DEMOGRAPHIC PROFILE AND ASSOCIATIONS OF DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE PATIENTS IN FEDERAL CAPITAL OF PAKISTAN.

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ABSRACT

Objectives: Depression is quite prevalent in patients with chronic kidney disease. Knowing the frequency of depression in such patients and its association with different variables may be helpful in devising strategies for better and timely management of such patients in our setup. **Materials and methods:** This cross sectional study was conducted by recruiting 315 patients of either gender, ≥ 18 years of age with chronic kidney disease (CKD) and receiving care at Pakistan Institute of Medical Sciences, Islamabad. Patients were divided into two groups; group A: pre-dialysis and group B: dialysis (End Stage Renal Disease). Prevalence of depression in CKD and dialysis group and its association with gender, level of formal education and socioeconomic status was evaluated using descriptive statistics and chi-square test. **Results:** Out of 204 (100%) patients in group B, 171 (83.8%) patients had depression while in group A, 68 (61.3%) out of 111 (100%) patients were depressed. The prevalence of depression in all stages of CKD combined was 75.87 % (239 out of 315) and that in dialysis group was 83.82% (171 out of 204). Frequency of depression was significantly higher in the dialysis group (p=0.01). Those with higher level of education less commonly suffered from depression (p=0.01). No such association was found with gender (p=0.68) or socioeconomic status (p=0.12).**Conclusion:** Frequency of depression is significantly higher in dialysis dependent CKD patients with an overall prevalence of 75.87% in CKD and 83.82% in dialysis dependent ones. Higher level of formal education positively affects the outcome while gender and socioeconomic class have no significant association.

KEY WORDS: Chronic kidney disease, prevalence, depression, pre-dialysis, dialysis, gender, level of education, socioeconomic status.

INTRODUCTION

Chronic kidney disease (CKD) is associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Most common causes of CKD are diabetes mellitus, hypertension, glomerular and interstitial disease and idiopathic illness. [1, 2] Due to very high prevalence of hypertension and diabetes, CKD is also a common condition in Pakistani population. [3] CKD is a chronic illness with increased morbidity and life style changes and often causes depression with an estimated prevalence of 20-47%in end stage renal disease (ESRD).[4, 5] [5] There is scarcity of data related to depression in CKD and dialysis patients in Pakistan. [6] the objective of this study was to determine the prevalence of depression and its association with other variables in CKD and dialysis patients at a tertiary care setup.

MATERIALS AND METHODS

This study was approved by the Ethical Review Committee of Pakistan institute of Medical Sciences for Research. All patients provided informed written consent. All the work was performed in accordance with the ethical standards of the responsible committee on human experimentation and with the latest (2008) version of Helsinki Declaration of 1975. This single centre, cross-sectional study was conducted by recruiting 315 patients of either gender, ≥ 18 years of age with CKD diagnosed according to the Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation clinical practice guidelines for the evaluation, classification and stratification of chronic kidney disease including patients with ESRD on maintenance hemodialysis (MH). All those included were receiving care at Pakistan Institute of Medical Sciences, Islamabad. The study was conducted over a period of one year i-e-, from June 2013 to July 2014. [1] Age > 90 years, chronic medical illnesses, patients already receiving treatment for depression, other psychiatric diseases and somatic symptoms of uremia were the exclusion criteria. Patients with history of depression prior to start of dialysis and those identified to have other possible stressors contributing towards

depression were also excluded.History was taken from the patient and detailed examination was done. Demographic and clinical data were recorded including history of cardiovascular, respiratory, endocrine, nervous, musculoskeletal, psychiatric and other co-morbid conditions.CKD was defined as the presence of kidney damage or decreased kidney function for ≥ 3 months with or without decreased GFR, irrespective of the cause. Kidney damage was ascertained via pathologic abnormalities, whether established via renal biopsy or imaging studies, or inferred from markers such as urinary sediment abnormalities or increased rates of urinary albumin excretion (albuminuria). [1]Although a number of different measurement methods have been used to define albuminuria, albumin-to-creatinine ratio (ACR) in an untimed "spot" urine and the accepted threshold by KDOQI recommendation that albuminuria with ACR ≥ 30 mg/g (3.4 mg/mol) should be considered part of the definition of CKD, were practiced in this study. [1, 2] Based on clearance measurements, the widely accepted threshold for defining decreased GFR of less than 60 mL/min/1.73 m2 was used to define CKD. All definitions were in accordance with KDOQI guidelines. CKD was classified into five stages on the basis of GFR. [Table 1]

