Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 2197-2202 | ISSN:2251-6727

The Role of Positive Acute Phase Protein (Ferritin) In Chronic Kidney Disease

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Received Date: 11/07/2025 ***Revised Date: 10/08/2025*** ***Accepted Date: 20/09/2025***

KEYWORDS

Ferritin, Inflammation, Chronic Kidney Disease.

ABSTRACT:

Background: Renal failure is a major health issue, which has been increasing worldwide [1]. Oxidative stress and inflammation are associated with higher risk of chronic kidney disease (CKD). Serum ferritin concentrations correlate with systemic inflammation, found in most tissues as a cytosolic protein, but small amounts are secreted into the serum where it functions as an iron carrier. Ferritin concentrations increase drastically in the presence of an infection. The aim of this (Retrospective) study is to know the associations between serum ferritin levels and CKD.

Method: Chemiluminescence.

Results: A total No of 100 cases (Retrospective) were studied by dividing them into two group's controls (50) and cases (50). The results so obtain were compared with 50 healthy controls Statistical evaluation was carried out to confirm any deviation from the normal values.The mean serum FERRITIN values in cases is having higher level as compared to the mean value of controls This increase (Ferritin <0.0001) is statistically highly significant.

Conclusions: where ferritin is elevated in its capacity as an inflammatory acute phase protein and not as a marker for iron overload.CKD can disrupt normal iron metabolism and lead to inflammation, it is clear that ferritin serves as a vital biomarker.

INTRODUCTION

In Normal healthy persons Kidneys filter blood, remove waste, and maintain the balance of essential bodily fluids, electrolytes, and toxins. They help regulate blood pressure, contribute to the formation of red blood cells, and even influence the body's calcium and vitamin D metabolism. Without these organs functioning efficiently, life itself would not be possible. While filtration removes waste from the blood, it also removes substances that the body needs. Therefore, the kidneys must carefully reabsorb essential compounds to maintain the body's balance.The amount of re-absorption that takes place is finely tuned to the body's needs.

The kidneys constantly monitor the body's fluid balance and adjust blood pressure as needed to ensure that tissues receive an adequate blood supply. This function is critical for preventing complications like kidney failure or stroke, which can result from uncontrolled high or low blood pressure.Chronic kidney disease (CKD) is characterized by the presence of kidney damage which involves a progressive loss of kidney function, often leading to the need for renal replacement therapy, such as dialysis or transplantation. CKD is often associated with complications that increase mortality, such as iron deficiency anaemia and cardiovascular disease. CKD affects millions globally and its prevalence continues to rise characterized by a gradual loss of kidney function over time. The progression of CKD can lead to significant complications.

Measuring the ferritin level in patients can provide core fact regarding their iron status, especially in conditions like CKD where iron metabolism is often disrupted. Ferritin is present in every cell type. (1) It serves to store iron in a non-toxic form, to deposit it in a safe form, and to transport it to areas where it is required. (2)Ferritin is an evolutionarily conserved globular protein, composed of 24 poly-peptide chains. It forms a spherical shape that is approximately 8nm in diameter, allowing it to store

Journal of Chemical Health Risks

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JCHR (2025) 15(5), 2197-2202 | ISSN:2251-6727

approximately 4,500 Fe atoms. [3–5] Serum ferritin is heterogeneous due to glycosylation. The glycosylation and direct relationship of serum ferritin concentration to iron storage in macrophages suggest it is secreted by macrophages in response to changing iron levels.

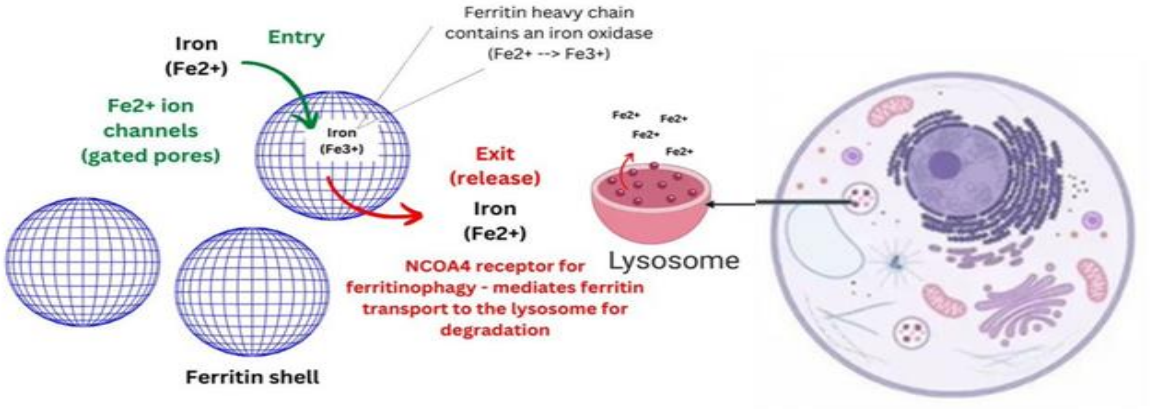

Figure 1: Distribution of iron in ferritin (fig1)

