

# Epidemiologic characteristics and outcomes of renal transplantation in hospitals affiliated to Kermanshah University of Medical Sciences, Kermanshah, Iran: 1989-2015

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## Abstract

**Background and Objective:** Renal transplantation outcomes are affected by variables including age and gender of recipient and donor, tissue matching, background conditions, health status before transplantation, comorbidities of recipients, surgeon's experience and expertise, and nature and extensiveness of immunosuppressive therapy. The objective of this study was to investigate the effective factors and outcomes of renal transplantation in patients who received this therapy in Kermanshah University affiliated hospitals from 1989 to 2015.

**Methods:** This multi-center study included medical records of all patients who received renal transplantation during the study period. The data were analyzed using SPSS software (ver. 19.0). Central and dispersion indices were used to express continuous variables. The categorical data were reported using frequency and percentage. The chi-squared test and independent t test were used to analyze data.

**Results:** The most common cause of chronic kidney disease was glomerulonephritis (42.1%). About 0.2% was due to Sport Supplemental Products. The highest number of kidney rejection was documented in the first 6 months after transplantation (10.06%). There was no significant difference between age groups ( $P= 0.15$ ) and gender ( $P= 0.12$ ) regarding survival of the recipients.

**Conclusion:** Despite improvement regarding irreversible transplanted kidney rejection compared to previous studies in the studied centers, the outcomes in particular at the first 6-month period is not satisfactory. Also, mortality rate was higher in comparison to other reports.

**Key words:** Epidemiology; renal transplantation; chronic kidney disease

## Introduction

End-stage renal disease (ESRD) is the most severe form of chronic kidney disease (CKD). ESRD is defined as irreversible decline in renal function (1).

Diabetes mellitus, hypertension and chronic glomerular diseases are common causes of ESRD (2). The incidence of this disease is different in different parts of the world, but in general its incidence has been reported to be more than 200 cases per million people a year (3). In the United States, the unadjusted prevalence of CKD with stages of 1 to 5 (except ESRD) between 2011 and 2014 has been reported as 14.8%. Stage 3 CKD had the highest prevalence. The United States Renal Data System (USRDS) shows that 117,162 patients had ESRD at the end of 2013. The prevalence of ESRD is 363 persons per 1 million subjects. This increased to 120,688 persons (1.1% increase) in 2014. Also, the overall population of ESRD patients (678,383 subjects) at the end of 2014 (3.5% higher than 2013) is the result of a reduction in mortality among these patients (4). In Europe, the average incidence of ESRD is 171 patients per 1 million persons (2), and in England it is 100 persons per million (5). At present, more than one million and nine hundred patients are affected by ESRD globally (6). According to a previous study from 1997 to 2006, a 130% growth in ESRD rate has been observed in Iran, which poses a need for more attention to this condition (7). According to available statistics, just in 2008, there were more than 24,000 new cases of ESRD in Iran and this is growing (8).

Treatment options for CKD patients include hemodialysis, peritoneal dialysis, and kidney transplantation (9, 10). The first organ transplantation was performed in Germany in 1954 from a living relative donor, and the first renal transplantation was performed in Iran in 1967 in Shiraz (9). Currently, the rate of kidney transplantation in Iran is 24 transplants per 1 million persons (11). Despite the growth in the number of deceased donors in the United States since 2003, reaching 8,021 donors in 2013, the kidney transplant waiting list in December faced a 3% increase compared to the preceding year (4). Despite the widespread use of kidney transplantation in the treatment of advanced renal disease in Western countries over the past 30 years, Asian countries are still at the beginning of the path due to cultural and religious conditions (12). While over the past few years, the number of transplantations including non-relative living donors has increased in comparison with relative and deceased donors (13), at the end of 2014, the number of patients awaiting kidney transplantation in the United States was 88,231 cases, of whom 83% were on the transplant list for the first time. The statistics also indicate that mortality rate in patients with ESRD (dialysis, kidney transplant) has been declining in recent years, with a net decline of 30% (28% dialysis, 40% kidney transplantation) from 1996 to 2013. However, with more than 18,000 kidney transplants performed in 2014, the active waiting list for transplantation is 2.8 times higher than kidney donors (4). However, various studies indicate that the population of patients who require dialysis

due to unsuccessful kidney transplants is increasing (14, 15). Despite the progression in renal transplantation procedures, which has had a significant effect on the reduction of acute kidney rejection, its effect on the long-term survival of transplanted kidney has been disappointing (16, 17). Late failure of this treatment is still a major clinical problem (16).

