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Depressive symptoms and chronic kidney disease: results from the National Health and Nutrition Examination Survey (NHANES) 2005–2006

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Abstract

Background and objective—Depression is common in individuals with end-stage renal disease. However, its relationship with earlier stages of chronic kidney disease (CKD) is less well known. In this study, we examined the association between depressive symptoms and CKD.

Methods—Cross-sectional analysis of the prevalence and correlates of depressive symptoms were measured by the Patient Health Questionnaire (PHQ-9) among adult participants with CKD in the National Health and Nutrition Examination Survey 2005–2006. CKD was defined according to estimated glomerular filtration rate by Modification of Diet in Renal Disease Study equation of <60 ml/min/1.73 m^2 or the presence of microalbuminuria (≥30 mg/g creatinine), using the Kidney Disease Outcomes Quality Initiative classification. A PHQ-9 score ≥10 was considered to be indicative of depressive symptoms.

Results—Among 3653 subjects in our study sample, 683 (15.2%) met laboratory criteria for CKD. The prevalence of depressive symptoms was 7% (95% confidence interval [CI] 3.2–10.8%) in subjects with CKD and 6% (95% CI 4.6–7.4%) in subjects without CKD ($P = 0.6$). In regression analysis, the presence of CKD was not significantly associated with depressive symptoms (adjusted odds ratio = 0.96 [95% CI 0.51, 1.78], $P = 0.9$).

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Conclusions—We found no difference in the prevalence of depressive symptoms among individuals with or without CKD.

Keywords

Chronic kidney disease; Depression; National Health and Nutrition Examination Survey; Prevalence

Introduction

Depression is the most common mental health disorder in patients with end-stage renal disease (ESRD) on long-term hemodialysis or following a kidney transplant, with an estimated prevalence between 15 and 40% [1–6]. Moreover, depression is associated with high hospitalization rates and substantial morbidity and mortality rates in these patients [7]. However, little is known about the prevalence and risk factors for depression in patients with early stages of chronic kidney disease (CKD). A study by Hedayati et al. [8] at a single urban outpatient clinic found that 21% of veterans with CKD stages 2–5 had major depressive disorder, and prevalence did not vary significantly by CKD stage. In a secondary analysis of data from hospitalized patients with congestive heart failure (CHF), the same authors reported that depression was significantly more prevalent among patients with severe CKD [9]. In contrast, other observational studies of patients with coronary artery disease [10], ambulatory CKD patients [2, 11], and a population-based cohort [12] found no difference in the prevalence of depressive symptoms between adults with and without CKD. These heterogeneous findings might be the result of study limitations such as small sample size and sampling of a single geographic region and therefore justify studying a larger and more representative sample of the US population.

The purpose of this study is to examine the prevalence of depressive symptoms among individuals with early stages of CKD and to evaluate the relationship between levels of kidney function and depressive symptoms among a large representative adult sample in the United States. We hypothesize that the prevalence of depression symptoms in adults with CKD will be higher than in the general population and that there will be a significant association between depression symptoms and severity of CKD.

Materials and methods

Study design

NHANES is a cross-sectional, multistage, stratified, clustered probability sample survey of the US civilian, non-institutionalized population, conducted by the National Center for Health Statistics (NCHS). The survey protocol was approved by the NCHS institutional review board. All participants provided informed consent. Participants underwent a home interview followed by a physical examination and blood and urine sampling [13].

We examined data from NHANES 2005–2006 participants who were 20 years of age or older and were not pregnant. Participants included in the study had complete demographic information, results reported for serum creatinine, urine creatinine and albumin, and answered questionnaires of interest (Patient Health Questionnaire [PHQ-9], Medical Conditions, Diabetes, and High Blood Pressure questionnaires) (n=3653, out of 4,841 eligible participants ≥20 years of age). Eighty-six percent of excluded participants had missing data on the outcome and/or exposure variables.

