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HYPER- AND HYPO- FERRITINEMIA

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ABSTRACT

Ferritin is an iron storage protein found mainly in liver and spleen and in small amounts in human serum. The ferritin in serum is chiefly derived from macrophages. It is critical to iron homeostasis. During liver damage, ferritin leaks from hepatocytes, and plasma concentration rises (hyperferritinemia). Hyperferritinemia observed in obesity, inflammation and daily consumption of alcohol. Hypoferritinemia (low levels of ferritin) is associated with iron deficiency anemia, crohn's disease, ulcerative colitis, celiac disease, hemorrhoids etc. Ferritin concentrations vary by age and gender. SF is the most common laboratory investigation requested these days from various departments. This study was planned to see the ferritin levels in serum samples of both males and females attending the outpatient department (OPD) of various clinical departments in a tertiary care hospital.

KEYWORDS: Ferritin, iron deficiency anemia, hypoferritinemia, hyperferritinemia.

INTRODUCTION

French scientist Laufberger in 1937 isolated a new protein from horse spleen (containing 23% by dry weight of iron), called as ferritin. Iron free ferritin (apoferritin) is a 24- subunit protein that is composed of two types of subunits, termed H and L. H form is isolated from human heart and kidneys and L form from human liver and spleen. The ratio of H and L subunits varies depending upon the tissue. Genes for the H and L subunit are located on chromosomes 11q and 19q respectively.[1,2]

Ferritin is ubiquitous in nature and is an iron storage protein found mainly in liver and spleen and in small amounts in human serum. The secretion processes are still unclear. The ferritin in serum is chiefly derived from macrophages. It is critical to iron homeostasis (free iron is toxic to cells) but is relatively iron poor. Serum ferritin (SF) has no role in iron transport or cellular iron uptake. That is the role of transferring. SF is entirely made of L subunit. Ferritin makes iron available for critical cellular processes. It protects lipids, DNA, and protein from the potentially toxic effects of iron.[3]

During liver damage, ferritin leaks from hepatocytes, and plasma concentration rises (hyperferritinemia). It is increasingly recognized that ferritin (non-specific acute phase protein because it increases in stresses such as anoxia) is deranged in inflammatory conditions adult-onset still's disease (AOSD), systemic juvenile idiopathic arthritis, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (MAS), neurodegenerative, autoimmune diseases and malignant diseases. High levels of ferritin are also observed in COVID-19. There are different mechanisms which inhibit the ferritin-mediated suppression of the immune cell, and in turn, this immune suppression may favour the loss of tolerance and development of autoimmune diseases. Expression of ferritin is also regulated by oxidative stress, hormones (thyroid hormone), growth factors, second messengers and hypoxia-ischemia and hyperoxia. Cyclopentenone prostaglandins, induce L subunit ferritin in human monocytes.[4-6]

Elevated ferritin levels (hyperferritinemia) are observed in obesity, inflammation and daily consumption of alcohol. Hereditary hemochromatosis is the most likely primary cause of elevated SF. A patient with typical C282Y homozygote for hemochromatosis is likely to have an elevated SF. Phlebotomy is usually recommended for such patients until SF falls <50ng/ml. If a patient is having an elevated SF and is not a typical C282Y homozygote, treatment options include observation, magnetic resonance imaging (MRI), liver biopsy, and empirical phlebotomy can be attempted. SF levels >1000µg/L is associated with high prevalence of advanced fibrosis and cirrhosis in hereditary hemochromatosis.[7,8]

Hypoferritinemia (low levels of ferritin) is associated with iron deficiency anemia (IDA), crohn's disease, ulcerative colitis, celiac disease, hemorrhoids, colon cancer, peptic ulcer disease, menorrhagia, hematuria, pregnancy (due to increase iron demand) and puberty. A concentration of <15µg/L is diagnostic of IDA. Therefore, the measurement of ferritin levels is crucial for the diagnosis, treatment, assessment of disease progression and post-operative prognosis of abnormal iron metabolism and IDA.[9,10]

Ferritin concentrations vary by age and gender. Males have a higher value as compared to females. In females, ferritin concentrations remain relatively low until menopause and then rise.[11]

SF is the most common laboratory investigation requested these days from various departments. SF can be measured by immunoassays [enzyme linked immunosorbent assay (ELISA), immunochemiluminescence or immunoturbidometric assay]. Most immunoassays use antibodies to either liver or spleen ferritin. This study was planned to see the ferritin levels in serum samples of both males and females attending the outpatient department (OPD) of various clinical departments in a tertiary care hospital.

METHODOLOGY

For measuring SF level, Nephelometry method was used.

Principle: "latex particles coated with anti-ferritin antibody (rabbit) are agglutinated when mixed with samples containing ferritin. The agglutination is directly proportional to the concentration of ferritin in the sample." The following values were used as reference range of SF.

