Anxiety and Depression - A Suicidal Risk in Patients with Chronic Renal Failure on Maintenance Hemodialysis

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Abstract- **Background:** Depression and anxiety is well established as a prevalent mental health problem in end-stage renal disease patients treated with hemodialysis. However these problem remains difficult to assess and is undertreated.

Aims & Objective: To assess the demographic and psychological factors associated with depression among hemodialysis patients and elucidated the relationships between depression, anxiety, fatigue, poor health-related quality of life, and increased suicide risk.

Method: This cross-sectional study enrolled 150 end-stage renal disease patients age >18 years on hemodialysis. Psychological characteristics were assessed with the Mini-International Neuropsychiatric Interview, the Hospital Anxiety and Depression Scale, the short-form Health-Related Quality of Life Scale, and Chalder Fatigue Scale, and structural equation modeling was used to analyze the models and the strength of relationships between variables and suicidal ideation.

Results: Of the 150 patients, 70 (46.6%) had depression symptoms, and 43 (28.6%) had suicidal ideation in the previous month. Depression was significantly correlated with a low body mass index (BMI) and the number of co morbid physical illnesses. Depressed patients had greater levels of fatigue and anxiety, more common suicidal ideation, and poorer quality of life than nondepressed patients. Results revealed a significant direct effect for depression and anxiety on suicidal ideation.

Conclusion: Among hemodialysis patients, depression was associated with a low BMI and an increased number of comorbid physical illnesses. Depression and anxiety were robust indicators of suicidal ideation. A prospective study would prove helpful in determining whether early detection and early intervention of comorbid depression and anxiety among hemodialysis patients would reduce suicide risk.

Index Terms- anxiety, depression, chronic kidney disease, dialysis

I. INTRODUCTION

Depression and anxiety are the primary psychiatric problems of end-stage renal disease (ESRD) patients.[1–5] Depression and anxiety symptoms has been gaining increasing attention as an authoritative measure of psychopathology in ESRD populations. [6–8] Hemodialysis significantly and adversely affects the lives of patients, both physically and psychologically. [1–3] The global influence on family, work competence, fear of death, and dependency on treatment may negatively affect quality of life and exacerbate feelings associated with a loss of control.[2,3] Postulated explanations for high incidence and prevalence of ESRD in India include high prevalence of diabetes and incidence of chronic kidney disease, failure to identify patients with an early stage of chronic kidney disease. Roughly 95% of ESRD patients in India are on hemodialysis.[5]Among ESRD patients undergoing hemodialysis, besides the disease itself; accompanying modifications in the occupational, marital, familial, social, and personal life provide a sufficient base to give rise to anxiety. The effects of illness, dietary constraints, time restrictions, financial burdens, feeling of handicap, psychological strain of awareness of impending death, and many such factors impede the normal life, therefore, it is important to determine the psychological effects of hemodialysis.

The co morbidities of depression and anxiety increased over time in subjects who were on hemodialysis.[11] The incidence of anxiety a common disorder in hemodialysis patients, is 27%–46%.[10,11] Suicide may be the gravest result of depression. A high suicide rate is also related to poor quality of life.[22] Fatigue is also one of the most debilitating symptoms reported by hemodialysis patients, and it is negatively correlated with quality of life.[14] Approximately 60%– 97% of patients on hemodialysis experience some fatigue.[13] This is a subjective symptom characterized by tiredness, weakness, and lack of energy.[12] Health-related quality of life is an important measure of how a disease affects the lives of patients. The quality of life domains include physical, psychological, and social functioning and general satisfaction with life.[15] Numerous studies have demonstrated that hemodialysis patients had a lower quality of life than that of a healthy population.[16–18]

Identification of the relationships between psychological issues and suicide risk for dialysis patients is crucial. Currently, the relationships between suicide, depression, anxiety, fatigue, and life quality remain poorly understood. The objective of this study is to identify the demographic and psychological factors associated with depression in hemodialysis patients, to establish the relationships among depression, anxiety, fatigue, health-related quality of life, and suicide risk.

II. MATERIAL AND METHOD

Study Population- A hospital based cross sectional comparative observation study was conducted in Nephrology Unit, Department of Medicine CSM Medical University

(Erstwhile KGMC) Lucknow India from March 2009 to July 2011. One hundred fifty patients, age >18 years, on hemodialysis were enrolled in this study. Written informed consent was obtained from each patient before participation. This study was approved by the ethical & research committee of CSMMU, Lucknow to use human subject in the research study.