Measurements

Random spot urine albumin and creatinine were measured using frozen specimens as previously described [13, 14]. Serum creatinine was measured using a kinetic rate Jaffé method and recalibrated to standardized creatinine [14]. We used the formula developed by NCHS to adjust the NHANES 2005–2006 serum creatinine values to ensure comparability with standard creatinine [14]. The glomerular filtration rate (GFR) was estimated using the abbreviated Modification of Diet in Renal Disease (MDRD) Study formula: estimated GFR (eGFR) = 175 × (standardized serum creatinine in mg/dL)$^{-1.154}$ × (age)$^{-0.203}$ × 0.742 (if female) × 1.212 (if African American).

Definitions

The outcome variable was the presence of depressive symptoms defined as a PHQ-9 ≥10. The PHQ-9 is a 9-item screening instrument with high reliability and validity in the primary care population [15] that evaluates the frequency with which depressive symptoms are present over the prior 2 weeks. Watnick et al. [6] showed validity of the PHQ-9 as screening tool in comparison with gold standard criteria for the diagnosis of depression in long-term dialysis patients, with an optimal cutoff value of ≥10, same as used in the general US population.

Microalbuminuria was defined as a urine albumin-to-creatinine ratio ≥30 mg/g creatinine. We evaluated CKD based on the Kidney Disease Outcomes Quality Initiative (KDOQI) classification:[16] eGFR (in ml/min/1.73 m^2) < 30 (stages 4 or 5), 30–59 (stage 3), and ≥60 with microalbuminuria (stage 1 or 2). Participants with eGFR ≥60 and no microalbuminuria were classified as not having CKD. For logistic regression analyses, CKD was dichotomized (eGFR < 60 or microalbuminuria, yes/no). Most medical conditions were defined based on subject self-report of the specific disease, including CHF, stroke, and cancer. The self-reported use of antihypertensive or diabetes medications was used to define hypertension or diabetes. Obesity was defined as body mass index (BMI) ≥30 kg/m^2.

Statistical methods

All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC) and incorporating the 2-year sample weights to adjust for oversampling of ethnic minorities, elderly persons, and those of low income. NCHS recommendations were followed to account for stratification and clustering of the survey design [13]. Unadjusted prevalence estimates of depressive symptoms were assessed by CKD status. A P value of <0.05 was considered significant for hypothesis testing. Differences in the distribution of sociodemographic and clinical characteristics were tested by using the Student's t test for continuous variables or Wald log-linear chi-square test for categorical variables. The association between depressive symptoms and covariates was assessed using logistic regression models and expressed as odds ratios (95% confidence intervals [CI]). Potential covariates were selected based on the published literature [4, 9, 10]. The final model was determined using manual backward selection to identify significant covariates. Interactions were tested by adding a product term for CKD category and each of the potential covariates.

Results

Study participants

Of a total eligible sample of 4841 NHANES 2005–2006 participants 20 years or older, 3,653 met the inclusion criteria. Of these, 248 (6.1% [95% CI 4.8–7.5%]) had depressive symptoms (i.e., PHQ-9 ≥10) (Table 1). There were 683 participants (15.2% [95% CI 12.9–17.5%]) with CKD (eGFR < 60 ml/min/1.73 m^2 or microalbuminuria) and 2,970

participants (84.8% [95% CI 82.5–87.1%]) without CKD (eGFR ≥60 ml/min/1.73 m^2 and no microalbuminuria). Among those participants with CKD, the distribution was as follows: 322 (7.1% [95% CI 6.2–7.9%]) with CKD stage 1 or 2; 336 (7.7% [95% CI 5.9–9.5%]) with CKD stage 3; and 25 (0.4% [95% CI 0.2–0.6%]) with CKD stage 4 or 5.

Characteristics of participants by PHQ-9 Score

Participants with depressive symptoms (PHQ-9 score ≥10) were significantly more likely to be aged 40–59 years, women, non-Hispanic Black, uninsured, current smoker, widowed, divorced or separated, to have less than a high school education, and a family income of less than US $20,000 compared to those without depressive symptoms (PHQ-9 score < 10) ($P < 0.05$) (Table 1). Participants with depressive symptoms were also more likely to be obese and to self-report a history of diabetes, hypertension, CHF, stroke, or cancer.

