

## Role of serum ferritin in dengue and its correlation with disease severity.

Dr. Asha Khubchandani<sup>1</sup>, Dr. Vidhi Patel<sup>2\*</sup>, Dr. Disha Gajjar<sup>3</sup>, Dr. Binal Prajapati<sup>4</sup>

<sup>1</sup>Professor & Head, <sup>2</sup>Second year Resident doctor, <sup>3</sup>Third year Resident doctor, <sup>4</sup>First year Resident doctor, Department of Biochemistry, B.J. Medical College, Ahmedabad.

### Abstract:

**Background:** 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. **Aims and Objectives :**The present study was conducted to observe role of raised serum ferritin levels of dengue patients with the disease severity. **Material and Methods:** The present cross sectional study was conducted among 50 dengue patients in Civil hospital Ahmedabad, Gujarat. Laboratory investigations included Ferritin, Packed cell volume, and platelet count. Serum Ferritin was done by kit based Chemiluminescent Micro particle Immunoassay , Packed cell volume and platelet count was done on Fully Automated Hematology Analyzer Horiba ABX Pentra 80. **Results:** 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. **Conclusion:** 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.

**Key Words:** Dengue, Ferritin, Packed cell volume, platelets.

### Introduction:

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 disturbances. A

#### \* Corresponding Author:

Dr. Vidhi Patel

Email: [vidzpatel.91@gmail.com](mailto:vidzpatel.91@gmail.com)

#### QR Code:



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].

### **Materials and method:**

#### ***Study area:***

The study was conducted among 50 dengue patients with the mean age of  $35 \pm 10$  years in Civil hospital, Ahmedabad, Gujarat from October 2019 to July 2020. With necessary permission and all due precautions serum sample were collected and analyzed for serum Ferritin, PCV, and platelets.

#### ***Inclusion criteria:***

Patients with confirmed NS1 positive or positive IgM antibodies for dengue, Age  $35 \pm 10$  years.

#### ***Exclusion criteria:***

Unknown cause of fever, Pregnancy, Liver dysfunction, Blood coagulopathy, Mixed infections, Patients on heparin, aspirin, Cardiac patients, Thyroid dysfunction, Kidney dysfunction, Patients with qualitative and quantitative platelet disorders.

#### ***Biochemical Analysis***

Serum ferritin levels of all the patients were analyzed by Fully Automated Immunochemistry Analyzer in Hitech Biochemistry Laboratory of Civil Hospital, Ahmedabad, Gujarat. For PCV and platelets samples were sent to Central Laboratory of Pathology department of Civil Hospital, Ahmedabad, Gujarat and measured by Fully Automated Hematology Analyzer Horiba ABX Pentra 80.

#### ***Data Analysis***

Muster chart was prepared using Excel 2007 software. Data statistically analyzed by IBM SPSS Statistics v.25 on basis of p value.

### **Results:**

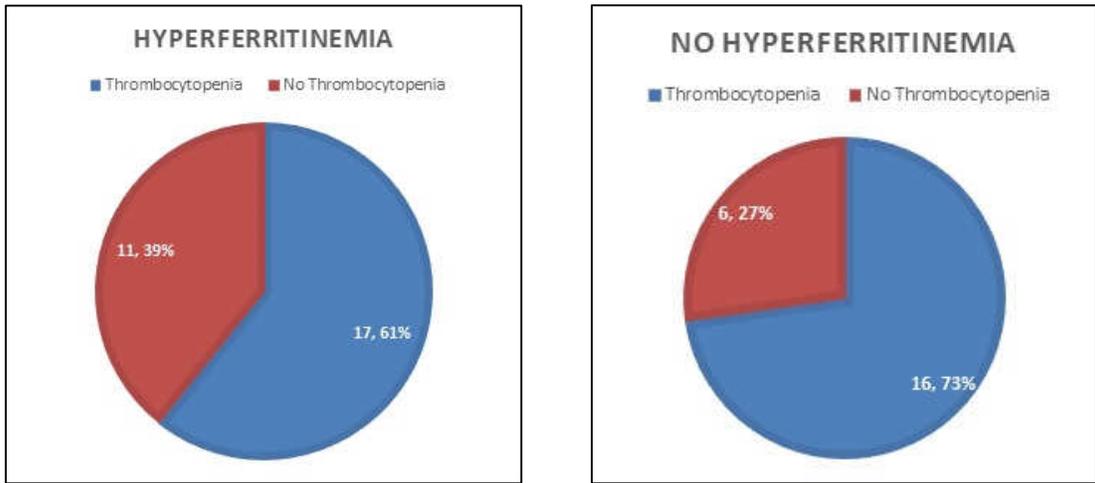
**Table 1: Significance between serum Ferritin levels and platelets.**

