on admission. Diagnosis was based on dengue serology (Immunochromatography assay) who presented in febrile phase of illness. 3ml of venous blood sample was taken and investigated for Serum ferritin (Chemiluminescence Immunoassay), Hb, PCV, platelet, WBC (cellpack reagent lysercell WNR), SGOT, SGPT, serum albumin levels. The following was sent on admission for all patients fulfilling the inclusion criteria and after excluding those who met the exclusion criteria. Consent was obtained from the patient's side for the study and data which included preliminary data and the above lab parameters with clinical diagnosis on admission was compiled in an exel sheet.

Statistical Analysis

The statistical association serum ferritin done on admission with severity of dengue and with various laboratory parameters was studied with a study population of 65 patients.

Kruskal Wallis ANOVA was used to compare serum levels of ferritin with different groups of dengue. The Spearman's rank correlation was done to compare the values of serum ferritin concentration with other parameters of blood like Hb, PCV, platelet, WBC, SGOT, SGPT, serum albumin. The software used is SPSS 20 version.

RESULTS

In our study, out of 65 cases who met the inclusion criteria, dengue fever (DF)group had 6 cases, dengue Haemorrhagic fever-(DHF)group had, DHF-1 had 32 cases, DHF-2 had 4 cases, DHF-3 had 23 cases and no case in DHF-4 group according to WHO criteria. Case distribution was as following, DF*(9.23%), DHF-1(49.23%), DHF-2(6.15%), DHF- 3(35.38%), DHF-4 (0%). Mean Serum ferritin level of 750.18, 1400.66, 2142.93 and 1671.7 ng/ml in DF, DHF-1, DHF-2 and DHF-3 groups respectively, with the (p-value of 0.1600) on comparing the level of serum ferritin with different groups of dengue fever based on severity according to WHO(2021) classification.

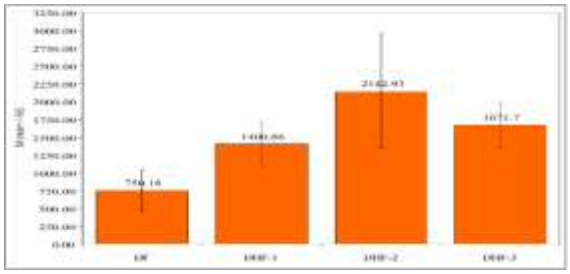

Figure 1: Comparison of four groups of dengue with serum FERRITIN levels.

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Table 1: Comparison of four groups of dengue with FERRITIN (B) levels by Kruskal Wallis ANOVA

Groups	Mean	SD	SE	Mean Rank
DF	750.18	718.55	293.35	24.08
DHF-1	1400.66	1763.32	311.71	29.81
DHF-2	2142.93	1609.86	804.93	44.38
DHF-3	1671.70	1526.35	318.27	37.78
H-value	5.1640			
P-value	0.1600			

Serum ferritin level was correlated with other laboratory parameters like Hb, PCV, platelet, WBC, SGOT, SGPT, serum albumin by using Spearman's rank correlation, in all the 65 cases irrespective of the WHO classification as shown in [Table 2].

Table 2: Correlation between Ferritin (b)with clinical parameters by Spearman's rank correlation.

Laboratory parameters	Correlation between Ferritin (b)with			
	N	Spearman R	t-value	p-value
Hb	65	0.1260	1.0080	0.3173
PCV	65	0.1014	0.8090	0.4216
Platelets	65	-0.3428	-2.8959	0.0052*
SGOT	65	0.6791	7.3428	0.0001*
SGPT	65	0.3560	3.0234	0.0036
Albumin	65	-0.3308	-2.7818	0.0071*
WBC	65	0.2387	1.9613	0.0500*

In [Figure 2] the negative correlation of serum ferritin with platelets (r-value of -0.3428) is shown. The result was statistically significant (p-value of 0.0052).

In [Figure 3] the positive correlation of serum ferritin with SGOT (r-value of 0.6791) is shown.

The result was statistically significant (p-value of 0.0001).

In [Figure 4] the positive correlation of serum ferritin with SGPT (r-value of 0.3560) is shown.

The result was statistically significant (p-value of 0.0036).

In [Figure 5] the negative correlation of serum ferritin with serum albumin (r-value of -0.3308) is shown. The result was statistically significant (p-value of 0.0071).

In Figure 6 the positive correlation of serum ferritin with WBC (r-value of 0.2387) is shown.

The result was statistically significant (p-value of 0.0500).

However significant correlation was not established with Hb and PCV levels.