Association of kidney disease status with depressive symptoms

The prevalence of depressive symptoms was 7% (95% CI 3.2–10.8%) in participants with CKD and 6% (95% CI 4.6–7.4%) in those without CKD ($P = 0.6$) (Fig. 1). Furthermore, the prevalence of depressive symptoms was not significantly different across KDOQI stages of CKD (P for trend 0.7). There was a non-significant increase in the percentage of participants with depressive symptoms among those with CKD stage 4 or 5 (11.6%) compared with no CKD (6%). In multivariate regression analyses, the risk of depressive symptoms was not increased in the presence of CKD (odds ratio [OR] = 0.96 [95% CI 0.51, 1.78], P value = 0.9) There was no evidence of interaction between CKD status and any covariate included in the model. Because depression is known to be more common in women, we conducted a gender-stratified analysis of the prevalence of depression among participants with and without clinically defined CKD; however, results were similar to those obtained from the population as a whole.

Discussion

While the risk for depressive symptoms among patients with ESRD has been well described, the risk for depression in the early stages of CKD has not been as thoroughly investigated. To our knowledge, this is the first evaluation of the relationship between depressive symptoms and kidney disease in a large representative sample of the US adult population and across the full spectrum of kidney function. We found that depressive symptoms affect a similar proportion of individuals with and without CKD, 7 and 6%, respectively. While the prevalence of depressive symptoms was more pronounced and present in nearly 12% of participants with CKD stages 4 and 5, definitive conclusions cannot be made due to the limited number of participants with advanced disease.

Previous studies of smaller samples from hospital-or clinic-based CKD patients have reported a wide range of depressive symptoms prevalence from 15 to 50% [2, 8–10]. This variability could be due to small sample size, heterogeneity in CKD severity between samples, and differences in instruments used to measure depression and depressive symptoms. The use of a larger dataset such as NHANES allows for examination of a sample where the racial/ethnic groups as well as persons from all ages and socioeconomic backgrounds are well represented. Our results are therefore generalizable to the broad US population. In contrast to prior reports, our study sample afforded a comparison of depressive symptoms between CKD and non-CKD individuals. Interestingly, we did not find a significant association between depressive symptoms and CKD stages. However, similar to prior reports [17], we found a non-significant increase in depressive symptoms among individuals with CKD stage 4 or 5. It is possible that the psychological and lifestyle burdens and losses associated with planning and initiation of dialysis account for these

observations [18]. Because of sample size limitations, more definitive conclusions about this association cannot be made.

This study has some limitations. First, the design was cross-sectional; therefore, we could not assess the change in depressive symptoms as renal disease progresses. Second, although a large number of patients were included in our sample, 1,188 out of 4,841 participants could not be analyzed due to missing data for key covariates, which may have introduced selection bias. Third, although the PHQ-9 has been validated for use in patients with ESRD [6], it has not yet been validated against a gold standard psychiatric diagnosis of depression in patients with CKD.

In conclusion, prevalence of depressive symptoms did not differ significantly by CKD status. It has been demonstrated that depressed CKD patients are at risk for having poor quality of life and dialysis patients with depression are at risk for increased rates of morbidity and mortality. Therefore, it is important for healthcare providers to be especially mindful of depression in their patients with CKD. Future research should be dedicated to assess the impact of worsening renal function in the presence of depressive symptoms and vice versa.

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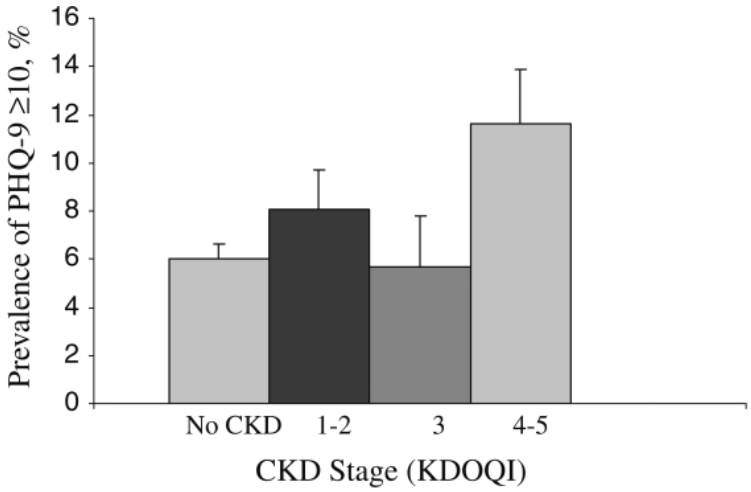

