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ROLE OF SERUM FERRITIN IN CHRONIC KIDNEY DISEASE: IMPLICATIONS AND CLINICAL SIGNIFICANCE

Biochemistry

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ABSTRACT

Millions of people worldwide suffer from chronic kidney disease (CKD), which frequently results in serious side effects such anaemia, cardiovascular illness, and higher mortality. Serum ferritin has become more popular among the biomarkers used to track the development of CKD and its related consequences. In the past, serum ferritin was thought to be an indirect indicator of the body's iron level and a kind of iron storage. Beyond iron metabolism, though, it plays a crucial role in chronic kidney disease (CKD) as a measure of oxidative stress and inflammation, two major pathogenic aspects of the disease. Infections and cardiovascular problems are linked to higher morbidity and mortality rates in CKD patients with elevated blood ferritin levels. The inflammatory condition that many CKD patients experience makes it difficult to evaluate blood ferritin levels clinically since they may not always appropriately indicate iron shortage. The significance of serum ferritin as an inflammatory measure as well as an iron storage marker in chronic kidney disease (CKD) is covered in the current review. Aside from emphasising the difficulties in detecting functional iron insufficiency, the review also discusses the relevance of serum ferritin in the therapy of anaemia associated with CKD. In addition, we investigate the therapeutic implications of high ferritin levels and how to maintain iron homeostasis in patients with chronic kidney disease. Through more individualised and efficient treatment plans, a better understanding of the complex function serum ferritin plays in chronic kidney disease (CKD) can lead to better patient outcomes.

KEYWORDS

INTRODUCTION

Untreated chronic kidney disease (CKD) can progress to end-stage renal disease (ESRD) due to the progressive decrease of kidney function over time. Since 10% of people worldwide suffer with CKD, it is a serious public health issue. Anaemia, which results from decreased erythropoietin production, iron shortage, and inflammation, is one of the most prevalent and crippling side effects of chronic kidney disease (CKD). Previously thought to be a measure of iron reserves, serum ferritin has become an important factor in determining iron status and treating anaemia in individuals with chronic kidney disease. However, because serum ferritin serves as both an acute-phase reactant and an iron storage marker, interpreting its levels in chronic kidney disease (CKD) is challenging. Increased serum ferritin levels can be brought on by inflammation, a typical CKD trait that might conceal actual iron deficiency and make managing anaemia more difficult. This raises questions about the diagnostic accuracy of serum ferritin as a measure of iron adequacy or shortage, especially in patients with chronic kidney disease (CKD) who are more likely to experience chronic inflammation.

Furthermore, increased risk of infections and cardiovascular events are two more negative outcomes associated with raised blood ferritin levels in patients with chronic kidney disease (CKD). Beyond its involvement in iron metabolism, this emphasises the need for a sophisticated understanding of serum ferritin in the context of chronic kidney disease (CKD). Serum ferritin's effects on chronic kidney disease (CKD) will be examined in this review, with particular attention paid to its management of anaemia, its relationship to inflammation, and its overall clinical relevance.

AIMS AND OBJECTIVES

This review's objective is to thoroughly investigate serum ferritin's involvement in chronic kidney disease, with an emphasis on its dual roles as an inflammatory and an iron storage marker. One of the specific goals is to investigate the connection between iron deficiency and serum ferritin in patients with chronic kidney disease.
2. To investigate how inflammation affects the management of anaemia by raising serum ferritin levels in individuals with chronic kidney disease.
3. To look into the clinical relevance of higher serum ferritin levels in CKD patients' infections and cardiovascular problems.
3. To evaluate treatment plans for controlling iron homeostasis and serum ferritin levels in individuals with chronic kidney disease.
4. To draw attention to the shortcomings of the current recommendations for the interpretation of serum ferritin in CKD. By tackling these goals, this review hopes to improve knowledge about serum ferritin's function in chronic kidney disease (CKD) and offer suggestions for enhancing the clinical outcomes of CKD patients. difficulties in people with CKD.

Methodology

This review article's foundation is a thorough examination of the body of research on serum ferritin's function in chronic renal disease. The following steps are part of the methodology that was chosen:

Literature Search: To find pertinent research on the function of serum ferritin in CKD, a thorough search was carried out utilising electronic databases such as PubMed, Scopus, Web of Science, and Google Scholar. To find papers, search terms including "serum ferritin," "chronic kidney disease," "CKD," "anaemia," "inflammation," and "iron deficiency" were utilised. In the search, both original research articles and reviews were taken into account.

1. Inclusion Criteria: Included studies those that addressed serum ferritin levels in patients with chronic kidney disease (CKD), including those that addressed the protein's function in iron metabolism, anaemia control, and inflammation. To make sure that the most recent developments in the subject were covered, articles released within the last 15 years (from 2008 to 2023) were taken into account.

2. Exclusion criteria: Research on paediatric populations or without a particular mention of serum ferritin in the setting of chronic kidney disease were not included. Articles that were not written in English or that had inadequate data were also disqualified.

3. Data Extraction: Based on their abstracts, the selected papers were vetted for relevancy. After meeting the inclusion criteria, full-text articles were examined. The study design, patient characteristics, serum ferritin levels, correlation with clinical outcomes (such as cardiovascular events, mortality, and infections), and anaemia management techniques in chronic kidney disease were among the data taken from these studies.

4. Analysis of Results: To find patterns and trends pertaining to serum ferritin levels in patients with chronic kidney disease, data from the included studies were thoroughly examined. The significance of

ferritin's dual function as an inflammatory and an iron storage marker was emphasised. Studies examining the relationship between increased ferritin levels and unfavourable clinical outcomes in individuals with chronic kidney disease (CKD) received special attention.