Procedures- In this cross-sectional study, all hemodialysis patients underwent assessments for fatigue symptoms with the Chalder Fatigue Scale (CFS), for depressive symptoms with the Hospital Anxiety and Depression Scale (HADS), and the Short-Form Health-Related Quality of Life Scale (SF–36), as well as psychiatric diagnostic interviews, using the Mini-International Neuropsychiatric Interview (MINI). Psychiatric diagnoses were made by Diagnostic and Statistical Manual of Mental Disorders (DSM–IV) after a structured psychiatric interview using the MINI. The MINI is a short, structured diagnostic interview for psychiatric disorders.[23] This module uses specific questions to assess suicidal ideation, suicide plans, and suicide attempts within the past month and lifetime suicide attempts.

The Chalder Fatigue Scale (CFS) - Fatigue symptoms were evaluated with the self-report CFS.[29] This scale consists of 11 items covering the physical and mental aspects of fatigue. Total fatigue score, which is obtained by adding the scores for all 11 items, has a range of 0–33. The CFS has a high degree of internal consistency, with a Cronbach-α of 0.89. Principal-component analysis supports the use of a two factor solution (Physical Fatigue and Mental Fatigue).[29]

The Hospital Anxiety and Depression Scale (HADS) - The HADS is a 14-item, self-administered questionnaire for assessing the severity of depression.[26] The HADS is commonly used in hospital practice and primary care, and for the general population. Seven items assess anxiety, and the other seven items assess depression. Each item has four possible responses (scored 0–3); the anxiety and depression subscales are independent measures. Patients with Anxiety scores (HADS–A) >8 are diagnosed with anxiety disorders (sensitivity: 0.89; specificity: 0.75), and patients with depression scores (HADS–D) >8 are diagnosed with depression disorders (sensitivity: 0.80; specificity: 0.88).[26]

The Short-Form Health-Related Quality of Life Scale (SF–36) - The SF–36 assesses eight dimensions of physical and mental health. The score range is 100 (optimal) to 0 (poorest). The eight subscales are the following: physical functioning (PF); physical role-functioning (RP); bodily pain (BP); general health (GH); vitality (VT); social functioning (SF); emotional role-functioning (RE); and mental health (MH).[27] A standard scoring algorithm aggregates scores from the eight SF–36 subscales into two summary scores for the Physical Component Summary (PCS) and Mental Component Summary (MCS).[28] The SF–36 has demonstrated sensitivity to change, and score changes can be interpreted as changes in the health-related quality of life of patients.

III. STATISTICAL ANALYSIS

Data were analyzed with SPSS Version 16 statistical software. Variables are presented as mean ± standard deviation (SD) or frequency. An HADS score >8 is the dichotomous cutoff for significant depression or anxiety symptoms. Descriptive statistics were analyzed by independent *t*-test and paired *t*-test; metric variables were analyzed by one-way analysis of variance (ANOVA); and x^2 test and Fisher's exact test were used for categorical variables. The Mann-Whitney test and Wilcoxon signed-ranks test were also applied to metric variables when the data distribution violated parametric assumptions. Partial correlation was used to analyze the relationships among suicide risk, and HADS, SF–36, and CFS scores, while controlling for body mass index (BMI) and number of comorbid physical illnesses. Structural-equation modeling, using maximum-likelihood estimation, was further utilized to analyze the strength of variable relationships among depression, anxiety, fatigue, quality of life, and suicide risk. All tests were two-tailed, and the level of significance was p < 0.05.

