ORIGINAL ARTICLE

PREVALENCE OF ANEMIA AND ITS IMPACT ON THE QUALITY OF LIFE OF RENAL TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL STUDY

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Summary

Background: Renal transplant patients show a high incidence of anemia, which is often responsible for cardiovascular morbidity and graft rejection. Anemia reportedly impacts the health-related quality of life (HRQoL); however, only a limited number of related studies have been conducted on renal transplant recipients. In this study, we estimated the prevalence of anemia and its effects on QoL of renal transplant patients in Saudi Arabia.

Methods: Seventy-four patients were recruited in this study. They were asked to fill a self-reported EuroQoL instrument (EQ-5D-5L). We measured the hemoglobin levels (Hgb) of the patients to assess their anemia status. Anemia and severe anemia were defined as Hgb < 12 g/dL and Hgb < 10 g/dL, respectively.

Results: Of the 74 recruited patients, 53 patients (71.6 %) were anemic. Around 33.7 % patients were reported to be completely healthy, with a 5-digit of 11111. With respect to EQ-5D-5L, the responses of anemic and non-anemic patients did not differ significantly. However, the response to anxiety-related questions for patients belonging to severe and mild-to-moderate anemia groups differed significantly. The final multivariate logistic model analysis revealed that the gender of patient was significantly associated with incidence of anemia postoperatively [OR: 6.72, 95 % CI: 1.7 - 25.6, P-value = 0.000; (25 males, 47.2 %) vs. (28 females, 52.9 %)]. The use of intravenous (IV) immunoglobulin in the induction phase was significantly associated with incidence of late anemia [P-value = 0.012].

Conclusions: Interestingly, our findings revealed a higher prevalence of anemia among the Saudi kidney patients compared to those of other nations. The incidence of anemia was shown to be significantly associated with renal function, female gender, and IV immunoglobulin use at the induction phase. Furthermore, multicentric prospective studies are warranted to elucidate other clinical factors that are associated with anemia and the underlying pathophysiological mechanisms.

Key words: Anemia; post-transplant; quality of life; renal; Saudi

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INTRODUCTION

In Saudi Arabia, renal replacement therapy is administered via three methods: hemodialysis, peritoneal dialysis, and renal transplantation. The first renal transplantation in the country was done in 1979 at Riyadh Military Hospital. By 2017, 11509 kidney transplantations had been conducted, among which 7838, 563, and 3108 procedures involved related, unrelated, and deceased donors, respectively (1).

Anemia is commonly found in patients with end-stage renal disease, who harbor damaged kidneys that produce inadequate amount of erythropoietin, which leads to fewer red blood cells in the bone marrow, thus, reducing the oxygen-carrying capacity of the blood (2). Anemic males and females are defined as hemoglobin level (Hgb) < 13.5 g/dL and 12 g/dL, respectively (3). Renal transplant patients showed a high incidence of anemia, which, in turn, is associated with cardiovascular morbidity and graft rejection. Post-renal transplant anemia exhibited multi-factorial pathogenesis, including graft rejection, iron deficiency, chronic infection, and immunosuppressive therapy (4). Previous studies have reported that anemia impacts the HRQoL of patients. A previous study in USA was conducted with the primary objective of determining the impact of anemia management on improving the HRQoL domains, regardless of the disease type. Interestingly, the study showed that efficient treatment of anemia significantly improved the selected HRQoL subdomains in patients with renal insufficiency and cancer. Their findings indicated that erythropoiesis stimulating protein-mediated anemia management could improve the overall HRQoL of patients (5). Another study in Japan conducted on pre-menopausal women with iron-deficiency anemia showed that iron-supplementation helped in hemoglobin recovery in patients, which, in turn, improved the overall HRQoL scores (6). In 2018, another study revealed that anemia not only reduced HRQoL but also deteriorated the clinical conditions of patients, impaired their work productivity, and gave rise to other comorbidities (7). However, a limited number of investigators have investigated the effect of anemia on HRQoL of post-renal transplant patients. A study conducted in Istanbul University on post-renal transplant patients reported 19 % of patients suffered from anemia and 4.5 % of patients suffered from severe anemia. As expected, anemic patients showed lower QoL than that of non-anemic patients (3). Univariate regression analyses employed in another study showed significant association of positive proteinuria and low Hgb with low HRQoL and anemia incidence. After adjustment for other parameters, low Hgb was still significantly associated with both the abovementioned outcomes (8). In another study, 887 renal transplant recipients were retrospectively analyzed. This study showed significant association between anemia and postoperative outcomes, such as death-censored graft survival, patient survival, or graft function (9).

