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Prevalence of anemia and its impact on the quality of life of renal transplant recipients in a Saudi setting

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ABSTRACT

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. Seventy-four patients were recruited in this study. They were asked to fill a self-reported EuroQoL instrument (EQ-5D-5L). Anemia and severe anemia were defined as Hgb < 12 g/dL and Hgb < 10 g/dL, respectively. 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 female gender of patient was significantly associated with incidence of anemia postoperatively [OR: 6.72, 95% CI: 1.7 - 25.6, P-value = 0.000]. Interestingly, our findings revealed a higher prevalence of anemia among the Saudi kidney patients compared to those of other nations. Furthermore, multicentric prospective studies are warranted to elucidate other clinical factors and the underlying pathophysiological mechanisms.

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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 (Al-Sayyari and Shaheen, 2011).

Anaemia is commonly found in patients with end-

stage renal disease, who harbour damaged kidneys that produce an inadequate amount of erythropoietin, which leads to fewer red blood cells in the bone marrow, thus, reducing the oxygen-carrying capacity of the blood (Bielesz *et al.*, 2020). Anaemic males and females are defined as haemoglobin level (Hgb) < 13.5 g/dL and 12 g/dL, respectively (Abacı *et al.*, 2015). Renal transplant patients showed a high incidence of anaemia, which, in turn, is associated with cardiovascular morbidity and graft rejection. Post-renal transplant anaemia exhibited multifactorial pathogenesis, including graft rejection, iron deficiency, chronic infection, and immunosuppressive therapy (Yabu and Winkelmayer, 2011). Previous studies have reported that anaemia impacts the HRQoL of patients. A previous study in the USA was conducted with the primary objective of determining the impact of anaemia management on improving the HRQoL domains, regardless of the disease type.

Interestingly, the study showed that efficient treatment of anaemia significantly improved the selected HRQoL subdomains in patients with renal insufficiency and cancer. Their findings indicated that erythropoiesis-stimulating protein-mediated anaemia management could improve the overall HRQoL of patients (Ross *et al.*, 2003). Another study in Japan conducted on pre-menopausal women with iron-deficiency anaemia showed that iron-supplementation helped in haemoglobin recovery in patients, which, in turn, improved the overall HRQoL scores (Ando *et al.*, 2006). In 2018, another study revealed that anaemia not only reduced HRQoL but also deteriorated the clinical conditions of patients, impaired their work productivity, and gave rise to other comorbidities (Staibano *et al.*, 2019). However, a limited number of investigators have investigated the effect of anaemia on HRQoL of post-renal transplant patients. A study conducted at Istanbul University on post-renal transplant patients reported 19% of patients suffered from anaemia, and 4.5% of patients suffered from severe anaemia. As expected, anaemic patients showed lower QoL than that of non-anaemic patients (Abacı *et al.*, 2015). Univariate regression analyses employed in another study showed a significant association of positive proteinuria and low Hgb with low HRQoL and anaemia incidence. After adjustment for other parameters, low Hgb was still significantly associated with both the abovementioned outcomes (Ichimaru *et al.*, 2016). In another study, 887 renal transplant recipients were retrospectively analyzed. This study showed a significant association between anaemia and postoperative outcomes, such as death-censored graft survival, patient survival, or graft function (Huang *et al.*, 2015).

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

MATERIALS AND 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 $\geq$ 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 the donor, Hbg, platelets, use of iron, use of immunosuppression 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 before transplantation were also recorded. At three months postoperatively and last clinical visit, other haematological 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 (Herdman *et al.*, 2011). 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 based on the user manual. Based on the patient responses, a five-digit code was derived, with each digit about each domain. A code of 11111 represented no problem in any domain and completely healthy patient. The questionnaire also included a

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. Inductionphase: use of either basiliximab or thymoglobulin. Continuous data was presentedas mean (SD) and range. Categorical data was presented as frequencies (n) and percentage (%).

