Does Hypertension Remain after Kidney Transplantation?

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Abstract- Hypertension is a common complication of kidney transplantation with the prevalence of 80%. Studies in adults have shown a high prevalence of hypertension (HTN) in the first three months of transplantation while this rate is reduced to 50- 60% at the end of the first year. HTN remains as a major risk factor for cardiovascular diseases, lower graft survival rates and poor function of transplanted kidney in adults and children. In this retrospective study, medical records of 400 kidney transplantation patients of Sina Hospital were evaluated. Patients were followed monthly for the 1st year, every two months in the 2nd year and every three months after that. In this study 244 (61%) patients were male. Mean ± SD age of recipients was 39.3 ± 13.8 years. In most patients (40.8%) the cause of end-stage renal disease (ESRD) was unknown followed by HTN (26.3%). A total of 166 (41.5%) patients had been hypertensive before transplantation and 234 (58.5%) had normal blood pressure. Among these 234 individuals, 94 (40.2%) developed post-transplantation HTN. On the other hand, among 166 pre-transplant hypertensive patients, 86 patients (56.8%) remained hypertensive after transplantation. Totally 180 (45%) patients had post-transplantation HTN and 220 patients (55%) didn't develop HTN. Based on the findings, the incidence of post-transplantation hypertension is high, and kidney transplantation does not lead to remission of hypertension. On the other hand, hypertension is one of the main causes of ESRD. Thus, early screening of hypertension can prevent kidney damage and reduce further problems in renal transplant recipients.

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Introduction

Hypertension is the most important risk factor for the development of renal failure. Hypertension is a major risk factor for atherosclerosis and increased cardiovascular morbidity and mortality, and causes half of the deaths among dialysis and transplant patients. Moreover, hypertensive transplant recipients are at an increased risk of allograft dysfunction. One of the complications of organ transplantation after transplantation is hypertension (HTN) (1).

In transplant recipients, HTN is usually defined as a blood pressure greater than 140/90 mmHg that is treated by antihypertensive drugs (2,3). A cut-off of 150/90 has been determined for blood pressure (4). We have chosen the first definition that is accepted in the general population for hypertension.

Systemic arterial HTN is a common complication of kidney transplantation, and that different studies have shown the prevalence of 80%. It remains as a major risk factor for cardiovascular diseases, lower graft survival rates and poor function of transplanted kidney in adults and children (5-8). Studies in adults have shown a high prevalence of HTN in the first three months of transplantation while this rate is reduced to 50- 60% at the end of the first year (9).

Factors commonly associated with essential HTN (age, sex, and race) have only a minor role in post-transplantation HTN and the greatest risk for HTN after transplantation is seen in patients with retained natural kidney and/or cadaveric donor. Although high blood pressure is usual in patients with well-functioning grafts, but HTN and graft dysfunction are closely associated after transplantation.

Multiple causes are identified including immunological processes, rejection and stenosis of transplanted renal artery that lead to a specific form of HTN after transplantation accounting for 5- 10 percent of cases (1). Before using immunosuppression therapy based on cyclosporine, patients' natural kidneys were

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the most important cause of HTN after transplantation. It is observed that HTN is less occurred in transplant recipients underwent bilaterally native nephrectomy (10). Currently, cyclosporine is a key factor in hypertensive patients after transplantation with well-functioning grafts (11,12). The most common etiology of HTN after renal transplantation are remaining patients' kidney, treatment with corticosteroids and calcineurin inhibitors, graft dysfunction, and obesity (13).

Before introduction of cyclosporine as a maintenance immunosuppressor in 1983, HTN after transplantation was observed in more than half of patients, but since the introduction of Calcineurin inhibitors, systemic HTN is seen in 70-90% of patients (14,15). Blood pressure control is an important part of post-transplantation medical care to protect kidneys from harmful effects of high blood pressure (16).

Corticosteroid therapy is not considered as a major cause of chronic HTN in transplant recipient, due to rapid discontinuation of dosing. However, steroids may be associated with HTN early after transplantation (in high doses) or during pulse treatment. Veenstra *et al*., estimate the incidence of corticosteroid associated HTN to be about 15 percent (17). In addition to calcineurin inhibitors and steroids, different factors before and after transplantation, predict the occurrence of HTN after renal transplantation. The main factors are listed in Table 1.

Considering the importance of HTN in patients with renal transplant, we aimed to evaluate the incidence of HTN in these patients after transplantation and assess some factors that may probably contribute to the development of HTN.

Table 1. Causes of post-transplant HTN (6)

Recipient related	Pre- existing HTN and LVH Body Mass Index Primary kidney disease (native kidneys)
Donor related	Elderly and female donor Hypertensive donor Use of right – sided donor kidneys
Transplantation related	Prolonged ischemia Delayed graft function
Immunosuppressive therapy	Calcineurin inhibitors (cyclosporine > tacrolimus) Corticosteroids
Transplant Dysfunction	Acute rejection Chronic allograft nephropathy Recurrent or denovo glomerular disease
Transplant obstruction	Ureteric stenosis Lymphocele
Renal transplant artery stenosis	--

HTN: Hypertension, LVH: Left ventricular hypertrophy??

Materials and Methods

In this retrospective study, medical records of 400 patients with kidney transplantation (September 1994 to February 2013) of Sina Hospital were evaluated.

Institutional Review Board approval was granted by the Research Ethics Committee of Tehran University of Medical Sciences.

