The Role of Psychosocial Factors in Depression and Mortality Among Urban Hemodialysis Patients

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The prevalence of chronic kidney disease (CKD) has increased by 29.3%, and the all-age mortality rate from CKD has increased by 41.5% since 1990 worldwide.[1] The overwhelming fatigue, complex treatment regimens, and diet restrictions constraining the lives of patients with CKD increases their psychological distress,[2] which can induce hyperactivity of the hypothalamus-pituitary-adrenal axis, the commonest neurobiological change observed in depressive patients.[3] The lifetime prevalence of depression is 10.8% in the general population,[4] whereas in CKD stage 5D patients, it is 22.8% based on the interview method and 39.3% based on self- or clinician-administered rating scales, according to a meta-analysis in 2013.[5]

Depression in CKD is due to a combination of behavioral mechanisms, such as burden of illness, poor quality of life, and lack of social support, and biological causes such as comorbidities, inflammation, hormonal abnormalities, and altered autonomic activity.[6] Depression is associated with mortality, increased hospital admissions, fatigue, decreased sexual functioning, cognitive impairment, low adherence to medication and fear of death in dialysis patients.[7,8] When patients' priorities for health research were studied, they felt that health professionals often overlooked the psychological and social issues of the dialysis-dependent CKD population.[9]

This study evaluated the prevalence of depression, its risk factors, and association with sociodemographic factors, quality of life, and self-perception of caregiver burden in hemodialysis patients.

RESULTS

The Consolidated Standards of Reporting Trials diagram of the study participants consisting of 150 hemodialysis patients is shown in Figure 1, and their baseline characteristics are listed in Supplementary Table S1. Depression was detected in 110 patients (73.3%), and the stratification into 3 categories based on severity is depicted in Supplementary Figure S1. The mean Beck Depression Inventory score was 24.17 $\pm$ 12.47.

A comparison of the depressed cohort with the rest of the study participants is shown in Table 1. Factors associated with greater severity of depression were lower level of education, higher pill burden, poor quality of life, and higher self-perception of caregiver burden. These variables are represented as box-and-whisker plots (Figure 2), and the detailed subgroup analysis between the 3 strata of depression is presented in Supplementary Table S2. A significant inverse relationship was observed between the Beck Depression Inventory score and quality of life scores, and a positive correlation was noted between the Beck Depression Inventory score and advancing age, pill burden, and the Cousineau score (Supplementary Table S3).

In univariate logistic regression analysis, risk factors for depression were higher body mass index (BMI) (odds ratio [OR], 1.14 per unit increase; 95% confidence interval [CI], 1.02–1.29), lower level of education (OR, 2.52; 95% CI, 1.18–5.37), offspring (OR, 5.63; 95% CI 1.16–27.4) or spouse (OR, 2.61; 95% CI, 1.18–5.77) as primary caregiver compared with parent, and higher self-perception of caregiver burden (OR, 1.06 per unit increase; 95% CI, 1.03–1.08). Improved quality of life in the form of increment in 36-Item Short Form Health Survey scores was associated with lesser likelihood of depression: physical functioning (OR, 0.97 per unit increase; 95% CI, 0.96–0.99), role functioning (OR, 0.98; 95% CI, 0.96–0.99), bodily pain (OR, 0.96; 95%

