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Evaluation of Hemodialysis Patients Regarding Anemia Related Factors

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Abstract

Background: To evaluate hemodialysis patients in terms of anemia and mortality-related factors.

Methods: A retrospective evaluation was conducted on ninety-nine hemodialysis patients from Bitlis, Turkey. The analysis involved comparing hemoglobin and ferritin levels and doses of ESA and iron administered. Additionally, mortality-related factors were analyzed.

Results: Patients with lower hemoglobin levels had significantly higher CRP and PTH levels but lower ferritin, total cholesterol, LDL, and glucose levels. The dose of ESA was higher, and the surface area of dialyzers was significantly lower in patients with lower hemoglobin levels. Patients with high ferritin levels had significantly higher CRP, lower hemoglobin levels, and longer dialysis vintage. Patients who received more than 200 mg of intravenous iron per month had significantly higher numbers of patients with diabetic nephropathy, higher CRP, and glucose levels but lower PTH and creatinine levels, lower transferrin saturation, and lymphocyte counts. Patients who received lower doses of ESA had significantly higher LDL, total cholesterol, hemoglobin levels, and higher surface area of dialyzers used but lower ferritin levels. Finally, hemoglobin levels < 9 g/dl and increasing IV iron doses were associated with mortality.

Conclusion: Hyperparathyroidism and inflammation were associated with anemia. Anemia and increasing doses of iron were associated with increased mortality.

Keywords: Nonsteroidal anti-inflammatory drugs, gastroduodenal lesions, celecoxib, indomethacin, proton pump inhibitors

INTRODUCTION

Anemia can manifest early in the early stages of chronic kidney disease (CKD) and can become prominent with a decline in glomerular filtration rate. Research indicates that 15% of Stage 3 CKD patients, 50% of pre-dialysis patients, and over 80% of dialysis patients experience anemia. Anemia negatively affects the quality of life in dialysis patients and leads to increased morbidity and mortality (1-3). Relative erythropoietin deficiency, iron deficiency, blood loss, reduced red cell lifespan, vitamin deficiencies, inflammation, hyperparathyroidism, and bone marrow suppression secondary to uremia are common causes of anemia in dialysis patients. Erythropoiesis-stimulating agents (ESA) and intravenous (IV) iron are the primary treatments for managing anemia (4). Before the discovery of ESA, erythrocyte transfusion and IV iron were the only available options for treating anemia. The introduction of ESA in dialysis patients led to a significant decrease in serious hemochromatosis cases, viral infections, and the number of sensitized patients on waiting lists (5). However, despite these advancements, resistant anemia is still a common complication of CKD among dialysis patients (6). ESA resistance primarily stems from iron deficiency. However, some dialysis patients remain resistant even after receiving adequate iron supplementation. Other contributors to ESA resistance in patients with sufficient iron stores include, infection, neoplasia, chronic hemolysis, hemoglobinopathies, aluminum intoxication, insufficient dialysis, myelosuppressive

agents, myelodysplasia, antibody-mediated pure red cell aplasia, thyroid dysfunction, and certain medications such as renin-angiotensin-aldosterone blockers. While increasing ESA and IV iron doses may be appropriate in some cases, it's crucial to carefully assess the risks and benefits of such interventions considering potential adverse effects such as cardiovascular complications and iron overload (7-9).

In this study, we aimed to evaluate anemia and mortality-related factors in HD patients in Bitlis, Turkey.

METHODS

Patient Evaluation

Ninety-nine patients receiving HD treatment in Bitlis City were evaluated retrospectively. Blood samples were obtained from these HD patients before dialysis in the middle of each month from April 2017 to March 2018 for testing.

Data Collection

The patients' gender, age, body mass index (BMI), medications, duration of HD, causes of end-stage renal disease (ESRD), comorbid diseases, all-cause mortality, development of cardiovascular events, hospitalizations, and infections were recorded. Additionally, the surface area of the dialyzers, Kt/V, urea reduction rate (URR), and doses of ESA and IV iron were also recorded.

