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Original article

Evaluation of Serum Ferritin Status in Patients with Chronic Kidney Disease: A Cross-Sectional Study

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Abstract
Serum ferritin levels are a key marker for assessing iron status, but various factors, including age, can influence them. In individuals with chronic kidney disease (CKD), serum ferritin levels may be altered due to factors such as inflammation, impaired kidney function, and disease severity. Elevated ferritin levels in CKD patients can reflect both iron overload and increased inflammation, complicating the interpretation of iron status. The goal of this study was to investigate the distribution of serum ferritin levels in individuals with chronic kidney disease (CKD) and to compare them with those of healthy controls. A case-control design involving 100 participants, including 80 individuals with chronic kidney disease (CKD) as the case group and 20 healthy individuals as the control group. Serum ferritin levels were measured for all participants using standardized laboratory techniques. Data analysis was conducted using SPSS version 25, and independent t-tests were performed to compare the mean serum ferritin levels between the CKD and control groups. Serum ferritin levels were significantly higher in the case group (202.0 ± 217.5) compared to the control group (79.1 ± 72.8), with a p-value of 0.000. However, there was no significant difference in ferritin levels between male and female participants in the case group (p = 0.480). This study demonstrated that serum ferritin levels were significantly higher in individuals with chronic kidney disease (CKD) compared to healthy controls. Although there were differences in age and gender distributions between the groups, gender did not have a significant effect on ferritin levels within the CKD group. The results suggest that CKD-related factors, such as inflammation and impaired kidney function, have a more substantial impact on serum ferritin levels than gender.
Keywords. Chronic Kidney Disease, Serum Ferritin, Age, Gender.

Introduction

Chronic Kidney Disease (CKD) represents one of the most critical health challenges globally, affecting an estimated 750 million individuals with renal disorders [1]. It ranks as the 12th leading cause of mortality worldwide [2]. CKD is characterized as a clinical condition resulting from irreversible changes in the structure and/or function of the kidneys, marked by a gradual and progressive decline [3]. A diagnosis of chronic kidney disease is established when an adult exhibits a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for a period of three months or longer [4]. The primary etiological factors for CKD include diabetes, hypertension, autoimmune disorders, and prolonged acute renal injury [4]. CKD is categorized into five distinct stages based on GFR levels [5]. For patients in stage 5 CKD or those with specific conditions, kidney replacement therapy is strongly advised. One commonly employed form of kidney replacement therapy for individuals with stage 5 CKD or end-stage renal disease (ESRD) is hemodialysis [6].

Iron plays a vital role in the binding of oxygen within red blood cells and is integral to numerous cellular processes. Research has shown that iron deficiency, even in the absence of anemia, constitutes an independent risk factor for heightened mortality rates [7]. Iron deficiency is the most common nutrient deficiency worldwide, thus constituting a major health problem [8]. Notably 1, 6 billion people, corresponding to a fifth of the world population, are iron-deficient, of which about 1 billion have a severe form with subsequent anemia [9]. Nephrologists have increasingly directed their attention towards iron deficiency in patients undergoing hemodialysis, where intravenous iron is commonly administered during dialysis sessions. Factors contributing to iron loss in these patients include blood loss associated with dialyzer and tubing, routine blood sampling, impaired dietary iron absorption, and gastrointestinal losses [10]. In CKD, it has been shown that ID is highly prevalent and associated with an increased risk of morbidity and mortality, independent of potential confounders, including anemia [11-13]. Conversely, the identification of iron deficiency in non-dialysis chronic kidney disease (ND-CKD) patients is often inconsistent, and the use of intravenous iron therapy at this stage is relatively uncommon.

The primary contributor to iron deficiency in ND-CKD patients is thought to be inadequate dietary intake, compounded by reduced iron absorption linked to elevated hepcidin levels. Additionally, the depletion of circulating iron may occur due to increased erythropoiesis stimulated by erythropoiesis-stimulating agents (ESAs) [14]. Ferritin is an iron storage protein present in all cells of the organism. A small amount is found in plasma and serum, which reflects iron stores in healthy individuals [15,16]. The main indicator used to diagnose absolute iron deficiency is ferritin concentration. Although doctors can accurately identify absolute iron deficiency in patients with dialysis-dependent chronic kidney disease (CKD) with low ferritin concentrations (<100 ng/dL for non-dialysis patients and <200 ng/dL for dialysis-dependent patients), there is disagreement on the top ferritin limit [17-18].