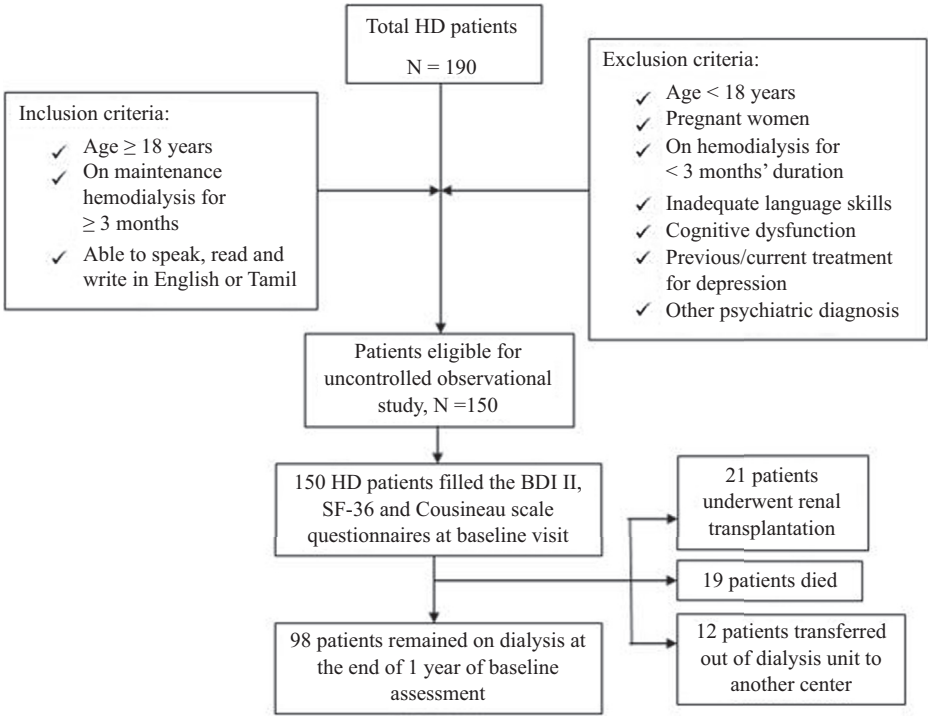

Figure 1. Consolidated Standards of Reporting Trials. HD, hemodialysis; BDI, Beck Depression Inventory score; SF-36, 36-Item Short Form Health Survey.

CI, 0.95–0.98), general health (OR, 0.94; 95% CI, 0.91–0.96), fatigue (OR, 0.96; 95% CI, 0.93–0.98), emotional well-being (OR, 0.94; 95% CI, 0.91–0.96), emotional functioning (OR, 0.97; 95% CI, 0.96–0.98), and social functioning (OR, 0.98; 95% CI, 0.96–0.99). In multivariate logistic regression, the level of education, perception of caregiver burden, and 3 quality of life domains—bodily pain, general health and emotional well-being—remained significant predictors of depression (Table 2).

All patients were monitored for 1 year from the time of assessment of their depressive symptoms. Nineteen patients (16.24%) had died, of whom 16 had been diagnosed with depression at the start of the study. By the Cox multivariate regression model, the only significant predictor of mortality in our cohort was increased number of comorbidities, with a hazard ratio of 0.40 (95% CI, 0.20–0.80; $P = 0.010$), and the analysis is depicted in Supplementary Table S4. The median patient survival on dialysis was 7.7 years in the depressed cohort and 8.9 years in the rest of the study population ($P = 0.427$). The survival curves and cumulative hazard ratio for all-cause mortality are depicted in Supplementary Figures S2 and S3. The hazard ratio for all-cause mortality was 0.61 (95% CI, 0.18–2.10; $P = 0.433$) in the depressed population after adjusting for all confounding variables, including age, sex, body mass index, number of failed vascular accesses, hypertension, coronary artery disease, tuberculosis, number of comorbidities, shift, duration, and frequency of dialysis, travel time, prior renal allograft loss, number of hospitalizations, pill burden, anemia, serum phosphorus, calcium and albumin levels, out-of-pocket expenditure, quality of life, and Cousineau scores.