This aim of this study was to estimate anemia prevalence and its impact on QoL of renal transplant patients in Saudi Arabia.

METHODS

Patient Recruitment

In this cross-sectional, retrospective study, the individuals who underwent renal transplant from April 2014 to April 2019 were recruited. The inclusion criteria included mentally stable patients, age ≥ 18 years, and registered at Transplantation Outpatient Clinic of Prince Sultan Military Medical City, Riyadh, Saudi Arabia. The exclusion criteria were as follows: suffering from hematologic disorders, dementia, impaired cognitive function, solid organ malignancy, and/or no consent for the study. All the included patients agreed to participate and signed a consent form.

Data Collection

The electronic medical records of the patients were used to obtain the following data: age, body mass index, gender, duration since transplant, living/dead status, relation to donor, Hbg, platelets, use of iron, use of immuno-suppression therapy, including induction phase therapy (basiliximab vs. thymoglobulin), maintenance phase therapy (tacrolimus-based vs. cyclosporin-based), intravenous (IV) immunoglobulin, supportive therapies (antiviral, antibiotic, and diabetes medications), and vitamin supplements (ferrous, B12, folate, etc.). Dialysis status and type prior to transplantation were also recorded. At 3 months postoperatively and at last clinical visit, other hematological parameters were recorded, such as Hbg, mean cell volume (MCV), hematocrit (Hct), platelets, and leucocyte counts. Mild-to-moderate and severe anemia were defined by Hbg < 12 g/dL and Hbg < 10 g/dL, respectively.

EQ-5D-5L questionnaire and QoL assessment

Patient QoL was assessed using the EQ-5D-5L questionnaire (10). The questionnaire consisted of five domains: self-care, anxiety/depression, mobility, usual activities, and pain/discomfort. For every question, five responses were available: no, slight, moderate, severe, and extreme problem. All the responses were coded on the basis of user manual. Based on the patient responses, a five-digit code was derived, with each digit pertaining to each domain. A code of 11111 represented no problem in any domain and completely healthy patient. The questionnaire also included a visual analog scale (VAS) that recorded the opinion of the patients regarding their current health on a visual equivalent scale ranging from a score of 0 (least QoL) to 100 (highest QoL). Thus, EQ VAS essentially provided a quantitative measure of patients' health based on their own perception (10).

STATISTICAL ANALYSIS

SPSS (version 27) was used to conduct all statistical analyses. Initially, the data distribution was examined for normality using the Smirnov Test. Univariate analyses was used to assess the association between patient variables and anemia prevalence. The variables that were found to be significantly associated with anemia prevalence were fitted into a multivariate logistic regression model to assess their final significance using forward and backward selection methods. Intervariable differences were assessed using the Pearson's Chi-square test. P-value < 0.05 represented statistically significant differences.

RESULTS

Table 1 shows the clinical, laboratory, and demographic data of all patients. Most of the patients were middle-aged (median age: 49 years; range: 21-78 years) with 58.1 % male and 41.9 % female patients.

Table 1. Population characteristics

Continuous data	Mean (SD), Range	
Age (y)	49 (14.9), 21-78	
Weight (kg)	74.7 (12), 44-103	
Height (cm)	160 (20), 1.6-177	
BMI	28 (4.8), 19-44.5	
Categorical data	Frequency (n)	Percent (%)
Gender		
Male	43	58
Female	31	41.9
Kidney donor state		
Living	68	91.9
Deceased	6	8
Type of living donor		
Related	49	66
Unrelated	25	33.8
Hypertension		
No	14	18.9
Yes	60	81
Dyslipidemia		
No	64	86.5
Yes	9	12
Cardiovascular		
No	68	91.9
Yes	6	8
Diabetes		
No	43	58
Yes	31	41.9
ESA use		
No	35	47
Yes	39	52.7
Induction phase		
No	41	55
Yes	33	44.6
IV immunoglobulin		
No	67	90.5
Yes	7	9.5
Dialysis		
Yes	52	70
Type of dialysis		
Hemodialysis	42	56.8
Peritoneal dialysis	10	13.5

Abbreviations: ESA, erythropoiesis-stimulating agent. Induction phase: use of either basiliximab or thymoglobulin. Continuous data was presented as mean (SD) and range. Categorical data was presented as frequencies (n) and percentage (%).

Of all patients, 53 (71.6 %) patients were anemic. During induction phase, 55.4 % patients received basiliximab and 44.6 % patients received thymoglobulin. Moreover, during maintenance phase, 91.9 % patients received tacrolimus-based regimen, while 8.1% patients received cyclosporin-based regimen. Around 9.5 % patients received IV immunoglobulin. Among supportive therapies, antiviral, antibiotic, and diabetes medications were administered in 8.1 %, 39.3 %, and 2.7 % patients, respectively.

