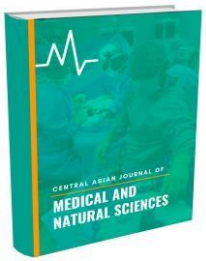

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 05 Issue: 04 | October 2024 ISSN: 2660-4159

Article

Anemia and Depression in Patients with End Stage Renal Disease on Hemodialysis

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Abstract: End-stage renal disease (ESRD) represents a global health challenge. Anemia and depression are frequent complication. Depression may be affected by reduction in tissue oxygenation, deterioration of physical performance due to anemia, that affects the progression of disease. The objective of the study is to assess the relation between anemia and depression among patients with ESRD. Across section study in Baghdad from the 1st of February to 1st of May 2024 in the Iraqi hemodialysis center /Baghdad medical city. Depression assessed using PHQ9 criteria. Laboratory data were recorded for hemoglobin, red blood cells, hematocrit, serum iron and ferritin. P value < 0.05 was considered statistically significant. This study included 173 patients with mean age (53.11±14.8) years. Depression was found in (67.1%) of them. Most patients were anemic, (80.9 %) had hemoglobin ≤11 g/dl. This study supports the association of depression with serum iron level, but did not support its relation with serum ferritin and anemia.

Keywords: Anemia, Depression, Hemodialysis

Citation: Rasheed, R. S., Ali, B. M., Hussien, S. S., & Ismaeel, Z. H. E. Anemia and Depression in Patients with End Stage Renal Disease on Hemodialysis. Central Asian Journal of Medical and Natural Science 2024, 5(4), 461-469.

Received: 25th Jul 2024
Revised: 1st Aug 2024
Accepted: 8th Aug 2024
Published: 15th Aug 2024

1. Introduction

End-stage renal disease (ESRD) is the advanced stage of CKD where the kidneys have lost most of their function and the patients rely on hemodialysis (HD) as part of renal replacement therapy, this represents a common global health challenge [1].

Anemia and depression represent frequent complications among ESRD patients. Anemia affects almost all HD patients, while depression has been recognized to be the most common psychological complication in ESRD patients [1-5]. Globally, the prevalence of depression is reported to be 10% higher among patients with chronic renal failure [6].

Anemia represents the absolute reduction in the number of circulating red blood cells (RBCs). It is considered when one or more of the following are decreased: hemoglobin level (Hb), hematocrit (HCT), or RBC count [7]. Iron is an essential micronutrient for the production heme protein, which is involved in the synthesis of hemoglobin and the production of red blood cells [8].

In chronic kidney disease (CKD), Anemia is caused by a deficiency of erythropoietin, short red blood cell half-life and iron deficiency [9]. This condition impairs the delivery of

oxygen to tissues and organs throughout the body [10], leading to many symptoms like shortness of breath, fatigue, weakness, headaches, dizziness, and depression [9].

Depression may be affected by the decrease in tissue oxygenation, deterioration of physical performance due to anemia, and by altered monoamine synthesis due to malnutrition [11]. That plays a crucial role in the progression of chronic disease. as individuals experiencing depression may lose hope and compliance with treatment, adversely affecting outcomes [12,13].

Moreover, depression may increase mortality in chronic hemodialysis patients. as it can be linked to poor oral intake and the activation of proinflammatory cytokines that could further increase mortality through malnutrition [12,13].

This study aims to assess the relation between anemia and depression among patients with ESRD. Such research can provide valuable insights into the management of these conditions, leading to better outcomes and overall well-being for patients.

2. Patients and Methods

The study is a cross section study conducted in Baghdad from the 1st of February to 1st of May 2024 in the Iraqi hemodialysis center /Baghdad medical city. Patients with end stage renal disease on maintenance hemodialysis were included in the study, while patients with malignancy, recent trauma, patients on medical treatment for psychiatric illness and patients already on antidepressant were excluded from the study.

The center had a fixed dialysis schedule for their patients. The center was visited to cover all the sessions throughout the day. All eligible patients were asked to participate. A total of 173 patients who fulfilled the selection criteria and agreed to participate were included. The research objectives and methods were explained to the patients and informed consent were obtained from all participants.