Renal transplantation outcome is affected by several factors including gender, age, donor and recipient tissue matching, primary disease, general health status of recipients before surgery, comorbid conditions, experience and expertise of the surgeon, and nature and extensiveness of immunosuppressive therapies. Understanding the factors that affect the quality of renal transplantation and its outcomes such as increasing life expectancy and reducing complications and the number of hospital admissions and costs imposed on the health system is of paramount importance. The aim of this study was to investigate the effective factors and outcomes of renal transplantation in hospitals affiliated to our medical university from 1989 to 2015.

## Materials and Methods

This multi center historical cohort study was performed on medical records of all renal transplantation recipients (1,571 patients). These patients had received renal transplantation from 1989 to 2015 at Imam Reza and Chaharom Shahid Mehrab hospitals.

The exact time of the transplant was considered as the initial event and irreversible rejection during surgery, during the first 6-month period postoperatively, and one year later which resulted in requirement for dialysis treatment or death of the recipient were regarded as the end point. Also survival time of the patients from surgery time to the last follow-up time in this study was determined.

Data were collected using meticulous review of the medical records at the above mentioned hospitals, records at nephrology clinics and in case of defective data by directly calling the recipients. The gathered data were age, gender, blood type, transplanted kidney status, residential place of recipient, background disease leading to ESRD, the number of renal transplantations, kidney rejection, and survival.

### Statistical analyses

The collected data were analyzed using SPSS software (ver. 19.0). Data collected using SPSS version 19 software was analyzed. Central and dispersion indices were used to express continuous variables. The categorical data were reported using frequency and percentage. The chi-squared test and independent t test were used to analyze data. A P value of less than 0.05 was considered significant.

## Results

In this study, 1,571 medical records with census method who had received kidney transplantation from 1989 to 2015 were included. About 61.9% of the sample were residents of Kermanshah province, 35.1% were residents of other provinces, and 3% were residents of Iraq. There were 829 males and 742 females. Of these, 823 patients were younger than 35 years of age and 748 were older than 35 years. Mean (SD) age of the sample was 36.1 (12.4) years. About 66.9% (1,051 patients) had left-sided renal transplantation. Diabetes mellitus and hypertension were respectively documented in 209 patients (13.30%) and 378 patients (24.06%). Forty-three patients (2.74%) had received renal transplantation for the second time. No statistically significant association existed between gender and second renal transplantation ( $P=0.056$ ). However, a significant association was observed between age group and the requirement for repeated renal transplantation ( $P=0.007$ ). The repeated renal transplantation was more common in age group younger than 35 years. Also, no significant association was seen between repeated renal transplantation and survival ( $P=0.37$ ).

**Table 1: Frequency distribution of kidney transplantation recipients based on the studied variables**

|                                       |             | No. (%)       | P value |
|---------------------------------------|-------------|---------------|---------|
| Gender                                | Male        | 829 (52.8%)   | 0.459   |
|                                       | Female      | 742 (47.2%)   |         |
| Age                                   | < 35 years  | 823 (52.39%)  | 0.342   |
|                                       | > 35 years  | 748 (47.61%)  |         |
| Side of transplant                    | Right       | 520 (33.09%)  | 0.028   |
|                                       | Left        | 1051 (66.90%) |         |
| Diabetes mellitus                     | Yes         | 209 (13.30%)  | 0.001   |
|                                       | No          | 1362 (86.7%)  |         |
| Hypertension                          | Yes         | 378 (24.06%)  | 0.012   |
|                                       | No          | 1193 (75.94%) |         |
| Number of transplants                 | First time  | 1528 (97.26%) | 0.001   |
|                                       | Second time | 43 (2.74%)    |         |
| Nephrectomy before hospital discharge | Yes         | 60 (3.82%)    | 0.001   |
|                                       | No          | 1511 (96.18%) |         |