DISCUSSION

In our study, 73.3% of patients had depression, which is considerably higher compared with published literature.[5] Younger age, higher unemployment rate, lower socioeconomic status, lower level of education, fewer transplant prospects, longer commuting time, and the consequential lifestyle restrictions can account for the higher rate of depression in our cohort. It is remarkable to note that the depression scores did not differ significantly between patients infected with hepatitis B, C, or HIV and the rest of the study population, reflecting absence of discrimination by the caregivers. The longer the duration on hemodialysis, the higher the proportion of depression noted, as in other studies.[S1]

Even if patients had a prospective living kidney donor or were on the priority list of deceased donors and had a high probability of successful renal transplantation in the near future, they experienced

Table 1. Characteristics of patients with and without depression

	Prevalence of depression		
	Yes	No	
Variables	**110 (73.3)**	**40 (26.7)**	***P* value**
Age, y	39.08 ± 11.62	34.8 ± 13.39	0.05
≤30	31 (62)	19 (38)	0.080
31–50	61 (78.2)	17 (21.8)	
>50	18 (81.8)	4 (18.2)	
Sex			
Male	73 (71.6)	29 (28.4)	0.476
Female	37 (77.1)	11 (22.9)	
Body mass index,[a] kg/m^2	19.64 ± 3.98	17.97 ± 2.59	**0.020**
Underweight	38 (67.9)	18 (32.1)	0.119
Ideal weight	52 (75.4)	17 (24.6)	
Overweight	7 (87.5)	1 (12.5)	
Obese	11 (100)	0 (0)	
Level of education			
Illiterate	10 (100)	0 (0)	**0.030**
Primary school	14 (87.5)	2 (12.5)	
Secondary school	59 (74.7)	20 (25.3)	
Graduation	24 (63.1)	14 (36.9)	
Postgraduation	3 (42.8)	4 (57.2)	
No. of previous failed vascular access	1.4 ± 0.8	1.38 ± 0.8	0.867
0	79 (73.1)	29 (26.9)	0.410
1	24 (77.4)	7 (22.6)	
2	4 (57.1)	3 (42.9)	
3	1 (100)	0 (0.0)	
4	2 (100)	0 (0.0)	
5	0 (0.0)	1 (100)	
Charlson Comorbidity Index	3.25 ± 1.32	3.05 ± 1.50	0.421
Diabetes mellitus			
Yes	18 (100)	0 (0.0)	**0.006**
No	92 (69.7)	40 (30.3)	
Hypertension			
Yes	90 (73.2)	33 (26.8)	0.923
No	20 (74.1)	7 (25.9)	
Coronary artery disease			
Yes	20 (74.1)	7 (25.9)	0.923
No	90 (73.2)	33 (26.8)	
Past history of tuberculosis			
Yes	8 (57.1)	6 (42.9)	0.150
No	102 (75)	34 (25)	
Current tuberculosis			
Yes	6 (75)	2 (25)	0.913
No	104 (73.2)	38 (26.8)	
Viral serologic status			
Positive	27 (73)	10 (27)	0.503
Negative	83 (73.4)	30 (26.6)	
Shift of dialysis			
Morning	49 (76.6)	15 (23.4)	0.507
Afternoon	33 (75)	11 (25)	
Evening	28 (66.7)	14 (33.3)	
Dialysis duration, y	2.5 (0.57,4)	1.62 (0.5,4)	0.901
<2	93 (69.9)	40 (30.1)	**0.010**
≥2	16 (100)	0 (0)	
Frequency of hemodialysis			
Twice weekly	65 (68.4)	30 (31.6)	0.074
Thrice weekly	45 (81.8)	10 (18.2)	
Availability of prospective donor			
On living donor work-up	14 (66.7)	7 (33.3)	0.413

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Table 1. (Continued)