Parameter	Thrombocytopenia	No Thrombocytopenia	p value
Hyperferritinemia	17( $110 \times 10^3 \pm 15 \times 10^3$ /cmm)	11( $156 \times 10^3 \pm 4 \times 10^3$ /cmm)	<0.001
No Hyperferritinemia	16( $130 \times 10^3 \pm 10 \times 10^3$ /cmm)	6( $153 \times 10^3 \pm 2 \times 10^3$ /cmm)	

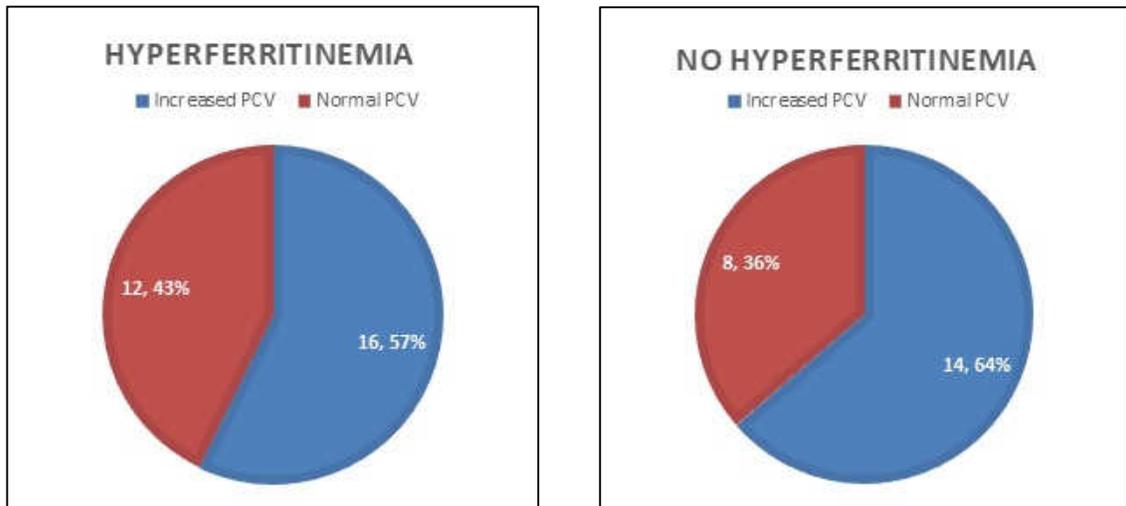
**Table 2: Significance between serum Ferritin levels and PCV.**

Parameter	Increased PCV	Normal PCV	p value
Hyperferritinemia	16(53.80%)	12(46.50%)	<0.001
No Hyperferritinemia	14(49.50%)	8(45.20%)	

**Image 1 Significance between serum Ferritin levels and platelets.**



**Image 2 Significance between serum Ferritin levels and PCV**



Current study included 50 dengue patients with confirmed NS1 positive or positive IgM antibodies. Out of 50 patients 56% (n=28) patients showed high serum ferritin level with mean of  $1358 \pm 733.28$  ng/ml, whereas 44% (n=22) had normal mean serum ferritin level with mean of  $127.82 \pm 51.92$  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.

**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%.<sup>[6,7,8]</sup>

**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.

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