Data Analysis

The data were analyzed by averaging the 12-month test results. Patients who had received dialysis treatment for less than three months, were under 18 years of age, experienced blood loss beyond the expected range, or had irregular dialysis schedules were not included in the study.

Dialysis Protocol

Low flux dialyzers were used. ESA preparations, specifically epoetin alpha and zeta, were administered intravenously. IV iron sucrose was given during HD sessions, with the frequency (1, 2, or 4 times per month) determined based on individual patients' serum transferrin saturation, ferritin, and hemoglobin levels.

STATISTICAL ANALYSIS

The statistical software R was used in this study. Descriptive statistics were utilized to show the distribution of the data. Independent Samples T-Tests were conducted to determine if there was a statistically significant difference between the means of the two groups. One-way ANOVA was employed to test whether the means of the groups differed when there were more than two groups. If differences were found, Tukey's HSD test was used to identify which groups these differences arose from. Furthermore, Chi-Square and Fisher's Exact Chi-Square tests were used to examine the relationships between categorical variables. In addition, multivariate logistic regression was applied if the dependent variable was binary.

Dialysis vintage was defined as the time elapsed from an individual's first dialysis session until their death or the end of March 2018. Cox Regression Analysis was also applied, with hazard ratios and p-values calculated. The level of statistical significance was set at 0.05.

Written informed consent was obtained from each patient. The study received approval from the Ethics Committee of Van Bölge Education and Research Hospital. It was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

The demographic and clinical data of the patients are shown in **Table 1**. The mean age of the patients was 58.2±14.69 years, and 52.5% were male. The mean dialysis vintage was 4.89±4.06 years. The number of patients with arteriovenous fistula and dialysis catheters was 89 and 10, respectively. Diabetic nephropathy was the cause of ESRD in approximately half of the patients (49.5%). The numbers of patients with hypertensive nephropathy, glomerulonephritis, nephrolithiasis, polycystic kidney disease, and others (familial Mediterranean fever n= 1, hemolytic uremic syndrome n= 1, chronic pyelonephritis n= 1, systemic

Table 1. Demographic and clinical characteristics of patients

Parameters	Results
Age (year, mean ± SD)	58.2 ± 14.69
Gender (male, %)	52.5
Dialysis duration (year, mean ± SD)	4.89 ± 4.06
Diabetic nephropathy (%)	49.50
Hemoglobin (g/dl, mean ± SD)	11.33 ± 1.21
Serum iron (µmol/l, mean ± SD)	74.03 ± 22.13
Transferrin saturation (mean ± SD)	0.29 ± 0.08
Ferritin (ug/l, mean ± SD)	567.16 ± 138.12
B12 (pg/ml, mean ± SD)	493.55 ± 269.71
Kt/V 1.2 (%)	97
Kt/V (mean ± SD)	1.56 ± 0.49
TSH (IU/ml, mean ± SD)	2.24 ± 4.12
Treatment Weekly ESA dose (IU, mean ± SD) Monthly iron dose (mg, mean ± SD)	 5030.73 ± 3046.56 274.74 ± 177.25
Hospitalization (%)	20
Infection (%)	14
Mortality (%)	10

SD; standard deviation, BMI; body mass index, ESA; erythropoiesis stimulating agents, TSH; thyroid-stimulating hormone

