Assessment of Serum Ferritin and Hemoglobin Levels in Chronic Hemodialysis Patients: An Observational Study in Sulaimani City, Kurdistan Region, Iraq

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Abstract

Background: Anemia management is critical for improving outcomes in chronic hemodialysis patients, particularly regarding iron status. The study aims to measure the serum ferritin and hemoglobin levels in hemodialysis patients in two Sulaimaniyah Governorate centers.
Methods: This descriptive cross-sectional observational study examines serum ferritin and hemoglobin levels in Sulaimani City, Kurdistan Region, Iraq. Conducted across two hemodialysis centers from November 2021 to August 2023, the study involved 180 patients on hemodialysis and aimed to evaluate iron and hemoglobin status for better anemia management in this cohort. Hemoglobin and ferritin levels were assessed pre-dialysis, with ferritin categorized into four zones: White (<200 µg/L), Green (200–500 µg/L), Yellow (500–1000 µg/L), and Red (>1000 µg/L).
Results: Results indicated that 65% of patients fell within the White Zone, indicating iron deficiency, while 8.33% were in the Red Zone, suggesting potential iron overload. Most patients presented with low hemoglobin levels (8.7 g/dL), below the recommended targets for anemia management in chronic kidney disease.
Conclusion: Regular iron and hemoglobin level monitoring is vital to prevent deficiency and overload, improving hemodialysis patients' quality of life. This study offers a regional perspective, enhancing the broader understanding of anemia management in the Middle East

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Introduction

Hemodialysis (HD) is the most prevalent treatment for end-stage renal disease (ESRD). This approach involves passing the patient's blood volume through a specific filter, eliminating excess fluids and waste elements. Although HD methods have improved over time, the morbidity and mortality rate among chronic HD patients remains high.[1] Hemodialysis can cause systemic hyperinflammatory states, hypercoagulation, and disruptions in iron homeostasis, frequently associated with elevated blood ferritin levels. Hemolysis can also occur during HD because of an oxidizing or reducing substance, heat, mechanical issues, or hyperosmolar dialysate.[2] Ferritin is the main protein for storing iron within cells and plays a vital role in the body's inflammatory response. It is strongly linked to iron metabolism and the body's inflammatory response.[3] Serum ferritin has long been investigated as an indicator of iron metabolism, and it is frequently used to guide iron therapy in CKD patients. [4] Serum ferritin, a measure of iron storage, has been linked to long-term mortality in typical HD patients. In patients undergoing hemodialysis, excess iron can worsen kidney damage by elevating oxidative stress, stimulating inflammation, causing greater iron buildup in

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tissues, and heightening the risk of infection.[5] Excess iron has been found to elevate plasma heparin levels, strongly linked to the progression of cardiovascular diseases, such as the formation of atherosclerotic plaques, greater plaque instability, and vascular sclerosis.[6]

Unfortunately, CVD is commonly recognized as the leading cause of death among HD patients. [7] Serum ferritin levels can be divided into three zones: green (200-500 µg/L), yellow (500-1000 µg/L), and red (>1000 µg/L). Ferritin levels above 1000 µg/L can be dangerous.[8] Serum ferritin levels of 346.05 µg/L were used in certain studies to predict hemodialysis patient outcomes.[9]

According to KDIGO, anemia is defined as a hemoglobin (Hb) level below 13 g/dL for men and below 12 g/dL for women.[10] With the development of erythropoiesis-stimulating agents (ESAs) therapy, it became clear that iron shortage was a critical component of the anemia that commonly occurs in patients receiving long-term hemodialysis. The Food and Drug Administration revised the ESA label, replacing the target hemoglobin range of 10-12 g/dL. The new guidance advises tailoring ESA treatment to minimize the need for red blood cell transfusions, stopping ESA use when hemoglobin levels near or exceed 11 g/dL, and halting further dose increases if patients show no response after three prior dose adjustments.[11]

Iron should be provided sufficiently to keep serum ferritin levels above 200 ng/mL.[12] Because of the importance of maintaining iron balance in HD patients, recent guidelines indicate that iron status assessments should be undertaken at least every three months. [13]

In iron deficiency anemia, transferrin saturation (TSAT), measured as the ratio of serum iron to total iron-binding capacity (TIBC), is often less than the normal range of 20–50%. In this scenario, TSAT is typically less than 20%, generally in the 10-15% range or lower. This decrease reflects a reduction in the quantity of iron available for binding to transferrin, the protein responsible for iron transport in the blood. Furthermore, serum ferritin levels are frequently low, although TIBC values are increased, confirming the diagnosis of iron deficiency anemia. [14]

The adequacy of dialysis is assessed by measuring the Kt/V. and to measure it by this equation: The equation KtV = In (R—0.008 x t) + (4 - 3.5 x R) x 0.55 UF/V can be used to resolve the Kt/V from the pre-dialysis to post-dialysis urea nitrogen ratio (R), the weight loss (UF), session length in hours (t), and anthropometric or modeled volume (V).[15]

Low serum albumin levels in hemodialysis patients can significantly affect the interpretation of iron markers like serum ferritin and transferrin saturation (TSAT), complicating the assessment of iron status. Serum albumin is a negative acute-phase protein that decreases during inflammation or malnutrition, both common in hemodialysis patients. [16]

The study aims were to measure the serum ferritin and hemoglobin levels in hemodialysis patients in two centers in Sulaimaniyah City.

