European Journal of Biology and Medical Science Research, 14(3),19-29, 2026
Print ISSN: ISSN 2053-406X,
Online ISSN: ISSN 2053-4078
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

Impact of Iron Injection on Dialysis Patients in Jordan

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doi: https://doi.org/10.37745/ejbmsr.2013/vol14n31929 Published July 12, 2026

Citation: Faris N.S. (2026) Impact of Iron Injection on Dialysis Patients in Jordan, *European Journal of Biology and Medical Science Research*, 14(3),19-29

Abstract: *Iron injections are frequently utilized to treat anemia in patients undergoing dialysis, given the essential function of iron in the production of red blood cells. [1] Nonetheless, administering excessive or improperly managed iron injections can result in complications, especially in dialysis patients who face existing metabolic and inflammatory issues. [2] This research examines the effect of iron injections on iron storage levels (ferritin) in dialysis patients at hospitals in Jordan. A total of 94 individuals, ranging from 20 to 80 years old, were examined between April 2025 and July 2025. The standard tests include assessing creatinine and hemoglobin levels, as well as measuring ferritin levels using hematology analyzers for hemoglobin and ELISA instruments for ferritin levels. Each 2ml ampoule of CosmoFer contains the equivalent of 100mg of iron in the form of an iron (III)-hydroxide complex, alongside 626mg of water for injection, administered as a bolus injection for 2 minutes for patients undergoing kidney dialysis. To determine the appropriateness of administering monthly iron injections to dialysis patients without prior checks of their blood ferritin levels, I separated the patients into two distinct groups after obtaining their informed consent and clarifying that this study aimed to benefit them. The first group did not receive iron injections, and their ferritin levels were evaluated, revealing normal results. The second group was administered monthly iron injections despite elevated ferritin levels according to hospital protocols. Ferritin levels were measured in both groups, and the group receiving monthly iron showed a notable increase in ferritin levels, with a statistically significant p-value (P-value is ‹‹0.001) indicating this difference. The research found that administering higher amounts of iron and reducing EPO for dialysis patients can decrease the likelihood of EPO-related side effects. Conversely, iron overload is a condition characterized by excessive total body iron content, which may carry a time-sensitive risk of organ dysfunction. Pathological iron overload refers to an elevated body iron content linked with indications of organ dysfunction that are likely due to excess iron. Elevated ferritin levels were correlated with increased mortality rates.***

Keywords: Iron Infusion, ferritin levels, hemoglobin, and creatinine assessments associated with dialysis patients.

INTRODUCTION

Individuals undergoing dialysis have end-stage renal disease and need elevated iron levels to produce blood cells. [2] For those with advanced kidney disease, intravenous iron is typically preferred over oral supplements due to its higher effectiveness. [3] The primary cause of iron deficiency is often related to

blood loss. [4] The correlation between blood loss and iron depletion is influenced by the hemoglobin (Hb) concentration (e.g., Hb 12 g/dl: 0.40 mg iron for every ml of blood; Hb 10 g/dl: 0.36 mg iron per ml of blood) [5]

