

	<div>ORIGINAL RESEARCH PAPER</div> <div>AN OBSERVATIONAL STUDY ON SERUM FERRITIN LEVEL IN DENGUE FEVER AND ITS CORRELATION WITH SEVERITY DENGUE FEVER</div>	<div>General Medicine</div> <div>KEY WORDS: Dengue, Ferritin, Packed cell volume, platelets</div>
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<div>ABSTRACT</div>	<div>Background:</div> Dengue is a self-limited, systemic viral infection transmitted between humans by mosquitoes. The rapidly expanding global footprint of dengue is a public health challenge with an economic burden that is currently unmet by licensed vaccines, specific therapeutic agents, or efficient vector control strategies. The present study is aimed at observing role of raised serum ferritin levels of dengue patients with the disease severity. <div>Aims and Objectives:</div> The present study was conducted to observe role of raised serum ferritin levels of dengue patients with the disease severity. <div>Material and Methods:</div> The present cross sectional study was conducted among 50 dengue patients in Pacific Institute of Medical Sciences, Udaipur, Rajasthan. Laboratory investigations included Ferritin, Packed cell volume, and platelet count. Serum Ferritin was done by kit based Chemiluminescent Microparticle Immunoassay, Packed cell volume and platelet count was done on Fully Automated Hematology Analyzer Horiba ABX Pentra 80. <div>Results:</div> Raised serum ferritin levels were observed in 56% of patients with dengue. Significant association was observed between raised serum ferritin with Packed cell volume and platelets. There was significant correlation between serum ferritin levels and thrombocytopenia (p=0.006). Patients with increased ferritin levels had significant decrease in platelet count. Bleeding tendencies were found to be higher in patients who had increased ferritin levels and thrombocytopenia. <div>Conclusion:</div> Present study showed 56% prevalence of raised serum ferritin in dengue patients. High level showed strong correlation with increased Packed cell volume and low platelet levels, clinically reported with hematological symptoms.	
	<div>INTRODUCTION:</div> 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. It is a mosquito borne viral disease and is transmitted to humans by infected Aedes mosquitoes, mainly Aedes aegypti. Dengue virus has four serotypes, all four cause similar illness ranging from asymptomatic infection to severe dengue. The four virus serotypes are designated as DEN-1, DEN-2, DEN-3 and DEN-4. At present DEN1 and DEN2 serotypes are widespread in India. Ferritin is an acute phase reactant and expressed by cells of reticuloendothelial system in response to infection or inflammation. Hyperferritinemia was found to be associated with severity of the dengue fever in terms of increased Packed cell volume(PCV) and decreased platelets in adult patients. It is also associated with immune activation and coagulation. <div>A distinctive key manifestation of the Dengue Hemorrhagic fever(DHF)/Dengue Shock syndrome(DSS) is hemorrhagic diathesis/ thrombocytopenia occurring at the time of defervescence of fever and suggested that it is mediated through soluble mediators, compliment activation and cytokines. Serial hematocrit determinations are essential guide for treatment, since they reflect the degree of plasma leakage and need for intravenous administration of fluids^[1,2,3,4,5].</div> Ferritin is a acute phase reactant produced by reticulo-endothelial cells in response to inflammation and infection. It is produced in significant amount by monocytes, macrophages and hepatic cells. It has been shown that synthesis of ferritin can be induced by cytokines. <div>The reticulo endothelial system plays a critical role in iron metabolism by processing heamoglobin from senescent red blood cells. Acute inflammation and infection induce the blockade of iron release resulting in a decreased in serum iron, A virulence factor for many microorganisms. Elevated levels of serum ferritin, an acute phase reactant reflect the</div> clinical response to deprive micro organisms of serum iron. <div>In dengue fever, serum ferritin is disproportionately raised compared to any bacterial or viral infection and this elevated level corroborates with an increased risk of developing complications. Some studies showed a very strong correlation between serum ferritin level and severity of dengue infection^[9]. Again, serum ferritin measured on 4th or 5th day roughly evaluates the prediction of dengue infection^[10]. A study from the Caribbean Island Aruba concluded that ferritin can be used as a clinical marker to discriminate between dengue and other febrile illnesses^[11]. The occur- rence of hyperferritinemia in dengue virus infected patients is indicative for highly active disease resulting in immune activation and coagulation disturbances. Therefore, patients with hyperferritinemia are recommended to be monitored carefully. The same study concluded that high serum ferritin level with a cut-off value of >1500 in confirmed DENV infection is associated with increased severity of dengue related illness in adults. Ferritin levels measured at Day 4 or 5 may be a good predictor in outcome in dengue^[10].</div> <div>AIM</div> To study serum ferritin level in dengue fever and its correlation with severity of dengue virus infection in a tertiary medical college. <div>MATERIALS AND METHOD:</div> <div>Study area:</div> The study was conducted among 50 dengue patients in PIMS hospital, Udaipur, Rajasthan from June 2023 to November 2023. With necessary permission and all due precautions serum sample were collected and analyzed for serum Ferritin, PCV, and platelets. <div>Inclusion criteria:</div> <ul style="list-style-type: none">Patients >18 years admitted in PIMS hospital medicine ward satisfying WHO Criteria for confirmatory diagnosis as DF, DHF & DSS.Patient willing to participate with informed consent.	