Variables	Prevalence of depression		*P* value
	Yes	No	
	110 (73.3)	40 (26.7)	
Priority in deceased donor waiting list	15 (65.2)	8 (34.8)	
Others	81 (76.4)	25 (23.6)	
Prior renal allograft loss			
Yes	14 (77.8)	4 (22.2)	0.649
No	96 (72.7)	36 (27.3)	
Hospitalizations in past 1 year, No.	3 (1, 4)	3 (2, 4)	0.633
Pills per day, No.	22.4 ± 6.03	21.5 ± 5.3	0.322
≤20	40 (69)	18 (31)	0.357
>20	69 (75.8)	22 (24.2)	
Dialysis center-home transit time, h	2 (1.5, 4)	3 (2, 4.75)	0.169
<2	29 (78.4)	8 (21.6)	0.365
2–4	64 (74.4)	22 (25.6)	
>4	17 (63)	10 (37)	
Out-of-pocket expenditure per dialysis session			
Indian rupees	375 (262.5, 500)	475 (300, 600)	0.084
Dollars	5.10 (3.57, 6.81)	6.47 (4.08, 8.17)	
Age of the caregiver, y	41.58 ± 11.87	44.15 ± 11.66	0.241
Relationship of the caregiver			
Parent	27 (58.7)	19 (41.3)	**0.028**
Spouse	63 (78.8)	17 (21.2)	
Offspring	12 (100)	0 (0)	
Sibling	4 (66.7)	2 (33.3)	
Others	4 (66.7)	2 (33.3)	
Laboratory values			
Plasma hemoglobin, g/dl	7.8 ± 1.6	8.1 ± 1.6	0.319
Serum phosphorus, mg/dl	6.8 ± 1.4	6.5 ± 1.8	0.346
Serum calcium, mg/dl	7.7 ± 0.9	7.6 ± 1.1	0.612
Serum albumin, g/dl	3.3 ± 0.5	3.3 ± 0.5	0.909
SF-36 scores			
Physical functioning	40 (20, 55)	57.5 (36.25, 80)	**<0.001**
Limitations due to physical health	0 (0, 25)	50 (0, 75)	**<0.001**
Body pain	32.5 (20, 65)	77.5 (53.1, 90)	**<0.001**
General health	40 (30, 55)	57.5 (46.25, 73.75)	**<0.001**
Energy/fatigue	0 (0, 33.3)	66.6 (33.3, 100)	**<0.001**
Emotional well-being	30 (20, 50)	55 (40, 70)	**<0.001**
Limitations due to emotional problems	52 (44, 60)	70 (60, 80)	**<0.001**
Social functioning	50 (25, 75)	75 (50, 96.88)	**0.001**
Cousineau score	55.5 ± 18.8	36.1 ± 19.9	**<0.001**
Outcome at the end of 1-year follow-up			
Death	16 (14.5)	3 (7.5)	0.084
Continuation on HD	75 (68.2)	23 (57.5)	
Transplantation	11 (10)	10 (25)	
Transfer out to another center	8 (7.3)	4 (10)	
Time from initiation of HD to death, y	1.8 (0.75, 4.28)	0.8 (0.7, 1.2)	0.239

HD, hemodialysis; No., number; SF-36, 36-Item Short Form Health Survey.
[a]Body mass index (kg/m^2) cutoff thresholds for the Asian population by the World Health Organization Expert Committee in 2004: underweight, <18.5; ideal weight, 18.5 to 22.9; overweight, 23 to 27.5; obesity, >27.5.
Continuous data are presented as the mean ± SD or as the median (interquartile range) and categorical data as n (%). Bold *P* values are statistically significant ($P < 0.05$).

depressive symptoms similar to those on maintenance hemodialysis without any prospective donors. We can infer that the diagnosis of end-stage renal disease itself is a major determinant of depression and that patients with living kidney donors felt apprehensive about the health risks they were imposing on the donors and the significant burden of being responsible for maintaining the donor's kidney.

Patients with offspring or spouse as primary caregivers had a significantly higher depression score compared with those who were accompanied by their parents to the hemodialysis center due to the cultural set-up unique to the Indian society. In contrast to a meta-analysis by Farrokhi *et al.*,[S2] our experience did not reveal an association between depression and mortality, probably because of the short duration of follow-up.