IV. RESULTS

Mean age of the 150 patients on hemodialysis in this study was 57.5 (13.5) years. Of all patients, 70 (46.6%) were men, and 80 (53.3%) were women. Of the 150 subjects, 50 (33.3%) fulfilled DSM–IV criteria for a major depressive disorder, and 36 (72%) reported having suicidal ideation within the past month. Of the 36 patients with suicidal ideation, 27(75%) fulfilled the DSM–IV criteria for major depressive disorder; 9 (25%) did not. The mean HADS–D score for all 150 patients was 6.5 (5.6); range: 0–21; 50 patients (33.3%) had depressive disorders (HADS–D score >8), and anxiety symptoms. **Table 1** summarizes the demographic characteristics of depressed and nondepressed patients, categorized using the >8 cutoff point of the HADS–D scale. There was no significant difference in gender ratio, age, and education, duration of hemodialysis, smoking, or alcohol drinking history between the depressed and nondepressed groups. Compared with nondepressed patients, patients' depression was significantly associated with low BMI and number of comorbid physical illnesses. **Table 2** shows the psychological characteristics of suicidality, anxiety, fatigue, and quality of life for depressed and nondepressed patients. Among the subjects, there is a significant difference in the rate of suicide attempts in their lifetime between the depressed and nondepressed patients. In 150 subjects, 70 (46.6%) fulfilled DSM–IV criteria for a major depressive disorder, 36 (51.4%) having suicidal ideation, 6(8.8%) having suicidal plan and 5(7.15%) suicidal attempts within the past month. Of the 36 patients with suicidal ideation, 27(75%) fulfilled the DSM–IV criteria for major depressive disorder; 9 (25%) did not. The mean HADS–D score for all 150 patients was 6.5 (5.6); range: 0–21; 50 patients (33.3%) had depressive disorders (HADS–D score >8), and anxiety symptoms. The depressed patients had significantly more suicidal ideation and suicide plans and had a higher incidence of anxiety disorders than nondepressed patients. Moreover, depressed patients had significantly higher scores on the HADS–D, HADS–A, and CFS, and significantly lower scores for all dimensions of the SF–36 than nondepressed patients. Physical functioning (PF); physical role-functioning (RP); bodily pain (BP); general health (GH); vitality (VT); social functioning (SF); emotional role-functioning (RE); and mental health (MH) were statistically significant in depressed patients (p<0.001).

The correlations between suicidal ideation and HADS scores for the Depression and Anxiety scales, CFS scores, and the PCS and MCS of the SF–36 are shown in **Table 3**. After controlling

for BMI and number of comorbid physical illnesses, suicidal ideation and scores on the HADS Depression and Anxiety scales and CFS were positively and strongly correlated. Scores on the SF–36 PCS were positively and strongly correlated with the SF–36 MCS, and both were negatively correlated with suicidal ideation and scores on the HADS Depression, Anxiety scales and the CFS. Significant and mutual correlations existed between fatigue, depression, anxiety, and quality of life. Structural-equation modeling revealed that depression and anxiety had a significant direct relationship with suicidal ideation, whereas fatigue and quality of life did not.

Table 1: Demographic Characteristics of Depressed and Non-Depressed Hemodialysis Patient

Characteristic	Total (N=150)	Non Depressed (N=80)	Depressed (N=70)	p
Gender (men/women),N %	70/80 (46.6/53.3)	46/34(57.5/42.5)	38/32 (54.3/45.7)	NS
Smoking, N (%)	36 (24)	19 (23.7)	17(25.0)	NS
Alcohol use, N (%)	22 (14.6)	10(12.5)	12(17.6)	0.058
Age, year	58 (13.9)	58.5(13.3)	58.8(15.0)	NS
Education, year	7.1+ (4.6)	7.3(4.4)	6.6(4.8)	NS
Body mass index (BMI: kg/m)	23.3 (4.0)	24.0(4.7)	20.3(2.8)	<0.001
Comorbidly physical illnesses,N	2.0(1.6)	1.8(1.4)	2.4(1.8)	0.018
Hemodialysis duration, month	68.1(65.8)	67.1(64.1)	69.7(69.5)	NS
Depression was defined as a Hospital Anxiety and Depression Rating Scale (HADS-D) score> 8.				

Table 2: Psychological Characteristics of Depressed and Non Depressed Hemodialysis Patients

Characteristic	Non- Depressed N=80	Depressed N=70	p
Suicidality, N			
Suicidal Ideation, past month	8 (6.2)	35 (50.0)	<0.001
Suicide plan, past month	1 (0.8)	6 (8.6)	0.008
Suicide attempt, lifetime	2 (1.5)	5 (7.1)	0.052
HADS-Anxiety score	3.0 (2.9)	7.7 (4.3)	<0.001
HADS- Depression score	2.9 (2.2)	13.2 (3.5)	<0.001
Fatigue srore	17.0 (4.2)	24.7 (5.5)	<0.001
Health- Related Quality of life			
physical Functioning	67.2 (23.2)	44.1 (34.0)	<0.001
Physical Role Functionig	71.9 (40.0)	34.6 (43.3)	<0.001
Emotional Role Functioning	87.1 31.0	36.2 (42.8)	<0.001
Vitality	60.8 (18.3)	29.1 (14.9)	<0.001
Mental Health	79.8 (13.7)	42.4 (17.1)	<0.001
Social Functioning	81.9 (22.9)	59.3 (24.8)	<0.001
Bodily Pain	76.2 (22.5)	59.3 (24.8)	<0.001
General Health	52.0 (24.0)		<0.001
Physical Component	57.9 (25.1)	39.6 (27.0)	<0.001
Summary			
Mental Component Summary	81.9 (18.4)	36.8 (22.7)	<0.001
Depression was defined as the Hospital Anxiety and Depression Rating Scale HADS-D =8			
Values are mean standard deviation unless otherwise indicated.			