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Elevated serum ferritin levels may be linked to longer hospital stays and higher rates of hospitalization [19]. In addition, it has been noted that a recent increase in serum ferritin levels in MHD patients indicates a relative risk of impending mortality [20]. A correlation has also been documented between a high serum ferritin level and dialysis morbidity, which includes the risk of infection and iron overload [21-23].
Regardless of iron status, ferritin is an acute-phase protein, meaning that it is elevated in both acute and chronic inflammatory environments [24]. Iron storage and inflammatory status can thus be linked by ferritin, which can be used as a surrogate marker. A high ferritin level is indicative of inflammation and iron overload, which leads to oxidative stress. Furthermore, patients, according to earlier research, have ferritin levels linked to increased mortality, infection, and risk of cerebro-cardiovascular diseases in hemodialysis [25,26]. Our understanding of inflammation as a novel risk factor for CKD-related morbidity and mortality has been evaluated because of the exponential growth in knowledge over the past 15 years regarding inflammation in CKD and end-stage renal disease (ESRD) [27].
Although ferritin is a good indicator of the body's iron levels, it can also be affected by non-iron-related illnesses like cancer, liver disease, inflammation, and malnourishment [28]. Given the limited research on this subject in Libya, this study aims to examine and compare ferritin levels between males and females with CKD, to analyze the impact of gender on iron deficiency treatment strategies in CKD patients through a comparative study of ferritin levels in men and women.

Methods

Study subject and classification

A cross-sectional study was conducted to evaluate ferritin levels in CKD patients at Janzour Centre for Kidney Services, Al-Maya Hospital, Al-Zahra Kidney Hospital, and Sarray Medical Laboratory. A total of 100 participants were included in the study and divided into two groups: the first study group (n = 80) consisted of male and female patients with CKD who were undergoing hemodialysis. In contrast, the second group (n = 20) consisted of patients with CKD who were not undergoing hemodialysis. However, the second group (n=20) consisted of healthy people, who were used as controls. All participants were Libyan individuals aged over 20 Years, diagnosed with CKD.

Population criteria

Inclusion and exclusion criteria

Patients aged 20-80 years old diagnosed with chronic kidney disease CKD at any stage, confirmed through clinical and laboratory assessments, and undergoing routine evaluation for iron status were included in this study. While we excluded patients with acute infection, inflammatory diseases, malignancies, or conditions that may independently alter ferritin levels (e.g., liver disease, active bleeding), patients currently receiving intravenous iron therapy or erythropoiesis-stimulating agents within the past three months were also excluded.

Sample collection and blood test

Sixty-nine samples were collected from the archive of AL-Zahra and AL-Maya Hospitals, and 11 fresh samples were taken from the Janzour Centre for Kidney Services laboratory. The examination was conducted in the Sarray laboratory. 20 control samples were collected from healthy people at Tripoli University Hospital. A total of 80 samples, comprising 47 males and 33 females, and 20 controls, with 7 males and 13 females, were collected. Approximately 3 mL of venous blood was drawn and placed in a serum separator tube (SST) for ferritin measurement.

Data analysis and presentation

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) program, version 25. The results obtained were presented in tables and figures. The level of significance is considered if the P-value < 0.05.

Results

The study investigated the distribution of age, gender, and serum ferritin levels among patients with chronic kidney disease. The age distribution of the study population (N = 100) showed that the largest proportion of participants fell within the 50–59 years age group (23%), followed by those 60 years and above (22%). The younger age groups were distributed as follows: 40–49 years (19%), 30–39 years (20%), and under 30 years (16%). Regarding gender distribution, the study included 54 males (54%) and 46 females (46%) (Table 1).
Among the case group (N=80), the highest percentage was observed in the 60 and above category (27.5%), followed by 50–59 years (25%) and 40–49 years (20%). In contrast, the control group (N=20) had a higher proportion of younger individuals, with 40% under 30 years and 30% in the 30–39 age range. Notably, there were no participants aged 60 or above in the control group. The case group had a higher proportion of males (60%), whereas the control group had more females (70%), suggesting a potential gender-related influence on the condition (Table 2). The analysis of serum ferritin levels showed a significantly higher mean in the

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case group (202.0 ± 217.5) compared to the control group (79.1 ± 72.8). A t-test was performed to compare the means, yielding a p-value of 0.000, indicating a statistically significant difference between the two groups. This confirms that serum ferritin levels are significantly elevated in the case group compared to the control group. Within the case group, males had a mean serum ferritin level of 187.95 ± 206.12, while females had a slightly higher mean of 223.30 ± 235.4. However, the t-test showed a p-value of 0.480, indicating that the difference in ferritin levels between males and females was not statistically significant (Table 3).

Table 1. Distribution of age group and gender among the study population (N=100)

Demographics	Frequency (N)	Percent (%)
Age groups		
Less than 30 years	16	16.0
30-39 years	20	20.0
40-49 years	19	19.0
50-59 years	23	23.0
60 and above	22	22.0
Gender		
Male	54	54.0
Female	46	46.0

Table 2. Distribution of age group and gender among case and control groups (N=100)

Demographics	Case		Control	
	Frequency (N)	Percent (%)	Frequency (N)	Percent (%)
Age groups				
Less than 30 years	8	10.0	8	40.0
30-39 years	14	17.5	6	30.0
40-49 years	16	20.0	3	15.0
50-59 years	20	25.0	3	15.0
60 and above	22	27.5	0	0.0
Gender				
Male	48	60.0	6	30.0
Female	32	40.0	14	70.0

Table 3. The mean and standard deviation of Serum ferritin of the case, control group, and gender among the case group.

