

Anxiety in patients with chronic kidney disease: sociodemographic, clinical and biochemical associations

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Background: Chronic kidney disease (CKD) is an important contributor to global disease burden and presence of anxiety in CKD is associated with poor quality of life and increased mortality. The relationship of anxiety symptoms with kidney function and sociodemographic factors remains poorly investigated.

Objectives: To assess the relationship between anxiety with socio-demographic factors as well as some clinical biomarkers in patients with CKD.

Methods: A cross-sectional study was conducted in nephrology department of a medical college hospital in 2021. By convenient sampling technique, 103 CKD patients of stages 3-5D were enrolled in the study. Sociodemographic and clinical data including CRP, hemoglobin, serum albumin, serum iPTH, blood urea was recorded from patients' clinical notes and interview. CKD staging was done by KDIGO 2012 criteria. Severity of anxiety symptoms was assessed by the Generalized Anxiety Disorder Scale-7 (GAD-7).

Results: Among the patients, 53 (51.5%) were in CKD stage of 3-5 and 50 (48.5%) were receiving hemodialysis. A significant number of patients (28.1%) had shown moderate to severe anxiety. CKD patients' age showed negative correlation with anxiety score ($r=-0.400$, $p=0.000$). No significant correlation was found between GAD-7 score and urea reduction ratio, serum creatinine level, eGFR, hsCRP, blood hemoglobin and serum parathyroid hormone level.

Conclusions: Anxiety symptoms are highly prevalent in CKD patients. However no significant association with sociodemographic factors or biochemical parameters were observed.

Declaration of interest: None

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Keywords: Chronic kidney disease; anxiety; hemodialysis, GAD-7.

Introduction

Chronic kidney disease (CKD) is characterized by the presence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m², persisting for three or more months.¹ The global burden of CKD is increasing and assumed to become the 5th most common cause of years of life lost globally by 2040.² While one in five adults in Bangladesh suffer from mental disorders, this number increases in many times when

associated with chronic diseases.^{3,4} Psychiatric problems like depression, anxiety, fatigue, suicidal tendency, impaired cognitive ability and decreased quality of life are widely reported in CKD, however, precise prevalence of anxiety symptoms are unclear. The prevalence reported range between 12% and 52% across different studies.⁵ Pathological anxiety can present with affective, cognitive, physiological or behavioral symptoms; the condition is

underdiagnosed in CKD but associated with high morbidity.⁶ Anxiety conditions can lead to substance abuse, major depression and adverse cardiac events.⁶ Also, it impairs one's ability to develop social relationship and worsen quality of life.

Some of the anxiety disorders are found to be associated with elevated level of circulating inflammatory biomarkers, such as high sensitivity C-reactive protein (hsCRP) which is also elevated in CKD.⁷ Other theories pointed to the vascular and hemodynamic similarities between renal and brain tissues for elevated risk of neuropsychiatric disorders in CKD.⁸ Brain damage related with inflammation, oxidative stress, involvement of renin-angiotensin system has also been hypothesized for emergence of anxiety symptoms in CKD.⁹ Considering the worldwide growing prevalence of CKD and increasing importance of mental health in chronic diseases, improving our knowledge about psychiatric disturbances and its predictors in CKD patients is important.

Selective serotonin reuptake inhibitors (SSRIs), commonly prescribed to manage anxiety have active metabolites that are renally excreted, leading to accumulation of potentially toxic metabolites in patients with decreased glomerular filtration rates. Therefore, identifying subjects with anxiety who may benefit from preventive measures before a complication begins to occur is also necessary.

Methods

A cross-sectional study was conducted at US-Bangla Medical College Hospital, Narayanganj, Bangladesh in 2021. Ethical clearance was taken from the respected authority before and informed written consent was taken from each participant. CKD stage 3 to 5D patients were enrolled from the outpatient department and hemodialysis unit of the hospital by convenient sampling technique. Inclusion criteria for the participants were age of 30 and above, and for stage 5D patients they had to receive hemodialysis treatment for at least 3 months. Exclusion criteria were previous diagnosis of psychiatric disorder (including depressive disorder), advanced dementia, active and severe illness at time of recruitment. Data included sex, age, marital status, education level, economic status, comorbidities, duration of dialysis, etc., were retrieved from medical records. From clinical notes information about biochemical variables such as hemoglobin (Hb), CRP, serum creatinine, serum albumin, parathyroid hormone (PTH) and blood urea were collected. GFR was calculated using Modification of Diet in Renal Disease (MDRD) formula. For descriptive purposes, patients were classified into CKD stages, according to the National

Kidney Foundation's Kidney Disease Outcomes Quality Initiative guidelines.