Anemia prevalence according to patient variables

The correlation between anemia prevalence and patient's variables was examined using the univariate and multivariate analyses (Table 2). Final model findings revealed that prevalence of anemia was most significantly associated with female gender [OR: 6.72, 95 % CI: 1.7- 25.6, P-value = 0.000; (25 males, 47.2 %) vs. (28 females, 52.9 %)]. None of the other demographic variables showed any significant association with anemia prevalence. Furthermore, the use of IV immunoglobulin was also significantly associated with the incidence of late anemia [P-value = 0.012; (57 % in females vs. 23 % in males)]. This finding was consistent with those of previous studies (11, 12). None of the used therapies were associated with anemia prevalence (all P-values ≥ 0.05). Surprisingly, prior use of and/or type of dialysis used preoperatively did not significantly affect anemia prevalence (P-value = 0.4).

Table 2. Post-transplant follow-up

Test	Mean (SD), Range	
	V1	V2
Leukocyte (×10³⁾)	8.6 (3.4), 2.2-20	7.5 (2.8), 3.1-17
Hgb (g/dL)	10.7 (2.2), 6.9-19	13 (1.9), 9-16
Hct (%)	0.33 (0.067), 0.21-0.49	0.41 (0.060), 0.27-0.54
MCH (pg)	28.7 (2.8), 19-39	27 (3), 19-36
Platelet (×10³)	249 (101), 71-497	263 (69), 112-439
Diagnosis of anemia	**Frequency (n)**	**Percent (%)**
Early anemia		
Mild-to-moderate	23	31
Severe	29	39
Late anemia		
Mild-to-moderate	16	21.6
Severe	4	5.4
Total	53	71.6

Abbreviations: Hgb, hemoglobin; Hct, hematocrit; MCH, mean corpuscular hemoglobin. V1; measurement at clinic visit within 1-3 months post renal transplant, V2; measurement at last clinic visit.

Table 3. EQ-5D-5L frequencies and proportions among post-transplant patients

	Mobility n (%)	Self-care n (%)	Activities n (%)	Pain/discomfort n (%)	Anxiety/depression n (%)
No problem	44 (59.5)	64 (86.5)	55 (74)	36 (48.6)	46 (62)
Slight problem	11 (14.9)	4 (5.4)	9 (12)	15 (20)	18 (24)
Moderate problem	12 (16.2)	3 (4.1)	5 (6.8)	19 (25.7)	6 (8)
Severe problem	6 (8.1)	2 (2.7)	3 (4)	3 (4)	3 (4)
Extreme problem/unable to do daily activities	1 (1.4)	1 (1.4)	2 (2.7)	1 (1.4)	1 (1.4)
Total	74 (100)	74 (100)	74 (100)	74 (100)	74 (100)

QoL assessment by EQ-5D-5L

Table 3 shows the EQ-5D-5L scores of all patients. Around 33.7 % patients corresponded to a 5-digit score of 11111 that represented full state of health. Table 4 shows no significant difference in EQ-5D-5L scores of patients in anemic and non-anemic groups. However, the response related to the anxiety domain of EQ-5Q-5L differed significantly between the patients of early severe and mild-to-moderate anemia groups (P-value = 0.02). Furthermore, the responses of the patients in the late anemia group and those of other groups were not significantly different.

Table 4. EQ-5D-5L frequencies and proportion according to incidence of anemia

Dimension	Anemia n (%)	Without anemia n (%)	P value
Mobility			
No problem	34 (64.2)	10 (47.6)	
Slight problem	8 (15.1)	3 (14.3)	
Moderate problem	6 (11.3)	6 (28.6)	0.416
Severe problem	4 (7.5)	2 (9.5)	
Extreme problems/unable to move	1 (1.9)	0 (0.0)	
Self-care			
No problem	47 (88.7)	17 (81.0)	
Slight problem	3 (5.7)	1 (4.8)	
Moderate problem	1 (1.9)	2 (9.5)	0.534
Severe problem	1 (1.9)	1 (4.8)	
Extreme problems/unable to do self-care	1 (1.9)	0 (0.0)	
Usual activities			
No problem	39 (73.6)	16 (76.2)	
Slight problem	8 (15.1)	1 (4.8)	
Moderate problem	3 (5.7)	2 (9.5)	0.706
Severe problem	2 (3.8)	1 (4.8)	
Extreme problem/ unable to do daily activities	1 (1.9)	1 (4.8)	
Pain /discomfort			
No pain /discomfort	25 (47.2)	11 (52.4)	
Slight pain /discomfort	12 (22.6)	3 (14.3)	
Moderate pain /discomfort	13 (24.5)	6 (28.6)	0.889
Severe pain /discomfort	2 (3.8)	1 (4.8)	
Extreme pain /discomfort	1 (1.9)	0 (0.0)	
Anxiety/depression			
Not anxious/depressed	32 (60.4)	14 (66.7)	
Slightly anxious /depressed	13 (24.5)	5 (23.8)	
Moderately anxious /depressed	5 (9.4)	1 (4.8)	0.378
Severely anxious /depressed	3 (5.7)	0 (0.0)	
Extremely anxious /depressed	0 (0.0)	1 (4.8)	