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Exclusion criteria:

- Patients with fever of any other aetiology, Unknown cause of fever
- Pregnancy
- Patients <18 years of age
- Patients with known liver, kidney and coagulation disorders.
- Patients with chronic inflammatory disease and mixed infections
- Patients on heparin, aspirin, Cardiac patients, Thyroid dysfunction.
- Patients with qualitative and quantitative platelet disorders.
- Patients of known case of anemia with Hb <10gm/dl.
- Patients with known iron overload status (hemochromatosis, multiple blood transfusions).
- Patients not willing to participate and doesn't give consent.

Table 2: Age Distribution of Study Participants (n=50)

Age	No. of patients (n)	Percentage (%)
11-25	19	38
26-40	12	24
41-55	13	26
56-70	2	4
71-85	4	8
Total	50	100

Table 3: Significance between serum Ferritin levels and platelets

Parameter	Thrombocytopenia	No Thrombocytopenia	p value
Hyperferritinemia	17 (110*103+15*103/cmm)	11 (156*103+4*103/cmm)	<0.001
No Hyperferritinemia	16 (130*103+10*103/cmm)	6 (153*103+2*103/cmm)	

METHODOLOGY

Study was started in Department of General Medicine-IPD patients, at Tertiary care Hospital, Udaipur the study was carried out on 50 patients admitted during the period of June 2023- November 2023 the hospital. This was an observational, Prospective study. study was started After taking ethical approval, patients were enrolled, the data was compiled, tabulated, analyzed and the results were finalised. Study was including all Patients who meet all the above mentioned criteria will be included in the study and those cases who did not, were exclude from this study. After satisfying the inclusion and exclusion criteria 50 dengue IgM positive patients were included in this study. Their serum ferritin levels on the day of admission was measured. The relationship between serum ferritin levels and platelets and severity of dengue fever was observed. Statistical analysis was done using the SPSS software.

RESULTS

Current study included 50 dengue patients with confirmed NS1 positive or positive IgM antibodies.

Out of 50 patients, 28 were males and 22 were females.

Most of the patients were in the age group of 11-25 (n=19) and least number of patients were in the age group of 56-70 (n=2).

Out of 50 patients 56% (n=28) patients showed high serum ferritin level with mean of 1358+733.28 ng/ml, whereas 44% (n=22) had normal mean serum ferritin level with mean of 127.82+51.92 ng/ml.

There was significant increase in PCV observed in 32%(n=16) patients who also developed hyperferritinemia, and 34%(n=17) patients out of 50 showed thrombocytopenia with increased ferritin levels.