Table 2. Comparison of patients regarding hemoglobin levels

Parameters	Hb <10 g/dl (n=12)	10≤ Hb ≤11.5 g/dl (n=45)	Hb >11.5 g/dl (n=42)	p-value
Age (year, mean ± SD)	51.00 ± 14.89	58.60 ± 15.28	59.88 ± 13.70	0.18[1]
Gender (male, %)	7.69	40.38	51.93	0.09[2]
BMI (kg/m^2)	37.42 ± 33.57	51.38 ± 27.16	51.26 ± 27.41	0.06[1]
Dialysis vintage (mean ± SD, year)	3.87 ± 3.10	4.56 ± 3.64	5.55 ± 4.66	0.34[1]
Dialysis vintage>5 years (%)	6.45	41.94	51.61	0.01[1,*]
Transferrin saturation (mean ± SD)	0.28 ± 0.10	0.30 ± 0.07	0.28 ± 0.08	0.28[1]
Ferritin (ug/l, mean ± SD)	592.37 ± 174.37	598.40[†] ± 87.16	526.47[†] ± 162.29	0.04[1,*]
Parathormone (pg/m, mean ± SD)	793.99[†,⊕] ± 711.51	380.64[†] ± 238.04	471.76[⊕] ± 260.04	0.00[1,*]
CRP (mg/l, mean ± SD)	31.78[†,⊕] ± 37.95	14.91[†] ± 13.87	12.53[⊕] ± 9.10	0.00[1,*]
Kt/V (mean ± SD)	1.56 ± 0.17	1.54 ± 0.21	1.59 ± 0.71	0.88[1]
URR (mean ± SD)	72.78 ± 4.23	72.48 ± 4.91	71.16 ± 3.92	0.31[1]
Dialyzer surface area (m^2, mean ± SD)	1.66[†] ± 0.26	1.80 ± 0.23	1.85[†] ± 0.17	0.03[1,*]
Monthly iron dose (mg, mean ± SD)	265.75 ± 190.56	289.65 ± 209.62	241.71 ± 141.55	0.47[1]
Weekly ESA dose (IU, mean ± SD)	7556.48[†] ± 2079.65	6430.86[⊕] ± 2761.52	2210.04[†,⊕] ± 1620.52	0.00[1,*]

1; One-Way ANOVA, 2; Chi-Square Test of Independence, *:statistically significant at 0.05, †,□; statistically significant Tukey HSD differences at 0.05, SD; standard deviation, BMI: body mass index, Hb; hemoglobin, CRP; c-reactive protein, URR; urea reduction rate, ESA; erythropoiesis stimulating agents

lupus erythematosus n: 1, vesicoureteral reflux n= 2, and unknown n= 8) were 18, 10, 4, 4, and 14, respectively.

The comparison of patients based on hemoglobin levels is detailed in **Table 2**. Patients with higher hemoglobin levels exhibited several notable differences compared to those with lower hemoglobin levels. Specifically, they had a significantly higher proportion of individuals undergoing HD for more than 5 years (p= 0.01), utilized dialyzers with larger surface areas (p= 0.03), received lower doses of ESA (p= 0.001), and demonstrated lower levels of C-reactive protein (CRP) (p= 0.00), parathormone (PTH) (p= 0.00), and ferritin (p= 0.04).

Concurrently, patients with hemoglobin levels below 10 g/dl were compared with those having hemoglobin levels of 10 g/dl or higher (these results are not provided in the tables). Glucose (p= 0.001), triglyceride (p= 0.010), and total cholesterol levels (p= 0.010) showed significant elevation among patients with hemoglobin levels of 10 g/dl or higher compared to those with hemoglobin levels below 10 g/dl. The dose of ESA used was significantly (p= 0.001) lower, and the number of patients with dialysis vintage >5 years (p= 0.010) was significantly higher among patients with higher hemoglobin levels.

When conducting multivariate logistic regression analysis with the dependent variable being hemoglobin levels (≥10 g/dl or not) and independent variables including cholesterol, triglyceride, dialysis vintage (>5 years or not), ferritin, PTH, CRP, ESA dose, and glucose, a significant association was observed between hemoglobin levels below 10 g/dl and both ESA dose (p=0.030) and PTH (p= 0.030). The number of patients with hemoglobin concentration below 9 g/dl was 3, and no patients had hemoglobin concentration below 8 g/dl.

