

Impact of Renal Transplantation on Erectile Dysfunction in Chronic Renal Failure Patients in Male

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ABSTRACT

Background & aim: Testicular dysfunction is well documented in patients with chronic renal failure. Our aim was to determine the incidence of erectile dysfunction among chronic renal failure patients who have undergone renal transplant. **Methods:** A cross sectional study was conducted in 60 renal transplant patients by means of International Index of Erectile Function (IIEF-5) questionnaires. Relationship between erectile dysfunction with patient's age and serum testosterone level was studied and analyzed. **Results:** Age and serum testosterone level were significantly associated with higher incidence of erectile dysfunction. 33 patients had no improvement in erectile dysfunction after transplant. Statistically significant changes were observed in the mean levels of testosterone. **Conclusion:** Incidence of erectile dysfunction after renal transplant is quiet high. IIEF-5 is an effective means to establish and diagnose the erectile dysfunction.

Keywords: Erectile dysfunction, renal transplantation, chronic renal failure.

INTRODUCTION

Erectile dysfunction (ED) can be defined as the persistent inability of man to achieve penile erection and maintain it sufficient for satisfactory coitus. Erection is a coordinated physiological process involving both central and peripheral nervous system. Vasodilatation and relaxation of smooth muscles layer in the corpora is caused by parasympathetic impulses leading to rushing of blood into it. This causes ballooning of the erectile tissue.^[2] Approximately 50% of men with end-stage renal disease (ESRD) and uremia display erectile dysfunction (ED). An even higher percentage of these patients show decreased sexual desire and a reduced number of sexual intercourses. The origins of this dysfunction are multifactorial deriving primarily from organic failure. In addition to the elevated blood urea nitrogen (BUN), these patients suffer from peripheral neuropathy, autonomic failure, peripheral vascular disease, and side effects of therapy with diuretics, antihypertensive, and immunosuppressant. Psychological and physical stress, which are usually present, exacerbate the situation.^[3] It is well established that sexual dysfunction is rather prevalent among hemodialysis patients; some authors have shown that renal transplantation restores libido and sexual capability.^[4] However, other studies have indicated that transplantation not always has a positive impact on sexual function.^[5] Comparative studies have shown that 32.2%–50.7% of renal transplant

recipients continued to experience ED and a high rate (48.9%) is even observed among the younger transplanted population. Erectile dysfunction cannot be attributed to a single cause but rather as a result of multi system disease, psychological factors and chronic illness. End stage renal disease is one of the chronic illnesses causing erectile dysfunction by organic diseases (neuro-endocrine disturbances, uraemia, anaemia and atherosclerosis), psychogenic factors (depression, anxiety) and the medications used for the treatment of diseases associated with chronic renal failure such as antihypertensive drugs, immunosuppressant, H2 blockers etc. It is known that approximately 25% of patients on dialysis are mentally depressed at any given time contributing in the erectile dysfunction due to end stage renal disease patients on regular hemodialysis. Renal transplantation is one of the renal replacement therapies in end stage renal disease widely used nowadays. With improving therapies and procedures, the total number of renal transplants has increased. The ability of patients to regain normal quality of life following renal transplantation has significantly increased now days.^[1]

Aims & Objectives: The objective of this study is to find out the impact of successful renal transplantation on the degree and frequency of erectile dysfunction.

MATERIALS AND METHODS

This is a prospective randomized control trial. All patients of end stage renal disease on regular hemodialysis and candidates of renal transplantation of age range 20-55 years are included in the study after getting informed consent. Erectile functions are

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to be assessed by history, examination, investigations and international index of erectile function (IIEF) prior to and on 3rd and 6th months after renal transplantation.

