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Outcomes following renal transplantation in elderly: A retrospective cohort study in a single tertiary care center

Abdulrahman Altamimi[1*], **Samar Algahtani**[2], **Leenah Aloufi**[2], **Elham Alharthi**[2], **Alaa Alselaimy**[2], **Badriah Alanazi**[2], **Norah Alharbi**[2], **Bayan Albdah**[3]

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Authors' Affiliation:
[1]Consultant of Hepatobiliary and abdominal organs transplant surgeon at King Abdulaziz Medical City (KAMC), Associate professor in the College of Medicine at King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Department of Biostatistics-King Abdullah International Medical Research Center (KAIMRC), Riyadh, Kingdom of Saudi Arabia
[2]Medical intern, College of Medicine, King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Riyadh, Kingdom of Saudi Arabia
[3]Biostatistician at King Abdullah International Medical Research Center (KAIMRC), Riyadh, Kingdom of Saudi Arabia

[*]**Corresponding Author**
Consultant of Hepatobiliary and abdominal organs transplant surgeon at King Abdulaziz Medical City (KAMC), Associate professor in the College of Medicine at King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Department of Biostatistics-King Abdullah International Medical Research Center (KAIMRC), Riyadh,
Kingdom of Saudi Arabia
Email: tamimiab@ksau-hs.edu.sa & altamimiab@ngha.med.sa

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ABSTRACT

Introduction: With the increasing number of elderly patients with end-stage renal disease, there is a growing use of renal replacement therapy. This includes dialysis or kidney transplantation (KT), with transplantation being the favorable option due to its decreased mortality rate. *Objective:* We aim to report our experience with KT outcomes in patients aged ≥65 at our center. *Methods:* This is a retrospective cohort study that reviewed elderly patients who underwent KT from January 2016 to December 2021 in Riyadh, Saudi Arabia. 38 patients who met our criteria were included. All statistical analyses were performed using SAS software. *Results:* Out of the 38 kidney donors, 24 were living relatives, 11 were living non-relatives and 3 were cadavers. Patients who stayed in the hospital for >8 days after transplantation had more complications, such as infections (38.89%), delayed graft function (11.11%) and new-onset diabetes (5.56%), than those who stayed less. The mean serum creatinine before transplant and six months post-transplant showed a statistically significant difference with a p-value of <0.0001. Post-transplant complications reported in patients include infection (34.21%), acute kidney injury (13.16%) and biopsy-proven acute rejection (5.26%). The estimated glomerular filtration rate (eGFR) greatly improved in patients after transplantation; when comparing the eGFR at 6 months and 12 months post-transplant, there was a statistically significant difference (p-value = 0.0056). *Conclusion:* Our study showed that KT in patients aged ≥65 yielded good outcomes, indicating that age alone should not be a contraindication to transplantation.

Keywords: Chronic kidney disease, Elderly, Kidney transplant, Saudi Arabia, Outcomes

1. INTRODUCTION

Chronic kidney disease (CKD) is a major health problem worldwide. It is defined by the presence of abnormal kidney function for >3 months with

either the presence of kidney damage markers (hematuria, proteinuria (albumin-to-creatinine ratio of 30 mg/g), or anatomic abnormalities) or a glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 (Hashmi et al., 2022). End-stage renal disease (ESRD) is the final stage of CKD with a GFR of 15 mL/min/1.73 m^2 (Hashmi et al., 2022). ESRD significantly affects the quality of life of patients due to its high morbidity and mortality rates (Ziemba et al., 2021).

Patients with ESRD would need renal replacement therapy (RRT) to sustain life, which includes regular dialysis (hemodialysis or peritoneal dialysis) or kidney transplantation (KT) (Hashmi et al., 2022). Out of all RRTs, KT is the most preferred modality due to its overall decreased mortality rate and improved quality of life (Hashmi et al., 2022; Tonelli et al., 2011). One study noted that in 2015, the total number of patients undergoing peritoneal dialysis in Saudi Arabia was 1,416 and those who underwent hemodialysis were 14,366 (Alkhlaif et al., 2020). Another study in 2021 reported that a total of 9,810 patients in Saudi Arabia had follow-up after kidney transplantation, whereas those still undergoing dialysis were over 20,000 (Mousa et al., 2021). ESRD in the elderly has increased over the years, thus adding to the controversy as to whether or not transplantation is the most appropriate treatment for this age group (Doyle et al., 2000). Elderly patients may develop complications that arise from transplantations, such as graft loss and/or death of the patient, which makes the choice of transplantation debatable (Doyle et al., 2000).