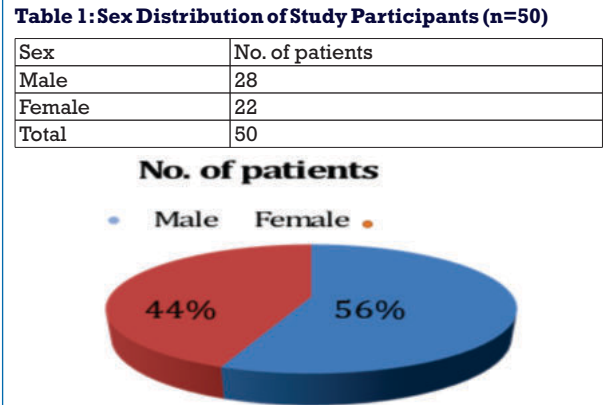


Figure 1: Sex Distribution of Study Participants

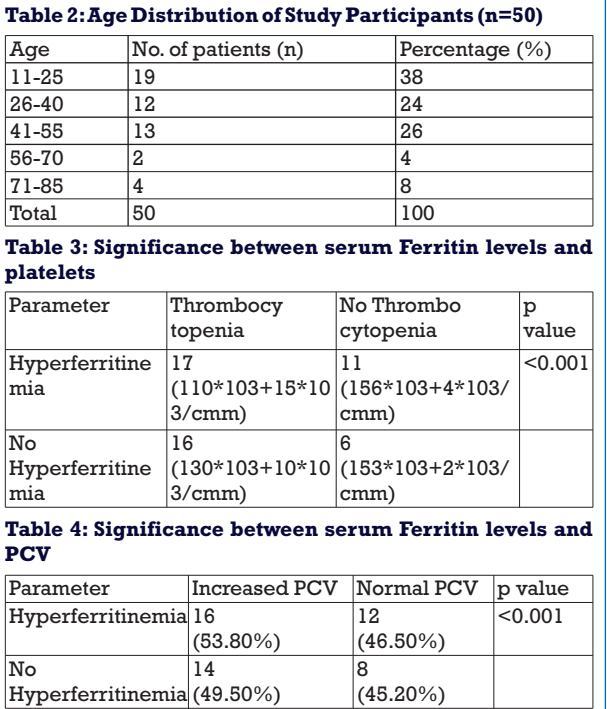
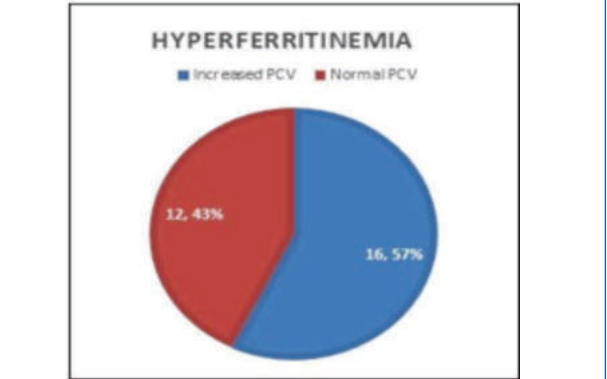


Figure 2: Significance between serum Ferritin levels and platelets.



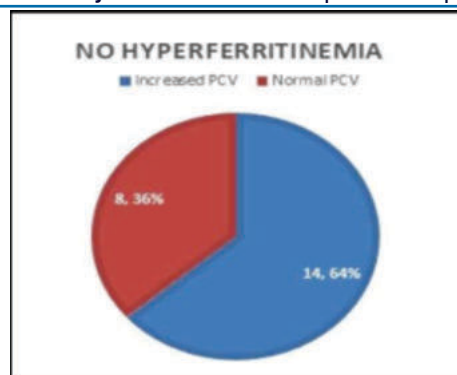


Figure 3: Significance between serum Ferritin levels and PCV

DISCUSSION:

Overall it can be said that in the present study, 56% (n=28) patients had high serum ferritin level significantly associated with thrombocytopenia 34% (n=17) and raised PCV 32% (n=16) (p value= <0.001). Mean serum ferritin was found significantly higher in patients with dengue.

Dengue fever is a dynamic febrile illness that can range from a mild self-limiting form to the other end of the spectrum which ranges from plasma leakage, hemorrhage, or severe multiorgan dysfunction leading to severe life threatening situation. The findings of present study are consistent with increased levels of ferritin associated with severe disease and a pro-inflammatory cytokine profile. Ferritin is an acute-phase reactant and a significant amount is produced by monocytes, macrophages and hepatic cells. It has been shown that synthesis of ferritin can be induced by cytokines and iron. In the earlier cohort studies from Aruba, increased concentrations of ferritin were significantly associated with a confirmed dengue diagnosis and viraemia.

The association of thrombocytopenia with dengue infection has been proved to be significant (p<0.001), a total of 34% patients had thrombocytopenia. This is in accordance with a study done by M. Anuradha et al, that showed thrombocytopenia in 89% of total patients.

Haematocrit (HCT) monitoring is used to evaluate the degree of plasma leakage and to determine what therapeutic intervention is needed. The increase in hematocrit in dengue is due to hemoconcentration attributed to plasma leakage induced by cytokine-mediated increase in vascular permeability and damage to vascular endothelium.

Results of current study correlate well with study done by Joshi, et al that showed 55% of cases with haematocrit >40%.^[6,7,8]

In a study conducted by Petchaiappan V et al. serum ferritin levels negatively correlated with the platelet count (r = 0.51, p < 0.001)

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.

CONCLUSION:

It is concluded that a higher prevalence of hyperferritinemia was found in the dengue patients along with thrombocytopenia and raised PCV. Thus hyperferritinemia is associated with thrombocytopenia and elevated PCV and such patients may require careful monitoring.

Raised serum ferritin level was found significantly associated with disease severity. Serum ferritin evaluated in dengue

could possibly aid clinical judgement and prompt early resuscitation which in turn could be useful in avoiding undue complications.

Conflict of Interest:

None.

Funding Statement:

Nil

Ethical Conduct of Research:

The authors have declared that they have obtained ethical approval for this study from the Institutional Ethics Committee.

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