5. Synthesis of Evidence: To give a thorough picture of serum ferritin's involvement in CKD, the literature's data were combined. The discussion of study discrepancies centred on figuring out the causes of contradicting data about the clinical importance of serum ferritin in patients with chronic kidney disease. Major haematological and nephrology organisations' guidelines were also examined in order to contextualise the current clinical management of blood ferritin levels in chronic kidney disease.

6. Quality Assessment: The methodology, sample size, and design of the included studies were taken into consideration while assessing their quality. To make sure the evidence was reliable, large-scale observational studies, cohort studies, and randomised controlled trials were given priority.

DISCUSSION

Because serum ferritin serves as both an acute-phase reactant and a measure of iron storage, its function in chronic kidney disease is multidimensional and complex. Optimising patient treatment requires an understanding of this dual role, especially when it comes to managing CKD-related anaemia, which continues to be a major burden for this population.

Serum Ferritin As An Iron Marker In CKD

Historically, serum ferritin has been used to measure iron stores; low levels indicate an iron deficit, whereas higher levels indicate adequate iron reserves. However, the presence of inflammation frequently makes this interpretation difficult in CKD. Serum ferritin levels may increase in CKD patients due to a persistent inflammatory condition that many of them suffer, regardless of real iron reserves. This condition, referred to as "functional iron deficiency," happens when ferritin levels are normal or increased but iron is trapped in macrophages and not available for erythropoiesis. Research have revealed that functional iron shortage, especially in dialysis patients, is prevalent in CKD patients[1,2].

Inflammation And Elevated Serum Ferritin Levels

As a result of the disease itself as well as its consequences, including infections, uremia, and oxidative stress, CKD is characterised by inflammation. Serum ferritin is an acute-phase reactant, and inflammation causes its levels to rise. This makes ferritin readings in CKD patients more difficult to interpret clinically. In this case, elevated ferritin levels may indicate an underlying inflammatory condition rather than iron deficiency[3,4]. Numerous investigations have revealed a robust association between elevated ferritin levels and inflammatory indicators, including C-reactive protein (CRP) and interleukin-6 (IL-6)[5,6].

Clinical Implications Of Elevated Ferritin In CKD

Beyond the treatment of anaemia, increased serum ferritin levels in CKD have significant therapeutic implications. High ferritin levels have been linked to poor outcomes for individuals with chronic kidney disease (CKD), including an increased risk of cardiovascular events, infections, and mortality, according to numerous studies[7,8,9].

This is especially worrying because inflammation is a known risk factor for cardiovascular disease (CVD), which is already present in patients with chronic kidney disease (CKD). According to a large cohort research, patients with chronic kidney disease (CKD) who had serum ferritin levels greater than 800 ng/mL were substantially more likely to die from cardiovascular causes than patients with lower ferritin levels[10].

Management Of Anemia And Iron Supplementation In CKD

In individuals with chronic kidney disease (CKD), iron supplementation and erythropoiesis-stimulating agents (ESAs) must be balanced. However, choosing an iron therapy course becomes more difficult when high ferritin is present. Guidelines state that if transferrin saturation (TSAT) is low, indicating functional iron shortage, then iron supplementation may be required even in the face of high ferritin levels[11,12].

However, iron overload needs to be avoided as it might aggravate oxidative stress and the prognosis of individuals with chronic kidney disease[13,14]. Dialysis patients frequently receive intravenous iron, but its delivery needs to be closely watched, particularly in those with increased ferritin[15,16].

The Controversy Of Ferritin Thresholds

There is disagreement over the proper ferritin thresholds, which makes iron therapy management in chronic kidney disease (CKD) difficult. For individuals with chronic kidney disease (CKD), the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines advise keeping ferritin levels between 100 to 500 ng/mL; however, there is little data to support this range[17]. According to recent research, ferritin levels exceeding 500 ng/mL are linked to a higher risk of unfavourable outcomes, especially when inflammation is present[18,19]. The question of whether the current standards are appropriate and should be modified in light of inflammatory markers like CRP has become increasingly contentious as a result.

New Therapeutic Approaches

New therapeutic approaches and diagnostic methods have drawn attention due to the limitations of serum ferritin as the only indicator of iron status in chronic kidney disease. One possible biomarker for evaluating iron status in CKD patients is hepcidin, a hormone that controls iron homeostasis. The functional iron shortage observed in patients with chronic kidney disease (CKD) is partly caused by high hepcidin levels[20,21]. In individuals with high ferritin, future treatments aimed at hepcidin control may provide a more efficient means of managing iron homeostasis in CKD[22].

CONCLUSION

Serum ferritin functions as a critical marker for inflammation and iron storage and is essential in the treatment of anaemia associated with chronic kidney disease (CKD). However, because of the intricate interactions between inflammation and iron metabolism in CKD patients, interpreting it can be difficult. Even while elevated ferritin levels frequently signify inflammation rather than iron overload, they are linked to unfavourable clinical consequences, such as elevated risks of infection and cardiovascular disease.

Ferritin thresholds and the taking of inflammatory markers into account are two areas where the current guidelines for iron supplementation and anaemia therapy in chronic kidney disease (CKD) may require revision. The discovery of novel biomarkers, such as hepcidin, may lead to more effective treatment plans and more accurate diagnoses for controlling iron homeostasis in CKD. Further studies ought to concentrate on improving these strategies in order to enhance patient outcomes and quality of life.

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