

# Renal transplantation experience in Cairo University hospitals

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## Background

Worldwide, the population treated with renal replacement therapy is increasing, representing ~1.3 million patients who undergo dialysis and 400 000 patients who are alive with a kidney transplant. Transplantation is more predictable than it was 20–30 years ago and innovation over the last 20 years has been rapid, delivering substantial short-term and medium-term improvements. Many reports have been published about the epidemiology of renal transplantation in different countries. The aim of this study was to identify the epidemiology of renal transplantation in Cairo University hospitals.

## Patients and methods

This is a retrospective study that was conducted at the King Fahd Unit, Faculty of Medicine, Cairo University, on 282 patients. All patients were followed up for a period of at least 1 year. Demographic data, history taking, clinical examination, immunosuppressive medications protocol, and laboratory investigations were recorded for every patient.

## Results

Of the 282 patients included in the study, 68.1% of recipients were male and 31.9% were female, whereas 52.5% of donors were male and 47.5% were female. An overall 98.6% of our patients received living kidney transplants, whereas 1.4% received cadaveric kidney transplants. The most common cause of end-stage renal disease was unknown etiology. The mean BMI increased significantly after transplantation to reach  $22.6 \pm 4.0$  ( $P=0.0001$ ). Hypertension was the most common disease among the patients; 82.2% of our patients were already hypertensive before transplantation.

## Conclusion

The majority of our recipients were male patients in their second and third decades of life. Moreover, the majority of donors were also male individuals in their second and third decades of life. Most of the transplants carried out by us are living-donor procedures.

## Keywords:

Cairo University, epidemiology, renal, transplantation

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## Introduction

Kidney transplantation is acknowledged as a major advancement of modern medicine that provides high-quality life-years to patients with irreversible kidney failure [end-stage renal disease (ESRD)] worldwide. What was an experimental, risky, and very limited treatment option 50 years ago is now a routine clinical practice in more than 80 countries. What was once limited to a few individuals in a small number of leading academic centers in high-income economies is now transforming lives as a routine procedure in most high-income and middle-income countries [1].

March 1976 was an important landmark for transplantation in Egypt: the first renal transplantation was performed in Mansoura [2].

Following a very slow start, the number of transplants gradually increased, reaching an annual rate of 90–100 transplants. Presently, there are 80 centers

that perform renal transplantation in Egypt, with the overall experience exceeding 7000 living donors [3].

In this study our aim was to evaluate the demographic and epidemiological aspects of renal transplantation in Cairo University Hospital.

## Patients and methods

This is a retrospective study that was conducted at the King Fahd Unit, Faculty of Medicine, Cairo University, on 282 patients (adults and pediatrics). All patients were followed up for a period of at least 1 year.

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In our study, serum creatinine was used to evaluate renal function; graft dysfunction was defined as serum creatinine exceeding 2.5 mg/dl.

The following variables were recorded for each patient:

- (1) Demographic and personal data:
  - (a) Sex and age at transplantation.
  - (b) BMI.
- (2) History taking and clinical examination, including:
  - (a) The original renal disease.
  - (b) Duration of dialysis before undergoing renal transplantation.
  - (c) Pretransplantation treatment modality.
  - (d) History of previous renal transplantation.
  - (e) Graft source.
  - (f) The presence of hypertension (HTN) and/or diabetes mellitus, history of ischemic heart disease.
  - (g) History of blood transfusion.
  - (h) History of any previous operation (urinary tract infection, nephrectomy, etc.).
  - (i) Post-transplantation complications.
- (3) Immunosuppressive medications.
- (4) Laboratory investigations, including:
  - (a) Hepatitis virus infection: hepatitis C virus (HCV), hepatitis B virus, cytomegalovirus, and HIV.
  - (b) Mean random blood sugar level and liver enzymes.
  - (c) Assessment of renal graft functions by serial measurement of serum creatinine in the follow-up.