There are many complications associated with KT in the elderly. One of the major complications of surgery is vascular complications, which account for 3–15% of all cases (Reyna-Sepúlveda et al., 2017). In addition, other complications from KT are infection, graft rejection, herniation, lymphocele and urological and cardiovascular complications (Reyna-Sepúlveda et al., 2017). Moreover, using immunosuppressive agents, especially in the elderly group, may lead to decreased immunity, leading to infection (Reyna-Sepúlveda et al., 2017). A study that compared death caused by infection showed 0.8% death in the younger group, whereas death in the elderly age group was 4.8% (Fabrizii et al., 2004).

Knowledge of the outcomes of KT in elderly recipients is limited in Saudi Arabia. Thus, this study aims to report our experience with KT outcomes in the elderly over the past six years in our center.

2. METHODOLOGY

Study Design

This is a consecutive, non-randomized, retrospective cohort study that reviewed elderly patients (≥65 years old) who underwent kidney transplantation from January 2016 to December 2021. It was conducted at King Abdullah Specialized Children Hospital (KASCH), Riyadh, Saudi Arabia.

Study Subjects

We reviewed 656 patients who underwent renal transplantation at KASCH from January 2016 to December 2021 and; only 38 patients who met our criteria were included. The selection criteria included in this study is patients aged ≥65 years who underwent kidney transplantation from 2016 to 2021. Patients aged <65 who underwent KT and patients aged ≥65 years who had combined organ transplant surgery (heart or liver) were excluded.

Outcomes

The outcomes that were measured in this study include the following: Delayed graft function (DGF), biopsy-proven acute rejection (BPAR), new-onset diabetes after transplantation (NODAT), graft and recipient survival, infection and other complications. The patients' kidney transplant outcomes were followed at 1 month, 3 months, 6 months and 12 months post-transplant.

Definitions

Estimated GFR (eGFR) was categorized into five groups: Category 1, >90 mL/min/1.73 m^2; category 2, 60–89 mL/min/1.73 m^2; category 3, 30–59 mL/min/1.73 m^2; category 4, 15–29 mL/min/1.73 m^2 and category 5, <15 mL/min/1.73 m^2 or in hemodialysis. DGF was defined as the need for at least one hemodialysis session during the first week post-transplantation.

BPAR (both cellular and antibody mediated either clinically or pathologically) was categorized according to the Banff classification: Category 1, normal biopsy or nonspecific changes; category 2, antibody-mediated changes; category 3, suspicious (borderline) for acute T cell-mediated rejection; category 4, T cell-mediated rejection; category 5, interstitial fibrosis and tubular atrophy and category 6, other nonrejection changes.

Data Analysis

Data were collected using electronic medical records (BEST Care system) at KASCH in Riyadh, Saudi Arabia. The results were obtained according to the inclusion criteria. The following variables were collected: (a) demographics; gender, age, body mass index (BMI) in kg/m^2 and habit of smoking; (b) medical history; diabetes mellitus (DM), hypertension (HTN), dyslipidemia, cardiovascular diseases, dialysis modalities and duration of initial stay after transplant; (c) lab results; eGFR in mL/min/1.73 m^2 and serum creatinine (SCr) in μmol/L; (d) outcomes; DGF, BPAR, NODAT, graft and recipient survival, infection and other complications and (e) follow-ups; assessment of graft and recipient survival, eGFR, SCr, acute kidney injury (AKI), infection and other complications at 1 month, 3 months, 6 months and 12 months.

Data were expressed as numbers, where frequencies and percentages were used to describe categorical variables and mean and standard deviation for continuous variables. The association between categorical variables was investigated by Fisher's exact test and the Wilcoxon two-sample test for continuous variables. All statistical analyses were performed using SAS software (version 9.4; SAS Institute). P-values of <0.05 were considered statistically significant.

3. RESULTS

A total of 38 patients with CKD (aged ≥65) were enrolled from 2016 to 2021. Of these patients, 27 (71.05%) were male and 11 (28.95%) were female. Patients with CKD had an average BMI of 28.48 ± 4.37. Moreover, 97.37% of the patients in this study had hypertension, 67.32% had diabetes mellitus, 63.16% had dyslipidemia, 55.26% had cardiovascular diseases and 68.42% had other comorbidities. The majority of patients with CKD before KT were on dialysis, with 89.19% on hemodialysis and 5.41% on peritoneal dialysis, while only 5.41% of the patients were not undergoing any form of dialysis. The kidney donors were as follows: 24 living relatives, 11 living non-relatives and 3 cadavers. The demographic details of all cases are listed in Table 1.

