

# Impact of Renal Transplantation on Anxiety-Depression and Quality of Life in Patients with End Stage Renal Disease on Dialysis

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## RESEARCH

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### ABSTRACT

**Background and objectives:** Chronic Kidney Disease is a significant health problem and little is known beyond traditional outcome measures. This study explores outcomes of renal transplantation in patients with End Stage Renal Disease (ESRD) on dialyses in terms of self-reported 'Quality of Life (QOL)' and further explores determinants of psychosocial aspects of health in terms of depression and anxiety. **Methods:** Consecutive patients from Jan 2011 till Mar 2012 with ESRD on dialyses were asked to self-assess QOL and case-ness for anxiety and

depression with World Health Organisation Quality of Life - BREF (WHOQOL-BREF) and Hospital Anxiety and Depression Scale (HADS) questionnaire respectively; 2 days before and 6 months after transplant. Data was also collected about duration of dialyses prior to transplant, clinical success of transplant, education level, marital status, employment status, insurance status, residence and relationship of donor with the recipient. **Results:** 50 patients with successful transplant were included. 6 (12%) and 13 (26%) patients had HADS anxiety and depression subscale scores respectively above the threshold defining case-ness preoperatively and this decreased to 2 (4%) and 3 (6%) patients respectively 6 months later. Scores increased significantly across all four domains of WHOQOL-BREF postoperatively. Depression predicted poor outcomes on 'physical health' and 'environment' domain while anxiety predicted a poor outcome in 'social relationship' domain of QOL. Employment and insurance status predicted outcomes in 'environment' domain of QOL even while adjusting for presence of depression and anxiety. **Interpretation and conclusions:** Anxiety and depression are significant contributors to QOL reported by patients with ESRD. While successful transplant ameliorates most such mood depression disorders yet employment and insurance status play a significant role in the ultimate improvement of QOL experienced.



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**Key Words:** Kidney transplantation; quality of life; renal insufficiency; anxiety; depression.

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## INTRODUCTION

Chronic kidney disease (CKD) is a significant public health problem whose reliable estimates in Indian population are difficult to derive. The only population based study from Bhopal estimated age adjusted incidence of End Stage Renal Disease (ESRD); and not CKD; to be 229 patients per million populations [1]. There is a worrying trend where economically backward regions of the world have to bear increasing share of ESRD global burden. There is evidence of a very strong correlation (Pearson's  $r = 0.94$ ) between the use of Renal Replacement Therapy (RRT) and regional income, and a wide gap between disease burden and treatment utilisation [2]. With advances in medicine, as 'traditional treatment outcomes' improve, the nephrology and transplant community worldwide are inclining to the concept of 'patient reported outcome measures' such as 'quality of life'. Determinants of psychosocial aspects of patient's health such as depression, anxiety, worrying, fear, hopelessness and experience of psychological and physical trauma through treatment are also increasingly being explored [3]. Evidence is also accumulating where such psychosocial determinants have been found to have a correlation with morbidity as well as important aspects such as treatment compliance [4,5]. Moreover recently physical Health Related Quality of Life (HRQOL) has been found to predict long term mortality and graft failure independent of socio-demographic and clinical risk factors [6]. Though Indian physician community is warming up to these concepts yet data from Indian subcontinent is few, and more efforts in this direction should be encouraged as evidence exists of ethnic and socio-economic variations in such measures allowing cautious applicability of western literature to Indian population [7-9].

All India Institute of Medical Sciences is a premier research medical institution in Delhi with renal transplant program operational for 30 years carrying out regular transplants in the Department of Surgical Disciplines. This

study was undertaken prospectively to assess the impact of renal transplantation on measures of anxiety, depression and quality of life in patients (with ESRD undergoing haemodialysis prior to transplant) before and six months after live related renal transplantation.