In many kidney facilities, patients typically have their blood tested approximately every month. [11] Numerous individuals receiving dialysis also require erythropoiesis-stimulating agents (ESAs) to enhance their red blood cell levels. [12] These ESAs are synthetic versions of the hormone erythropoietin, or EPO, which is produced by the kidneys and signals the bone marrow to generate red blood cells.[13] When the kidneys are damaged, they secrete less EPO, so ESAs are utilized to encourage the bone marrow to manufacture red blood cells. This form of treatment is referred to as EPO therapy. [14] . Elevated doses of EPO have been linked to a greater risk of cardiovascular incidents like strokes. Nevertheless, it is often feasible to achieve effective results with a lower EPO dosage paired with a higher intake of iron. [4]Once this occurs, it will be released into transferrin for transport to cells, provided that hepcidin levels are low.[13] If not, it will stay within ferritin granules located in [1] the cytoplasm of macrophages and other reticuloendothelial cells, including Kupffer cells found in the liver. [7]The conditions under which elevated iron levels lead to clinically significant adverse effects, as well as the specifics of these effects, are not clearly understood. Evidence from patients with inherited hemochromatosis indicates that excess parenchymal iron and labile iron may be detrimental, while iron stored within the cells of the reticuloendothelial system may pose less risk.[12]. Once this happens, it will be bound to transferrin for transport to cells, assuming that hepcidin levels are low. If hepcidin levels are high, it will remain confined within ferritin granules in the cytoplasm of macrophages and other reticuloendothelial cells, including Kupffer cells found in the liver. [13] The specific conditions that lead to clinically significant adverse effects due to elevated iron levels, as well as the nature of these effects, are not well understood. [14]Research involving patients with inherited hemochromatosis suggests that excess parenchymal iron and labile iron might be harmful, while iron stored within the reticuloendothelial system's cells may be less hazardous. Although intrahepatic iron could potentially cause liver damage through iron-induced mesenchymal activation.[17] Elevated serum ferritin levels do not necessarily reflect increased liver iron content. [18] Therefore, hyperferritinemia should not be equated with iron overload, and serum ferritin levels do not reveal whether iron is stored in parenchymal cells or in cells of the reticuloendothelial system (RES). [19]A significant concern arises when both high transferrin saturation and elevated serum ferritin coexist, particularly in patients with hereditary hemochromatosis and those experiencing iron overload from transfusions. [20] The toxicity of iron overload in hematologic disorders is influenced by several factors, including the extent and rate of iron accumulation. The primary organs affected include the liver, heart, endocrine glands, and joints. [21] However, the extent, distribution, and duration of iron accumulation in patients with chronic kidney disease (CKD) may not be enough to cause the toxicity seen in hemochromatosis.[22]

This research is important as it reveals the influence of iron injections on dialysis patients in Jordan, assisting in the improvement of treatment strategies. Iron supplementation plays a crucial role in treating anemia in dialysis patients but administering too much or improperly regulated iron can result in issues

like iron overload, oxidative stress, and damage to organs. By examining the effects on ferritin levels and patient wellbeing, this study aids in enhancing clinical guidelines, which leads to safer and more effective iron therapy. Additionally, the research offers significant insights into healthcare practices within Jordanian hospitals, promoting better patient care, informed medical choices, and potential policy improvements to optimize dialysis treatment outcomes.

MATERIALS AND METHODS

A total of 94 individuals, ranging in age from 20 to 80, were examined from April 2025 to July 2025; among them, 32 were female (30.08%) and 62 were male (58.28%); the female-to-male ratio was 1.1 to 8. These individuals were referred to the dialysis department at a specialized hospital located in Amman, the capital city of Jordan. Standard assessments included measuring creatinine and hemoglobin levels, with ferritin levels determined using hematology analyzer instruments for hemoglobin and ELISA instruments for ferritin levels. In my study, I categorized my dialysis patients into two groups: one group received a 200mg ferritin injection monthly, while the other group received ferritin based on their blood ferritin concentration. Additionally, I conducted routine creatinine tests for the dialysis patients, along with hemoglobin tests to indicate iron concentration. Most importantly, I performed a ferritin test to evaluate the impact of the monthly iron injections.

Every 2ml ampule of CosmoFer contains 100mg of iron in the form of an iron (III)-hydroxide complex, along with 626mg of water for injection, administered as a bolus injection over a period of 2 minutes for patients undergoing kidney dialysis. [3] Any adverse events were documented, which included acute anaphylactoid reactions resulting from the iron injection.

Statistical analysis

The results are displayed as the average. The Student's “t” test was employed to compare the findings, with P values under 0.05 regarded as statistically significant.

RESULTS

Table 1: The test outcomes for the patient undergoing dialysis.