**Table 2: Frequency distribution of surviving and patients who died based on gender and age group in 1571 recipients of kidney transplantation in Kermanshah province from 1989 to 2015**

|           |            | Survived |        | Died |        | P value |
|-----------|------------|----------|--------|------|--------|---------|
|           |            | No.      | %      | No.  | %      |         |
| Gender    | Female     | 536      | 72.2%  | 206  | 27.8%  | 0.12    |
|           | Male       | 627      | 75.6%  | 202  | 24.4%  |         |
| Age group | > 35 years | 551      | 73.66% | 197  | 26.34% | 0.15    |
|           | < 35 years | 612      | 74.36% | 211  | 25.64% |         |

Sixty patients (3.82%) required nephrectomy (transplanted kidney) before hospital discharge. About 85.04% of the patients (1,336 subjects) had satisfactory renal function without pharmacologic interventions. No significant association was observed between gender and transplanted kidney function ( $P=0.2$ ). On the other hand, a significant association was observed between age group and transplanted kidney function ( $P<0.001$ ). Rejection was more common in those younger than 35 years.

About 74.36% of the patients were younger than 35 years. About 74.02% of the patients survived. After 1 year, 94.3% of the patients survived and after 5 years, 84.5% survived. There was no significant difference regarding gender and mortality ( $P=0.12$ ). Likewise, no significant association was found between age group and survival ( $P=0.15$ ) and between kidney function and survival ( $P=0.68$ ).

Table 3 (next page) shows the frequency of etiologies of ESRD. As observed, the most frequent cause was glomerulonephritis (42.1%). The cumulative incidence rate of irreversible rejection of the transplanted kidney during surgery, during hospitalization after surgery, the first six-month post-operatively, the whole 6-month period after surgery, the second 6-month period after discharge and the first 1 year period was respectively 0.45%, 3.37%, 6.24%, 10.06%, 2.35%, and 12.41% (Table 4).

**Table 3: Frequency distribution of the etiology of chronic kidney disease in recipients of kidney transplantation in Kermanshah province**

| Etiology                  | Absolute frequency | Relative frequency |
|---------------------------|--------------------|--------------------|
| Glomerulonephritis        | 661                | 42.1               |
| Hypertension              | 378                | 24.1               |
| Diabetes mellitus         | 209                | 13.3               |
| Nephrotic syndrome        | 120                | 7.6                |
| Polycystic kidney disease | 114                | 7.3                |
| Nephrolithiasis           | 65                 | 4.1                |
| Urologic conditions       | 19                 | 1.2                |
| Supplemental products     | 3                  | 0.2                |
| Hemolytic anemia          | 1                  | 0.1                |
| Kidney trauma             | 1                  | 0.1                |
| Total                     | 1571               | 100                |

**Table 4: Frequency distribution of transplanted kidney rejection among 1571 kidney recipients**

| Time of rejection                         | Absolute frequency | Relative frequency |
|---|--------------------|--------------------|
| During surgery                            | 7                  | 0.45               |
| During hospitalization after surgery      | 53                 | 3.37               |
| The first 6 months after discharge        | 98                 | 6.24               |
| Whole 6 months after surgery              | 158                | 10.06              |
| The second 6 month period after discharge | 37                 | 2.35               |
| The whole one year                        | 195                | 12.41              |

## Discussion

With the application of modern surgical techniques and the use of new immunosuppressive therapies, renal transplant rejection rates have significantly decreased compared with the past. The cumulative incidence rate of irreversible rejection of the transplanted kidney during surgery, during hospitalization after surgery, the first six-month post-operatively, the whole 6-month period after surgery, the second 6-month period after discharge and the first 1 year period was respectively 0.45%, 3.37%, 6.24%, 10.06%, 2.35%, and 12.41%. In McCaughan et al's study in Northern Ireland, the prevalence of acute (6 months) kidney transplantation rejection (cadaver donor) was reported as 19% (18) which is higher than what we observed here. This could be attributed to cadaver donor in the mentioned study. In comparison to a former study from Kermanshah city which reported 6-month kidney rejection as 11% and 6-month survival of 89% (19), our results indicate that the rate of acute kidney rejection is decreasing.

According to the report by the Iranian Network for Transplant Organ Procurement, the probability of kidney rejection in one year is 3.5% (one-year survival of 94.7%) (20). Compared to the current results, average kidney rejection in one year is lower than the obtained findings. In a study in Kermanshah studying survival of 712 patients (received kidney transplantation from 1979 to 2001), one-year survival in non-relative patients was 85.6% (irreversible kidney rejection of 14.4%) (21). Another study which

addressed five-year survival rate of kidney transplantation in Kermanshah from 2001 to 2012, one-year survival of transplanted kidney was 87.4% and irreversible kidney rejection was 12.6% (19). Our results show that one-year survival of transplanted kidney has improved.