## MATERIAL AND METHODS

### Subjects

After obtaining institutional review board and university approval (work awarded as theses to one of the authors and all patients providing written informed consent) consecutive adult patients with ESRD undergoing haemodialysis and about to undergo live related renal transplant were prospectively enrolled over 1 year from Jan 2011 to Mar 2012 with further follow up for six months. Patients unwilling for 6 months follow up, undergoing prior treatment for anxiety or depression, and those undergoing second transplant were excluded. Apart from demographic information, data was also collected about education level, marital status, employment status, insurance status, residence (rural, urban, semi urban), and relationship of donor with the recipient. Duration of dialyses prior to transplant was also recorded. Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS) and quality of life was assessed with World Health Organisation Quality of Life - BREF (WHOQOL-BREF) questionnaire. Questionnaires were self-administered in a quiet room ensuring privacy two days before and again 6 months after transplant. Illiterate patients were provided help of a doctor in explaining a validated translation of the questionnaire in their native language.

### Instruments

#### Hospital Anxiety and Depression Scale (HADS)

It is self-assessment scale which has been widely used across diverse spectrum of physical comorbid clinical conditions to screen for anxiety and depression. Scores on anxiety and depressive subscales have been found to correlate with the severity of the underlying disorder [10]. It consists of 14 questions with 7 each relating to anxiety and depression administered separated in even and odd number

order. Each item on the questionnaire is scored from 0-3 and thus an ordinal score from 0-21 is assigned each for anxiety and depression. Rather than being diagnostic, the scale demonstrates the likelihood of a person developing these disorders. A score of 11 or higher specific to a domain was considered as significant case-ness while a score from 8-10 was considered to imply mood disturbances. 7 or lower score was considered within normal range. Originally in English, permission to use an Indian English and Hindi version of the same was obtained from the copyright holders of the instrument and the trust distributing its translated version [11,12]. Cross cultural validation in Indian population has been reported previously [13,14]. All patients with clinical case-ness were counselled to seek expert psychiatric attention.

### **World Health Organisation Quality of Life - BREF questionnaire (WHOQOL-BREF)**

WHO designed the self-administered WHOQOL-100 questionnaire consisting of 100 items in association with 15 countries including India in an effort to develop a responsive quality of life measure that was valid across diverse cultures. It assesses the "individual's perceptions in the context of their culture and value systems, and their personal goals, standards and concerns". WHOQOL-BREF is a brief version consisting of 26 items derived from the same in an effort to reduce the length suitable for large studies and clinical trials. It measures four broad domains namely: physical health, psychological health, social relationships, and environment, with items rated on a 5 point scale [15]. A Hindi version is also available and was used where appropriate [16]. Raw scores in each domain were determined separately and converted to transformed scores ranging from 4-20; scaling in a positive direction with higher scores indicating better QOL.

### **Statistical methods**

Data are described as mean [standard deviation (SD)] where normally distributed, and median [range/interquartile range (IQR)] otherwise. Non parametric comparative paired analyses (Mc Nemar test) was used

where questionnaires mostly returned ordinal scores and parametric paired t test otherwise. ANOVA (analyses of variance) and non-parametric counterpart Kruskal Wallis (with repeated measures consideration as necessary) were used as appropriate to compare multiple means/medians. Alpha less than 0.05 was set beforehand as significant and all tests were two tailed. Stepwise multivariable logistic regression model analyses were also performed (among patients prior to transplant) to assess relationship of anxiety-depression with 'physical health', 'social relationships' and 'environment' domains of quality of life. 'Psychological' domain was excluded in regression analyses as it directly represents a measure of anxiety-depression. Additional variables found significant in univariate analyses were also included in the model. For the purpose of logistic regression analyses the median scores in each domain of WHOQOL-BREF were used as a cut off to classify groups of patients with low and high QOL domain scores and cut off value of HADS anxiety/depression subscale score  $\leq 7$  was used to define absence of anxiety/depression.