Data were collected using interview questionnaire. and information about the age, gender, medical history and associated comorbidities was collected. Depression was assessed using PHQ9 criteria, and total score was calculated for each patient. According to PHQ9 score, depression was categorized into normal (≤4) and depression (≥5). Based on the participants' dialysis records, laboratory data were recorded for Hb, RBC, HCT, serum iron and serum ferritin, and classified into groups: (Hb; low ≤11 and normal >11 g/dl), (RBC; low < 4 $x10^6$ and normal ≥ 4 $x10^6$ μl), (HCT; low < 35% and normal ≥ 35%), (serum iron; low ≤ 9 and normal > 9 μmol/l) and (serum ferritin; < 500 and ≥ 500 ng/ml).

Analysis of data was carried out using SPSS-26 (Statistical Packages for Social Sciences- version 25). The data were presented as frequencies and percentages for categorical variables. Chi square test was used to determine the association the independent variables. P value < 0.05 was considered statistically significant. Confidentiality of data was maintained throughout the study.

3. Results

This study included 173 patients with mean age (53.11±14.8) years, and the age group (> 50) was the most prevalent (63.6%). Male constituent 96 (55.5%) of patients while females were 77 (44.5) as in Table 1.

Table 1. Age and Gender

Age	Number	%
< 30	16	9.2

30-50	47	27.2
> 50	110	63.6
Total	173	100
Gender		
Male	96	55.5
Female	77	44.5
Total	173	100

The majority of patients 146 (84.4%) had hypertension, while diabetes mellitus (DM) in 55 (31.8%), heart failure in 30 (17.3%), hepatitis C (HCV) in 66 (38.2 %) and hepatitis B (HBV) in 3 (1.7 %) as in Figure 1.

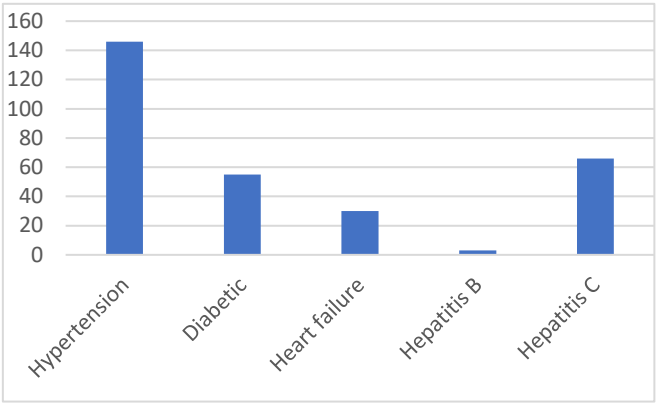

Figure 1. Distribution according to comorbidities

Out of the total number of patients, Depression was found in 116 (67.1%), compared to 57 (32.9%) without depression as in Figure 2.

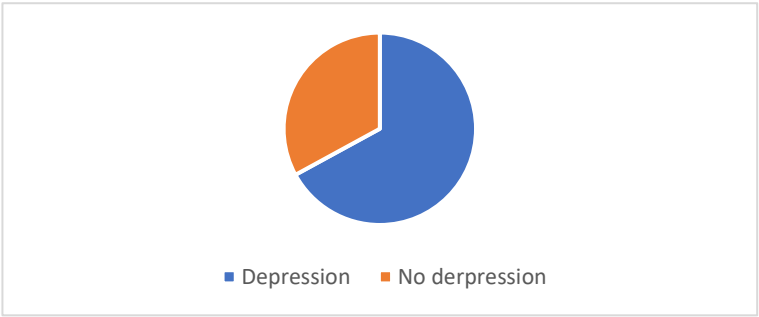

Figure 2. Distribution according to depression

Table 2 show that the majority of patients in this study were anemic, 140 (80.9 %) of patients had Hb level ≤11 g/dl, 163 (94.2%) had low RBC count, and 167 (96.5%) with low HCT compared with 33 (19.1%) with Hb level > 11 g/dl, 10 (5.8%) with normal RBC count and only 6 (3.5%) with normal HCT. Serum iron level was low in 70 (40.5%) and normal in 103 (59.5%) patients. Serum ferritin level was found ≥ 500 ng/ml in134 (77.5%) compared to 39 (22.5%) with level < 500 ng/ml.

Table 2. Distribution of Blood Parameters.