Table 1 Demographic details of 38 patients who underwent renal transplantation from 2016 to 2021

Variable	Frequency (%)
Gender	
Male	27 (71.05)
Female	11 (28.95)
Age	
65	7 (18.42)
66	6 (15.79)
67	5 (13.16)
68	3 (7.89)
69	3 (7.89)
70	2 (5.26)
71	3 (7.89)
72	2 (5.26)
73	1 (2.63)
74	3 (7.89)
75	2 (5.26)
80	1 (2.63)
DM	
No	9 (23.68)
Yes	29 (76.32)
HTN	
No	1 (2.63)
Yes	37 (97.37)
Dyslipidemia	
No	24 (63.16)
Yes	14 (36.84)

Cardiovascular disease	
No	21 (55.26)
Yes	17 (44.74)
Smoking history	
No	36 (94.74)
Yes	2 (5.26)
Dialysis modality	
No dialysis	2 (5.41)
Hemodialysis	33 (89.19)
Peritoneal dialysis	2 (5.41)
Kidney donor type	
Living relatives	24 (63.16)
Living non-relatives	11 (28.95)
Cadavers	3 (7.89)
BMI (mean ± standard deviation)	28.48 ± 4.37

Table 2 Correlation between length of stay with delayed graft function, infection and new-onset diabetes after transplantation

Length of stay	Delayed graft function (DGF)	Infection	New-onset diabetes after transplantation (NODAT)
8 or less, n (%)	0 (0.00)	4 (23.53)	0 (0.00)
More than 8, n (%)	2 (11.11)	7 (38.89)	1 (5.56)
Fisher's exact test (two-sided probability)	0.4857	0.4857	1.0000

As shown in Table 2, 18 out of 35 patients who underwent KT stayed in the hospital for >8 days and developed more complications during their one-year follow-up. Of these, 7 patients developed an infection, 2 patients developed DGF and 1 patient developed NODAT. The variables were compared using Fisher's exact test with the length of hospitalization in days. It was found that infection, DGF and NODAT were statistically insignificant with the length of hospitalization with a p-value of 0.4857, 0.4857, and 1.0000, respectively.

Post-transplant infections were reported in 13 patients (34.21%). Infections that developed during and after transplant were caused by different organisms such as *Escherichia coli*, *Klebsiella pneumoniae*, parvovirus B19, extended-spectrum beta-lactamases (ESBLs), and *Streptococcus pneumoniae*. Most patients (61.54%) developed infections within the first month post-transplant. Out of 13 patients, urinary tract infection (UTI) was the most common post-transplant infection in 10 patients (76.92%). Moreover, AKI was documented in five patients (13.16%) in the first three months post-transplant. In addition, two patients developed BPAR (5.26%) with antibody-mediated changes (category II) based on the Banff classification. Other surgical complications such as central nervous system toxicity (5.26%), acute tubular necrosis (2.63%), deep vein thrombosis (2.63%), diabetic ketoacidosis (2.63%), pulmonary edema that leads to ICU admission (2.63%) and wound healing delay (2.63%) are documented in Figure 1.

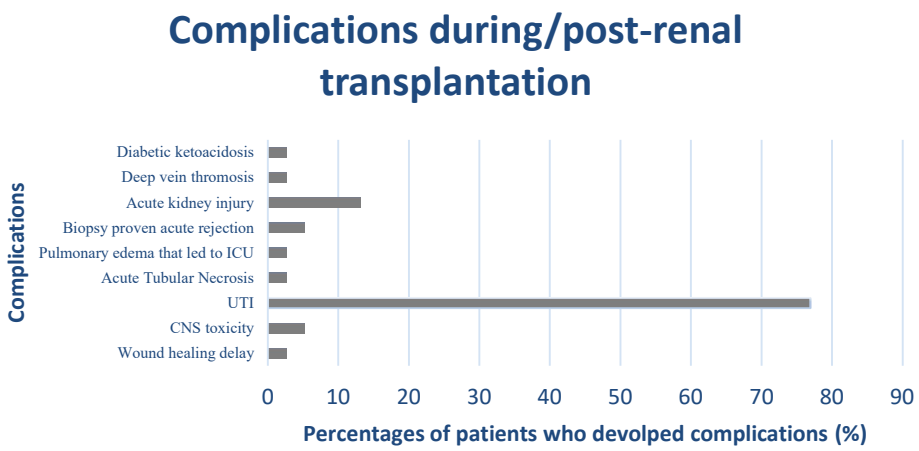

Figure 1 Bar chart showing the complications during and after renal transplantation