Inclusion criteria

- Age 20 to 55 yr
- Married
- ESRD on HD for renal transplantation
- Psychologically sound

Exclusion criteria

- Age < 20 yrs, >55 yrs
- H/O neurovascular injury
- H/O trauma to sex organs
- Congenital abnormality of sex organs

Trial protocol

- Consent for the study
- Counseling for non drop out from the study
- At 1st visit: 3rd month – history, examination, serum testosterone and IIEF score
- Second visit: 6th month – history, examination, serum testosterone and IIEF score

The study was carried out of 60 patients with end stage renal disease, on regular haemodialysis and was candidates for renal transplantation. All the patients were married and having no history of neurovascular injury or trauma to sex organs. All these patients were psychologically fit using general health questionnaire and having no congenital abnormality of sex organs. Erectile functions were evaluated by history general physical examination investigations and international index of erectile function-5 during the period of hemodialysis before renal transplantation. International index of erectile function is used to determine the presence of erectile dysfunction. It gives the degree overreaction (Severe erectile dysfunction; 5–7, Moderate erectile dysfunction; 8–11, Mild erectile dysfunction; 12–16, Moderately mild erectile dysfunction; 17–21, NO erectile dysfunction; 22–25).⁵ After successful renal transplantation these patients were reassessed for erectile dysfunction at 3 and 6 months. Data was entered into computer using SPSS10.00 used for analysis. Data was described in terms of frequency and percentages in case of categorical variable and Mean±SD for continuous variables. Student's t-test was used for continuous data and Chi-square for categorical data. A level of 5% was taken as significant.

RESULTS

In this study 60 patients were included. The age range was 20–55 years with the mean age 39±7.35 years. The number of patients in the 3rd decade were 14(23.3%), 4th decade 22 (35.7%) 5th decade 20 (33.3%) and 6th decade 4 (6.7%). The observed

causes and their frequencies of ESRD are shown in [Table 1].

Table 1: Causes of ESRD

Disease	Number	Percentage
Only Hypertension	22	36.6
Only Diabetes Mellitus	20	33.3
Both Hypertension & D.M	6	10
Drugs	6	10
Glomerulonephritis	4	6.6
Calculus Disease	2	3.3

In this study 54 (90%) patients out of 60 had haemoglobin level less than 10 gm/dl and 6 (10%) patients had haemoglobin 10–12 gm/dl before renal transplantation. The mean haemoglobin was (8.48±1.13) gm/dl before renal transplantation. After 3 months, 2 (3.3%) patient had haemoglobin less than 10 gm/dl and 58 (97.7%) patients had haemoglobin in range of 10–12 gm/dl. The mean haemoglobin was 11.75±0.97 gm/dl. After 6 months of renal transplantation 24(40%) and 36 (60%) patients had 10–12 gm/dl and 13–15 gm/dl respectively. The mean haemoglobin was (12.93±0.65) gm/dl [Figure 1].

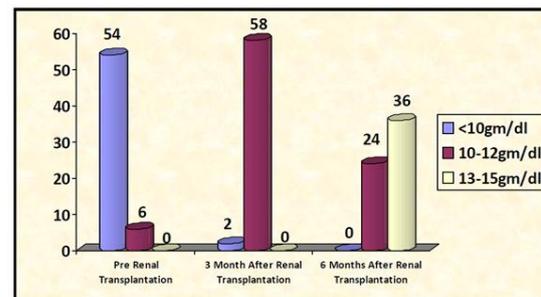


Figure 1: Serum haemoglobin level

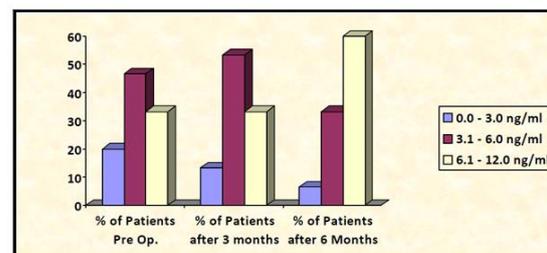


Figure 2: Serum testosterone level

In this study 12 (20%) patients had serum testosterone level in the range of 0.0–3.0 ng/ml, 28(46.6%) and 20 (33.3%) patients had serum testosterone levels ranging 3.10–6.00 ng/ml and 6.10–12 ng/ml respectively before renal transplantation. After 3 months of renal transplantation 8 (13.3%), 32 (53.3%) and 20(33.3%) patients had 3.10–6.00 ng/ml and 6.10–12 ng/ml respectively. After 6 months of renal transplantation 4 (6.6%), 20 (33.3%) and 36 (60%) patients had 3.10–6.00 ng/ml and 6.10–12 ng/ml respectively. There is no significant impact of haemoglobin level and serum testosterone on erectile

dysfunction in patients after renal transplantation.[Figure 2]