In **Table 3**, patients with ferritin levels ≤500 µg/l exhibited significantly higher hemoglobin levels (p= 0.04), and uric acid levels (p= 0.01), and utilized

Table 3. Comparison of patients regarding serum ferritin levels

Parameters	Ferritin ≤500 ug/l (n=19)	Ferritin >500 ug/l (n=80)	p-value
Age (year, mean ± SD)	54.42 ± 15.31	59.12 ± 14.49	0.23[1]
Gender (male, %)	28.85	71.15	0.02[2,*]
Dialysis vintage (mean ± SD, year)	4.22 ± 4.02	5.05 ± 4.08	0.42[1]
Dialysis vintage >5 years (n)	6	25	0.00[2,*]
Hemoglobin (g/dl, mean ± SD)	11.92 ± 1.45	11.18 ± 1.11	0.04[1,*]
WBC (/l , mean ± SD)	6.97 ± 1.54	7.02 ± 2.25	0.93[1]
Platelet /l, (mean ± SD)	204.24 ± 40.18	209.01 ± 51.29	0.66[1]
Urate (mg/dg, mean ± SD)	7.07 ± 1.08	6.35 ± 1.04	0.01[1,*]
Parathormone (pg/ml, mean ± SD)	378.73 ± 268.94	490.93 ± 372.44	0.14[1]
CRP (mg/l, mean ± SD)	11.61 ± 6.93	16.97 ± 19.47	0.04[1,*]
Kt/V (mean ± SD)	1.44 ± 0.16	1.59 ± 0.53	0.03[1,*]
URR (mean ± SD)	69.77 ± 3.53	72.47 ± 4.5	0.01[1,*]
Dialyzer surface area (, mean ± SD)	1.91 ± 0.14	1.78 ± 0.22	0.01[1,*]
Weekly iron dose (mg, mean ± SD)	288.48 ± 261.17	261.17 ± 186.33	0.77[1]
Weekly ESA dose (IU, mean ± SD)	4717.91 ± 4587.98	4790.60 ± 2765.88	0.95
Infection (yes, %)	28.57	71.43	0.46[3]
Hospitalization (yes, %)	25	75	0.73[3]

1; One-Way ANOVA, 2; Chi-Square Test of Independence, *:statistically significant at 0.05, †,□; statistically significant Tukey HSD differences at 0.05, SD; standard deviation, BMI: body mass index, Hb; hemoglobin, CRP; c-reactive protein, URR; urea reduction rate, ESA; erythropoiesis stimulating agents

Table 4. Comparison of patients regarding iron treatment

Parameters	IV Iron <200 mg (n=40)	IV Iron >200 mg (n=59)	p-value
Age (year, mean ± SD)	56.05 ± 16.76	59.69 ± 13.04	0.25[1]
Gender (male, %)	42.31	57.69	0.84[2]
Diabetic nephropathy (yes, %)	29.09	70.91	0.03[2,*]
Dialysis vintage (mean ± SD, year)	5.36 ± 3.68	4.58 ± 4.30	0.33[1]
Serum iron (µmol/l, mean ± SD)	73.64 ± 19.53	74.26 ± 23.89	0.89[1]
Transferrin saturation (mean ± SD)	0.34 ± 0.08	0.26 ± 0.06	0.00[1,*]
IV iron (mg, mean ± SD)	104.19 ± 19.53	376.40 ± 23.89	0.001
Glucose (mg/dl, mean ± SD)	140.24 ± 77.56	170.90 ± 73.10	0.04[1,*]
Creatinine (mg/dl, mean ± SD)	7.90 ± 3.08	6.53 ± 1.48	0.01[1,*]
Hemoglobin (g/dl, mean ± SD)	11.40 ± 1.29	11.28 ± 1.15	0.63[1]
Lymphocyte (/l, mean ± SD)	1.69 ± 0.47	1.48 ± 0.51	0.04[1,*]
Albumin (g/dl, mean ± SD)	3.76 ± 0.28	3.66 ± 0.34	0.11[1]
Parathormone (pg/ml, mean ± SD)	562.90 ± 455.39	406.01 ± 255.25	0.04[1,*]
Ferritin (ug/l, mean ± SD)	586.24 ± 149.38	554.22 ± 129.65	0.27[1]
CRP (mg/l, mean ± SS)	10.19 ± 8.58	19.84± 21.23	0.00[1,*]
Weekly ESA dose (IU, mean ± SD)	4312.09 ± 2835.44	5091.61± 3361.28	0.22[1]
Hospitalization (yes, %)	25	75	0.06[2]
Infection (yes, %)	28.57	71.43	0.48[2]