Table 3 Mean serum creatinine values before transplant, after transplant and 1 month, 3 months, 6 months and 12 months after transplantation

Variable	Mean ± SD	Number of patients
SCr before transplant	675.83 ± 227.93	35
SCr after transplant	346.58 ± 226.36	38
SCr 1 month	96.14 ± 39.37	37
SCr 3 months	91.89 ± 29.94	37
SCr 6 months	92.24 ± 22.20	35
SCr 12 months	98.06 ± 58.40	33

As shown in Table 3, the mean SCr before transplant was 675.83 ± 227.93 and it improved by 48.72% (346.58 ± 226.36) after a few days of transplantation. The SCr mean difference improved by 85.77%, 86.40%, 86.35% and 85.49% in comparison to SCr before transplantation and 1 month, 3 months, 6 months and 12 months post-transplantation, respectively. However, when comparing the difference in the mean value of SCr between 6 months and 12 months, a reduction of 6.31% was noted.

Table 4 Difference between serum creatinine before transplant and 6 months post- transplant and between 6 months and 12 months post-transplant

	Serum creatinine (SCr)	
	Before transplant to 6 months post-transplant	6 months to 12 months post-transplant
Mean ± SD	604.14 ± 228.02	5.29 ± 50.98
Sign test (M) (p-value)	<0.0001	0.2962

From the period before transplant until six months post-transplant, 32 patients demonstrated a mean SCr difference of 604.14 ± 228.02 and showed a statistically significant difference calculated using the Sign test with a p-value of <0.0001. From the period of 6–12 months post-transplant, 33 patients showed a mean SCr difference of 5.29 ± 50.98, which was statistically insignificant with a p-value of 0.2962 (Table 4).

Table 5 Difference between eGFR before transplant and at 6 months and 12 months post-transplantation

eGFR (before transplant)	eGFR (6 months)			
Range	>90	60–89	30–59	Total

15–29, n (%)	0 (0.00)	1 (5.26)	1 (16.67)	2
<15 or in HD, n (%)	7 (100.00)	18 (94.74)	5 (83.33)	30
Fisher's exact test (p-value)	0.3871			
eGFR (6 months)	eGFR (12 months)			
Range	>90	60–89	30–59	Total
>90, n (%)	5 (50.00)	3 (16.67)	0 (0.00)	8
60–89, n %)	5 (50.00)	12 (66.67)	1 (20.00)	18
30–59, n (%)	0 (0.00)	3 (16.67)	4 (80.00)	7
Fisher's exact test (p-value)	0.0056			

As shown in Table 5, 30 patients with CKD before KT had eGFR of <15 mL/min/1.73 m^2 or in hemodialysis and 2 patients had eGFR between 15 and 29 mL/min/1.73 m^2. In addition, six months post-transplantation showed a higher eGFR with 60–89 mL/min/1.73 m^2 in 19 patients, >90 mL/min/1.73 m^2 in 7 patients and 30–59 mL/min/1.73 m^2 in 6 patients. Fisher's exact test showed a statistically insignificant difference with a p-value of 0.3871.

However, there were improvements in eGFR 12 months post-transplant, with 18 patients having eGFR between 60 and 89 mL/min/1.73 m^2, 10 patients having eGFR of >90 mL/min/1.73 m^2 and 5 patients having eGFR between 30 and 59 mL/min/1.73 m^2. Fisher's exact test showed that there was a statistically significant difference in eGFR 6 months and 12 months post-transplant with a p-value of 0.0056.

4. DISCUSSION

Compared to dialysis, KT offers a better outcome due to the decreased mortality rates in patients with ESRD (Tonelli et al., 2011). However, much controversy exists regarding KT in the elderly group (≥60 years of age) due to the higher risk of morbidity and mortality post-KT (Doyle et al., 2000). In this retrospective cohort study, we aimed to report the outcomes of KT in patients aged ≥65. Assessment of renal function post-transplantation is measured by three main factors: SCr, blood urea nitrogen and eGFR. Monitoring these blood workups at serial intervals helps detect early signs of renal failure due to graft rejection (Maraghi et al., 2016).