Number	Gender	Age/ year	Creatinine 0,8-1.4 Mg/dl	Hb	Ferritin 20-200 Ng/ml
1	Male	63	5.1	11.4	905
2	“	78	3.9	8.5	47
3	“	37	10.2	7.6	380
4	female	53	6.5	12.6	32
5	male	56	8.1	10.6	265
6	“	65	9.5	8.5	699

7	female	8.7	8.7	9.4	≥ 1000
8	male	63	6.03	7.4	51
9	“	51	8.6	11.6	540
10	“	67	7.2	7.0	407
11	female	47	7.1	9.0	481
12	Male	62	7.9	9.0	≥ 1000
13	“	50	9.7	10.9	879
14	“	28	9.6	8.2	148
15	“	61	2.2	9.3	413
16	female	43	5.3	9.4	492
17	“	64	6.5	9.4	49
18	male	50	7.3	11.3	28
19	female	56	9.6	9.2	80.6
20	male	53	2.3	11	26
21	female	53	7.6	10.8	951
22	male	46	7.1	9.2	463
23	“	56	8.9	9.5	≥1000
24	female	67	5.3	9.1	≥ 1000
25	male	71	7.0	8.3	699
26	“	32	8.6	12.3	≥ 1000
27	“	42	10.2	8.8	611
28	“	45	7.0	9.5	723
29	“	48	9.6	11.2	57
30	“	70	8.0	10.0	≥ 1000
31	female	69	3.1	9.4	202
32	male	55	8.1	9.8	540
33	female	42	7.3	10.3	523
34	male	63	10.6	9.7	400
35	female	53	5.5	9.8	≥ 1000
36	male	64	9.3	11.0	615
37	“	68	7.1	11.4	659
38	“	59	5.5	9.5	≥ 1000
39	“	60	5.4	8.2	≥ 1000
40	“	39	4.1	6.5	205
41	“	35	10.6	4.9	≥ 1000
42	female	72	7.3	7.8	808
43	Male	51	5.1	10.4	323
44	“	68	7.0	9.0	≥ 1000
45	Female	56	6.2	9.7	222
46	Male	30	8.2	7.9	148

47	Female	52	4.2	10.0	143
48	“	64	7.5	7.8	185
49	“	51	5.7	9.5	70
50	Male	52	3,9	8.0	596
51	Female	60	4.3	12.1	57
52	“	80	5.7	8.1	516
53	Male	36	10.3	9.0	312
54	“	52	8.4	11.3	880
55	“	50	7.0	8.9	183
56	“	52	7.1	10.5	363
57	“	51	8.9	8.0	≥ 1000
58	female	59	5.6	9.0	187
59	“	20	8.4	7.7	842
60	Male	51	7.3	7.0	329
61	“	65	8.4	7.8	87
62	“	38	10.6	10.0	103
63	Female	78	5.0	9.3	295
64	Male	50	7.9	8.7	30
65	Female	61	5.4	11.8	320
66	“	66	4.2	8.3	161
67	Male	70	7.5	7.7	1000
68	“	61	5.2	11.3	347
69	“	56	7.8	8.0	522
70	“	62	9.4	9.5	149
71	“	35	8.6	9.1	35
72	“	71	6.5	9.5	1000
73	Female	46	9.3	12.8	1000
74	Male	41	9.9	10.9	22
75	“	41	8.9	10.6	17
76	Female	61	5.4	10.3	209
77	“	30	6.5	10.0	1000
78	Male	48	10.5	7.0	641
79	Female	62	5.4	9.2	73
80	Male	52	6.5	8.9	91
81	“	55	10.9	9.2	1000
82	Female	60	8.5	8.3	100
83	Male	57	8.6	7.7	970
84	“	45	2.9	9.4	217
85	“	53	6.8	10.4	380
86	“	67	7.5	9.6	888

87	Female	83	5.0	8.4	1000
88	Male	51	3.8	8.7	805
89	Female	51	4.7	9.5	242
90	"	78	5.8	9.9	700
91	Male	48	6.3	9.2	20
92	"	62	3.9	10.9	89
93	"	40	2.1	11.4	179
94	"	77	9.5	7.8	1000

Table 2: Ratio of gender classification among the patients

Gender	**Number n=94**	**Average age**
Male	63	58.08%
Female	31	30.08%

Table 3: Allocation of ferritin consumption among dialysis patients based on demographic information.