Stage	Description	GFR(mL/min/1.73 m2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15 (or dialysis)

Table 1: CKD classification according to KDOQI guidelines based upon GFR

Table1: KDOQI CKD classification based upon GFR. GFR = glomerular filtration rate, CKD = chronic kidney disease, KQOQI = Kidney Disease Outcomes Quality Initiative, ↓ = increased, ↓ = decreased.

GFR measurement by Cockcroft Gault formula was done using following equation: [1, 3]

$$eCcr = \frac{(140\text{-}Age) \times Mass(Kilograms) \times constant}{Serumcreatinine(\mu mol/L)}$$

[Where Constant is 1.23 for men and 1.04 for women] Patients were divided into two groups; group A: pre-dialysis and group B: dialysis (ESRD). The term "end-stage renal disease" (ESRD) was used to denote CKD patients receiving hemodialysis. [1]

The diagnosis of depression was made according to Diagnostic and Statistical Manual of Mental Disorders - 4th Edition (DSM-IV). Instruments used included Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale of depressive episode (HDRS). [5, 6] Each item was read out to the patient by researcher and responses were marked. Urdu translation of HDRS was used where needed. Socioeconomic status of the population was graded ashigh, middle and lower class. [7] and level of education as no formal education, middle or less (≤ eight years of school education), middle to matric (> eight years but ≤ ten years of school education), matric to graduation (> ten years but ≤ graduate level of education) and post-graduation (>graduate level of education). Sample size calculated for hypothesis testing for the population proportion using WHO SS (World Health Organization Sample Size) calculator[8]was 154 at significance level of 5%, power of test at 95% and anticipated population proportion at 20-47%. [5] A non-consecutive, non-probability sampling technique was used for patient selection. Data was analyzed using the Statistical Package for Social Sciences version 16 (SPSS Inc. USA). Descriptive statistics were used to calculate mean and standard deviation forquantitative variables and Frequency and percentages were calculated for qualitative variables, i.e. gender, socioeconomic status, level of formal educational and depression in the two groups.Pearson's Chi-square test was used to compare frequency of depression in both groups (pre-dialysis & dialysis) using the equation:

$$x^2 = \sum_{i-1}^{n} \frac{(Oi - Ei)^2}{Ei}$$

Whereas,

x^2=Pearson's cumulative test statistic, which asymptotically approaches a x^2 distribution;

Oi=an observed frequency;

Ei=an expected theoretical) frequency, asserted by the null hypothesis;

n=the number of cells in the table.

P-values less than 0.05 were considered statistically significant. The prevalence of depression in CKD and dialysis dependent population and the difference in frequency of depression between pre-dialysis and dialysis group was calculated. Association of gender, socioeconomic status and level of education with depression was done using chi-square. We further calculated the frequency of depression in different stages of CKD using Hamilton Depression Rating Scale of depressive episode.[5, 6]

RESULTS

Out of total 315 patients, 204 (64.76%) were in dialysis group and 111 (35.23%) were in pre-dialysis group. In pre-dialysis group, 52 (46.84%) were males with the mean age of 56.37 ± 17.07years and 59 (53.15%) were females with mean age of 49.36 ± 19.17 years. In dialysis group, 106 (51.96%) patients were males with the mean age of 49.49 ± 17.47 years and 98 (48.03%) were females with mean age of 44.17 ± 17.83 years. [Table 2]