DISCUSSION

To the best of our knowledge, this is the first study to determine anemia prevalence in post-renal transplant patients in Saudi Arabia. Interestingly, in this study, the anemia prevalence in Saudi patients was observed to be higher than that in patients of other countries. Around 31.1 % and 40.5 % of our patients suffered from mild-to-moderate and severe anemia, respectively. However, anemia incidence was not observed to affect the QoL of patients.

Study limitations

The study was conducted at only one center. Thus, our results could not be extrapolated or generalized to all Saudi renal transplant settings. Furthermore, anemia status of the patients was defined by their Hbg levels that were obtained in a retrospective manner, which might be prone to error due to inaccurate entry in the patients' medical files. Therefore, larger-scale, prospective-design, cohort studies are needed to further elucidate anemia incidence and its underlying pathophysiological mechanisms and sub-classifications.

CONCLUSIONS

The most significant predictors of anemia among the Saudi renal transplant patients were female gender and IV immunoglobulin use. Further studies need to focus on other patient parameters as potential predictors of anemia prevalence and their impact on QoL of post-renal and non-renal transplant patients.

Abbreviations

EQ-5D-5L: EuroQoL instrument
Hct: Hematocrit
Hgb: Hemoglobin levels
HRQoL: Health-related quality of life
MCV: Mean cell volume

Declarations

Ethics approval and consent to participate

The Institutional Review Board at PNU approved this study (20–0292). Before starting the study, the study aims were clarified to the participants, and their written informed consent was obtained. In addition, the participants were assured that their personal information would remain completely confidential.

Consent for publication

Not applicable

Availability of data and material

All data are available on demand from the corresponding author.

Competing interests

There are no conflicts of interest.

REFERENCES

1. Al-Sayyari AA and Shaheen FA. End stage chronic kidney disease in Saudi Arabia. Saudi Medical Journal. 2011;32(4):339-346.
2. Bielesz B, Reiter T, Hammerle FP, et al. The Role of Iron and Erythropoietin in the Association of Fibroblast Growth Factor 23 with Anemia in Chronic Kidney Disease in Humans. Journal of Clinical Medicine. 2020;9(8):2640.
3. Abacı SH, Alagoz S, Salihoglu A, et al. December. Assessment of Anemia and quality of life in patients with renal transplantation. In Transplantation proceedings. 2015;47(10):2875-2880.
4. Yabu JM and Winkelmayer WC. Posttransplantation anemia: mechanisms and management. Clinical Journal of the American Society of Nephrology. 2011;6(7):1794-1801.
5. Ross SD, Fahrbach K, Frame D, et al. The effect of anemia treatment on selected health-related quality-of-life domains: a systematic review. Clinical Therapeutics. 2003;25(6):1786-1805.
6. Ando K, Morita S, Higashi T, et al. Health-related quality of life among Japanese women with iron-deficiency anemia. Quality of life research. 2006;15(10):1559-1563.
7. Staibano P, Perelman I, Lombardi J, et al. Patient-centered outcomes in the management of anemia: A scoping review. Transfusion medicine reviews. 2019;33(1):7-11.
8. Ichimaru N, Obi Y, Nakazawa S, et al. April. Post-transplant Anemia has strong influences on renal and patient outcomes in living kidney transplant patients. In Transplantation Proceedings. 2016;48(3):878-883.
9. Huang Z, Song T, Fu L, et al. Post-renal transplantation anemia at 12 months: prevalence, risk factors, and impact on clinical outcomes. International urology and nephrology. 2015;47(9):1577-1585.
10. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of life research. 2011;20(10):1727-1736.
11. Markvardsen LH, Christiansen I, Harbo T, et al. 2014. Hemolytic anemia following high dose intravenous immunoglobulin in patients with chronic neurological disorders. European Journal of Neurology. 2014;21(1):147-152.
12. Elsayed H, Sany D, Eldin EN, et al. Prevalence and association of post-renal transplant anemia. Saudi Journal of Kidney Diseases and Transplantation. 2012;23(3):461-466.