Table 2: Improvement in erectile dysfunction

		Erectile dysfunction improved	Erectile dysfunction not improved	p-value
Age (Mean age = 39 yrs)	Above mean(35)	10	25	0.023
	Below mean(25)	17	8	
Haemoglobin		22	38	0.862
Serum testosterone	Above mean	20	26	0.218
	Below mean	2	18	

The study showed that all 60 patients had erectile dysfunction with difference in severity. In prerenal transplantation period 28 (46.6%) patients had severe erectile dysfunction and 32 (53.3%) patients were having moderate erectile dysfunction. There was no patient who had mild or moderately mild erectile dysfunction in the pre renal transplantation period. After three months of renal transplantation 30 (50%) patients had severe erectile dysfunction; 12 (20%) patients had moderate erectile dysfunction; 18 (30%) patients had mild erectile dysfunction. After six months of renal transplantation 22 (36.6%) patients had severe erectile dysfunction; 20(33.3%) patients had moderate; 16(26.6%) patients had mild and 2 (3.3%) patients had moderately mild erectile dysfunction.

At 6 month follow up ED improved in 10 and 12 patients while 18 and 20 patient ED did not improved in patients above and below mean age 39 years respectively. Erectile dysfunction improved in 22 patients but not improved in 38 patients at 6 month in respect of haemoglobin. At 6 month follow up ED improved in 20 and 2 patients while 26 and 18 patients ED did not improved in patients above and below mean serum testosterone 6.33ng/ml respectively. [Table 2]

DISCUSSION

Erectile dysfunction defined by National Institute of health (NIH) consensus development conference as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance.^[4] Renal failure is a major risk for erectile dysfunction and half of patients with chronic renal failure may be impotent. The genesis is multi factorial and is primarily organic. In addition to the uraemic milieu, peripheral neuropathy, autonomic insufficiency, peripheral vascular disease and pharmacotherapy, all play an important role in the genesis of erectile dysfunction. Although laboratory based diagnostic procedures are available, it has been proposed that sexual function is best assessed in a naturalistic setting with patient self-reporting technique. The International Index of Erectile Function (IIEF) is the most widely accepted self-administered questionnaire and is statistically validated in many languages. Initial IIEF was a 15-item questionnaire which addresses and quantifies five domains: erectile function, sexual desire, orgasmic function, intercourse satisfaction and overall satisfaction.^[4,5] These questionnaires are

cumbersome and to make it more useful, 5-item questionnaire of the IIEF -15 has been developed which mainly deals with erectile function and overall satisfaction. We had also included question pertaining to ejaculatory problem because of high prevalence of ejaculatory dysfunction.

Major risk factors associated with high incidence of erectile dysfunction in our study were diabetes mellitus, older age, smoking and longer duration of dialysis. Diabetes mellitus causes erectile dysfunction through its vascular, neurologic, endothelial and psychogenic complications. Molecular mechanism responsible for erectile dysfunction were pathologic changes in cavernous arteries, ultra structural changes in cavernous smooth muscle cell and impaired endothelium dependent relaxation of corporeal smooth muscle cell. All these changes are aggravated by uremia and basically do not revert back after renal transplantation, therefore responsible for high incidence of erectile dysfunction.

Longer duration of hemodialysis was also a risk factor for erectile dysfunction. This has been attributed to permanent damage of cavernous micro and macro vessels and smooth muscle, sustained during the long course of renal failure. Early transplantation is recommended because it is more effective and less costly than hemodialysis. Maintaining erectile function should be another reason for early transplant. Another risk factor for erectile dysfunction is increasing age. All the endocrinal and micro vascular changes with aging are aggravated by renal failure.