In addition to the demographic characteristics of the patients, We also assessed patients body mass index (BMI), cause of chronic kidney disease, duration of dialysis pre-transplantation co-morbidities (HTN, Diabetes Mellitus, hyperlipidemia and coronary artery disease), rejection episodes, post-transplantation immune suppressant regimen, donor source, graft and patients' survival. Patients had been followed monthly in the 1st year, every two months in the 2nd year and every three months after that.

Statistical analysis was performed by SPSS version 19. Statistical significance was considered as *P*. value<0.05.

Results

Among 400 patients, 244 (61%) were male. The Mean age of recipients was 39.3 ± 13.8 years. Table (2) shows characteristics of participants. In most patients (40.8%) the cause of end-stage renal disease (ESRD) was unknown followed by HTN (26.3%) (Table 3). Mean ± SD duration of dialysis pre-transplantation was 19.2 ± 23.1 months. A total of 48 (12%) patients had no experience of dialysis. Overall 166 (41.5%) patients were hypertensive before transplantation and 234 (58.5%) had normal blood pressure. Among these 234

individuals, 94 (40.2%) developed post-transplantation HTN. On the other hand, among 166 pre-transplant hypertensive patients, 86 (56.8%) remained hypertensive after transplantation. Totally 180 (45%) patients had post-transplantation HTN and 220 (55%) didn't develop HTN. Mean ± SD age of kidney recipients who developed post-transplant HTN was 42.3 ± 12.7 years and the mean age of individuals with no HTN after transplantation was 36.7 ± 14.1 years (P<0.001). Mean BMI of patients was 22.7 ± 3.7 kg/m2 in patients with post-transplantation HTN and 22.3 ± 3.7 kg/m2 in patients without HTN (P=0.4). A total of 200 (50%) patients had post-transplantation hyperlipidemia.

Table 2. Characteristics of participants

Variable	*P*.Value
Age (mean ± SD)	38.9 (9-67)
Body Mass Index (kg/m^2)	22.5 (13.8- 32.4)
Pre- TX dialysis (month)	19.2 (0-130)
Previous transplantation	11 (2.8)
Donor	
Living Related	16 (4)
Living unrelated	308 (84.5)
Cadaveric	76 (11.5)
Hospitalization (day)	22.6 (7-120)

Data are presented as either mean (range) or n [%]

Table 3. Causes of ESRD among patients

	Frequency	Percent (%)
Unknown	163	40.8
Hypertension	105	26.3
Diabetes Mellitus	52	13.0
Glomerulonephritis	22	5.5
APKD*	15	3.8
Stone	11	2.8
Neurogenic Bladder	6	1.5
Lupus	6	1.5
VUR*	5	1.3
Pyelonephritis	4	1.0
UTI*	4	1.0
Pre-eclampsia	2	0.5
Alport	2	0.5
PVU*	1	0.3
IgA Nephropathy	1	0.3
Congenital	1	0.3
Total	400	100

VUR: Vesicoureteral Reflux, UTI: Urinary Tract Infection, PVU: Posterior Urethral Valves, PKD: Adult Polycystic Kidney Disease

Discussion

Post-transplantation HTN is common and affects about 50 percent of patients and may occur anytime after transplantation. HTN remains a serious problem after transplantation, and cardiovascular disease is one of the leading causes of death in renal transplant recipients (10,18).

Opelz *et al*., (19) showed a significant correlation between systolic and diastolic blood pressure one year after successful transplantation and graft survival so that in a follow-up study of more than 29,000 recipients of cadaveric kidney transplant, they found that increasing levels of systolic and diastolic blood pressure after transplantation followed by graft failure.

The severity of post-transplantation HTN is usually mild to moderate. However, some patients with critical HTN are reported. Several factors such as rejection episodes, immunosuppressive drugs, weight gain and other factors increase blood pressure after transplantation. At present, for well-functioning graft patients, cyclosporine may be the main cause high blood pressure (10,18).

In this study, overall 41.5% of patients were hypertensive before transplantation and 58.5% were normotensive. Among these normotensive individuals, 40.2% developed post-transplantation hypertension and among pretransplant hypertensive patients, 56.8% of cases remained hypertensive after transplantation. Totally 45% of individuals were hypertensive after transplantation. So the incidence of post-transplantation hypertension was 45% in the current study. Meanwhile, 40.2% of patients experienced HTN after transplantation while they were normotensive before transplantation.

Present results are in good agreement with Kasiske's (20) study. He found that 55.5% of patients had blood pressure less than 140 mmHg 1 year after transplantation.

Malek-Hosseini *et al*., (1) reported an incidence of 60% for post-transplantation HTN, and they reported 19% new onset HTN. In the current research, there was a significant difference regarding age in developing HTN after transplantation so that the pot transplant hypertensive individuals were significantly older than normotensive cases. Our results do not correspond to Malek-Hosseini *et al*., findings. They found no significant difference regarding age between post-transplant normotensive and hypertensive subjects. In a follow-up study of more than 29,000 recipients of cadaveric kidney transplant, they found that increasing levels of systolic and diastolic blood pressure after transplantation followed by graft failure has been associated with a progressive increase (P<0.0001).

In current study BMI of patients with post-transplantation, HTN did not significantly differ from patients without HTN. In study by Mistnefes *et al.*, risk factors for developing hypertension have been evaluated 3 years after renal transplantation in children and 50.8%

patients were hypertensive and statistical significance was observed for body mass index 1 year after transplantation (6).

Based on the results of the present study, the incidence of post-transplantation HTN is high, and kidney transplantation does not lead to remission of HTN. On the other hand, HTN is one of the main causes of ESRD that relatively contributes to a high proportion of cases. So early screening of HTN at younger ages can prevent from kidney damage and reduce further problems recipients of renal transplant.

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