1; Independent Sample T-Test, 2; Chi-Square Test of Independence, 3; Fisher's Exact Test, *; statistically significant at 0.05, SD; standard deviation, IV; intravenous, CRP; c-reactive protein, ESA; erythropoiesis stimulating agents

dialyzers with larger surface areas (p= 0.01) compared to those with ferritin levels >500 µg/l. Additionally, patients with ferritin levels ≤500 µg/l showed statistically lower values for Kt/V (p= 0.030), URR (p= 0.010), and CRP levels (p= 0.040), as well as a lower proportion of patients undergoing HD for more than five years (p= 0.00). The number of patients with serum ferritin levels below 200 µg/l and above 500 µg/l was 5 and 80, respectively, with no patients having ferritin levels exceeding 800 µg/l. Additionally, there were 3 patients with transferrin saturation levels below 20% and ferritin levels below 200 µg/l. Functional iron deficiency was defined as transferrin saturation <20% and ferritin >200 µg/l, and the number of patients with functional iron deficiency was 7.

In **Table 4**, the comparison of patients based on IV iron dose is presented. Patients who received ≤ 200 mg/month of IV iron exhibited significantly lower levels of CRP (p= 0.00) and glucose (p= 0.04), as well as a reduced number of patients with diabetic nephropathy (p= 0.03). Conversely, they demonstrated significantly higher levels of creatinine (p= 0.01), transferrin saturation (p= 0.00), PTH (p= 0.04), and lymphocyte counts (p= 0.04) compared to patients who received >200 mg/month of IV iron. Notably, only three patients did not require IV iron during the study period.

The patients were also compared for weekly ESA doses given (not shown in Table). The patients receiving <25 units/kg/week ESA had significantly higher levels of hemoglobin (p= 0.001), total cholesterol (p= 0.001), and LDL cholesterol (p= 0.030), but significantly lower ferritin levels (p= 0.030) compared to those receiving ESA ≥25 units/kg/week. The sizes of the dialyzers used were also higher in the patients receiving <25 units/kg/week ESA (p= 0.040).

Table 5 presents factors associated with mortality. Mortality rates were found to increase significantly with hemoglobin levels <9 g/dl (p= 0.020). Additionally, mortality was observed to rise with increases in total IV iron dose (p= 0.020) and iron dose per kg (p= 0.020). However, no significant relationship was found between

Table 5. Mortality related factors

Parameters	HR	95% CI	p-value
Age ≥ 65 years	4.42	(1.14, 17.18)	0.03*
Diabetes mellitus	10.6	(1.27, 88.79)	0.02*
Body mass index ≥ 30 (kg/)	4.16	(1.15, 14.99)	0.02*
Hemoglobin<9 g/dl	0.22	(0.05, 0.85)	0.02*
Total IV iron dose (mg)	1.01	(1.001, 1.008)	0.02*
ESA dose (mg)	0.99	(0.99, 1.00)	0.25
IV iron per kg (mg)	1.30	(1.04, 1.62)	0.02*
Ferritin (ug/l)	1.006	(0.99, 1.015)	0.16
Transferrin saturation	0.001	(0.00, 4.81)	0.11
CRP (mg/l)	1.03	(1.02, 1,05)	0.00*
Albumin (g/dl)	0.07	(0.01, 0.41)	0.00*

*; statistically significant Cox Regression result at level 0.05, IV; intravenous, CRP; c-reactive protein, ESA; erythropoiesis stimulating agents; HR; hazard ratio, CI; confidence interval

mortality and ESA dose (p= 0.150), serum ferritin (p= 0.160), or transferrin saturation (p= 0.200). Moreover, mortality was significantly associated with age ≥65 years (p= 0.030), presence of diabetes (p= 0.020), BMI ≥30 kg/m² (p= 0.020), low serum albumin (p= 0.010), and high serum CRP levels (p= 0.001).