Table-3: Correlation of Suicide Rick, Depression, Anxiety, Fatigue, and Health-Related Quality of life, Contolling for body Mass Index BMI and Number of Comorbid Physical II Inesses.

	Suicide Risk	Depression	Anxiety	Fatigue	PCS	MCS
Suicide Risk	___					
Depression	0.46***	____				
Anxiety	0.46***	0.59***	___			
Fatigue	0.37***	0.68***	0.58***	___		
PCS	_0.19**	_0.35***	_0.39***	_0.54***	___	
MCS	0.39***	0.77***	_0.62***	_0.63***	0.21**	___
PCS: Physical Component Summary of Health-Related Quality of Life, MCS: Mental Component Summary of Health- Ralated Quality of life.						
*p<0.05,*** p<0.001.						

V. DISCUSSION

Study results demonstrate that depression was correlated with low BMI and a high number of comorbid physical illnesses. Depressed patients had a significantly higher incidence of anxiety and fatigue, more common suicidal ideation, and significantly lower quality of life than nondepressed patients. The intercorrelations between fatigue, depression, anxiety, and quality of life were significant. Suicidal ideation was strongly related to depression and anxiety, but not to fatigue or quality of life.

A high BMI is associated with increased survival rate and reduced risk of hospitalization for hemodialysis patients. [30,31] Poor nutrition and inflammation have been suggested as plausible explanations for this epidemiological phenomenon. [31] Interestingly, the correlation between BMI and survival rate was noted among most ethnic groups, with the exception of Asians. [30] Analytical results obtained by this study demonstrate that depressed patients had lower BMIs than nondepressed patients. Loss of appetite and decreased body weight are common manifestations of depression. Thus, the causal relationships among low BMI, depression, and mortality warrant further investigation.

Empirically, patients with many comorbid physical illnesses have worse physical condition and greater psychological stress than those with few comorbid physical illnesses. Our results also demonstrate that depression was significantly correlated with the number of comorbid physical illnesses. The comorbidity score of a major comorbid physical disease has been demonstrated to be a predictor of mortality in general-medical inpatients. [32]

In this study, 33.3% of patients had a major depressive disorder HADS-D score was 13.2+3.6 (p<0.001) as defined by DSM–IV criteria. To meet the diagnostic DSM–IV criteria for major depressive disorder, the subjects needed to fulfill the exclusion criteria "symptoms are not due to the direct physiological effects of a medication or a general medical condition." Therefore, a substantial proportion of subjects who met the criteria for "depressive disorders" defined by HADS–D scores >8 did not meet DSM–IV criteria for major depressive disorder. Some studies indicated that moderate depressive syndromes are common in roughly 25% of ESRD patients, and major depression is common in 5%–22% of ESRD patients. [32,33] The etiology of dialysis-related depression is multifactorial, and is related to biological, psychological, and social mechanisms. [3] Biological mechanisms include increased cytokine levels, [1] possible genetic predisposition, [34] and neurotransmitters affected by uremia. [35] Psychological and social factors include feelings of hopelessness, perceptions of loss and lack of control, job loss, and altered family and social relationships. [1,34] Depression is a significant factor influencing survival [9] and is strongly correlated with fatigue, anxiety, quality of life, and suicide. Fatigue can be a debilitating symptom for patients undergoing hemodialysis, and it is strongly correlated with depression. [36] The pathogenesis of fatigue among hemodialysis patients has been attributed to osmotic disequilibrium, change in blood pressure, intramuscular energy metabolism, and central activation failure. [13,37] Fatigue is not only strongly correlated with scores for many SF–36 subscales, but it is strongly correlated with dialysis patient survival. [38] Fatigue and depression may be closely related, and depression may manifest as feelings of tiredness and lack of energy. [13] In this study, significant mutual correlations existed between fatigue, depression, anxiety, and quality of life. This finding is generally compatible with those in the literature.