		KDOQI - CKD Classification		
	No CKD	**Stage 1, 2**	**Stage 3**	**Stage 4,5**
N (Weighted %)	2970 (84.8)	322 (7.1)	336 (7.7)	25 (0.4)
% PHQ-9 ≥10 (95% CI)	6.0 (4.6-7.4)	8.1 (5.3-10.9)	5.7 (0.7-10.7)	11.6 (0-27.8)
P Value	Referent	0.1	0.9	0.3

Fig. 1.
Prevalence of PHQ-9 ≥10 by kidney disease status (*vertical bars* represent standard errors)

Table 1

Characteristics of the US adult population, by PHQ-9 Score, NHANES 2005–2006

	No. of participants (weighted %)	PHQ-9 Score, % (SE)		
		<10	≥10	*P* value*
Overall	3,653 (100)	93.9 (0.6)	6.1 (0.6)	
Age group (years)				
20–39	1,214 (35.7)	36.2 (1.5)	27.9 (4.0)	0.004
40–59	1,259 (41.8)	40.9 (1.4)	54.9 (3.8)	
>60	1,180 (22.6)	22.9 (1.9)	17.1 (3.6)	
Gender				
Female	1,765 (51.1)	50.3 (0.6)	62.8 (3.1)	0.001
Male	1,888 (48.9)	49.7 (0.6)	37.2 (3.1)	
Race/ethnicity				
Mexican–American	679 (7.1)	7.2 (0.9)	6.2 (1.6)	0.01
NH-White	1,935 (74.8)	75.2 (2.5)	68.7 (5.0)	
NH-Black	806 (10.3)	9.9 (1.7)	15.6 (3.2)	
Other/multiracial	233 (7.8)	7.7 (1.1)	9.5 (3.2)	
Education[a]				
≤High school	1,815 (40.9)	40 (2.1)	54.3 (3.4)	0.001
>High school	1,838 (59.1)	60 (2.1)	45.7 (3.4)	
Family income (US$)[a]				
<20,000	855 (16.2)	14.9 (0.8)	36.5 (3.3)	<0.001
≥20,000	2,798 (83.8)	85.1 (0.8)	63.5 (3.3)	
Current smoker[a]	854 (24.7)	23.7 (1.3)	40.1 (4.1)	0.0006
Marital status[a]				
Married/living with partner	2,299 (66.8)	67.4(1.5)	57.6 (3.4)	0.008
Widowed/divorced/separated	806 (18.8)	18.1 (0.9)	28.8 (2.8)	
Never married	548 (14.4)	14.5 (1.0)	13.6 (3.0)	
Health insurance (yes)[a]	2,866 (77.6)	82.7 (1.8)	71.2 (4.2)	0.006
Obesity[a]	1,309 (35)	34.2 (1.5)	48.2 (5.9)	0.02
eGFR < 60 or Microalbuminuria	683 (15.2)	15.0 (1.0)	17.3 (4.5)	0.6
Self-reported comorbidities[a]				
Diabetes	393 (8.0)	7.8 (0.6)	12.4 (2.2)	0.05
Congestive heart failure	120 (2.3)	2.1 (0.2)	4.5 (1.4)	0.02
Stroke	131 (2.6)	2.2 (0.3)	8.8 (1.9)	<0.001
Cancer	312 (8.3)	7.7 (0.6)	16.6 (2.7)	0.0004

SE standard error, *eGFR* estimated glomerular filtration rate, and *RA* rheumatoid arthritis

*Wald log-linear Chi-square test

[a]Missing values were distributed as follows: PHQ-9 score (498), education (7), family income (138), smoking status (4), marital status (5), health insurance (6), BMI (95), eGFR (313), microalbuminuria (473), kidney disease awareness (14), hypertension (14), CHD (2), CHF (14), stroke (7), COPD (5), RA or osteoarthritis (10), and cancer (4)