DISCUSSION

The relationship between dialysis adequacy and anemia is well-known, with evidence suggesting that anemia can be more effectively treated with increasing Kt/V doses (10). In our study, there was no statistically significant difference between the groups in terms of URR and Kt/V when comparing patients based on hemoglobin levels and ESA doses. Notably, nearly all of our patients had dialysis adequacy.

Hyperparathyroidism leads to bone marrow fibrosis, ultimately resulting in lower hemoglobin levels (11). Tanaka et al. highlighted the correlation between anemia and hyperparathyroidism, suggesting that anemia could be ameliorated through hyperparathyroidism treatment (12). Another study by Mpio et al. demonstrated that treatment of secondary hyperparathyroidism with calcimimetics improves hemoglobin levels in HD patients (13). Kalantar-Zadeh et al. also observed that patients with high PTH levels exhibit resistance to ESA (14). In this study, we also observe an obvious relationship between hyperparathyroidism and anemia.

Inflammation triggers elevated hepcidin levels, leading to reduced iron absorption from the gastrointestinal tract, disruption of iron transport from bone marrow stores, and ultimately leading to anemia (15,16). In our study, where the relationship between low hemoglobin levels and high CRP levels was observed, it can be stated that inflammation causes anemia.

We observed that patients with higher hemoglobin levels exhibited significantly elevated levels of glucose, total cholesterol, and LDL cholesterol compared to those with lower hemoglobin levels. Additionally, we found that patients with higher hemoglobin levels had statistically longer dialysis vintage, with a higher proportion of patients having a dialysis vintage longer than five years. Among patients with high hemoglobin levels, total cholesterol and LDL cholesterol levels were also higher in those who received lower doses of ESA. These findings are in line with the study conducted by Nafar et al., where it was found that patients with hemoglobin levels ≥10 g/dl had significantly lower CRP levels, lower ESA doses, longer dialysis vintage, and higher ferritin levels compared to those with hemoglobin levels <10 g/dl. Moreover, Nafar et al. defined malnutrition criteria in their study as triglyceride < 150 mg/dl, total cholesterol <150 mg/dl, creatinine < 8 mg/dl, and serum albumin <4 mg/dl and reported that malnutrition was significantly more prevalent in patients with hemoglobin levels <10 g/dl.

In our study, no significant difference was found in terms of ESA or IV iron doses, serum iron, and transferrin saturation when the patients were compared regarding their ferritin levels. CRP levels were significantly higher in patients with higher serum ferritin levels. Since ferritin is a positive acute-phase reactant, the elevation of ferritin in these patients can be due to inflammation (17). Additionally, the number of patients who had a dialysis vintage longer than five years was also significantly higher in the group with higher ferritin levels. The high level of ferritin in these patients could be due to the accumulation of iron that has developed over the years. In our study, hemoglobin level was significantly lower in patients with higher ferritin levels than in patients with lower ferritin levels. Low levels of hemoglobin in patients with high ferritin levels could be due to inflammation, which leads to functional iron deficiency, resulting in anemia (15).

High ferritin levels and low transferrin saturation are frequently detected in inflammation (15,16). In our study, although there was no significant difference between hemoglobin and ferritin levels in both patients receiving IV iron >200 mg/month and ≤200 mg/month, transferrin saturation was significantly lower and CRP levels were significantly higher in the group receiving >200 mg/month IV iron. Additionally, we found that diabetic nephropathy was significantly higher, glucose levels were higher, and PTH and creatinine levels were lower in patients who received >200 mg/month IV iron. Kalantar-Zadeh et al. showed that patients who received IV iron at baseline had significantly lower levels of creatinine and transferrin saturation and a significantly higher number of diabetic patients than those who did not (14). Feldman et al. also found that the group who were given more IV iron had a significantly higher number of diabetic patients and a significantly lower transferrin saturation than the group who were given less IV iron (18).