Patients and Methods

This descriptive cross-sectional observational study interviewed hemodialysis patients at the Qirga Hemodialysis Centre (100 patients) and Shar Teaching Hospital (80 patients) in Sulaimani City, Kurdistan region, Iraq. The study was performed from November 2021 to August 2023. A standardized questionnaire collected personal information, medical history, including the cause of renal failure if it is known, and dialysis specifics.

Each participant provided verbal agreement, and a questionnaire was provided via direct interviews. Interviews were conducted before and during hemodialysis sessions.

Patient selection was based on specific inclusion criteria: adults 18 or older undergoing regular hemodialysis treatment for at least six months before the study. In contrast, patients with recent blood loss, acute illness, history of acute infection or inflammation [high level of C-reactive protein (CRP), high parathyroid hormone (PTH), and high hepcidin], recent hospitalization, patients with active malignancy and patients with a kidney transplantation were all excluded from the study to minimise confounding factors.

The questionnaire asked about age, gender, location of residence, dialysis history, and weekly hemodialysis sessions. Each participant underwent a venipuncture to obtain venous blood.

Regarding the types of hemodialysis machines, they used the 5008 Fresenius machine, AK 98 Baxter, and AK 200 Gambro. For the dialyzers, they use Fresenius high flux dialyzers (40, 60, 80, and 100).

Epoetin alfa (Eprex) is used to treat anemia in both centers.

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Blood samples were collected on the day of hemodialysis and analyzed to measure a range of blood parameters. The parameters of interest included hemoglobin (gm/L), blood urea nitrogen before and after the dialysis, the weight of the patients and the amount of ultrafiltration to assess the adequacy of dialysis by measuring the Kt/V, serum folate (ng/mL), serum ferritin (ng/ml), serum vitamin B12 (pg/mL), serum albumin (gm/dL), serum creatinine (mg/dL), C- reactive protein and parathyroid hormone, and high hepcidin. The measurements for these parameters were conducted using standardized laboratory techniques, including automated chemistry analyzers and immunoassay methods.

Serum ferritin is measured through immunoassays, specifically enzyme-linked immunosorbent assay (ELISA) and chemiluminescent immunoassay (CLIA). These methods use antibodies that bind specifically to ferritin in the blood, allowing for its quantification.

Ethical norms require any participant in this observational study to provide verbal agreement before being included. The participants were thoroughly informed about the study's nature, objective, and techniques. Furthermore, safeguards were taken to ensure participants' personal and health-related data privacy throughout the study.

We divided the patients into four groups or zones based on their serum ferritin levels. The first was the white zone, which included patients with serum ferritin levels less than 200 µg/L. The second was the green zone, which included patients with serum ferritin levels between 200 and 500 µg/L. The third was the yellow zone, which comprises serum ferritin levels ranging from 500 to 1000 µg/L, whereas the fourth group was the red zone, which includes serum ferritin levels beyond 1000 µg/L.

These zones are essential for assessing the patients. As for the white zone, they need iron supplement treatment, and the target of the treatment is to have patients in the green zone. The yellow zone is a message to stop any iron supplements with close follow-up, and the red zone is dangerous for the patients.

We also asked the patients if they were still receiving iron supplements during the study to determine whether they were aware of their condition regarding the ferritin level.

The College of Medicine's Ethics Committee, University of Sulaimani, approved the study by document number (311) on 22/9/2024

The study's statistical analysis was performed using SPSS version 24, a robust data management and analysis software. It facilitated descriptive (e.g., mean, frequency) and inferential statistics (e.g., Chi-square tests), enabling detailed examination and interpretation of the study's data.

The data were coded, tallied, and presented descriptively. The analysis involved inferential data techniques, including descriptive statistics such as frequency, percentage, mean, standard deviation, and the Chi-square test. The significance of the test results was assessed using probabilistic criteria based on the p-value. Specifically, a p-value of less than 0.001 was considered highly significant, less than 0.05 was considered significant, and greater than 0.05 was deemed non-significant.