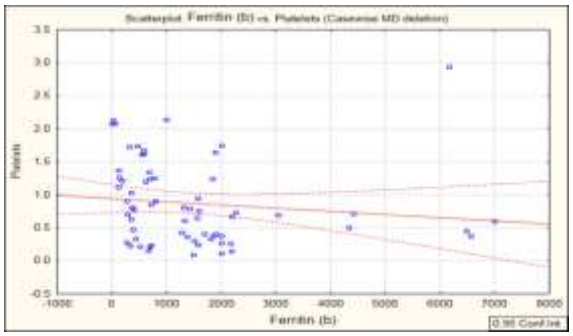

Figure 2: correlation of serum ferritin and platelets.

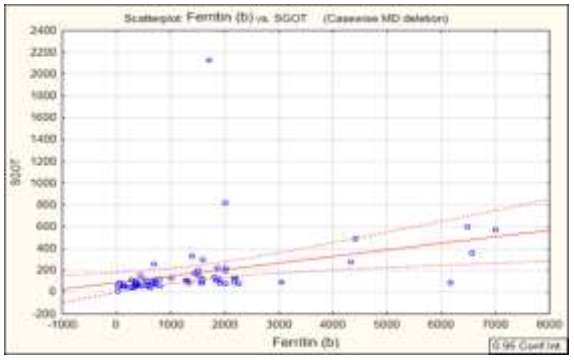

Figure 3: correlation of serum ferritin and SGOT.

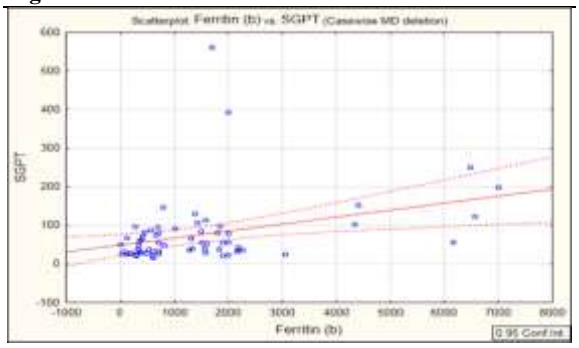

Figure 4: correlation of serum ferritin and SGPT.

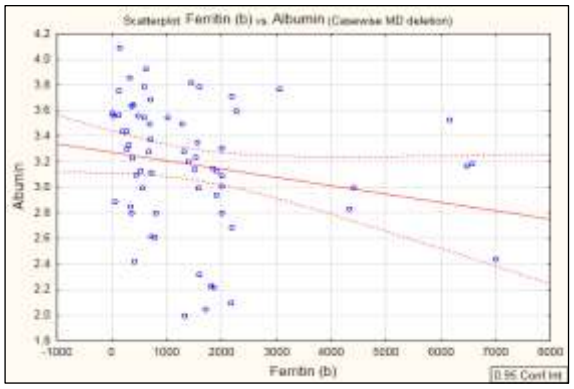

Figure 5: correlation of serum ferritin and serum Albumin.

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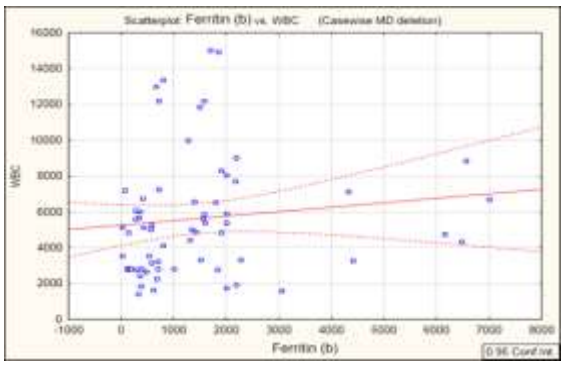

Figure 6: correlation of serum ferritin and WBC.

DISCUSSION

Dengue fever is a dynamic febrile illness that can range from a mild self-limiting form to plasma leakage, haemorrhage, or severe multiorgan dysfunction leading to severe life threatening situation. An array of mechanisms have been proposed to explain the pathogenesis of severe dengue that includes antibody-dependent enhancement [ADE] of viral infection.[7,8]

Ferritin is a reliable inflammatory marker to differentiate between dengue and fever of other origin.[6] Other studies show that serum ferritin done in febrile phase helps to predict the severity of dengue fever.[9-12] The presence of thrombocytopenia with concurrent haemoconcentration differentiates DHF/DSS from other diseases. In patients with no significant rise in haematocrit as a result of severe bleeding and/or early intravenous fluid therapy, demonstration of pleural effusion/ascites indicates plasma leakage.

Hypoproteinaemia/albuminaemia supports the presence of plasma leakage.[5] However hyperferritinemia in dengue illness is associated with elevation of both SGOT and SGPT, as reported in the paper on DENV infection in the Aruba Islands by the Brazilian and the Dutch medical researchers.[9] A study conducted by Itha et al. showed that 43 out of 45 patients with DENV infection had elevated levels of SGOT and SGPT,[10] and Chhina et al,[11] also showed that elevation of liver enzymes secondary to hepatic dysfunction was common in all forms of dengue infection with a preferentially high SGOT than SGPT being found in 90% of the patients with dengue fever.