The relation between mortality and iron is perhaps due to the elevated risk of infections, oxidative stress, endothelial dysfunction, and cardiovascular disease with iron treatment (19). Kalantar-Zadeh et al. showed increased mortality in patients who received >400 mg/month IV iron (8). Feldman et al. reported that compared with none, billing for more than 1000 mg IV iron over a 6-month period was associated with an increased risk of hospitalization and mortality (20). Bailie et al. found that as both monthly total iron and IV iron per kg increased, mortality also increased (21). However, Feldman et al. could not demonstrate a statistically significant association between cumulative iron dose and mortality. In their study, the baseline model found a statistically significant association between mortality and IV iron dose, though this disappeared after using time-

dependent models (19). Finally, Hougen et al. reported in their meta-analysis that a higher dose of IV iron does not seem to be associated with a higher risk of mortality, infection, cardiovascular events, or hospitalizations in adult patients on dialysis (22). In our study, we found associations between both total IV iron and IV iron per kg and mortality. Furthermore, elevated mortality rates were observed in patients with hemoglobin levels <9 g/dl, consistent with findings from prior studies (1,3).

Limitations of the Study

Two major limitations of our study are its retrospective design and the small number of participants. The retrospective nature of the study means that we were limited to analyzing pre-existing data, which could introduce bias and affect the reliability of our findings. Additionally, the small sample size limits the generalizability of our results and reduces the statistical power to detect significant differences. Furthermore, the study's observational design prevents us from establishing causality between the variables studied. Another limitation is the single-center setting, which may not reflect the practices and patient characteristics of other dialysis centers. Finally, the study period of twelve months may not be sufficient to capture long-term trends and outcomes related to anemia and mortality in dialysis patients.

CONCLUSION

Our study highlights the association between dialysis adequacy, anemia, inflammation, and iron management in hemodialysis patients. Despite the limitations of a retrospective design and a small sample size, our findings underscore the importance of addressing hyperparathyroidism and inflammation to improve anemia management. The association between higher ferritin levels, inflammation, and lower hemoglobin levels emphasizes the need for careful monitoring and individualized treatment strategies. Furthermore, the observed correlations between IV iron dosing, diabetic nephropathy, and mortality risk call for a cautious approach to iron supplementation. Future prospective studies with larger, multi-center cohorts are essential to validate these findings and develop comprehensive guidelines for anemia management in dialysis patients..

DECLARATIONS

Ethics Committee Approval: An informed consent form was obtained from each patient. The study approval was obtained from Van Bölge Education and Research Hospital's Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki..