Some of the patients in our series had cyclosporine based immunosuppression. Cyclosporine (calcineurin inhibitor) is a proven inhibitor of nitric oxide mediated smooth muscle relaxation, which is an essential factor for erection. No statistically significant difference was seen in erectile dysfunction patients and normal renal transplant patients. Similarly betablocker and central acting antihypertensive like clonidine which have been implicated in erectile dysfunction but did not reveal any significant association in this series.

Gittes and Walter reported that higher incidence of erectile dysfunction in patients who underwent bilateral renal transplantation using both internal iliac artery,^[5] explanation given for that was bilateral ligation of internal iliac artery leads to penile revascularization. Penile arteries are branches of internal iliac artery, when internal iliac artery used for end to end anastomosis with renal artery, this

leads to decrease in penile blood flow and may affect subsequent erection. In our series internal iliac artery was used in 19 cases and no significant difference for erectile dysfunction was observed in internal iliac artery and external iliac artery group respectively. Second transplantation was done in three patients and the external iliac artery was used second time and none had erectile dysfunction. It therefore appears that using unilateral internal iliac artery is not a risk factor for erectile dysfunction. 36.6% patients had moderate to severe erectile dysfunction while 26.6% had mild to moderate erectile dysfunction and this grading may help in future for decision of treatment option like psychological counseling, oral drug therapy and invasive therapy like intracavernosal injection therapy.

Presently sildenafil citrate has provided a significant improvement in the treatment with erectile dysfunction because it is effective, safe, easy to handle and causes no serious side effects. Its efficacy has been proven in renal transplant patients without significant interaction with cyclosporine /FK50615. So both nephrologists and transplant surgeon alike should be aware of the patients unexpressed problems and possible therapy. In this respect self-administered questionnaire like IIEF - 5 provides an easy and rapid way for accumulating data and could be used routinely for diagnosis and treatment evaluation.

Sexual dysfunction is common in men with chronic renal failure. In a survey of 69 men on hemodialysis, only 55% were sexually active and the predominant sexual dysfunctions were loss of or diminished sexual needs (84.7%), erectile dysfunction (44.5%), and inhibited or lack of ejaculation (51.5%) (Lew-Starowicz and Gellert, 2009).^[6] Similarly, ED was reported in 52% of men undergoing peritoneal dialysis. The presence of depressive symptoms, highly prevalent in hemodialysis patients, is an independent factor of sexual dysfunction in male hemodialysis patients. Significant improvement of sexual function has been reported after kidney transplantation. Many of the effects of uremia can potentially contribute to the development of ED including disturbance of the hypothalamic-pituitary-testis sex hormone axis, hyperprolactinemia, accelerated atheromatous disease, and psychologic factors (Ayub and Fletcher, 2000).^[7]

Evidence of autonomic neuropathy as a factor contributing to ED in men with chronic renal failure comes from studies that found a high rate of abnormality in vascular and bulbocavernous reflexes, suggesting nerve dysfunction. Neuropathy is a common complication of end-stage kidney disease (ESKD), typically presenting as a distal symmetric process with insidious onset progressing over months. Neuropathy has been estimated to occur in 60% to 100% of patients on dialysis. Nerves of uremic patients have been shown to exist in a chronically depolarized state before initiation of

dialysis, with subsequent improvement and normalization of resting membrane potential after initiation of dialysis. The degree of depolarization correlates with serum K(+), suggesting that chronic hyperkalemic depolarization plays an important role in the development of nerve dysfunction in ESKD. Investigation of cavernous vascular function in 20 men undergoing renal replacement therapy showed that 80% had both arterial insufficiency and veno-occlusive dysfunction. A link between impairment of the NO-cGMP pathway relating to failure of cavernous relaxation is provided by the finding of increased serum levels of asymmetric dimethyl arginine (ADMA) in uremic patients.⁸ Sexual function was assessed by the IIEF, which was considered by the World Health Organization to be the most important document to address efficacy in clinical studies. It has a high sensitivity and specificity to detect changes related to treatment of patients with erectile dysfunction.