### Statistical analysis

Statistical package for the social science (SPSS, version 9.0), was used for analysis of data. Data were summarized as mean, SD, and percentage. Nonparametric test (Mann-Whitney *U*) was used for analysis of two independent variables as data were not symmetrically distributed. The  $\chi^2$ -test was used for analysis of qualitative data. Significance was judged at two-sided 0.05 levels. All parameters were significant at 5% significance level.  $R^2$  is an indicator of the goodness of fit for the line.

### Results

As shown in Table 1, of the 282 patients included in the study, 68.1% of recipients were male and 31.9% were female, whereas 52.5% of donors were male and 47.5% were female.

Tables 2 and 3 show that 5% of our patients were under 10 years of age, 27.7% were between 10 and 18 years of

age, 33.4% were between 19 and 30 years of age, 21.6% were between 31 and 40 years of age, 8.7% were between 41 and 50 years of age, and 3.6% were more than 50 years old, as shown in Table 2.

Thirty-nine percent of the donors were between 21 and 30 years of age, 33.7% were between 31 and 40 years of age, 20.9% were between 41 and 50 years of age, 4.6% were between 51 and 60 years of age, and 1.8% were more than 60 years old, as shown in Table 4.

As shown in Tables 4 and 5, 98.6% of our patients received living kidney transplants, whereas 1.4% received cadaveric kidney transplants; these were the only cadaveric transplantations performed in Egypt (Kasr Al-Aini) until then. Of the living donors, 61.9% were related, 93% of whom were first-degree relations (mother, father, sibling, children) and 7% of whom were second-degree relations (aunt, uncle, cousin, grandparent). Of the living donors 38.1% were unrelated, 7.5% of whom were spouses and 92.5% were emotionally related friends.

Table 6 shows the etiology of ESRD in adult and pediatric groups. In adult patients the most common cause of ESRD was unknown etiology (60%), followed

**Table 1 Sex distribution of recipients and donors**

Sex of recipients	N (%)	Sex of donors	N (%)
Males	192 (68.1)	Males	148 (52.5)
Females	90 (31.9)	Females	134 (47.5)

**Table 2 Age of recipients at the time of transplantation**

Age	N (%)
<10 years	14 (5.0)
10–18 years	78 (27.7)
19–30 years	94 (33.4)
31–40 years	61 (21.6)
41–50 years	25 (8.7)
>50 years	10 (3.6)

**Table 3 Age of donors at the time of transplantation**

Age	N (%)
21–30 years	110 (39.0)
31–40 years	95 (33.7)
41–50 years	59 (20.9)
51–60 years	13 (4.6)
>60 years	5 (1.8)

**Table 4 Graft source**

Graft source	N (%)
Living donors	278 (98.6)
Cadaveric donors	4 (1.4)

by obstructive uropathy (10%), glomerulonephritis (8.4%), and HTN nephrosclerosis (5.3%).

A total of 92 pediatric patients (<18 years of age) were transplanted between 1976 and 2010. The most common cause of ESRD in this age group was unknown etiology (46.7%), followed by obstructive uropathy (16.3%), glomerulonephritis (13%), and chronic pyelonephritis (7.6%).

Tables 7 and 8 show that at the time of transplantation, the mean BMI before transplantation for all patients was  $21.7 \pm 3.6$  SD. This mean BMI increased significantly after transplantation to reach  $22.6 \pm 4.0$  ( $P=0.0001$ ).

Nephrectomy was performed in 28 (9.9%) patients; of them, 24 underwent the procedure before transplantation and four after transplantation either

**Table 5 Relation between recipients and living donors**

Consanguinity	N (%)
Related donors	172 (61.9)
First-degree relatives	160 (93)
Second-degree relatives	12 (7)
Unrelated donors	106 (38.1)
Spouse	8 (7.5)
Emotionally related (friends/neighbors)	98 (92.5)