### **RESULTS**

50 patients were finally included after excluding 4 patients due to loss to follow up. Both questionnaires were successfully administered to all study subjects. Transplant was successful in all cases and all patients were free from dialysis six months later. The demographic and socioeconomic details are shown in table 1. Most patients were educated males in 26-35 year age group. 30 (60%) patients reported being meaningfully employed despite adhering to haemodialysis schedule and the minimum duration of dialyses prior to transplant was 6 months. 33 (66%) patients were married and not surprisingly majority of the donors were either wives or mothers (n=32). Majority (n=31, 62%) resided in urban or semi-urban localities. Only 9 (18%) patients reported having an insurance cover.

### **Anxiety and Depression**

Before transplant 6 patients (12%) had HADS anxiety subscale scores above the threshold defining case-ness and this decreased to 2 patients (4%) six months after

transplant (Figure 1). The mean (SD) HADS Anxiety subscale score decreased from 7.16 (3.14) to 3.64 (2.80),  $p$  value  $<0.001$  (mean paired difference 3.52). Both patients having anxiety case-ness six months after transplant also had its presence prior to it, while 4 patients having anxiety case-ness present prior to transplant had HADS anxiety subscale score within normal range six months following transplant.

Clinical case-ness for depression was found in 13 patients (26%) before transplant and this decreased to 3 patients (6%) six months later (Figure 2). The mean (SD) HADS Depression subscale score decreased from 8.30 (2.76) to 4.40 (2.63),  $p$  value  $<0.001$  (mean paired difference 3.90). 2 patients having depression case-ness following transplant also had its presence prior it while another patient progressed from equivocal score to clinical case-ness following transplant. Scores of 11 patients having clinical case-ness for depression prior to transplant showed improvement among who scores of 9 cases became normal.

### Quality of life

Preoperatively comparatively lower scores were noted in environmental and social relationship domains (Table 2). Environmental domain assesses facets of - 'physical safety and security', 'home environment', 'financial resources', 'availability and quality of health and social care', 'opportunities for acquiring new information and skills', 'participation and opportunities for recreation and leisure', 'physical environment (pollution/noise/traffic/climate)', and 'transport'. Social relationship domain assesses facets of - 'personal relationships', 'social support', and 'sexual activity'.

Post operatively scores improved significantly across all four domains and became comparable among each other too.

### Relationship analyses

No significant relationship was observed between age, gender, marital status, education level, locality of residence, relationship with donor, and duration of dialyses with any domain of QOL or anxiety-depression (Table 3),

except that of age with social relationship domain of WHOQOL-BREF.

However, employment status and presence of insurance were found significantly associated with psychological and environment domain of quality of life. Psychological domain assesses facets of - 'bodily image and appearance', 'positive and negative feelings', 'self-esteem', 'spirituality/religion/personal beliefs', 'thinking, learning, memory and concentration'.

### Regression analyses

Patients with higher scores on HADS depression subscale had higher odds of reporting poor outcomes on 'physical health' and 'environment' domain of quality of life (Table 4). Anxiety predicted a poor outcome in 'social relationship' domain. Employment and insurance status (included because found significant in univariate analyses; Table 3) were also found important predictors of quality of life outcomes in 'environment' domain even while adjusting for presence of depression and anxiety.

### DISCUSSION

Depression remains the most common psychiatric disorder found in patients with dialyses with similar incidence even in earlier stages of disease. It has been found keenly associated with socio-demographic characteristics and functional capacity [17]. Also, depression and anxiety have been found to be more prevalent among patients undergoing haemodialysis compared to transplant, affecting activities of daily living apart from QOL [18]. Despite the presumed strong family support system in the Indian culture, our study similarly found an important number of patients with ESRD to have case-ness for anxiety and depression prior to transplant. Although successful transplant ameliorated most such cases yet they may provide a point for specific attention in patient population awaiting transplant, as by itself QOL assessment offers little by way of any specific focus of medical intervention, and anxiety and depression were significant explanatory variables to observed QOL scores. All patients with still

remaining case-ness for anxiety or depression six months following transplant were referred to the psychiatry service.