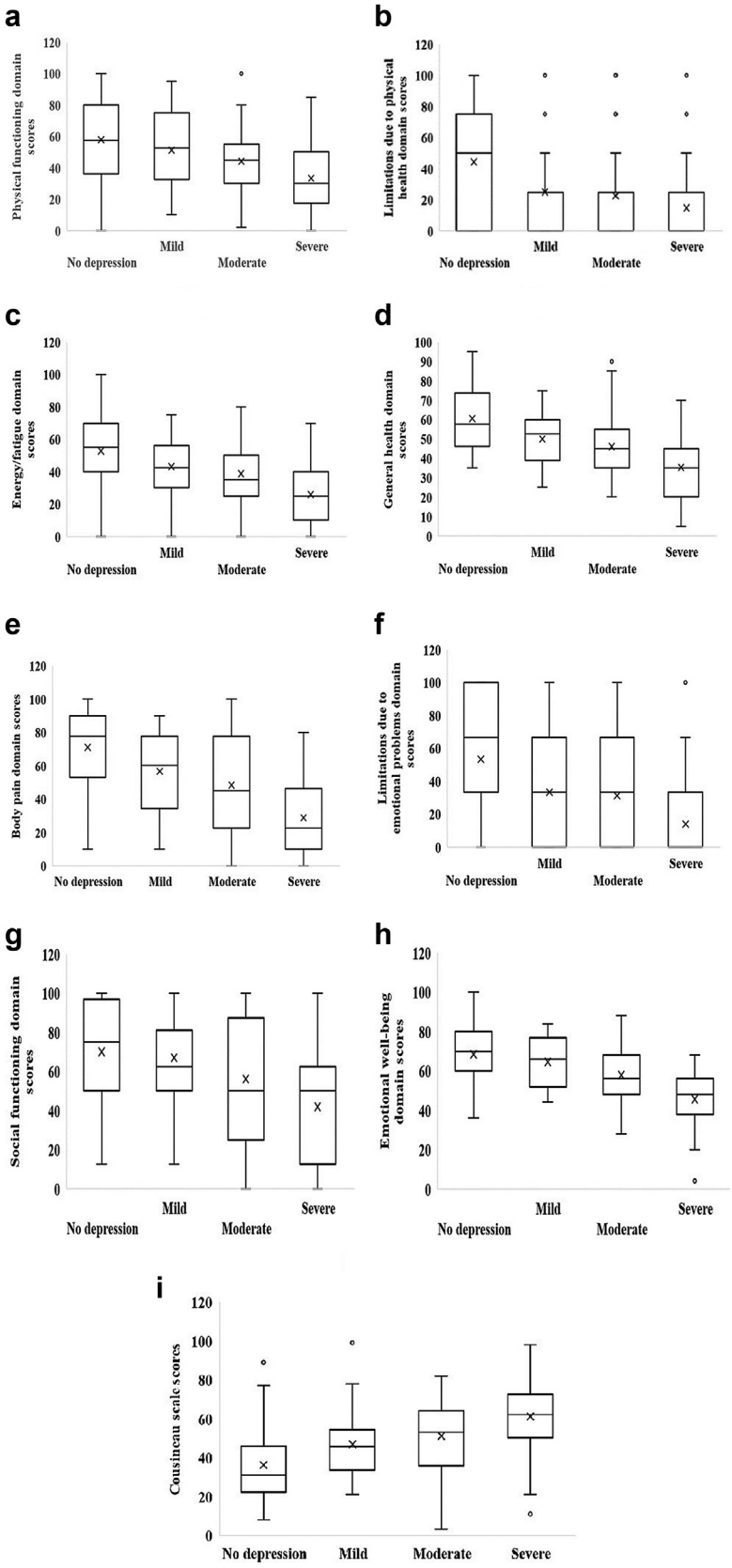

Figure 2. Box-and-whisker plots of (a-h) 36-Item Short Form Health Survey and (i) Cousineau scores. As the quality of life scores decrease and self-perception of caregiver burden increases, there is worsening of severity of depression. (a) Physical functioning. (b) Role functioning/limitations due to physical health. (c) Energy/fatigue. (d) General health. (e) Bodily pain. (f) Emotional functioning/limitations due to emotional problems. (g) Social functioning. (h) Emotional well-being. (i) Cousineau score. The bottom and top of the boxes indicate the 25th and 75th percentiles, respectively, of the SF 36 and Cousineau scores. The horizontal line and cross-mark inside the boxes indicate the median and mean, respectively. The lower and upper whiskers indicate the minimum and maximum values, respectively. The circles represent the outliers.