Iron ***enters*** ferritin through pores as Fe2+, where it is oxidized to Fe3+ and stored inside the shell. Iron ***exits*** ferritin through iron-regulatable NCOA4-mediated autophagic proteolytic degradation of the ferritin shell in lysosomes – a process called ferritinophagy. Inflammation associated with CKD increases ferritin and hepcidin independent of the body's iron composition. Hepcidin prevents iron egress from cells and increases intracellular ferritin expression.

Inflammation associated with CKD increases ferritin and hepcidin independent of the body's iron composition. Hepcidin prevents iron egress from cells and increases intracellular ferritin expression.[7] Serum ferritin has since remained mainstay for evaluation of systemic iron stores despite evidence suggesting that ferritin is elevated during infection and malignancies. These underlying co-morbid conditions often confound the interpretation of serum ferritin levels (reviewed in[8], [9] Until recently, it was assumed that serum ferritin is a leakage product, derived from damaged cells and studies demonstrate that serum levels correlate with disease severity. [10,11,12]

While it is possible that damaged cells contribute to an increase in ferritin during disease states, emerging evidence support that ferritin is actively secreted by uninjured cells as a normal physiological process. [13,14] Ferritin transfer from cells to serum in humans; less active secretion, more simply leakage from damaged cells.

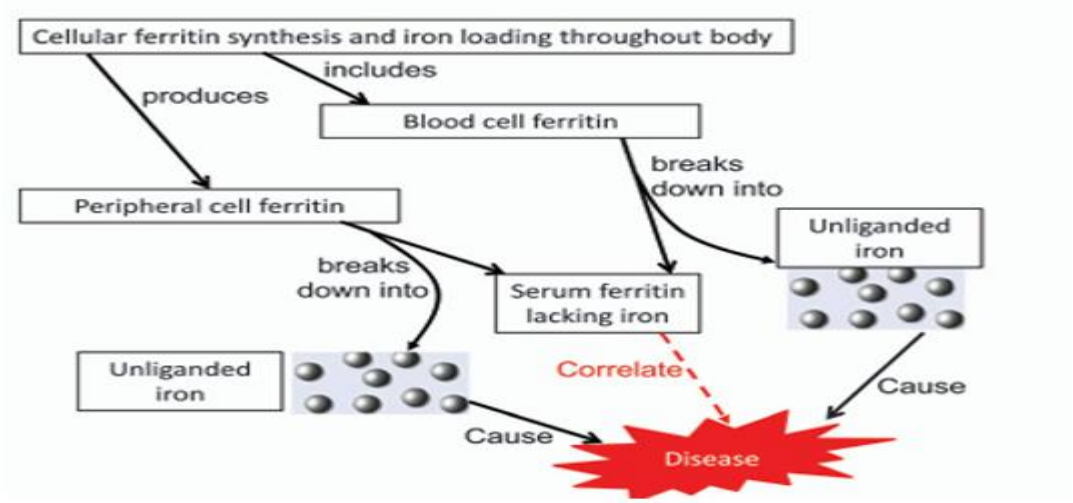

Figure 2: A high-level systems approach to serum ferritin

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JCHR (2025) 15(5), 2197-2202 | ISSN:2251-6727

Fig 2 high-level systems approach to serum ferritin. The diagram serves to illustrate why there tend to be correlations between the amount of ferritin in cells, the rate of its excretion by cell damage (involving liberation of unliganded iron) and the levels of serum ferritin. The serum ferritin correlates with disease but the cause is iron, with which it too can correlate. As with any systems biology network, multiple differences in different elements of the network can lead to the same overall effects, explaining the lack of a perfect correlation with any individual process. Thus, a first order rate of efflux of ferritin is the product of (and thus contains contributions from) both the internal ferritin concentration and the rate constant for efflux, which may vary independently. For these purposes we do not discriminate the many individual iron species. (15)