Table 2: Post-transplant follow-up

Test	Mean (SD)	Range
	V1	**V2**
Leukocyte ($\times 10^3$)	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 (%)	.33 (.067), .21-.49	.41 (.060), .27-.54
MCH (pg)	28.7 (2.8), 19-39	27 (3), 19-36
Platelet ($\times 10^3$)	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)

visual analogue 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 perception (Herdman *et al.*, 2011).

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 were used to assess the association between patient variables and anaemia prevalence. The variables that were found to be significantly associated with anaemia 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 Pearson's Chi-square test. P-value < 0.05 represented statistically significant differences.

RESULTS AND DISCUSSION

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.

Of all patients, 53 (71.6%) patients were anaemic. During the induction phase, 55.4% of patients received basiliximab, and 44.6% of patients received thymoglobulin. Moreover, during the

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)	.416
Slight problem	8 (15.1)	3 (14.3)	
Moderate problem	6 (11.3)	6 (28.6)	
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)	.534
Slight problem	3 (5.7)	1 (4.8)	
Moderate problem	1 (1.9)	2 (9.5)	
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)	.706
Slight problem	8 (15.1)	1 (4.8)	
Moderate problem	3 (5.7)	2 (9.5)	
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)	.889
Slight pain /discomfort	12 (22.6)	3 (14.3)	
Moderate pain /discomfort	13 (24.5)	6 (28.6)	
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)	.378
Slightly anxious /depressed	13 (24.5)	5 (23.8)	
Moderately anxious /depressed	5 (9.4)	1 (4.8)	
Severely anxious /depressed	3 (5.7)	0 (0.0)	
Extremely anxious /depressed	0 (0.0)	1 (4.8)	

maintenance phase, 91.9% of patients received a tacrolimus-based regimen, while 8.1% of patients received cyclosporin-based regimen. Around 9.5% of patients received IV immunoglobulin. Among supportive therapies, antiviral, antibiotic, and diabetes medications were administered in 8.1%, 39.3%, and 2.7% patients, respectively.

Anaemia prevalence according to patient variables

The correlation between anaemia 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 anaemia prevalence. Furthermore, the use of IV immunoglobulin was also significantly associated with the incidence of late anaemia [P-value = 0.012; (57% in females vs 23% in males)]. This finding was consistent with those of previous studies (Markvardsen *et al.*, 2014; Elsayed *et al.*, 2012). None of the used therapies was associated with anaemia prevalence (all P-values $\geq$ 0.05). Surprisingly, prior use of and/or type of dialysis used preoperatively did not significantly affect anaemia prevalence (P-value = 0.4).

QoL assessment by EQ-5D-5L

Table 3 shows the EQ-5D-5L scores of all patients. Around 33.7% of patients corresponded to a 5-digit score of 11111 that represented a full state of health. Table 4 shows no significant difference in EQ-5D-5L scores of patients in anaemic and non-anaemic 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 anaemia groups (P-value = 0.02). Furthermore, the responses of the patients in the late anaemia group and those of other groups were not significantly different.

Study limitations

The study was conducted at only one centre. Thus, our results could not be extrapolated or generalized to all Saudi renal transplant settings. Furthermore, the anaemia 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 elucidate further anaemia incidence and its underlying pathophysiological mechanisms and sub-classifications.

CONCLUSION

To the best of our knowledge, this is the first study to determine anaemia prevalence in post-renal transplant patients in Saudi Arabia. Interestingly, in this study, the anaemia 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 anaemia, respectively. However, anaemia incidence was not observed to affect the QoL of patients. The most significant predictors of anaemia among Saudi renal transplant patients were female gender and IV immunoglobulin use. Further studies need to focus on other patient parameters as potential predictors of anaemia prevalence and their impact on the QoL of post-renal and non-renal transplant patients.

Conflict of Interest

The authors declare that they have no conflict of interest.

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