Variables	N	Mean ± std	p. value
Study groups			
Case	80	202.0 ± 217.5	0.000
Control	20	79.1±72.8	
Gender			
Male	48	187.95±206.12	
Female	32	223.30± 235.4	

Discussion

Iron metabolism is essential for maintaining overall health, and serum ferritin serves as a key indicator of iron storage in the body. Abnormal ferritin levels have been linked to various health conditions, including chronic diseases, inflammation, and disorders affecting iron metabolism [29]. This study investigated the relationship between age, gender, and serum ferritin levels in a defined population, comparing the findings with those of previous research to identify patterns and differences. The study population (N = 100) showed the highest concentration of participants in the 50–59 years age group (23%), followed by those aged 60 and above (22%). Among the case group (N = 80), individuals aged 60 and above formed a higher proportion (27.5%). In contrast, the control group (N = 20) consisted mainly of younger participants, with 40% under 30 years old and 30% in the 30–39 age range.

These findings align with previous research indicating that serum ferritin levels tend to increase with age. This trend is often attributed to prolonged dietary iron absorption and decreased iron utilization over time [30]. Studies such as those by Suleiman et al. (2019) and Wong et al. (2020) have reported elevated ferritin levels in older individuals, particularly in patients with chronic kidney disease (CKD). They suggest that chronic inflammation and impaired iron metabolism contribute to this increase [30-31]. Razaq et al. (2019) further emphasized that iron markers, including ferritin, progressively increase with age in CKD patients, reinforcing our findings [32]. The gender distribution in our study was relatively balanced, with 54% males and 46% females. However, differences emerged between the groups. The case group had a higher proportion of males (60%), whereas the control group had a higher proportion of females (70%). This gender disparity

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suggests that biological or lifestyle factors may influence serum ferritin levels. This agrees with a study done by Suleiman et al., 2019found that 53.5% were male and 46.5% were female [30].

Previous studies have consistently found that males tend to have higher ferritin levels than females. One of the primary reasons for this difference is the regular iron loss in premenopausal women due to menstruation [33]. Shreewastav et al. (2023) and Wong et al. (2020) both observed that male CKD patients exhibited significantly higher ferritin levels, likely due to differences in iron absorption and mobilization (33-31). Sanni et al. 2022) also reported similar findings [34]. However, in our study, there was no statistically significant difference in ferritin levels between males and females (p=0.480). This suggests that while gender plays a role in iron metabolism, other factors—such as disease severity, inflammation, and genetic predisposition—may have a greater influence on ferritin levels.

A significant difference in serum ferritin levels was observed between the case and control groups. The case group had a markedly higher mean serum ferritin level (202.0 ± 217.5 ng/mL) compared to the control group (79.1 ± 72.8 ng/mL), with a highly significant p-value of 0.000. These findings support the well-established association between elevated ferritin levels and chronic diseases, including CKD, inflammatory disorders, and metabolic syndromes. Research by Suleiman et al. (2019) confirmed that CKD patients have significantly higher ferritin levels than healthy controls, highlighting the role of ferritin as a marker of disease progression rather than just iron overload (30). Wong et al. (2020) and Shreewastav et al. (2023) also found that high ferritin levels may indicate underlying inflammation or oxidative stress rather than excessive iron storage [31-33]. Furthermore, Raji et al. (2018) and Shukla et al. (2019) demonstrated that increased ferritin levels in CKD patients correlate with a higher risk of anemia, suggesting that ferritin alone is not a direct measure of iron status, but rather a marker of overall disease burden [35, 36]. Interestingly, despite previous studies consistently reporting higher ferritin levels in males, our study did not find a significant gender-based difference. This discrepancy indicates that additional factors, including comorbidities, dietary habits, and genetic influences, may play a crucial role in determining ferritin concentrations.

Study findings align with existing literature demonstrating an age-related increase in serum ferritin levels and a general trend of higher ferritin levels in males. The research by Suleiman et al. 2019 Wong et al. 2020 reinforces the idea that ferritin levels are influenced by both physiological and pathological factors (30-31). Razaq et al. 2019emphasized that ferritin, along with transferrin saturation and total iron-binding capacity, serves as a critical marker in evaluating iron status in CKD patients [32].

Our study suggests that gender alone may not be a primary determinant, particularly in disease conditions where inflammation plays a dominant role. Sanni et al. 2022 and Raji et al. 2018 also supported this idea, emphasizing that functional iron status assessments require consideration of multiple factors beyond just age and gender [34-35].

Conclusion

The findings indicate that CKD is more prevalent among older individuals, with the majority of cases occurring in those aged 50 years and above. In contrast, the control group had a higher proportion of younger participants. Gender distribution showed a higher prevalence of CKD among males, while females were more dominant in the control group, suggesting a potential gender-related influence. Serum ferritin levels were significantly elevated in CKD patients compared to the control group, as confirmed by a highly significant p-value (0.000). However, the difference in ferritin levels between male and female CKD patients was not statistically significant. These findings highlight the potential role of serum ferritin as a biomarker in CKD and underscore the importance of monitoring iron metabolism in affected patients. Future studies should adopt a more comprehensive approach to understanding iron metabolism and its clinical implications. It is recommended that other iron markers and inflammatory markers provide better context in diagnosing iron-related disorders and raise awareness about CKD risk factors.

Conflict of interest. Nil

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