Formation of inflammation chronic kidney disease (CKD) is defined as "abnormalities of the kidney structure or function, present for more than 3 months, with implications for health". (16) There is no question that inflammation plays a part in CKD progression and outcome. (17)

Dialysis and inflammation Chronic, low-grade inflammation is regarded as a common comorbid condition in CKD, and particularly in chronic dialysis patients (18) Several circulating markers are commonly assessed as indicators of systemic inflammation. IL-1 is a pro-inflammatory mediator of both acute and chronic inflammation, and induces synthesis and expression of hundreds of secondary inflammatory mediators. (19) Multiple factors likely contribute to chronic inflammatory activation in kidney disease patients (Fig 3). (20) With declining renal function. Frequent infectious and thrombotic events provide additional inflammatory stimulations, particularly in dialysis patients (21)

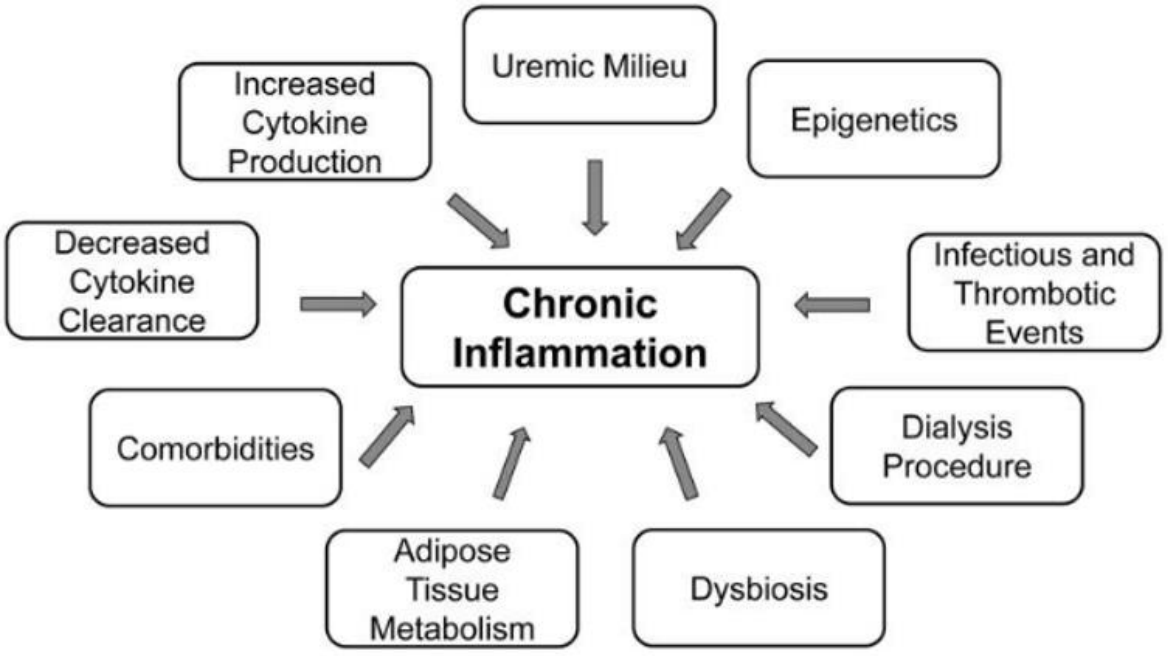

Figure 3: Factors Contributing to Increased Inflammation in Chronic Dialysis Patients.

Dialysis and ferritin

Chronic kidney disease (CKD) is defined by sustained and impaired renal function that may result from a loss of functional nephrons. CKD is often associated with complications that increase mortality, such as iron deficiency anaemia and cardiovascular disease. (22,23,24)

Inflammation associated with CKD increases ferritin and hepcidin independent of the body's iron composition. Hepcidin prevents iron egress from cells and increases intracellular ferritin expression. As both of these iron regulatory molecules increase, total iron availability for red blood cell synthesis decreases, leading to a functional iron deficiency. Thus, the discrepancies in serum ferritin levels could result in a misleading diagnosis of iron stores during CKD

MATERIAL AND METHODS

Study Design: Retrospective observational study.

Study Period: March 2025 to May 2025.

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Sample Size: contain 50 cases of CKD and 50 normal healthy individuals as control.

Sampling technique: Convenient Sampling from the patients who are attending nephrology department.

Study Setting: Malla Reddy Medical College for women's and Maharajah's Institute of Medical Sciences.