Gender distribution				
Gender	**Pre-dialysis n(%)**	**Mean Age ± SD (years)**	**Dialysis n (%)**	**Mean Age ± SD (years)**
Male	52 (46.84)	56.37 ± 17.07	106 (51.96)	49.49 ± 17.47
Females	59 (53.15)	49.36 ± 19.17	98 (48.03)	44.17 ± 17.83
Total	111 (100)	52.64 ± 18.86	204 (100)	47.20 ± 17.74
Socioeconomic status				
Socioeconomic status	Frequency (n)	Percent (%)	Valid Percent (%)	Cumulative Percent (%)
Low	96	30.47	30.50	30.50
Middle	120	38.09	38.10	68.60
High	99	31.42	31.40	100.0
Education				
Level of education	Frequency (n)	Percent (%)	Valid Percent (%)	Cumulative Percent (%)
No formal education	117	37.14	37.10	37.10
Middle or less	76	24.12	24.10	61.20
Middle to Matric	57	18.09	18.10	79.30
Matric to graduation	52	16.50	16.50	95.80
Post-graduation	13	4.12	4.10	100.0
Total	315	100.0	100.0	-

Table 2: Demographic data

Table 2: Demographic data for gender, socioeconomic status and level of education. SD = standard deviation, n = number of individuals. Overall, 239 (75.87%) patients developed depression. Out of 204 (100%) patients in dialysis group, 171 (83.82%) had depression. In pre-dialysis group, 68 out of 111 had depression.[Table 3]On evaluation of frequency of depression in different stages of CKD, most of the patients were mildly depressed in almost all stages of CKD. [Table 4] Frequency of depression did not differ significantly among classes(p=0.12).[Table 3]Gender was also not significantly associated with depression (p=0.68).[Table 3]

Prevalence of depression in dialysis and pre-dialysis groups of CKD				
	Depression			
Category	**Present**	**Absent**	**Total**	**P value**
	n (%)	**n (%)**	**n (%)**	
Dialysis	171(83.82)	33 (16.17)	204 (100.00)	
Pre-dialysis	68 (61.26)	43 (38.73)	111 (100.00)	0.00*
Total	239 (75.87)	76 (24.12)	315 (100.00)	
Association of depression with gender				
Male	117 (74.05)	41 (25.94)	158 (100.00)	
Female	122 (77.70)	35 (22.29)	157 (100.00)	0.68
Total	239 (75.87)	76 (24.12)	315 (100.00)	

Association of depression with socioeconomic status				
Category	**Present n (%)**	**Absent n (%)**	**Total n (%)**	**P value**
Low	80 (83.33)	16 (16.66)	96 (100.00)	
Middle	87 (72.50)	33 (27.50)	120 (100.00)	0.12
High	72 (72.72)	27 (27.27)	99 (100.00)	
Total	239 (75.87)	76 (24.12)	315 (100.00)	
Association of depression with level of formal education				
No formal education	80 (68.37)	37 (31.62)	117 (100.00)	
Middle or less	61 (80.26)	15 (19.73)	76 (100.00)	
Middle to Matric	45 (78.94)	12 (21.05)	57 (100.00)	0.01*
Matric to graduation	46 (88.46)	06 (11.53)	52 (100.00)	
Post-graduation	07 (53.84)	06 (46.15)	13 (100.00)	
Total	239 (75.87)	76 (24.12)	315 (100.00)	

Table 3: Prevalence of depression in dialysis and pre-dialysis groups and association with socioeconomic status, level of formal education and gender

Table 3: Prevalence of depression in dialysis and pre-dialysis groups of CKD and association with socioeconomic status, level of formal education and gender. CKD = chronic kidney disease, n = number of individuals, * = statistically significant.

CKD Stage	**Depression ratings**			
	None	**Mild**	**Moderate**	**Severe**
CKD I	0	0	0	0
CKD II	6	12	0	0
CKD III	21	20	3	0
CKD IV	15	23	6	3
CKD V	34	134	34	4

Table 4: Frequency of depression in different stages of CKD

Table 4: Frequency of depression in different stages of CKD (I-V) calculated using Hamilton depression rating scale of depressive episode (HDRS). CKD = chronic kidney disease.Out of 117 (37.14%) patients with no formal level of education, there were 80 (68.37%) had depression. Frequency of depression was significantly lower in patients with post-graduate level of education i-e-, 7 (53.84%) (p=0.01). [Table 3]