A previous study reported that measuring the SCr level for one month or less after transplantation was a poor predictor value (Hariharan et al., 2002). They argued that the SCr level would not reach its lowest level upon discharge (Hariharan et al., 2002). Also, high doses of immunosuppressants within the first month after transplant could show a falsely high SCr level (Hariharan et al., 2002). Therefore, it was recommended that serum creatinine best be measured at 6 months and 1 year after transplantation (Hariharan et al., 2002).

Our study compared the SCr levels in 32 patients aged ≥65 from the period before the transplant until 6 months after the transplant. The mean SCr was 604.14063 ± 228.01978 μmol/L, which shows great improvement after transplantation with a significant p-value of <0.0001. However, when comparing the SCr from 6 months to 12 months post-transplantation in 33 patients, there was no significant difference, with a mean SCr of 5.28787879 ± 50.9799333 μmol/L and a p-value of 0.2962. Our results were similar to the findings of a study done in 2011 comparing SCr levels in elderly patients aged ≥65 at 1 month and 12 months after KT (Eufrásio et al., 2011). The study noted that good graft function was evaluated by SCr levels, which were as follows: 2.1 mg/dL (185.68 μmol/L) at 1-month post-transplant and 1.52 mg/dL (134.4 μmol/L) at 12 months post-transplant (Eufrásio et al., 2011).

In this study, the overall surgical outcomes of KT in patients aged ≥65 were satisfactory. There was no graft loss in the first year following the transplant. This study assessed the mortality rate only in the first-year post-transplant, with no deaths reported. A study published in 2022 evaluated the mortality rate at 5-years post-transplant and found that the overall 5-year patient survival rate was 76% (Yilmaz et al., 2022). Several studies demonstrated that the post-transplant mortality rate in elderly patients is directly

related to other comorbidities like infection and cardiac diseases rather than graft loss or decline in kidney function (Karim et al., 2014; Yilmaz et al., 2022).

Furthermore, 36 of our patients (94.75%) did not develop DGF or BPAR. These results are also similar to other studies that suggested that KT in elderly patients is safe and effective; in fact, there is a published study that compared the outcome of KT between patients older than 60 and a younger group of patients. The results of that study demonstrated better surgical outcomes of KT in the elderly groups because the acute rejection rate was lower in the older group of patients (22.7%) than it was in the younger ones (37.6%) (Mendonça et al., 2007; Pedroso et al., 2006). Another study has also compared the outcomes between KT recipients aged >65 years and a younger group of transplant recipients. BPAR was found less in the elderly group (6.8%) compared to BPAR in the younger group (22.00%) (Dempster et al., 2013). This can be explained by the immunosenescence that the elderly group experiences, which can aid in the prevention of BPAR by lowering the dosage of immunosuppressant medication post-transplant (Panda et al., 2009). Studies have shown that the reduction of immunosuppressant medication can help in lowering cardiovascular risk, aid in graft survival and reduce medications' side effects (Friedman, 2011).

In this study, post-transplant infections were reported in 13 patients (34.21%). The majority of the infections developed in the first month after the transplant in 8 of the patients (21.62%). Urinary tract infection (UTI) was the most common post-transplant infection in 10 patients (76.9%). A recent study published in 2021 reviewed infections in older kidney transplant recipients and found that UTI was also the most common post-transplant infection (Abidi & Erlandson, 2021).

Limitations and recommendations

This study has some limitations. Our data were collected from a single center only and in a retrospective manner by electronic chart review. In addition, we had a relatively small sample size and a short follow-up period. Furthermore, some patients failed to attend their follow up appointments hence, no further lab results obtained. Also, most of the other studies have measured outcomes such as graft survival at 5- and 10-year survival, which was not measured in our study. We recommend expanding the research by looking at more centers with a larger sample size and a longer follow-up period to obtain more accurate results.

5. CONCLUSION

In conclusion, our study found that elderly patients aged ≥65 have shown good outcomes following KT. Clinicians should be aware that elderly patients with ESRD should not be excluded from receiving a renal transplant as long as there are no contraindications.

Author's contribution

All Authors have contributed to the development of the research idea, literature review, data collection and interpretation, manuscript writing, editing and revision of the manuscript. Approved for publication and agreed to take responsibility for the content.

Bayan Albdah: Contributed to the data analysis and interpretation, editing and revising of the manuscript.

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Ethical approval

This study has been reviewed and approved by the Institutional Review Board (IRB) at KAIMRC, Riyadh, Saudi Arabia. Reference number: RYD-22-419812-58266.

Informed consent

This study uses chart review for data collection; therefore, no ethical consent was needed. However, the patient's information/identity was kept confidential and was coded into a serial number to ensure privacy.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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