Variable	Number	%
Hb		
Low ≤11 g/dl	140	80.9
Normal > 11 g/dl	33	19.1
Total	173	100
RBCs Count		
Low < 4 x10⁶ µl	163	94.2
Normal ≥ 4 x10⁶ µl	10	5.8
Total	173	100
HCT		
Low < 35%	167	96.5
Normal ≥ 35%	6	3.5
Total	173	100
Iron		
Low ≤ 9 µmol/l	70	40.5
Normal > 9 µmol/l	103	59.5
Total	173	100
Ferritin		
< 500 ng/ml	39	22.5
≥ 500 ng/ml	134	77.5
Total	173	100

Table 3 show, the peaks of age for depression was at 30-50 years, and < 30 years for no depression. These differences were not statistically significant. According to gender, 59 (76.6%) of females had depression compared to 18 (23.4%) without depression. The gender was significantly related to depression (p = 0.02). Out of total patients with DM ,44 (80%) had depression compared to only 11(20%) without depression. There was significant association between DM and depression (p= 0.01), similar significant association was seen with heart failure (p=0.01), while hypertension and hepatitis C infection were not related with depression.

Table 3. Distribution of Patients' Characteristics According to Depression

		Depression		No depression		**Total**
Age	< 30	8	50%	8	50%	16
	30-50	37	78.7%	10	21.3%	47
	> 50	71	64.5%	39	35.5%	110
	X^2= 5.31		d.f= 2	P = 0.07		
Gender	Male	57	59.4%	39	40.6%	96
	Female	59	76.6%	18	23.4%	77
	X^2= 5.75		d.f= 1	P = 0.02		
Hypertension	Yes	100	68.5%	46	31.5%	146

	No	16	59.3%	11	40.7%	27
	X^2= 0.88	d.f= 1	P = 0.35			
Diabetes	Yes	44	80%	11	20%	55
	No	72	61%	46	39%	118
	X^2= 6.11	d.f= 1	P = 0.01			
Heart failure	Yes	27	90%	3	10%	30
	No	89	62.2%	54	37.8%	143
	X^2= 8.65	d.f= 1	P = 0.01			
Hepatitis C	Yes	46	70.8%	19	29.2%	65
	No	70	64.8%	38	35.2%	108
	X^2= 065	d.f= 1	P = 0.42			

Serum iron level was significantly related to depression (p= 0.04), 53 (75.7%) of patient with low serum iron level had depression compared to 17 (24.3%) without depression. The variation in the level of Hb, RBC, HCT and ferritin were not related to depression as shown in Table 4.

Table 4. Distribution of Blood Parameters According to Depression.

Variable			Depression		Not depression		Total
Hb	Low	≤11 g/dl	96	68.6%	44	31.4%	140
	Normal	> 11 g/dl	20	60.6%	13	39.4%	33
		X^2= 0.77	d.f= 1	P = 0.38			
RBC	Low	< 4 x10^6 µl	110	67.5%	53	32.5%	163
	Normal	≥ 4 x10^6 µl	6	60%	4	40%	10
		X^2= 0.24	d.f= 1	P = 0.63			
HCT	Low	< 35%	111	66.5%	56	33.5%	167
	Normal	≥ 35%	5	83.3%	1	16.7%	6
		X^2= 0.75	d.f= 1	P = 0.39			
Iron	Low	≤ 9 µmol/l	53	75.7%	17	24.3%	70
	Normal	> 9 µmol/l	63	61.2%	40	38.8%	103
		X^2= 3.99	d.f= 1	P = 0.04			
Ferritin	Normal	< 500 ng/ml	26	66.7%	13	33.3%	39

High ng/ml	≥ 500	90	67.2%	44	32.8%	134
		X^2= 0.03	d.f= 1	P = 0.95		

4. Discussion

End stage renal disease impacts patients psychologically and physically. Anemia is the commonest physical complication, while psychologically, the commonest impact is depression [6]. In this study depression was found in the majority (67.1%) of participants. This finding was similar to other studies worldwide [14-16]. There was no significant association between depression and age. It is similar to that reported in a study from Saudi Arabia [16,17].

Depression in hemodialysis was significantly more prevalent among females than males (p=0.02). this is consistent with a study from western Rajasthan and Saudia Arabia [19,20]. Females have more restricted lifestyle and more responsibilities than males. so, they might be more vulnerable to depression. In Saudi Arabia, a study revealed females were more prevalent than males in depression and anxiety symptoms [20]. On the other hand, other study found that depression was not related to gender [16].