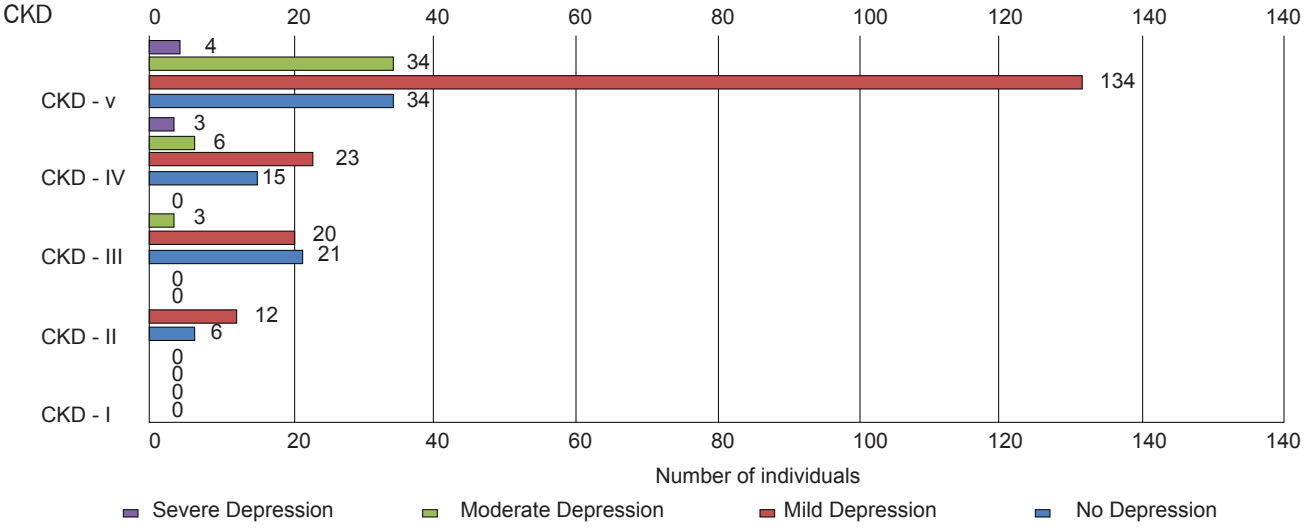

Figure 1: Frequency of depression in different stages of CKD

Figure 1: Frequency of depression in different stages of CKD (I-V)calculatedusing Hamilton depression rating scale of depressive episode (HDRS). CKD = chronic kidney disease.