Bangla version of the Generalized Anxiety Disorder Scale-7 (GAD-7)^{10,11} was used in the study to assess the frequency and severity of anxiety symptoms over the previous 2 weeks. Each question rates symptom severity from 0 to 3 with total scores ranging from 0 to 21. Scores between 0-4, 5-9, 10-14 and 15-21 points correspond to minimal, mild, moderate and severe anxiety, respectively. This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories of "not at all," "several days," "more than half the days," and "nearly every day", respectively, to the seven questions of GAD-7. Statistical analysis of the results was done by using computer based statistical software, SPSS-IBM version 23. P value of less than 0.05 was considered as statistically significant.

Results

Sociodemographic characteristics and selected biochemical parameters are shown in Table 1. A total of 103 CKD patients were enrolled for this study and among them 53 (51.5%) were in CKD stage of 3-5 and 50 (48.5%) were receiving hemodialysis. Hemodialysis group patients were older, had more incidences of comorbid diabetes mellitus, higher levels of PTH and lower levels of serum albumin and hemoglobin than CKD stage 3-5 patients.

Table 1: Sociodemographic and clinical characteristics of the CKD patients (N=103)

Characteristic	CKD Stage 3-5 (n=53)	CKD Dialysis (n=50)
Age (mean±SD)	55.2±12.7	59.2±6.8
Gender		
Male	31 (30)	24 (23.3)
Female	22 (21)	26 (25.2)
Education		
Below SSC	25 (24.2)	28 (27.1)
SSC	24 (23.3)	16 (15.5)
HSC and above	4 (3.8)	6 (5.8)
Residence		
Semi-urban	26 (25.2)	36 (34.9)
Rural	27 (26.2)	14 (13.5)
Marital status		
Married	43 (41.7)	36 (34.9)
Widow/widower	10 (9.7)	14 (13.5)
Monthly expenditure (1000 BDT)		
5-10	19 (18.4)	10 (9.7)
11-30	22 (21)	22 (21)
31-50	12 (11.6)	18 (17.4)

Characteristic	CKD Stage 3-5 (n=53)	CKD Dialysis (n=50)
Profession		
Service	6 (5.8)	14 (13.5)
Business	6 (5.8)	2 (1.9)
Cultivator	8 (7.7)	20 (19.4)
Dependent	21 (20.3)	14 (13.5)
Others	12 (11.6)	-
Comorbidity		
None	8 (7.7)	38 (36.8)
Diabetes	25 (24.2)	50 (48.5)
Hypertension	45 (43.6)	-
Investigation		
Serum creatinine	3.14±1.77	-
URR	-	65±7.0
eGFR	24.07±9.67	-
hsCRP	28.8±46.5	16.4±10.1
Serum albumin	3.48±1.05	3.08±0.79
Hemoglobin	9.99±2.17	8.86±1.44
iPTH	185.3±152.9	203.6±108.4

*URR, urea reduction ratio; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitive C-reactive protein; iPTH, intact parathyroid hormone

The mean score in anxiety severity falls in the mild range. A significant number of patients (28.1%) had moderately to severe anxiety. Table 2 shows the severity of depressive symptoms in CKD patients. T tests and ANOVA were used to see the differences in anxiety severity between various sociodemographic variables (Table 2).

Table 2: Severity of anxiety symptoms in CKD stages (N=103)

Anxiety state	CKD stage 3-5 (n=53)	CKD dialysis (n=50)	Total (n=103)
GAD-7 score (mean±SD)			
	8.1±4.3	6.6±3.9	7.4±4.2
Anxiety severity			
Minimal	14 (26.4)	12 (24)	26 (25.2)
Mild	18 (34)	30 (60)	48 (46.6)
Moderate	17 (32.1)	6 (12)	23 (22.3)
Severe	4 (7.5)	2 (4)	6 (5.8)

GAD-7, Generalized Anxiety Disorder Scale-7, cell values are expressed as frequency (percentage)

No significant difference was observed between CKD stage 3-5 and hemodialysis patients. Patients with monthly expenditure between 11-30,000 BDT reported higher anxiety than others. No significant difference was observed between across different gender, residence, education, marital status or profession (Table 3).