**Table 6 Causes of end-stage renal disease in adult and pediatric age groups**

Original disease in adults	N (%)	Original disease in children	N (%)
Unknown	114 (60)	Unknown	43 (46.7)
SLE	5 (2.6)	SLE	4 (4.3)
GN	16 (8.4)	GN	12 (13)
Polycystic kidney	5 (2.6)	Polycystic kidney	2 (2.2)
Obstructive uropathy	19 (10)	Obstructive uropathy	15 (16.3)
Neurogenic bladder	3 (1.6)	Neurogenic bladder	2 (2.2)
Chronic pyelonephritis	4 (2.1)	Chronic pyelonephritis	7 (7.6)
HTN nephrosclerosis	10 (5.3)	Congenital hypoplastic kidney	1 (1.1)
Amyloidosis	2 (1.05)	Alport disease	1 (1.1)
FMF	1 (0.5)	Prune belly	1 (1.1)
Failure of first transplant	2 (1.05)	Cystinosis	1 (1.1)
RTA	1 (0.5)	Chronic interstitial nephritis	1 (1.1)
Pre-eclampsia	5 (2.6)	Posterior urethral valve	2 (2.2)
Reflux	2 (1.05)	Reflux	2 (2.2)
NSAIDs	1 (0.5)		

FMF, familial Mediterranean fever; GN, glomerulonephritis; HTN, hypertensive; RTA, renal tubular acidosis; SLE, systemic lupus erythematosus.

due to persistent urinary tract infection or after failure of the first transplant.

Pre-emptive transplantation was carried out only in 5% of patients, whereas the majority of the patients were on hemodialysis, as shown in Table 9.

In the patients treated with dialysis (95%) the median length of time from initiation of dialysis to transplantation was between 2 and 84 months; 89.6% of them underwent hemodialysis for less than 5 years, whereas 10.4% underwent hemodialysis for more than 5 years (Table 10).

Tables 11–13 show that 16.6% of the recipients were anti-HCV antibody positive but their PCR for HCV was negative. However, 1.4% of them received allograft from an anti-HCV-positive donor, whereas the rest of the donors were seronegative for HCV.

In our study, comparison between HCV-positive and HCV-negative recipients revealed that HCV-positive patients had longer duration of dialysis and had received more blood transfusions, but this result was statistically insignificant ( $P=0.5$ ).

Among our 90 female patients, five were married, in child-bearing period, and not on contraception. Only two (40%) of them became pregnant after transplantation. They completed their full term and their babies were in good health (Table 14).

**Table 7 Body mass index before and after transplantation of recipients**

BMI	Before transplantation (mean $\pm$ SD)	After transplantation (mean $\pm$ SD)	P-value
BMI (kg/m <sup>2</sup> )	$21.7 \pm 3.6$	$22.6 \pm 4.0$	0.0001*

\*Significant.

**Table 8 Nephrectomy of recipients**

Nephrectomy	N (%)
No	254 (90.1)
Yes	28 (9.9)

**Table 9 Pretransplantation treatment modality and duration of dialysis in recipients**

Modality of treatment	N (%)
On dialysis	268 (95.0)
Pre-emptive	14 (5.0)

**Table 10 Duration of dialysis in recipients**

Duration of dialysis (268 patients)	N (%)
<5 years	240 (89.6)
>5 years	28 (10.4)

**Table 11 Hepatitis C virus antibodies of the recipients and donors**

Variables	N (%)
Recipients	
Positive	47 (16.6)
Negative	235 (83.4)
Donors	
Positive	4 (1.4)
Negative	278 (98.6)

**Table 12 Hepatitis C and duration of dialysis for patients on heart disease**

Variables	Negative HCV (mean±SD) (N=235)	Positive HCV (mean±SD) (N=47)	P-value
Duration of dialysis (years)	1.7±1.7	1.9±1.5	0.5

HCV, hepatitis C virus.

**Table 13 Hepatitis C and blood transfusion before transplantation of recipients**

Variables	HCV negative (235 patients) [N (%)]	HCV positive (47 patients) [N (%)]	P-value
Blood transfusion			
Negative	72 (30.6)	11 (23.4)	0.6
Positive	163 (69.4)	36 (76.6)	

HCV, hepatitis C virus.