Results

*Note: All tables mentioned in this section are provided at the end of the article

According to the demographics and distribution of patients across centers,180 participated, distributed across two hemodialysis centers: 100 patients in Qirga and 80 patients in Shar. The blood parameters reveal several key health indicators. The mean hemoglobin level is 8.7 g/L, with a median of 8.6 g/L, indicating that many participants may be experiencing anemia. This is a common concern in individuals with chronic kidney disease (CKD) or other underlying health conditions. The standard deviation of 1.53 suggests some variation in hemoglobin levels among the participants.

The Kt/V value, which measures dialysis adequacy, has a mean of 1.18 and a median of 1.21. These values are close to the recommended threshold of ≥1.2, suggesting that most participants receive adequate dialysis. The standard deviation of 0.16 indicates relatively consistent dialysis effectiveness across the group.

Serum folate levels show a mean of 24.01 ng/ml and a median of 21.1 ng/ml. However, the high standard deviation (14.37) and interquartile range (24.50) suggest a large variability in folate levels among participants. While the median value suggests generally sufficient folate status, the wide variation could indicate that some individuals have much lower levels.

The serum vitamin B12 levels reported in the study show a mean of 420.7 pg/mL, a median of 511.1 pg/mL, and a standard deviation of 110 pg/mL, with an interquartile

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range of 521 pg/mL. These values suggest most patients have adequate B12 levels, as the median falls within the normal reference range (typically 200–900 pg/mL). The relatively small standard deviation indicates that the B12 levels are reasonably consistent across the study population, with fewer extreme variations.

The median (511.1 pg/mL) is higher than the mean (420.7 pg/mL), suggesting a slightly skewed distribution, with some participants having notably lower values. However, the reported values suggest that B12 deficiency is not widespread.

Ferritin levels exhibit significant variability, with a mean of 252.01 ng/mL, a median of 101.1 ng/mL, and a high standard deviation of 389.98. This suggests that while some participants have adequate iron stores, many patients have very low ferritin levels, potentially due to variations in iron supplementation.

Serum albumin levels appear stable, with a mean of 3.89 g/dL and a median of 3.90 g/dL. The relatively low standard deviation (0.44) suggests that most participants have similar albumin levels, a positive nutritional and protein status indicator. All the above results are shown in

The ferritin levels and mean transferrin saturation among 180 hemodialysis patients were categorized into four zones based on ferritin levels. The majority of patients (65%) fall within the "< 200 ng/mL (White Zone)" category, with a mean transferrin saturation of just 10%. This indicates that most patients have low iron stores and poor iron availability, contributing to anemia and iron supplementation.

The "200–500 ng/mL (Green Zone)" includes 18.88% of the patients, with a mean transferrin saturation of 26%. This range suggests a more optimal iron status, as transferrin saturation is closer to the recommended levels for adequate iron transport and utilization. Patients in this group likely have better iron availability than White Zone patients.

In the "500–1000 ng/mL (Yellow Zone)," 7.77% of patients are present, with a mean transferrin saturation of 49%. This suggests that iron stores are significantly higher, and transferrin saturation is approaching the upper limit of the recommended range.

The "Red Zone" (>1000 ng/mL) contains 8.33% of the patients, with the highest mean transferrin saturation of 54%. This indicates a risk of iron overload.

Overall, the results highlight that most patients have low ferritin levels and inadequate iron availability, with only a minority showing high iron stores. As shown in

The comparison of ferritin levels with the number of patients receiving iron supplements shows a significant relationship between iron therapy and ferritin status ($p < 0.05$). This suggests that patients with different ferritin levels are not equally likely to receive iron supplementation, indicating a targeted approach to iron therapy in hemodialysis patients.

A large proportion of patients (65%) fall into the <200 ng/mL (White Zone) category, reflecting low iron stores. However, only 20 out of 117 patients (17%) in this group receive iron supplementation, raising concerns about whether iron-deficient patients are adequately treated.

In the 200–500 ng/mL (Green Zone), only 4 out of 34 patients (11.8%) receive iron therapy. This range is often considered adequate for iron stores, which may explain the lower supplementation rates. However, given the variability in individual iron needs, some patients in this category might still benefit from iron therapy.

A different pattern is observed in the 500–1000 ng/mL (Yellow Zone), where 10 out of 14 patients (71%) receive iron supplementation.

In the >1000 ng/mL (Red Zone), 13 out of 15 patients (86.7%) are receiving iron supplements. High ferritin levels typically indicate either excessive iron stores.

Overall, the significant p-value (< 0.05) confirms a strong association between ferritin levels and iron supplementation. However, the findings highlight potential inconsistencies in treatment, particularly in the White Zone, where iron deficiency is prevalent but supplementation rates are relatively low. A more structured and individualized approach to iron management in hemodialysis patients may help optimize treatment outcomes. As shown in Table 3. Ten patients in both centers have Adult Polycystic Kidney disease; all have no anemia with normal serum ferritin.