In a study by El-Husseini et al in Egypt, one-year survival of kidney recipients was 93% and irreversible rejection was 7% (22). In some studies, this rate has been reported as 1.7% (23), which indicates that one-year survival is higher than our study results. The observed differences in various studies may be due to different reasons such as the lack of coincidence of the studies, differences in experience of kidney transplantation centers, surgical procedures, post-operative care, and the process of selecting kidney donors.

Although long-term survival of patients after kidney transplantation is still lower than the general population, mortality rates are significantly lower than that of dialysis patients. The results of the studies show that, over the past three decades, the survival of patients undergoing kidney transplant has clearly increased. The analysis of the United States Renal Data System information reveals that out of a total of 50,000 dialysis patients who were on the kidney transplant list, the risk of death among kidney recipients was 68% lower than those on the waiting list. At present, the expectation of a one-year survival rate after renal transplantation is estimated at 95% and for 3-5-year survival is about 90% (24).

The results of this study showed that one year after renal transplantation, 94.9% of the patients survived. Following 5 years, survival rate was 84.5%. At present, the expectation of one-year survival rate after renal transplantation is estimated at 95% and for 3-5-year expectation is 90% (24). Also, McMillan et al., in a study in an educational hospital in Glasgow, reported overall one-year, 3-year, and 5-year survival of diabetics who received kidney transplantation as 83%, 59% and 50%, respectively (25). The lower 5-year survival rate in this study compared to international figures can be due to low awareness of patients about self-care principles or non-compliance with therapeutic guidelines. This requires further investigation. The better survival rate we observed in comparison with findings by McMillan et al. could be attributed to the fact that the mentioned study included diabetic patients only and time difference between our study and that study and better therapeutic approaches in our study.

In the mid-1970s, one-year survival in patients over 35 years old was only about 60%, and in patients younger than 35 was about 80%. Age of the patients was a major contributor to post-transplantation survival. But in the 1990s, this difference became less prominent. In patients older than 35 years, one-year survival rate increased to 90%. In younger patients, this rate increased to 95% (24). The results of this study also show that survival rate did not differ between patients younger and older than 35 years ( $P=0.15$ ). This indicates that the role of age in survival of patients is becoming less important.

The most common cause of renal failure and the requirement for kidney transplantation was glomerulonephritis, followed by hypertension and diabetes mellitus. In a previous study in China, the most common causes of ESRD were glomerulonephritis, hypertension and diabetes mellitus, respectively (26). In a study from Guilan province, Iran on hemodialysis, hypertension, glomerulonephritis, and urolithiasis were reported as most common causes of CKD (27). In another study in Lorestan, Iran the most common causes of kidney failure were described as hypertension, diabetes mellitus and kidney stones, and glomerulonephritis was regarded as the fourth most common cause (28). The results of this study regarding the common causes of kidney failure are compatible with most international and domestic results. The difference in the rate of glomerulonephritis, hypertension, diabetes mellitus, and kidney stones and what was reported in neighboring Lorestan province can be related to the prevalence of high blood pressure, diet, and drinking water.

## Conclusion

Despite the decreasing rate of renal transplantation rejection, the observed rate of rejection was higher in comparison with other studies. Also, one- and five-year mortality rates that we observed were higher than international rates. Implementation of arrangements for updating surgical, therapeutic, and pharmacologic protocols as well as training self-care principles and highlighting the role of community health nurses in this field can be helpful. At the end, it is recommended that, given the increasing

prevalence of ESRD, and the high costs of managing this medical problem and high rate of hypertension and diabetes mellitus, screening procedures can diagnose these patients earlier and therefore the rate of ESRD can be reduced. Improving the collaboration of health-care teams, increasing the number of specialized diabetes and blood pressure clinics in the province of Kermanshah will be helpful in addressing early diagnosis of hypertension and diabetes mellitus. Also, the implementation of the plan for monitoring CKD patients in the early stages and training through social media, especially public media, in raising awareness about early diagnosis of diabetes and hypertension, as well as recognizing the early signs of kidney diseases, can reduce the incidence of ESRD and its consequences (dialysis and kidney transplantation) are helpful.

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