**Table 14 Pregnancy after transplantation in female recipients**

Pregnancy after transplantation	N (%)
Nonpregnant	3 (60)
Pregnant	2 (40)

As shown in Tables 15 and 16 HTN is the most common disease among all patients; 82.2% of our patients were already HTN before transplantation. This proportion reached 87.9% after transplantation. Another 1.8% of the patients had early post-transplant hyperglycemia due to steroids; this was managed by lowering the prednisolone dose and insulin therapy, and 1.6% of the patients developed ischemic heart disease after transplantation.

Thirty of our recipients experienced early graft dysfunction due to the following reasons: acute rejection (15.6%), acute tubular necrosis (13.5%), and hyperacute rejection (1.1%). Of these patients 2.1% underwent early post-transplant dialysis, whereas 13.1% developed chronic allograft dysfunction. Patients who developed rejection received intravenous methyl prednisolone, following which 28.6% of the cases were completely reversed, 48.8% of the cases were partially reversed, and 22.6% of the cases ended in graft failure and are on hemodialysis.

**Table 15 Comorbidities in recipients before and after transplantation**

Variables	N (%)	Variables	N (%)
HTN before RTx		HTN after RTx	
Negative	50 (17.8)	Negative	34 (12.1)
Positive	232 (82.2)	Positive	248 (87.9)
DM before RTx		DM after RTx	
Negative	278 (98.5)	Negative	273 (96.7)
Positive	4 (1.5)	Positive	9 (3.3)
IHD before RTx		IHD after RTx	
Negative	281 (99.6)	Negative	277 (98.2)
Positive	1 (0.4)	Positive	5 (1.8)

DM, diabetes mellitus; HTN, hypertensive; IHD, ischemic heart disease; RTx, renal transplantation.

Proteinuria was discovered in 17.8% of the patients after transplantation during the follow-up by urine analysis.

Complications other than uremia included the following: 18.8% of the recipients had infection, of whom 32.1% were infected with cytomegalovirus and 67.9% were infected with other bacterial and fungal infections; 5.7% of our patients had bone problems; 8.6% had teeth problems, mainly gum hyperplasia; 1.4% had neurological problems, mainly epilepsy; 0.8% had malignancy, wherein one patient had colon cancer and the other had lymphoma; and finally 0.4% of our patients had liver cell failure.

Before 2003, almost all the patients were on cyclosporine (CsA), prednisolone, and azathioprine (AZA) regimen, but after 2003 the proportion of patients who received mycophenolate mofetil increased, as shown in Table 17.

Gross mortality represented 20.2% of patients in the last 30 years.

Mortality in pediatric transplant patients younger than 10 years was 0%, and mortality in pediatric transplant patients older than 10 years was 3.7%, as shown in Tables 18 and 19.

## Discussion

The concept of transplantation attracted the attention of ancient Egyptians. The Great Sphinx, which has been standing for 50 centuries, is a symbol of a human head transplanted onto a lion's body. The Egyptians never gave up the dream until the transplantation practice became a reality.

October 1976 was a memorable date in Cairo University: the first renal transplantation was performed in Kasr El-Aini Hospital. Just 7 months earlier, the first renal transplantation in Egypt was carried out in Mansoura [3].

**Table 16 Post-transplant complications in recipients**

Variables	N (%)	Variables	N (%)
Infection		Teeth and gum	
Negative	299 (81.2)	Negative	259 (91.4)
Positive	53 (18.8)	Positive	23 (8.6)
CMV	17 (32.1)		
Others	36 (67.9)		
Bony complications		Hyperacute rejection	
Negative	266 (94.3)	Negative	279 (98.9)
Positive	16 (5.7)	Positive	3 (1.1)
Neurological		Acute rejection	
Negative	278 (98.6)	Negative	238 (84.8)
Positive	4 (1.4)	Positive	44 (15.6)
LCF		Chronic rejection	
Negative	281 (99.6)	Negative	245 (86.9)
Positive	1 (0.4)	Positive	37 (13.5)
Malignancy		ATN	
Negative	280 (99.2)	Negative	244 (86.5)
Positive	2 (0.8)	Positive	38 (13.3)
Proteinuria		Early post-RTx dialysis	
Negative	232 (82.2)	Negative	267 (97.8)
Positive	50 (17.8)	Positive	6 (2.2)

ATN, acute tubular necrosis; CMV, cytomegalovirus; DM, diabetes mellitus; LCF, liver cell failure; RTx, renal transplantation.