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Discussion

The results of this study provide important insights into anemia and iron metabolism in hemodialysis patients at the Qirga and Shar centers, focusing on hemoglobin levels, serum ferritin, transferrin saturation (TSAT), and iron supplementation. The data reveal significantly lower levels of hemoglobin below the normal range. This is consistent with findings from other studies in the Middle East and Iraq (Basrah Center), as seen in Abed et al. and Al-Jabi et al., where anemia is a common and serious issue among hemodialysis patients. [17,18]

High serum ferritin levels reported in the other study that was done by Ali et al. indicate a risk for iron overload, a prominent cause of death among HD patients in both local and worldwide studies.[19]

Studies undertaken in other Middle Eastern nations have shown difficulties with iron control in HD patients. A study done by Malaki found that many HD patients had serum ferritin levels less than 200 µg/L. with a high prevalence of anemia.[8]

While inflammation may cause ferritin to be elevated in some regions, it is less of a factor in this Iraqi cohort, as all patients with evidence of infection and inflammation were excluded from the study (normal CRP, PTH, serum hepcidin, and normal serum albumin), where iron deficiency seems to be the primary concern. The mean TSAT in our study (11%) falls within the iron deficiency range seen in many studies in the region, suggesting that iron therapy protocols may need to be improved to ensure better management of iron status in these patients. Similar findings have been reported in other Middle Eastern studies, where other vitamin deficiencies often exacerbate anemia in hemodialysis patients (which is not the issue in our research). [19]

Research by Shaheen et al. revealed that despite iron supplementation, many HD patients suffered from anemia and raised serum ferritin.[20]

According to studies in Europe and North America, HD patients frequently have serum ferritin levels that may offer a risk of iron overload, potentially raising the risk of CVD.[21]

Similarly, a cohort study by Toida et al. showed that frequent monitoring of ferritin and hemoglobin levels in HD patients, combined with personalized iron supplementation, could enhance patient outcomes, notably regarding anemia and CVD risk reduction.[22]

The Kt/V values measuring dialysis adequacy are close to the recommended threshold of ≥1.2, suggesting that most participants receive adequate dialysis.

However, our study has a high percentage of patients with low serum ferritin. This does not align with findings from Ayesh et al., who reported that improving dialysis adequacy through enhanced dialysis techniques may help improve anemia control in hemodialysis patients. [23]

Future research should involve multicenter cohorts to validate findings. Routine monitoring of iron and hemoglobin levels is essential to improve patient outcomes. Patients with low ferritin should receive iron supplementation to support ESA therapy, while those with elevated ferritin levels require monitoring for iron overload and related complications.

Conclusion

This study highlights the high prevalence of iron deficiency and anemia among hemodialysis patients in Sulaimaniyah City, emphasizing important clinical implications for patient care and management. Although most patients need iron supplementation, a few are at risk of iron overload, highlighting the importance of personalized treatment strategies. Adhering to international guidelines, enhanced monitoring, and personalized iron therapy could improve anemia and iron management in this high-risk group, potentially reducing morbidity and mortality rates.

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Table (1) Blood parameters of study participants (n=180).

Blood Parameters	Mean	Median	Standard deviation	Interquartile range
Hemoglobin (gm/L)	8.7	8.6	1.53	2.1
Kt/V	1.18	1.21	0.16	0.16
Serum Folate (ng/ml)	24.01	21.1	14.37	24.50
Serum vitamin B12 (pg/ml)	420.7	511.1	110	521
Ferritin level ng/mL	252.01	101.1	389.98	239.83
Serum albumin (gm/dl)	3.89	3.90	0.44	0.42

Table (2) Ferritin and mean transferrin saturation levels according to the zones and the patient numbers in both hemodialysis units

Ferritin level ng/mL (Zones)	Frequency	%	Mean Transferrin saturation for both centers (%)
< 200 (white)	117	65%	10%
200 - 500 (Green)	34	18.88%	26%
500 - 1000 (Yellow)	14	7.77%	49%
> 1000 (Red)	15	8.33%	54%
Total	180	100.0%	19.7%

Table (3) compares the ferritin level and the number of patients receiving iron supplements.

Ferritin level ng/mL (Zones)	Number of patients receiving iron supplements		Total number of patients and percentage	p value
	Yes	No		
< 200 (white)	20	97	117 (65%)	< 0.05
200 - 500 (Green)	4	30	34 (18.88%)	
500 - 1000 (Yellow)	10	4	14 (7.77%)	
> 1000 (Red)	13	2	15 (8.33%)	
Total	30 (100%)	150 (100%)	180 (100%)	

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