Table 2. Predictors of depression in hemodialysis patients

	Patients with depression (Beck Depression Inventory score > 14)						
	Univariate analysis					Multivariate analysis	
Covariates	β	Standard error	Wald	Odds ratio (95% CI)	*P* value	Odd ratio (95% CI)	*P* value
Age[a]	0.031	0.017	3.553	1.03 (0.99–1.07)	0.059	1.03 (0.97–1.09)	0.345
Sex							
Male (reference)	…	…	…	…	…		
Female	0.29	0.408	0.506	1.34 (0.60–2.97)	0.477		
Body mass index[a]	0.135	0.059	5.145	1.14 (1.02–1.29)	**0.023**	0.98 (0.80–1.19)	0.813
Level of education							
Postgraduation (reference)	…	…	…	…	…	…	
Others	0.922	0.387	5.668	2.52 (1.18–5.37)	**0.017**	3.33 (1.14–9.73)	**0.028**
No. of failed vascular accesses[a]	−0.085	0.217	0.153	0.92 (0.60–1.41)	0.696		
No. of comorbidities[a]	0.115	0.155	0.553	1.12 (0.83–1.52)	0.457		
Charleson Comorbidity Index[a]	0.116	0.144	0.652	1.12 (0.85–1.49)	0.419		
Hypertension							
No (reference)	…	…	…	…	…		
Yes	0.047	0.484	0.009	1.05 (0.41–2.70)	0.923		
Coronary artery disease							
No (reference)	…	…	…	…	…		
Yes	−0.047	0.484	0.009	0.96 (0.37–2.46)	0.923		
Current tuberculosis							
No (reference)	…	…	…	…	…		
Yes	−0.092	0.838	0.012	0.91 (0.18–4.72)	0.913		
Viral serology status							
Negative (reference)	…	…	…	…	…		
Positive	0.185	0.435	0.181	0.83 (0.36–1.95)	0.671		
Shift of dialysis							
Morning (reference)	…	…	…	…	…		
Afternoon	0.491	0.441	1.239	1.63 (0.69–3.87)	0.266		
Evening	0.085	0.456	0.035	1.09 (0.44–2.66)	0.852		
Duration of dialysis[a]	−0.003	0.087	0.001	0.99 (0.84–1.18)	0.973		
Frequency of dialysis							
Twice weekly (reference)	…	…	…	…	…		
Thrice weekly	0.731	0.413	3.125	2.08 (0.92–4.67)	0.077	0.53 (0.16–1.75)	0.296
Availability of living donor							
Living donor available (reference)	…	…	…	…	…		
Deceased donor waiting list priority	−0.482	0.516	0.873	0.62 (0.22–1.70)	0.35		
No donors	−0.547	0.494	1.226	0.58 (0.22–1.52)	0.268		
Prior renal allograft loss							
No (reference)	…	…	…	…	…		
Yes	−0.272	0.6	0.206	0.76 (0.24–2.47)	0.65		
No. of hospitalizations in 1 year[a]	−0.081	0.071	1.289	0.92 (0.80–1.06)	0.256		
Pill burden per day[a]	0.025	0.032	0.585	1.02 (0.96–1.09)	0.444		
Dialysis center–home transit time[a]	−0.034	0.049	0.481	0.97 (0.88–1.06)	0.488		
Out-of-pocket expenditure[a]	−0.001	0.001	0.725	0.999 (0.998–1.001)	0.395		
Age of caregiver[a]	−0.018	0.016	1.379	0.98 (0.95–1.01)	0.24		
Relationship of care-giver							
Parent (reference)	…	…	…	…	…		
Offspring	−1.728	0.808	4.579	5.63 (1.16–27.4)	**0.032**		
Spouse	−0.959	0.405	5.59	2.61 (1.18–5.77)	**0.018**	2.43 (0.90–6.53)	0.079
Others	−0.342	0.916	0.139	1.4 (0.23–8.48)	0.709		
Plasma hemoglobin[a]	−0.127	0.127	1.002	0.88 (0.69–1.13)	0.317		
Serum phosphorus[a]	0.134	0.142	0.892	1.14 (0.87–1.51)	0.345		
Serum calcium[a]	0.113	0.219	0.263	1.12 (0.73–1.72)	0.608		
Serum albumin[a]	−0.038	0.331	0.013	0.96 (0.50–1.84)	0.908		
SF-36 scores[a]							
Physical functioning	−0.027	0.008	12.524	0.97 (0.96–0.99)	**<0.001**	0.99 (0.96–1.02)	0.392
Role functioning	−0.025	0.006	16.912	0.98 (0.96–0.99)	**<0.001**	1.02 (0.99–1.04)	0.154
Bodily pain	−0.038	0.008	24.776	0.96 (0.95–0.98)	**<0.001**	0.975 (0.95–0.99)	**0.001**