In our study, comparision of 4 groups of dengue with gender, was made, the distribution in each droup was not statistically significant (p-0.9030). Further the 4 groups were compared according to categories of dengue like primary and seconday dengue, no significant difference was noted (p0.839) meaning, the distribution of all cases into different categories like primary and secondary dengue, and male and in males and females was statistically insignificant.

Hypothesis was formed that serum ferritin level in febrile phase of dengue illness, can predict and classify the severity and serum ferritin has correlation with other laboratory parameters like Hb, PCV, platelets, WBC, SGOT, SGPT, serum albumin done routinely in a dengue patients to access the severity.

Limitations: The major limitation of the study is that the analysis involved small number of samples, unequally distributed in 4 groups as follows DF(9.23%), DHF-1(49.23%), DHF- 2(6.15%), DHF-3(35.38%) and no case in DHF-4 group. Statistically significant correlation could not be established, however, rising trend of serum ferritin was noted in different groups as the severity increased. The trend of the ferritin was not monitored as the disease progressed in individual patient. Clinical correlation with the onset of symptoms was not studied.

However the data adds to the existing literature on correlation between severity of dengue and serum ferritin. In this study significant correlation was established between serum ferritin and Hb, PCV, WBC, Platelets, SGOT, SGPT, Serum Albumin which is done routinely to predict the severity.

CONCLUSION

From this study we conclude that the level of serum ferritin done at admission wasnot useful to classify the severity of dengue. The ferritin level was increased as the severity increased, but statistical correlation could not be established.

However statistically significant positive correlation was established between serum Ferritin with SGOT, SGPT, WBC separately. Satistically significant negative co-relation was established between Serum Ferritin with level of platelets and serum albumin.

REFERENCES

1. Worwood, 1990; Griffiths, 1991; Woodldridge and Williams, 1993; Krol and Cunha, 2003.
2. Nimmannitya S. Clinical manifestations of dengue/yellow haemorrhagic fever. In: WHO Regional Office for South-East Asia. Monograph on dengue/dengue haemorrhagic fever. New Delhi: WHOSEARO 1993. p. 48–61.
3. Nimmannitya S, Halstead SB, Gohen SN, Margotta MR. Dengue and chikungunya virus infection in Thailand 1962–64: Observations on hospitalized patients with haemorrhagic fever. Am J Trop Med Hyg. 1969; 18: 954–71.
4. World Health Organization. (2009). Dengue guidelines for diagnosis, treatment, prevention and control : new edition. World Health Organization.
5. World Health Organization. Regional Office for South-East Asia. (2011). Comprehensive Guideline for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. Revised and expanded edition. WHO Regional Office for South-East Asia..
6. Roy Chaudhuri S, Bhattacharya S, Chakraborty M, Bhattacharjee K. Serum Ferritin: A Backstage Weapon in Diagnosis of Dengue Fever. Interdiscip Perspect Infect Dis. 2017;2017:7463489. doi: 10.1155/2017/7463489. Epub 2017 Oct 2. PMID: 29098002; PMCID: PMC5643150.
7. R. De Alwis, K. L. Williams, M. A. Schmid et al., "Dengue Viruses Are Enhanced by Distinct Populations of Serotype Cross-Reactive Antibodies in Human Immune Sera," PLoS Pathogens, vol. 10, no. 10, 2014.
8. A. L. Rothman and F. A. Ennis, "Immunopathogenesis of dengue hemorrhagic fever," Virology, vol. 257, no. 1, pp. 1–6, 1999.
9. T. Ho, S. Wang, R. Anderson, and C. Liu, "Antibodies in dengue immunopathogenesis," Journal of the Formosan Medical Association, vol. 112, no. 1, pp. 1-2, 2013.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

10. S. Itha, R. Kashyap, N. Krishnani, V. A. Saraswat, G. Choudhuri, and R. Aggarwal, “Profile of liver involvement in dengue virus infection,” National Medical Journal of India, vol. 18, no. 3, pp. 127–130, 2005.
11. R. S. Chhina, O. Goyal, D. K. Chhina, P. Goyal, R. Kumarb, and S. Puric, “Liver function tests in patients with dengue viral infection,” Dengue Bulletin, vol. 32, pp. 110–117, 2008.
12. Petchiappan, Velammal & Hussain, Thaha & Thangavelu, Saravanan. (2019). Can serum ferritin levels predict the severity of dengue early?: an observational study. International Journal of Research in Medical Sciences. 7. 876. 10.18203/2320-6012.ijrms20190940.

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