Table 3: Differences in anxiety severity between different characteristics of CKD patients (N=103)

Variable	Frequency (n)	GAD-7 Score*	t/F	P Value
CKD group				
CKD stage 3-5	53	8.1±4.3	1.72	0.088
CKD dialysis	50	6.6±3.9		
Gender				
Male	55	6.7±3.1	-1.82	0.071
Female	48	8.2±5.1		
Education				
Below SSC	53	7.3±3.9	0.17	0.912
SSC	40	7.5±4.9		
HSC and above	10	6.8±1.5		
Residence				
Urban	62	7.1±4.2	-0.63	0.527
Rural	41	7.7±4.1		
Marital status				
Married	79	7.7±4.2	1.43	0.154
Widow/widower	24	6.3±4.1		
Monthly expenditure (thousand BDT)				
5-10	29	6.9±3.6	4.86	0.010
11-30	44	8.7±4.8		
31-50	30	5.8±3.1		
Profession				
Service	6	10.6±1.3	2.12	0.083
Business	20	6.8±2.5		
Cultivator	10	6±3.5		
Dependent	41	6.8±4.1		
Others	26	8.6±5.3		

*Mean±SD

There was moderately strong negative correlation between age and anxiety severity. No significant correlation was found between GAD-7 score and urea reduction ratio, serum creatinine level, eGFR, hsCRP, blood hemoglobin and serum parathyroid hormone level (Table 4).

Table 4: Correlation of GAD-7 score with age and biochemical profile of the CKD patients (N=103)

Variable	Pearson's correlation coefficient (r)	P Value
Age (year)	-0.400	0.000
URR (%)	0.086	0.551
Serum creatinine (mg/dl)	0.088	0.529
eGFR (ml/min/1.73 m ²)	-0.016	0.941
hsCRP (mg/L)	0.147	0.155
Serum albumin (g/L)	0.082	0.433
Hemoglobin (g/dl)	-0.007	0.947
iPTH (pg/ml)	0.051	0.610

URR, urea reduction ratio; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitive C-reactive protein; iPTH, intact parathyroid hormone

Discussion

Mosleh et al. conducted a study in Saudi Arabia where 19.7% CKD patients showed anxiety symptoms¹² while Kumar et al. from India cited the figure as 28%.¹³ Through the administration of GAD-7 questionnaire, we found that most of the patients fall in the mild range of anxiety severity. A significant number of patients had moderate to severe anxiety. Similar findings were observed in some of the previous studies.¹⁴

Anxiety appears to be caused by an interaction between biopsychosocial factors where genetic vulnerability interacts with stressful and traumatic events to produce clinically significant symptoms.¹ Apart from age and monthly expenditure, we did not observe any significant correlates of anxiety symptoms in CKD patients. In general, the prevalence rate of anxiety disorders is reported to be lower among older adults compared to younger adults which was also found in our observation.¹⁵ People with less education, lower socioeconomic status tend to show more and persisting anxiety symptoms.¹⁶ Female gender and widowhood reportedly increase the risk of anxiety disorders.¹⁷ However, such associations may not be

found in patients with chronic disease.¹⁸ We observed no significant correlation between GAD-7 score and urea reduction ratio, serum creatinine level, eGFR, hsCRP, blood hemoglobin and serum parathyroid hormone level. Similarly, in patients on hemodialysis, hemoglobin, iron, TIBC, ferritin and albumin levels were not significantly correlated with anxiety.¹⁹

Personality traits are one of the factors that might explain anxiety symptoms in such patients. Traits like high neuroticism, low extraversion predict anxiety.²⁰ Cognitive styles such as tendency to ruminate, worry, intolerance of uncertainty, negative reappraisal of situations and looming cognitive style may also contribute to development of anxiety symptoms in CKD patients.^{21,22} One study reported acceptance, religion, planning, positive reframing, instrumental support, emotional support, self-distraction and venting were the most frequently used coping strategies in persons with chronic disease.²³ Lack of such strategies may thereof predict emergence of anxiety.

We acknowledge several limitations in our study. It was a single center study with a limited sample size. Also, as a cross-sectional study, we could only estimate the association and not the causal relevance of an exposure.

Conclusions

A significant number of patients with CKD showed moderate to severe anxiety symptoms. The symptoms showed no significant association with several routinely measured biochemical parameters; hence, personality traits, cognitive style and coping strategies might play important role in development of anxiety in CKD patients.