In this study all patients with end stage renal disease had some degree of erectile dysfunction during regular haemodialysis before renal transplantation. Out of these 46.6% patients had severe erectile dysfunction while 54.4% had moderate erectile dysfunction. A study conducted by

In this study the major causes of end stage renal disease were diabetes mellitus, hypertension. It was observed that 36.6% patients had hypertension, 33.3% patients had diabetes mellitus and 10% patients were having both diabetes mellitus and hypertension in the same individual. Anantharaman et al has mentioned this that above 70% of end stage renal disease is caused by diabetes mellitus or hypertension.^[9] Our results are comparable with these results.

In our study it was observed that 40% patients had improved erectile functions 53.3% patients erectile functions remained static, and 6.6% patients presented with deteriorated erectile functions after renal transplantation for end stage renal disease. Study performed by Akbari et al showed that erectile functions improved in 32.5% disappeared in 20%, static in 42.5% and worsened in 5%.^[10] In another study done by Bahanswayet al showed that erectile functions improved in 43.5%, deteriorated in 12.5% and remained static in 44% of patients after successful renal transplantation.^[11] The study of Burgos PJ et al showed that the presence of erectile dysfunction in pre transplant stage of end stage renal disease and during haemodialysis was 92% and 50% of the patients after renal transplantation.^[12] There is no significant difference between the international studies and observed results.

The impact of age, haemoglobin and serum testosterone observed in the study at 6 months showing that age has significant negative correlation in the improvement of ED while Hb and serum testosterone has no positive impact on the erectile dysfunction. The same was observed by

Bahnsawy et al and Burgos et al.^[11,12] There may have been a bias regarding the ED evaluation, probably caused by sociocultural issues, since it's quite common in our environment for men to try to affirm their manhood by overestimating their sexual health. Another factor that may help to explain these results is the relatively lower mean age among the ESRD (32.7 years) compared with the transplant group (36.7 years); age itself is one of the most important isolated risk factors for ED. This may also explain our positive results of kidney transplantation as whole when compared with the literature, wherein the mean age of included subjects was up to 50 years in our review. From the 5 components on the IIEF, 3 showed significant differences: orgasmic function, sexual desire, and intercourse satisfaction. The group of patients undergoing hemodialysis showed a greater prevalence of decreased sexual desire than the control group ($P < .001$). The decreased libido may have organic or psychological causes. The main cause is organic hypogonadism in its several variants. Another important question is hyperprolactinemic that in principle has organic causes, but may be due to psychological stress.^[13,14] Although sexual dysfunction is a benign disorder, it may have an important impact on the quality of life of many men and their partners. It can adversely affect self-esteem, quality of life, and interpersonal relationships.^[15] Most kidney transplants are performed in middle-aged men whose sexual function and fertility are still of great importance.^[16] Further studies are required to achieve a better comprehension of the matter.

CONCLUSION

Erectile dysfunction is present in almost all patients' of chronic renal failure. There is significant improvement in erectile functions of the patients with end stage renal disease treated by renal transplantation. Erectile dysfunction is an extremely common problem in hemodialysis patients and has a major negative effect on the quality of life in these patients. Also, many patients with ED will not seek treatment themselves. Thus, respecting the development of effective oral therapies for ED, discussions about this problem should be a part of the routine management of the patients on hemodialysis. Prevalence of erectile dysfunction before renal transplant is quite high and most of these problems are never discussed with the patients during routine evaluation. IIEF-5 is an effective means to establish and diagnose the erectile dysfunction. Advance age, prolonged dialysis, diabetes mellitus and smoking were important risk factors for erectile dysfunction. Finally, ED improvement seems to be higher when the kidney transplantation is performed at lower ages.

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