In this study hypertension was the most common comorbidity (84.4%), followed by hepatitis C infection 66 (38.2 %), DM 55 (31.8%) and heart failure 30 (17.3%). A study in Brazil observed that hypertension was the most common, followed by diabetes and heart failure [17]. Another study from Pakistan reported that (85%) of patients had hypertension, followed by DM (59%), heart failure (8.5%) and hepatitis C (2.8%) [21]. This indicates the need to increase the prevention and control actions with strict infection control measures. In our study depression was significantly associated with DM and heart failure (P= 0.01, 0.01) respectively, but not related with hypertension and hepatitis c infection. In Amsterdam, Cardiac disease was associated with depression while diabetes mellitus was not associated [22]. The association of depression with heart disease may arises from shared environmental factors. Risk factors for heart disease are likely to be causally related with depression [23].

Anemia was prevalent among patients in this study, (80.9 %) of patients had Hb level ≤11 g/dl, low RBC count was found in (94.2%), and (96.5%) with low HCT. This finding agreed with a studies from Pakistan and India [21,24]. In India the severity of anemia was related with the stage of disease [24]. Another study from Baghdad reported that low RBC count is common among hemodialysis patients and the majority of patients (96%) had lower count than the healthy control group [25]. Across section study in Egypt found that hematocrit was ranging from (20.60 – 44.30%) with a mean of 31.79%, compared to a mean of 38.86% in the healthy control group [26]. The possible reasons for that could be attributed to poor nutritional status, with decline in general health, erythropoietin deficiency, comorbid conditions and hemolysis [21].

The levels of Hemoglobin, RBC and HCT in this study were not related to depression significantly. This agreed with a study in Egypt that showed no differences in patient groups with mild, moderate and severe depression when compared to each other and to the non-depressed patient group regarding hemoglobin level [30]. Another study from turkey, also reported no correlation between hemoglobin levels and depression [31]. These results are inconsistent with studies from Pakistan and turkey that displayed association of depression with anemia, and poor nutritional status among patients with end stage kidney disease on hemodialysis [27,28]. In a descriptive retrospective study, the number of erythrocytes and hemoglobin were significantly lower in depressed patients than in the control group, but no statistically significant difference was found on hematocrit [29]. Factors like anemia severity, using different assessment methods for depression and variation

in patients' demographic characteristics may be contributed to the different results between studies.

Iron plays an important role in body's physiological functions and the development of brain, including DNA synthesis and repair, oxygen transport, and neurotransmitter metabolism [32]. In patients with CKD, Iron deficiency is a common and reversable cause of anemia. It contributes to impairing erythropoiesis. This deficiency may be due to absolute iron deficiency or a relative deficiency which prevents the utilization of available iron stores [33]. Sufficient iron stores are essential to Improve the effects of erythropoietin stimulating agents [24]. Decrease of iron also result in the accumulation of monoamine oxidase and affects the metabolism of neurotransmitters related with depression [32].

In this study, serum iron level was significantly related with depression (p=0.04). Among patients with low iron levels, (75.7%) of them had depression compared to only 24.3% with no depression. This agreed with a cross section study that revealed low iron status is associated with higher depressive mood and lower memory, and seemed to be modified by nutritional status [34]. Similarly, iron deficiency is found to be related with young adult depression when stratified by sex [35].

One of the best tests of iron status is serum ferritin [24]. In patients with CKD, serum ferritin is increased Repeatedly, as a result of underlying systemic inflammation, and trial of iron repletion is recommended if the serum ferritin level is ≤500 ng/ml [33].

Many studies found significant relation between serum ferritin level and depression [31,36,37]. However, no associations were found in this study. This agreed by a study carried out in Turkey [38]. Another study at Najaf Governorate showed an inverse correlation between ferritin level and depression [37]. This may reflect the impact of low iron in the development of depression, while a study among patients with chronic kidney disease, illustrated patients with depression had higher ferritin levels than those without depression [36]. The development of depression in this condition might be attributed to the inflammatory process.

5. Conclusion

This study supports the association of depression with serum iron level, but did not support its relation with serum ferritin and anemia, as reflected by the levels of (Hb, RBCs and HCT). Further multi center studies with a larger sample are needed to support these relations.

Funding

This report did not receive any specific funding.

Conflict of interests

The authors declare that they have no relevant financial or non-financial interests to report.

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