High rate of co morbid depression and anxiety was noted in hemodialysis patients. Those with a persistent course of depression had marked decreases in quality of life and self-reported health status; however, this pattern did not emerge with an anxiety diagnosis. [11] In this study, 33.3% of subjects had co morbid depression and anxiety, and in depressed patients HADS-Anxiety score was 9.5+4.5 (p<0.001). Furthermore, anxiety is also a factor strongly correlated with suicidal ideation. Uncertainty regarding the future and fear of losing control in life are important factors associated with anxiety that adversely affect emotional stability. [22] The importance of anxiety may have been underestimated for hemodialysis patients. Notably, anxiety is a common psychological problem that may emerge during the initial course of dialysis; [11] thus, it is important to identify anxiety symptoms in dialysis patients.

Improved quality of life is correlated with high self-esteem and low levels of mood disturbances. [17] Decreased health-related quality of life is strongly correlated with depression, anxiety, [39–41] and increased mortality in hemodialysis patients. [8,17] Poor exercise tolerance and muscle weakness may limit daily activity, further resulting in poor quality of life. [5,42] Depression scores

were independently correlated with all SF–36 dimensions.[18] Nevertheless, composite scores for all eight SF–36 subscales were aggregated into the PCS and MCS. The MCS had a stronger correlation with depression than did the PCS.[8] Although our results showed that the correlation coefficient between depression and the MCS (– 0.76) was higher than that for depression and the PCS (– 0.36) both were significant (p<0.0001). Fatigue, anxiety, depression, or reduced quality of life may be a primary response when a patient begins hemodialysis; nevertheless, suicide is undoubtedly an adverse consequence.[22] The suicide rate of ESRD patients was approximately 15 times greater than that for the general United States population. Suicide was associated with several demographic characteristics.[20] A preexisting anxiety disorder was identified as an independent risk factor for subsequent onset of suicidal ideation and attempts.[43] Depression is also a prominent predictor for suicide for many chronic illnesses.[20,44]

Results of this study revealed a significant direct effect for depression and anxiety on suicidal ideation. Several limitations of this study must be considered. First, this is an observational, cross-sectional study. The causal inferences of fatigue, anxiety, depression, and reduced quality of life remain unclear. Second, the Charlson Co morbidity Index,[45] which been shown to be an effective measure of co morbidity severity, was not computed for patients in this study. Third, diagnosing depressive disorders or anxiety disorders is difficult for hemodialysis patients when we apply DSM–IV criteria. To meet the diagnostic DSM–IV criteria for major depressive disorder or anxiety disorders, the subjects need to fulfill the exclusion criterion "The symptoms are not due to the direct physiological effects of a medication or a general medical condition." It is difficult to judge arbitrarily whether the depressive symptoms are due to the direct physiological effects of a medication or a general medical condition in hemodialysis patients. The DSM–IV criteria may have a higher specificity but a lower sensitivity than the HADS. Therefore, the authors used the HADS to define cause of depressive disorders and anxiety disorders. Last, subjects in this study were from a single site. Hence, the external validity may be limited. Ethnic differences in quality of life have been identified among hemodialysis patients.[46] It was postulated that Asian patients perceive kidney disease as a social burden.[46] Perceived "burdensomeness" has been reported to be correlated with suicidal ideation.[47,48] Whether Asian hemodialysis patients perceive their illness as a greater burden to their family or society than other ethnic populations do, and whether this could account for the high incidence of suicidal ideation in this population are areas for further study. We would recommend further research with samples from multiple sites and other ethnicities to improve generalization. Although this cross-sectional design could not determine causal relationships, this study provides a path-analysis for the complex relationships between depression, anxiety, fatigue, quality of life, and suicide risk in hemodialysis patients.

In conclusion, depressed hemodialysis patients had greater levels of fatigue and anxiety, greater suicide risk, and poorer quality of life than nondepressed patients. In this population, depression was associated with a low BMI and an increased number of comorbid physical illnesses. Depression and anxiety were robust indicators of suicide risk. Depressed and anxious patients should be identified early and offered appropriate treatment. A prospective, controlled study will prove helpful in determining whether early detection and early intervention of comorbid depression and anxiety among hemodialysis patients will reduce their suicide risk.

Conflict of Interest: None

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