We found employment status and presence of insurance to be significantly associated with psychological and environment domain of quality of life. They remained important predictors of quality of life outcomes in the 'environment' domain even while adjusting for presence of depression and anxiety on multivariate analysis. Social and economic circumstances often drive many personal decisions of a patient [19]. Their importance can be gauged when one comes across evidence from India that organ donation 'improves' the quality of life of donor [7,20]. This can be partly explained as CKD entails considerable financial and social burden on the 'entire family unit' as frequently the person affected is the sole bread winner, and which may have a varying impact on the QOL of every individual in the family. A previous study in our institution found that mothers (as donors) experienced maximum improvement in QOL and emphasized 'difference in outlook towards donation' as well as 'role shifts' in family towards decision making process apart from 'proto altruism'[20]. Together these factors may explain why living unrelated donors experience worse QOL indicators in comparison [21]. Financial security could play an important role in helping families overcome adversity in this challenging disease and is amenable to health policy intervention.

### LIMITATIONS

The numbers in our series are small and most patients in our study were less than 45 years of age. This reflects our case mix where younger patients are given priority by caregivers as well as the health care system. Although this study tries to investigate relationship between mood depression disorder and quality of life yet we did not explicitly evaluate the specific causes of anxiety or depression in patients. We used generic HRQOL questionnaire although disease specific QOL measures following therapeutic interventions in kidney disease patients are available [22,23]. However, generic QOL indicators are still helpful in many ways such as cost effectiveness analyses where 'treatment effects on disease

specific measures are frequently mapped on to generic QOL measures', and have been recommended to be used in randomised controlled studies [24]. Moreover, generic QOL measures may provide better precision above a certain threshold of sample size. Generic HRQOL questionnaire unmasked the important aspect of association between employment status and presence of insurance with psychological and environment domain of the quality of life.

We hope future studies would endeavour towards a structured equation model approach with a larger sample size which may be better suited to fully investigate the diverse spectrum of other variables that may additionally influence this complex situation such as - side effects of medications, critical or infectious illness in the recent past, side effects related to body modification, sexual health, and many more.

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## PEER REVIEW

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**TABLES****Table 1:** Demographic and socio-economic details of the entire study population, n=50.

Variable	Distribution
Age, years, mean (SD)	32.3 (10.2)
18-25 years, n (%)	14 (28%)
26-35 years, n (%)	21 (42%)
36-45 years, n (%)	9 (18%)
>45 years, n (%)	6 (12%)
Gender, male, n (%)	45 (90%)
Marital status, married, n (%)	33 (66%)
Education status	
Illiterate, n (%)	4 (8%)
Primary education, n (%)	7 (14%)
Intermediate education, n (%)	14 (28%)
Graduation and above, n (%)	25 (50%)
Employment status, employed, n (%)*	30 (60%)
Residence	
Rural, n (%)	19 (38%)
Urban, n (%)	22 (44%)
Semi urban, n (%)	9 (18%)
Insurance, present, n (%)	9 (18%)
Relationship of donor with the recipient	
Wife, n (%)	13 (26%)

Mother, n (%)	19 (38%)
Others, n (%)	18 (36%)
Duration of dialyses, months, mean (SD) (Range)	10.4 (4.6) (6-24)

n = Number of patients

\* All 5 female patients were housewives and have been considered unemployed

**Table 2:** Comparison of scores in each of four domains of WHOQOL-BREF assessed two weeks before and six months after transplant, n=50.