**Table 17 Immunosuppressive treatment protocols**

Protocol of treatment	N (%)
Steroid and azathioprine and cyclosporine	120 (42.6)
Steroid and azathioprine	2 (0.7)
Steroid and MMF and cyclosporine	160 (56.7)

MMF, mycophenolate mofetil.

**Table 18 Gross mortality**

Mortality	N (%)
No	224 (79.8)
Yes	58 (20.2)

In our study, we retrospectively analyzed renal transplants in King Fahd Unit. Our aim was to identify the epidemiology of renal transplantation in Cairo University hospitals.

The majority of our recipients were male (86.1%) and in their second and third decades of life. The majority of donors were also male (52.5%) and in their second and third decades of life.

Living-donor procedures were performed in 98.6% patients compared with only 1.4% cadaveric kidney procedures. These are the only cadaveric transplants carried out in Egypt until now. The program could have suffered a setback by the unfortunate fact that the organs were procured from criminals. They were executed in Alexandria, intubated immediately after hanging, ventilated, and transferred by ambulance to Cairo (Kasr El-Aini), where a surgical team transplanted two livers and four kidneys in 1992. This provoked an

**Table 19 Mortality in pediatric transplantation in children more than 10 years old**

Variables	N (%)
No	52 (96.3)
Yes	2 (3.7)

intense ethical reaction in the media, leading to the abandonment of deceased donor transplantations [3].

Among living-donor transplantations, 172 (61.9%) were related donors [160 donors were first-degree relations (mother, father, sibling, children); 12 donors were second-degree relations (aunt, uncle, cousin, grandparent)] and 106 (38.1%) were unrelated (eight were spouses and 98 were emotionally related friends).

In our patients the most common cause of ESRD was unknown etiology (60%), followed by obstructive uropathy (10%), glomerulonephritis (8.4%), and HTN nephrosclerosis (5.3%). The large percentage of unknown etiology in our cases might be because most of our patients presented late.

Kidney transplant numbers in the USA have not changed in a decade. Since 2004, the total number of candidates on the waiting list has increased annually. The discard rate of deceased donor kidneys has also increased, and the annual number of living-donor transplants has decreased [4].

There is wide variation in the use of living and deceased kidney donors around the world. These differences

reflect varying medical and societal cultural values. Differences can also be driven by the availability of deceased donor organs relative to the number of patients waiting for transplants [5].

Regarding patients' characteristics in our study, pre-emptive transplantation was performed in 5%, whereas the majority of patients (95%) were on heart disease for variable periods ranging between 2 and 84 months before they underwent transplantation. Regarding pregnancy in our cases, among our 90 female patients, only five were married, in child-bearing period, and not on contraception. Only two (40%) of them became pregnant after transplantation. It can be concluded that successful pregnancy is possible after transplantation with acceptable maternal risk and fetal outcome.

Pre-emptive kidney transplant is considered the preferred treatment for end-stage kidney disease, but only about 20% of kidney transplants are performed pre-emptively in the USA [6].

In the Mansoura experience, pre-emptive transplantation was carried out in 13% of patients and 49 pregnancies occurred in 92 recipients [7].

In our study, 16.6% of recipients were HCV antibody positive PCR negative; 1.4% of them received allograft from an HCV-positive donor. Moreover in our study, HCV-positive patients had longer mean duration of dialysis ( $1.9 \pm 1.5$ ), whereas in HCV-negative patients the mean duration of dialysis was  $1.7 \pm 1.7$ . We found that HCV patients had received more blood transfusions.

HCV infection should not be considered a contraindication for kidney transplantation because patient survival is better with transplantation than with dialysis [8].

These figures are matched with the Mansoura experience; it was reported that HCV-positive patients had longer duration on dialysis, had received more blood transfusions, and had frequent pretransplant liver diseases [7].