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Table 2. (Continued)

Covariates	Patients with depression (Beck Depression Inventory score > 14)						
	Univariate analysis					Multivariate analysis	
	β	Standard error	Wald	Odds ratio (95% CI)	*P* value	Odd ratio (95% CI)	*P* value
General health	−0.066	0.014	23.652	0.94 (0.91–0.96)	**<0.001**	0.97 (0.942–0.99)	**0.024**
Emotional functioning	−0.026	0.006	20.196	0.97 (0.96–0.98)	**<0.001**	1.01 (0.99–1.03)	0.195
Energy/fatigue	−0.046	0.01	19.494	0.96 (0.93–0.98)	**<0.001**	0.99 (0.94–1.02)	0.529
Emotional well being	−0.067	0.015	21.243	0.94 (0.91–0.96)	**<0.001**	0.96 (0.94–0.99)	**0.031**
Social functioning	−0.022	0.007	10.532	0.98 (0.96–0.99)	**0.001**	0.99 (0.98–1.02)	0.791
Cousineau score[a]	0.055	0.012	21.05	1.06(1.03–1.08)	**<0.001**	1.03 (1.01–1.06)	**0.032**

CI, confidence interval; No., number; SF-36, 36-Item Short Form Health Survey.
[a]Per unit increase.
Bold *P* values are statistically significant ($P < 0.05$).

This is the first detailed epidemiologic study of depression among hemodialysis patients in the Indian setting with a significant sample size. There is minimal scope for patient recall bias because the questionnaires were based on activities of daily life. Because of the time lag of 1 year between assessment of depressive symptoms and the outcome measure of mortality, the temporal association between them cannot be inferred. There is considerable overlap between the domains of the Beck Depression Inventory II and 36-Item Short Form Health Survey scores; therefore, this redundancy in measurement may have contributed to a part of the association observed between depression and quality of life. Owing to few atypical characteristics of our study cohort compared with the average hemodialysis population worldwide, the results may not be applicable to all clinical settings.

To conclude, a regular formal screening will aid clinicians in early diagnosis and treatment of this major mental health problem in this vulnerable population.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods

Supplementary Table S1. Baseline characteristics of the study cohort

Supplementary Table S2. Comparison between categories of severity of depression

Supplementary Table S3. Correlation between BDI score and clinical parameters

Supplementary Table S4. Impact of depression on all-cause mortality in hemodialysis patients

Supplementary Figure S1. Prevalence of depression in the study participants

Supplementary Figure S2. Kaplan-Meier survival curve of hemodialysis patients with and without depression.

Supplementary Figure S3. Cumulative hazard ratio for all-cause mortality in hemodialysis patients with and without depression.

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