WHOQOL-BREF domain	Score two weeks before transplant, mean (SD)	Score 6 months after transplant, mean (SD)	p value*
Physical domain	10.08 (1.23)	14.72 (0.95)	<0.001
Psychological domain	10.42 (1.69)	14.68 (1.27)	<0.001
Social relationship domain	9.66 (1.78)	14.26 (1.97)	<0.001
Environment domain	9.68 (1.36)	13.98 (1.76)	<0.001

\* paired t test

**Table 3:** Univariate relationship analyses between studied clinical variables and patient reported outcome scores of WHOQOL-BREF and HADS prior to transplant, n=50.

Variable	Statistical parameter	Patient reported outcome					
		WHOQOL-BREF				HADS	
		Physical domain	Psychological domain	Social relationship domain	Environment domain	Anxiety	Depression
Age	Correlation coefficient*	-0.172	0.02	<b>-0.28</b>	-0.11	-0.24	-0.03
	p value	0.23	0.91	<b>0.045</b>	0.46	0.09	0.83
Gender	Mann Whitney U statistic	95.5	108.5	74.5	67.5	69	74.5
	p value	0.55	0.89	0.20	0.14	0.15	0.21
Marital status	Mann Whitney U statistic	231	275	239.5	271.5	263.5	269
	p value	0.27	0.90	0.39	0.85	0.72	0.81
Education	Chi square <sup>α</sup>	0.20	1.02	2.31	0.49	1.76	0.50
	p value	0.98	0.80	0.51	0.92	0.62	0.92
Employment	Mann Whitney U statistic	130	<b>104</b>	162	<b>70</b>	172	181.5



	p value	0.16	<b>0.03</b>	0.63	<b>0.001</b>	0.66	0.88
Residence	Chi square <sup>α</sup>	7.29	2.02	2.17	2.85	0.54	2.41
	p value	0.26	0.36	0.34	0.24	0.76	0.30
Insurance	Mann Whitney U statistic	137	<b>109.5</b>	169.5	<b>75</b>	165.5	177.5
	p value	0.20	<b>0.04</b>	0.70	<b>0.005</b>	0.63	0.86
Relationship with donor	Chi square <sup>α</sup>	6.34	2.69	0.46	4.81	5.25	2.00
	p value	0.27	0.75	0.99	0.44	0.39	0.85
Duration of dialyses	Correlation coefficient <sup>π</sup>	0.14	0.20	0.07	0.04	0.07	0.03
	p value	0.32	0.16	0.63	0.76	0.64	0.85

\* Spearman's rho correlation coefficient

<sup>α</sup> Kruskal Wallis test statistic

<sup>π</sup> Pearson's correlation coefficient

Significant values marked **bold** and *italicised*

Refer Table 1 to see how individual variables are stratified

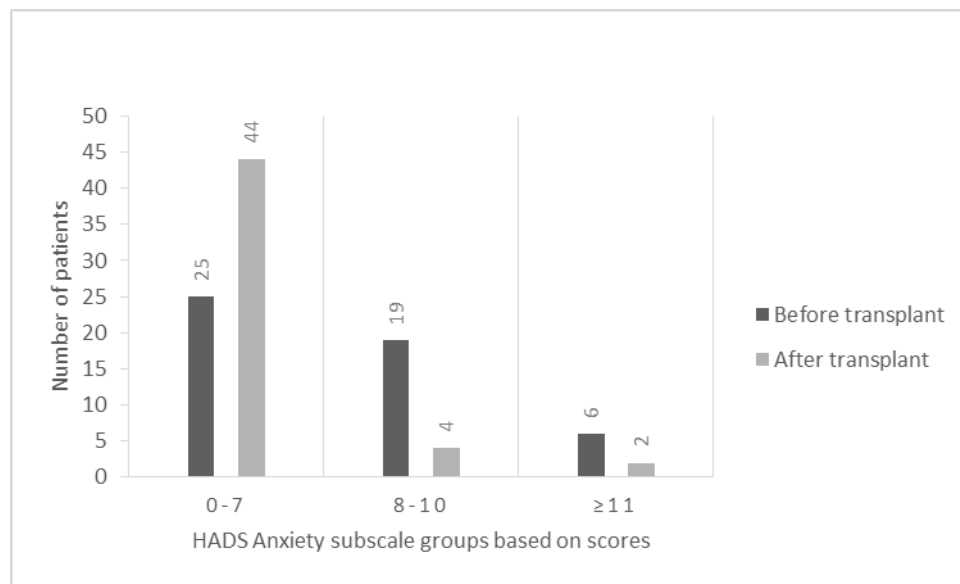
**Table 4:** Multivariable logistic regression analyses to assess contribution of anxiety and depression in predicting patient reported outcomes in physical, social and environment domains of WHOQOL-BREF.