Different immunosuppressive protocols were used by our patients. Before 2003, almost all the patients were on CsA, prednisolone, and AZA regimen. After 2003, the proportion of patients who received mycophenolate mofetil increased. The dose of each of these maintenance immunosuppression medications was correlated with age and with body weight.

Induction with ATG was applied in six cases only, whereas plasmapheresis before transplantation was carried out in 12 cases.

Regarding complications encountered after transplantation in our current study, HTN was found to be the most common disease among all patients, followed by diabetes mellitus and cardiac disease.

Patients who developed rejection received intravenous methyl prednisolone. As a result, 28.6% of cases were completely reversed, 48.8% of cases were partially reversed and have renal impairment, and 22.6% ended in graft failure and are on hemodialysis.

Another 5.7% of the patients had bone problems. Osteoporosis remains a frequent and serious complication in transplant recipients. The risk factors for bone loss among transplanted patients included pre-treatment renal osteodystrophy, persistent hyperparathyroidism, and the use of immunosuppressive drugs.

Avascular bone necrosis of the femoral head in renal allograft recipients is a disabling problem.

In the Mansoura experience, 171 patients developed postoperative HTN. Post-transplant DM was diagnosed in 18% of their cases. Graft survival was comparable in the post transplant diabetes mellitus (PTDM) group and their controls, whereas patient survival was markedly inferior in the PTDM group and cardiovascular events were the leading cause of mortality.

A total of 164 patients had infection and 126 had hepatic problems. Overall, 53% of cases did not experience any episode of acute rejection. The condition at last follow-up revealed that 61% were living and enjoying normal graft function. Postoperative mortality occurred in 1.7% of the study cases. Osteoporosis remains a frequent and serious complication affecting transplant recipients. The study showed that early bone loss occurring during the first 12 months after transplantation could be prevented by the use of alfacalcidol. The study reported 52 malignancies in 50 patients. The commonly encountered malignancies in their recipients included Kaposi's sarcoma (48%), lymphoma (11%), breast cancer (11%), and bladder cancer (8%). The incidence of malignancy is higher among CsA-treated recipients in comparison with the AZA-based therapy group. The malignant group suffered from high incidence of both acute and chronic rejection episodes [7].

The most recent US data show that infectious complications cause 20.9% of kidney transplant recipient deaths even with a functioning allograft. Nonmelanoma skin cancers are the most common malignancies seen in the organ transplant population, and the incidence of these cancers is three to five times that of the general population. Although both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) occur, SCC tends to occur more frequently in transplant recipients, as compared with a predominance of BCC in the general population. Both SCC and BCC occur at a younger age when compared with that in the general population [9].

There is evidence that acute rejection can influence the long-term outcome of renal transplantation. Graft half-life is longer in patients who never experienced acute rejection. However, the long-term impact of rejection on graft function is related more to its characteristics than to its occurrence. Long-term graft survival is better in patients who have had only a single episode of rejection than in patients with two or more episodes of rejection [10].

With reference to pediatric transplantation, our experience at King Fahd Unit included 92 transplanted children between 1976 and 2010, of whom 58 underwent the procedure between 2005 and 2010. The most common cause of ESRD in the pediatric age group was also due to unknown etiology (46.7%), followed by obstructive uropathy (16.3%), glomerulonephritis (13%), and chronic pyelonephritis (7.6%).

The graft survival rates at 1 year and 3 years were 95.5 and 94.1%, respectively, whereas the gross mortality was 3.7% between 2005 and 2010.

The Mansoura experience included 164 transplanted children with a mean age of 13.1 years. The common causes of end-stage renal failure in this age group were

renal dysplasia, nephrotic syndrome, hereditary nephritis, and obstructive uropathy.

The graft survival rates at 1 year and 5 years were 92.5 and 71%, respectively, whereas the corresponding patient survival rates were 96 and 83.7% [3].

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## Conclusion

The majority of our recipients were male and in their second and third decades of life. Moreover, the majority of donors were also male and in their second and third decades of life. Most of our transplants are living-donor procedures. The most common etiology of ESRD is unknown cause.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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