DISCUSSION

Chronic kidney disease encompasses a spectrum of pathophysiological processes associated with abnormal kidney function and progressive decline in glomerular filtration rate. [1, 2]The exact prevalence of depression in dialysis patients is unclear but reported ranges in ESRD vary from 20-47%. [5] This wide variation is based in part upon the different criteria utilized for assessing mood disturbances. In two studies of 210 and 380 peritoneal dialysis patients, scores consistent with a possible diagnosis of clinical depression were observed in 42% and 49%, respectively. [9, 10] Of the patients who agreed to further testing, 87% and 84%, respectively, were diagnosed with clinical depression based upon DSM-IV. In addition, it has been suggested that some patients may overemphasize their somatic symptoms and may deny any mood disturbance or other symptoms directly attributable to depression. [11]Limited data exists related to CKD and dialysis related depression all the more limited. [3] Our study reports the local prevalence of depression and associated factors in CKD in Pakistan. Conflicting information exists concerning the association of depression with survival. [6] The effects of psychosocial factors on mortality were assessed in one study of 295 dialysis patients that used the Beck Depression Inventory. [12] Although variations in depression scores were not associated with survival, lower levels of social support, decreased compliance with treatment and increased negative perception of the effects of illness independently correlated with increased mortality. In contrast, other studies suggested poor survival among depressed dialysis patients. [13] Depression is also associated with an increased risk of hospitalization. This appears to be independent of other co morbidities and demographic variables. [14] Our results are in concordance with that of Hung et al. who explored possible correlation of depression with demographic, socio-economic, clinical and laboratory variables in CKD patients. [15][Table 3] They enrolled 146 MH patients in their cross-sectional study. The self-administered BDI was used to determine the presence or absence of depression symptoms. They found that the prevalence of depression (BDI ≥14) was 45.9% and no statistically significant association with age, gender, smoking habits or clinical characteristics. The rate of depression was significantly lower in elderly patients (age ≥75 years) compared with those below 64 years of age. No correlation was found with socio-economic status matching our observations. [15][Table 3] Similarly, like Hung et al., we also did not find any gender difference between people with and without depression in CKD.[Table 3] [Figure 1] Wuerthet al.screened all chronic peritoneal dialysis patients in their facility for depression. [16] Compared to our results depicting 83.82% individuals with depression, 87% dialysis dependent patients were diagnosed with clinical depression based on scores on the BDI, HDRS and DSM-IV. [16] Combined prevalence for all stages of CKD including pre-dialysis and dialysis patients was found to be 75.87% in our study.[Table 3]We further evaluated the frequency of depression in different stages of CKD usingHamilton Depression Rating Scale of depressive episode. [Table 4]Statistics revealed that patients of CKD I-IV were mostly categorized in pre-dialysis group while those in CKD V mostly were dialysis dependent. Out of all in CKD I-IV i-e-, 109 (34.60%) individuals, only 2 (1.83%) patients (both in CKD II) were dialysis dependent. Among the 206 (65.39%) in CKD V, 202 (98.05%) were on maintenance dialysis while only 4 (1.94%) were in the pre-dialysis group. On evaluation of frequency of depression in different stages of CKD, most of the patients with depression in almost all stages of CKD were mildly depressed. [Table 4] Those on dialysis (ESRD) were more frequently seen to be suffering from depression. [Table 4] Watnicket al. sought to assess the prevalence of depressive symptoms in patients with ESRD starting dialysis therapy, to identify patient characteristics associated with depression and to determine whether patients with serious depressive symptoms were receiving treatment. [17] They implemented a multicenter prospective cohort study at 14 dialysis centers in Connecticut. Patients with ESRD who were 18 years and older were interviewed within 10 days of initiating dialysis therapy. BDI was used to assess depressive symptoms. They found that among 123 patients, 44% (54 out of 123) had scores above the validated cutoff value in the BDI for depression. Depression was significantly associated with Caucasian race (OR=3.4; p=0.02), lower self-rated quality of life (OR=2.2; p=0.01), and no previous acquaintances on dialysis therapy (OR=10.2; p=0.03). They concluded that depressive symptoms are very common at the start of dialysis therapy and specific characteristics are associated with a greater burden of depressive symptoms. [17] Hedayattiet al. determined the prevalence of a major depressive episode and other psychiatric illnesses by using a structured gold-standard clinical interview and demographic and clinical variables associated with major depressive episode in patients with CKD. [18] In their observational

cross-sectional study, they used DSM-IV based structured interview administered by trained persons to 272 consecutive participants. The prevalence of a major depressive episode was 21% and did not vary significantly among different CKD stages. Variables associated with a major depressive episode were diabetes mellitus, co morbid psychiatric illness, and history of drug or alcohol abuse. [18] They concluded that one in 5 patients with CKD had a major depressive episode. They further suggested that patients with CKD should be screened routinely for depression given this high prevalence and the independent association of depression with poor outcomes in patients with ESRD receiving maintenance dialysis. [18] It is important to identify and treat depression in hemodialysis patients to improve their quality of life. [20] The KDOQI guidelines suggest that every dialysis patient should be evaluated by the dialysis social worker upon initiation of dialysis and at least biannually subsequently. The strengths of this study are that the study was conducted over substantial period of time i.e. more than one year. The sample size was also meaty. However, the study is limited by the fact that it was carried out at a single center and hence, the results cannot be readily generalized.

CONCLUSION

Frequency of depression is significantly higher in dialysis dependent CKD patients with an overall prevalence of 75.87% in CKD and 83.82% in dialysis dependent ones in Pakistan. Higher level of formal education positively affects the outcome while gender and socioeconomic class have no significant association.

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Abbreviations:
CKD (Chronic Kidney Disease); GFR (Glomerular Filtration Rate); eGFR (Estimated Glomerular Filtration Rate) ACR (Albumin-to-Creatinine Ratio); KDOQI (Kidney Disease Outcomes Quality Initiative); DSM-IV (Diagnostic and Statistical Manual of Mental Disorders - 4th Edition), HDRS (Hamilton Depression Rating Scale), BDI (Beck Depression Inventory), MH (Maintenance Hemodialysis), ESRD (End Stage Renal Disease.

Consent:
Written informed consent was obtained from every patient for participation in this study.