- Males: 30-220 ng/ml
- Females: 20-110 ng/ml

Values not between the above ranges were considered abnormal. Lower detection limit is 1ng/ml. The reagent used in our kit is linear up to 1000 ng/ml. If the concentration is greater than linearity, dilute the sample with normal saline and repeat the assay. Multiply the result with the dilution factor.

Calibration is not required since the calibration data is incorporated into the smart card.

Fig: serum ferritin measuring machine.

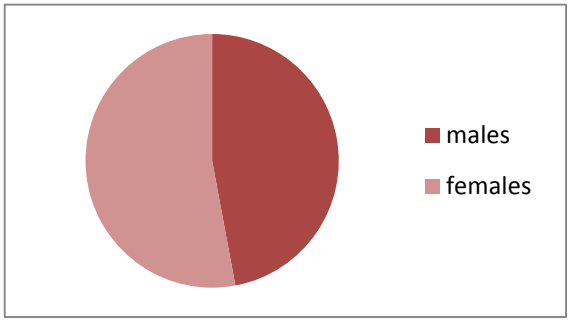
PROCEDURE

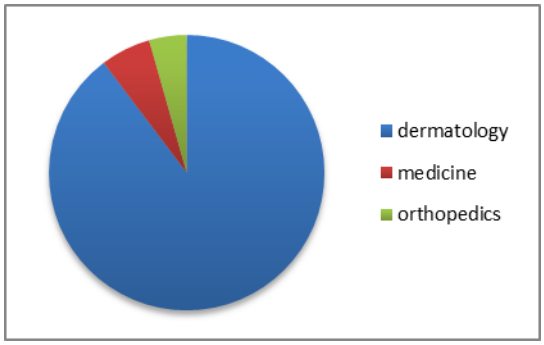
1. Insert the card to card reader slot an display will prompt to add R1+ sample
2. Pipette 100 µL R1 and 10 µL sample to cuvette and place the cuvette into cuvette holder
3. After incubation display will prompt to add R2
4. Pipette 150 µL R2 using attached sensor pipette to the cuvette
5. The result will show in the display and print out

RESULTS

This study included a total of 68 fresh serum samples for measuring SF levels from various departments of a tertiary care hospital. This study included both males and females.

Out of the 68 serum samples, 32 (47.06%) samples were from male patients and 36 (52.94%) from female patients. 61 serum samples were received from dermatology department, 4 samples from medicine department and 3 samples from orthopedics department.





5 male patients were have elevated SF levels of values 368.37ng/ml, 265.35ng/ml, 482.16ng/ml, 237ng/ml and 369ng/ml and 6 patients were having value less than the normal range.

Only 1 female patient was having an elevated SF (>150ng/ml) and 17 female patients were having SF less than the normal range. Out of the 17 female patients with hypoferritinemia, 2 patients had value of <1ng/ml.

DISCUSSION

SF is the most specific and effective test to reflect total body iron stores. SF concentrations were higher among males as compared to females. Very high ferritin levels are not just the product of inflammation but may have a pathogenic role. In a study conducted by Ling-ling Han and colleagues (2014) concentrations of SF were higher in males than females which is in concordance with the present study.[12]

Out of 68 patients, 39 (57.3%) had normal ferritin status, 23 (33.8%) with hypoferritinemia and 6 (8.8%) with hyperferritinemia.

Low levels of ferritin in females (hypoferritinemia 25%) can be attributed to the loss of blood during the menstrual cycle. Thereby, increasing the iron demand in these females. Also demand of iron is increased during pregnancy.[13]

Hyperferritinemia was 8.8% in the present study. More in men than women. It can be due to hepatitis, alcoholism, massive blood transfusions, increased consumption of iron rich diet and hereditary.[13]

CONCLUSION

SF tends to be a logical marker for the diagnosis of many diseases. The levels of ferritin vary according to the predisposing factor. SF is the most common indicator of iron deficiency.

Following conclusions were made

- ✓ 57.3% of the patients had normal SF levels
- ✓ Hypoferritinemia was more common in females than males and
- ✓ Hyperferritinemia was more common in males than females.
- ✓ It is also conclusive that women have more IDA.

In conclusion, measuring SF is essential to investigate the prevalence and distribution of iron deficiency and overload, thus leading to proper intervention and therapy. Hypoferritinemia in females in our study is most commonly due to IDA due to the loss of blood (more hemolysis than erythropoiesis) in females more frequently. So it is advised that females should take iron rich diet to keep up their iron stores replenished and hemoglobin balanced. Females should add iron tablets in their routine during menses. The limitation of doing SF is that it not only increases during inflammation but also during pregnancy and due to extensive exercise. So it is difficult to rule out whether the underlying condition (deranged ferritin levels) is due to a disease pathology or normal (eg: due to menses). Other investigations are needed, to rule out the differential diagnosis and reach to a probable or a final diagnosis for the deranged ferritin levels.

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