Dependent outcome	Significant explanatory variables	regression coefficient	Adjusted odds ratio (OR)	95% confidence interval of adjusted OR	p value
<b>WHOQOL-BREF domain*</b>					
Physical domain	Depression	-0.81	0.44	0.20-0.74	0.003
Social relationship domain	Anxiety	-1.32	0.27	0.16-0.78	0.001
Environment domain	Depression	-1.41	0.24	0.10-0.47	<0.001
	Employment	1.24	3.46	1.62-6.84	<0.001
	Insurance	1.14	3.13	1.54-8.23	0.021

\* Each domain adjusted for presence of anxiety and depression. Additional adjustment for employment and insurance has done for environment domain as these were found significant in univariate analyses (refer Table 3).

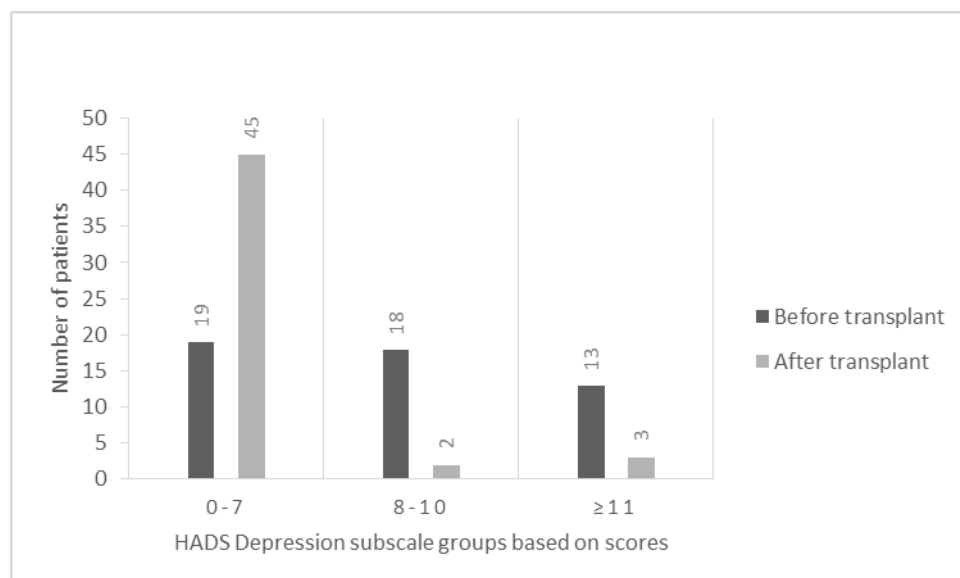
## FIGURES

**Figure 1:** Comparative frequency distribution of patients among different groups defined by HADS Anxiety subscale scores two weeks before and six months after renal transplant, n=50.



HADS Anxiety subscale score	Definition
0-7	Normal
8-10	Mood disturbances/equivocal
≥11	Anxiety case-ness present

**Figure 2:** Comparative frequency distribution of patients among different groups defined by HADS Depression subscale scores two weeks before and six months after renal transplant, n=50.



HADS Depression subscale score	Definition
0-7	Normal
8-10	Mood disturbances/equivocal
≥11	Depression case-ness present