Group	**Number n=94**	**Mean (approx.,)**	**Standard Deviation (approx.)**	**Interpretation/ p-value estimate**
Ferritin abnormal	63	≈760	≈230	
Ferritin normal	31	≈ 90	≈ 50	
Percentage of Abnormal ferritin	67%			
Percentage of Normal ferritin	32%			
P -value				‹‹0.001(high significant difference)

Dissection

Iron overload in patients undergoing dialysis poses a significant threat, primarily due to the persistent accumulation resulting from intravenous iron administration. [1] This condition results in oxidative stress, inflammation, and damage to various organs. [2]When iron levels exceed the binding capacity of transferrin, it exists in the bloodstream as non-transferrin-bound iron (NTBI), which promotes the

generation of reactive oxygen species (ROS) through the Fenton reaction.[3] This oxidative stress results in lipid peroxidation, damage to DNA, and oxidation of proteins, which together contribute to cellular harm and widespread inflammation.[4] Diligent observation and compliance with clinical protocols are essential in preventing and controlling this condition.[21]

To assess the appropriateness of administering monthly iron injections to dialysis patients without checking their blood ferritin levels according to standard hospital protocol, I divided the patients into two groups after obtaining their written consent and explaining that this study is intended for their benefit. The first group did not receive iron injections, and their ferritin levels were assessed, revealing that they were within the normal range. The second group was given monthly iron injections. Ferritin levels were measured in both groups, showing a notable increase in ferritin levels for the group that received iron, with a statistically significant p-value (P -value is ‹‹0.001) indicating this difference. This rise in ferritin levels may result in side effects that I have previously mentioned.

CONCLUSION

The research found that providing patients on dialysis with higher amounts of iron and lower doses of EPO can lessen the likelihood of experiencing side effects from EPO. Conversely, iron overload is characterized by an excessive total body iron content, which could be linked to a progressively increasing risk of organ dysfunction. Pathological iron overload refers to an elevated body iron level that presents with signs of organ impairment, which is likely attributed to the surplus of iron. High levels of ferritin were linked to a greater risk of mortality (compared to region-specific averages) in all three studied regions. While these variations in median ferritin levels might be influenced by differing genetic and environmental backgrounds.

Recommendation: I suggest monitoring the ferritin levels in dialysis patients prior to administering injections to avoid iron overdose.

Ethical Considerations

The study was reviewed and approved by the institutional ethics committee at Middle East University.

Acknowledgement: I would like to express my gratitude to Middle East University, particularly the university president, for permitting me to fully focus on scientific research. I also appreciate the hospitals for granting me the opportunity to conduct my research there. Lastly, I want to thank the nurses, and everyone involved for allowing me to collect samples from them.

Declarations

Ethical Considerations: Ethical approval was obtained from the Ethical committee of the institute and informed consent was obtained from patients. Approval attached

Consent for publication: Publication approval attached

Funding: This research is funded by I will fund personally

Declaration of generative AI and AI-assisted technologies in the writing process

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PRISMA 2020 Flow Diagram (Text Version)

Identification

Records identified from databases (e.g., PubMed, Scopus, Google Scholar): n = 346

Records removed before screening:

- Duplicate records removed: n = 98
- Records marked as ineligible by automation tools: n = 0
- Records removed for other reasons: n = 10