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REFERENCES

1. Macdougall IC, Tomson CR, Steenkamp M, Ansell D. Relative risk of death in UK haemodialysis patients in relation to achieved haemoglobin from 1999 to 2005: an observational study using UK Renal Registry data incorporating 30,040 patient-years of follow-up. Nephrol Dial Transplant. 2010;25(3):914-919. doi:10.1093/ndt/gfp550.
2. Teles F, Amorim de Albuquerque AL, Freitas Guedes Lins IK, Carvalho Medrado P, Falcão Pedrosa Costa A. Quality of life and depression in haemodialysis patients. Psychol Health Med. 2018;23(9):1069-1078. doi:10.1080/13548506.2018.1469779.
3. Shi Z, Zhen S, Zhou Y, Taylor AW. Hb level, iron intake and mortality in Chinese adults: a 10-year follow-up study. Br J Nutr. 2017;117(4):572-581. doi:10.1017/S000711451700040X
4. Anemia in CKD – KDIGO, https://kdigo.org/guidelines/anemia-in-ckd/ (accessed 7 September 2021)
5. Macdougall IC, Obrador GT. How important is transfusion avoidance in 2013?. Nephrol Dial Transplant. 2013;28(5):1092-1099. doi:10.1093/ndt/gfs575
6. Malyszko J, Malyszko JS, Mysliwiec M. Hyporesponsiveness to erythropoietin therapy in hemodialyzed patients: potential role of prohepcidin, hepcidin, and inflammation. Ren Fail. 2009;31(7):544-548. doi:10.1080/08860220903082606
7. Kuragano T, Matsumura O, Matsuda A, et al. Association between hemoglobin variability, serum ferritin levels, and adverse events/mortality in maintenance hemodialysis patients. Kidney Int. 2014;86(4):845-854. doi:10.1038/ki.2014.114
8. Kalantar-Zadeh K, Regidor DL, McAllister CJ, Michael B, Warnock DG. Time-dependent associations between iron and mortality in hemodialysis patients. J Am Soc Nephrol. 2005;16(10):3070-3080. doi:10.1681/ASN.2005040423
9. Koulouridis I, Alfayez M, Trikalinos TA, Balk EM, Jaber BL. Dose of erythropoiesis-stimulating agents and adverse outcomes in CKD: a metaregression analysis. Am J Kidney Dis. 2013;61(1):44-56. doi:10.1053/j.ajkd.2012.07.014
10. Nafar M, Samavat S, Khoshdel A, Alipour-Abedi B. Anemia Evaluation and Erythropoietin Dose Requirement Among Hemodialysis Patients: a Multicenter Study. Iran J Kidney Dis. 2017;11(1):56-65.
11. Komaba H, Kakuta T, Fukagawa M. Diseases of the parathyroid gland in chronic kidney disease. Clin Exp Nephrol. 2011;15(6):797-809. doi:10.1007/s10157-011-0502-5.
12. Tanaka M, Komaba H, Fukagawa M. Emerging Association Between Parathyroid Hormone and Anemia in Hemodialysis Patients. Ther Apher Dial. 2018;22(3):242-245. doi:10.1111/1744-9987.12685.
13. Mpio I, Boumendjel N, Karaaslan H, et al. Hyperparathyroïdie secondaire et anémie. Effets d'un calcimimétique sur le contrôle de l'anémie des hémodialysés chroniques. Étude pilote [Secondary hyperparathyroidism and anemia. Effects of a calcimimetic on the control of anemia in chronic hemodialysed patients. Pilot Study]. Nephrol Ther. 2011;7(4):229-236. doi:10.1016/j.nephro.2011.01.008.
14. Kalantar-Zadeh K, Lee GH, Miller JE, et al. Predictors of hyporesponsiveness to erythropoiesis-stimulating agents in hemodialysis patients. Am J Kidney Dis. 2009;53(5):823-834. doi:10.1053/j.ajkd.2008.12.040.
15. Małyszko J, Koc-Żórawska E, Levin-Iaina N, et al. New parameters in iron metabolism and functional iron deficiency in patients on maintenance hemodialysis. Pol Arch Med Wewn. 2012;122(11):537-542.
16. Ueda N, Takasawa K. Impact of Inflammation on Ferritin, Hepcidin and the Management of Iron Deficiency Anemia in Chronic Kidney Disease. Nutrients. 2018;10(9):1173. Published 2018 Aug 27. doi:10.3390/nu10091173.
17. Jairam A, Das R, Aggarwal PK, et al. Iron status, inflammation and hepcidin in ESRD patients: The confounding role of intravenous iron therapy. Indian J Nephrol. 2010;20(3):125-131. doi:10.4103/0971-4065.70840
18. Feldman HI, Joffe M, Robinson B, et al. Administration of parenteral iron and mortality among hemodialysis patients. J Am Soc Nephrol. 2004;15(6):1623-1632. doi:10.1097/01.asn.0000128009.69594.be.
19. Vaziri ND. Understanding iron: promoting its safe use in patients with chronic kidney failure treated by hemodialysis. Am J Kidney Dis. 2013;61(6):992-1000. doi:10.1053/j.ajkd.2012.10.02720.
20. Feldman HI, Santanna J, Guo W, et al. Iron administration and clinical outcomes in hemodialysis patients. J Am Soc Nephrol. 2002;13(3):734-744. doi:10.1681/ASN.V133734
21. Bailie GR, Larkina M, Goodkin DA, et al. Data from the Dialysis Outcomes and Practice Patterns Study validate an association between high intravenous iron doses and mortality. Kidney Int. 2015;87(1):162-168. doi:10.1038/ki.2014.275
22. Hougen I, Collister D, Bourrier M, et al. Safety of Intravenous Iron in Dialysis: A Systematic Review and Meta-Analysis. Clin J Am Soc Nephrol. 2018;13(3):457-467. doi:10.2215/CJN.05390517