Inclusion criteria: Patients who diagnosed with Chronic Kidney Disease.

Exclusion criteria: Patients with chronic complications and Patients with HIV and Hepatitis Positive.

Study Methodology: Ethical Committee approval was obtained. Patients who are eligible to the study are included and patients ferritin values measured with CLIA was recorded and data was compared with control group.

Statistical Techniques: The quantitative data was expressed with mean and standard deviation statistical significance was measured with Z test and statistical significance measured where p value is <0.0001.

Estimation of serum ferritin by Chemiluminescence method

Serum Ferritin level in Control and CKD patients

Table 1.

Groups	Ferritin (Mean ± SD)	Z Value	p value
Control	75.28 ± 25.79	21.73145	<0.0001
CKD Patients	1095.04 ± 330.80		

RESULTS

The ferritin levels were determined using the Fully Automated Biodirectionally Interfaced Chemi Luminescent Immune Assay Method. Table 1 presents the mean serum Ferritin levels in a sample of 50 individuals, including both males and females. The data indicates that the mean serum Ferritin levels in the cases are greater compared to the mean levels observed in the control group. The observed rise exhibits statistical significance.

DISCUSSION

The retrospective studies obtained from lab during the period from March 2025 to May 2025 in the Department of Medicine MIMS and MRMCW. A total No of 100 cases were studied by dividing them into two groups Controls and Cases and observation made were tabulated

The mean serum FERRITIN values in cases is having higher level as compared to the mean value of controls This increase (Ferritin <0.0001) is statistically highly significant Patients with Chronic Kidney Disease (CKD), ferritin levels can be unreliable indicators of iron stores due to the impact of inflammation and kidney function. Elevated ferritin levels in CKD patients are often attributed to inflammation rather than actual iron overload. While low ferritin levels generally suggest iron deficiency, elevated levels don't necessarily rule it out in the context of CKD. CKD disrupts iron metabolism, making it difficult to accurately assess iron status using traditional markers like serum ferritin and transferrin saturation.

Inflammation's Impact:

CKD patients often experience chronic inflammation, which can lead to increased ferritin levels, even if iron stores are low. This is because inflammation stimulates the release of hepcidin, a hormone that restricts iron absorption and utilization, leading to functional iron deficiency. patients with chronic kidney disease (CKD), ferritin levels can be unreliable indicators of iron stores due to the impact of inflammation and the body's altered iron metabolism. While low ferritin (<100 ng/mL in non-dialysis patients, <200 ng/mL in dialysis patients) is generally indicative of absolute iron deficiency, elevated ferritin levels don't always mean iron overload, as inflammation can mask functional iron deficiency.

Both inflammation and nutritional status are crucial factors influencing ferritin levels in CKD patients. Addressing these elements can lead to more personalized and effective treatment plans, ultimately improving patient outcomes

Summary of Key Insights

- Ferritin as a Biomarker: Ferritin is not merely an indicator of iron storage. It also reflects inflammatory processes and helps assess the severity of anemia in CKD patients.
- Clinical Implications: Abnormal ferritin levels can signal critical health shifts in CKD patients. Thus, regular monitoring is essential for timely interventions.

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JCHR (2025) 15(5), 2197-2202 | ISSN:2251-6727

- Management Strategies: Effective management requires a multifaceted approach, focusing on iron supplementation and anemia treatment while considering individual patient circumstances.
- Emerging Research: Novel studies propose new biomarkers and future directions, indicating that the understanding of ferritin's role in CKD is still evolving.

CONCLUSION

serum ferritin is known to associate with disease and/ or disease severity,factors such as the presence of other inflammatory markers, the severity of CKD, and the patient's overall iron status should be considered when interpreting ferritin levels. Elevated ferritin, especially in the context of inflammation, may impact erythropoietin responsiveness and iron therapy decisions. Serum ferritin levels can be affected by two largely independent causes, viz. iron status and inflammatory status.[25] "Ferritin levels are an essential piece of the puzzle in managing CKD-related anemia and inflammation.

"This topic has significant clinical relevance as it links ferritin not only to iron status but also to inflammation and overall patient health.Serum ferritin may in general be a better marker of inflammation than of iron status and need for further research.

The conclusion serves as a important point in this article, understanding ferritin in the context of CKD is not just a scientific curiosity; it has significant implications on clinical practice and patient management.

Acknowledgments;

Malla Reddy Medical College for Women & Maharaja's Institute of Medical Sciences

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