Records screened: n = 238

Records excluded: n = 190

Screening

Reports assessed for eligibility: n = 48

Reports excluded: n = 33

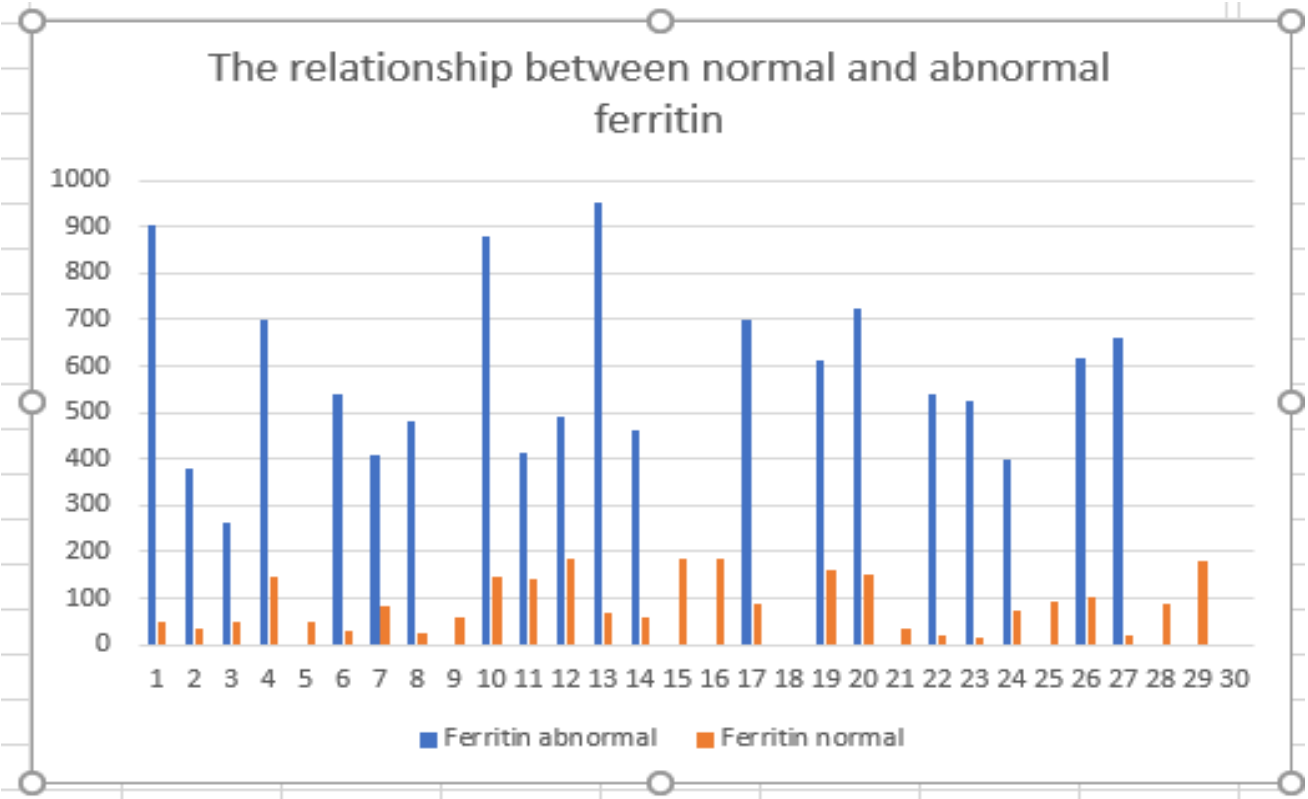
- Not relevant: n = 20

- Incomplete data: n = 8
- Language barrier: n = 5

Included

Studies included in review: n = 15

- Qualitative synthesis: n = 10
- Quantitative synthesis (meta-analysis): n = 5



European Journal of Biology and Medical Science Research, 14(3),19-29, 2026
Print ISSN: ISSN 2053-406X,
Online ISSN: ISSN 2053-4078
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

- The **Abnormal** box is much taller and shifted upward compared to **Normal**.
- This big gap visually represents the significant difference, matching the expected very low p-value.