References

- Vaidya SR, Aeddula NR. Chronic Renal Failure. [Updated 2021 Oct 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022
- Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all cause and cause specific mortality for 250 causes of death: Reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet* 2018; 392: 2052-90.
- Turner J, Kelly B. Emotional dimensions of chronic disease. *West J Med* 2000; 172(2): 124-8.
- National Institute of Mental Health. National Mental Health Survey 2019. Dhaka: NIMH Press, 2021.

- 5 Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: A systematic review. *Adv Chronic Kidney Dis.* 2007; 14: 82-99.
- 6 Davison GC, Neale JM. *Abnormal psychology* (8th ed.). New York, NY John Wiley & Sons, Inc, 2001.
- 7 Glaus J, von Känel R, Lasserre AM, et al. The bidirectional relationship between anxiety disorders and circulating levels of inflammatory markers: Results from a large longitudinal population-based study. *Depress Anxiety* 2018; 35(4): 360-71.
- 8 Mogi M, Horiuchi M. Clinical interaction between brain and kidney in small vessel disease. *Cardiol Res Pract.* 2011; 2011: 306189.
- 9 Simões E Silva AC, Miranda AS, Rocha NP, Teixeira AL. Neuropsychiatric disorders in chronic kidney disease. *Front Pharmacol.* 2019; 10: 932.
- 10 Spitzer RL, Kroenke K, Williams Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder. *Arch. Intern. Med* 2006; 166: 1092-7.
- 11 Dhira TA, Rahman MA, Sarker AR, Mehreen J (2021) Validity and reliability of the Generalized Anxiety Disorder-7 (GAD-7) among university students of Bangladesh. *PLoS ONE.* 16(12): e0261590.
- 12 Mosleh H, Alenezi M, Al Johani S, Alsani A, Fairaq G, Bedaiwi R. Prevalence and factors of anxiety and depression in chronic kidney disease patients undergoing hemodialysis: a cross-sectional single-center study in Saudi Arabia. *Cureus.* 2020; 12(1): e6668
- 13 Kumar V, Khandelia V, Garg A. Depression and anxiety in patients with chronic kidney disease undergoing hemodialysis. *Ann Indian Psychiatry* 2018; 2: 115-9.
- 14 Gadia P, Awasthi A, Jain S, Koolwal GD. Depression and anxiety in patients of chronic kidney disease undergoing haemodialysis: A study from western Rajasthan. *J Family Med Prim Care* 2020; 9(8): 4282-6.
- 15 Canuto A, Weber K, Baertschi M, Andreas S, Volkert J, Dehoust MC, et al. Anxiety disorders in old age: psychiatric comorbidities, quality of life, and prevalence according to age, gender, and country. *Am J Geriatr Psychiatry* 2018; 26(2): 174-85.
- 16 Green MJ, Benzeval M. The development of socioeconomic inequalities in anxiety and depression symptoms over the lifecourse. *Soc. Psychiatry Psychiatr. Epidemiol* 2013; 48(12): 1951-61.
- 17 Onrust SA, Cuijpers P. Mood and anxiety disorders in widowhood: a systematic review. *Aging Ment Health* 2006; 10(4): 327-34.
- 18 Nieder C, Kämpe TA. Does marital status influence levels of anxiety and depression before palliative radiotherapy? *In vivo* 2018; 32(2): 327-30.
- 19 Najafi A, Keihani S, Bagheri N, Ghanbari Jolfaei A, Mazaheri Meybodi A. Association between anxiety and depression with dialysis adequacy in patients on maintenance hemodialysis. *Iran J Psychiatry Behav Sci.* 2016; 10(2): e4962.
- 20 Brandes M, Bienvenu OJ. Personality and anxiety disorders. *Curr Psychiatry Rep* 2006; 8(4): 263-9.
- 21 Arditte Hall KA, Quinn ME, Vanderlind WM, Joormann J. Comparing cognitive styles in social anxiety and major depressive disorders: An examination of rumination, worry, and reappraisal. *Br J Clin Psychol* 2019; 58(2): 231-44.
- 22 Carnahan ND, Carter MM, Sbrocco T. Intolerance of uncertainty, looming cognitive style, and avoidant coping as predictors of anxiety and depression during COVID-19: a longitudinal study. *Int J Cogn Ther* 2021;1-19.
- 23 Tuncay T, Musabak I, Gok DE, Kutlu M. The relationship between anxiety, coping strategies and characteristics of patients with diabetes. *Health Qual Life Outcomes.* 2008; 6: 79.

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