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Factors predicting depressive symptoms in patients with chronic kidney disease and end-stage renal failure

Nazia Afrin Siddiqui, Babrul Alam, Mohammad Haris Uddin, Mohammad Afjal Hossain, Md. Ashrafal Alam, S M Nafeez Imtiaz, Md. Raquib Morshed

Background: In adults with chronic kidney disease (CKD), depression is highly prevalent and associated with poor quality of life and increased mortality. The relationship of depressive symptoms with kidney function and sociodemographic factors remains poorly investigated.

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

Methods: : A cross-sectional study was conducted in Nephrology Department of a non-government 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 done by KDIGO 2012 criteria. Severity of depressive symptoms was assessed by Patient Health Questionnaire-9 (PHQ-9).

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 (35%) had moderately severe to severe depression severity. Those with education level below SSC, rural residents, monthly expenditure below 10 thousand and above 31 thousand BDT, businessmen and dependent on other's income showed higher depression levels. There were positive correlations between age ($r=0.34$, $p=0.000$), serum creatinine level ($r=0.64$, $p=0.000$), serum parathyroid hormone level ($r=0.52$, $p=0.000$) and depression severity; and negative correlations between urea reduction ratio ($r=0.80$, $p=0.001$), serum albumin ($r=-0.71$, $p=0.000$) and hemoglobin levels ($r=-0.71$, $p=0.000$) with depression severity.

Conclusions: Depressive symptoms are highly prevalent in CKD patients and several biochemical parameters correlates with depression severity.

Declaration of interest: None

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Keywords: Chronic kidney disease; depression; hemodialysis, end stage renal failure.

Introduction

While one in four people suffer from mental disorders worldwide this number increases in many times when associated with chronic diseases. Worldwide, Chronic Kidney Disease (CKD) has a prevalence of 13.4% and number is increasing day by day.¹ Common psychological problems in patients with chronic kidney disease include depression, anxiety, fatigue, decreased quality of life, increased risk for suicide and impaired cognitive functions.² Depression is the most common psychiatric disorder in patients with advanced CKD, with prevalence of major depressive disorder is estimated between 22.8 and 39.3%.³ It is an emotional state characterized by somatic and cognitive symptoms including feelings of sadness, loss of enjoyment, worthlessness, sleeplessness, loss of appetite and sexual desires, and interest in usual activities. A clinical diagnosis of depression, most often major depressive disorder, is performed when symptoms of depression become persistent, often for more than 2 weeks.⁴

In the general population, circulating inflammatory biomarkers, such as interleukin-6 (IL-6), high sensitivity C-reactive protein (hsCRP) and tumor necrosis factor- α (TNF- α), are associated with depression.⁵ Depression with protein catabolism can increase cardiovascular morbidity and mortality resulting repeated in hospitalization. Relationship between depression, elevated inflammatory cytokine levels, protein catabolism, and cardiovascular disease have led to protein-energy wasting which acts as a potential mechanism for high comorbidity of depression with chronic medical illness like chronic kidney disease.^{6,7} Direct effects of uremic toxins can cause cognitive decline by microvascular and hemodynamic alteration in dialysis patients. This causes non adherence to food, poor response to antidepressant medications and become more difficult to treat.⁸ It is worth noting that depression in CKD comes with serious effects on the patients' quality of life and negatively affecting their social, financial, and psychological well-being.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. Many anti-depressants have active metabolites that are renally excreted, leading to accumulation of potentially toxic metabolites in patients with decreased glomerular filtration rates.¹⁰ In addition, there is the risk of drug–drug interactions in CKD and ESRD patients. Therefore, there is a need to develop strategies to identify “high risk” subjects who may benefit from preventive

measures before a complication begins to occur which will help in providing active and healthy life in CKD patients.

Methods

This was a cross-sectional study, conducted at US-Bangla Medical College Hospital, Naraynganj, Bangladesh in between months of January 2021 and July 2021. Study population was CKD stage 3 to stage 5D patients enrolled from the Outpatient Department and Hemodialysis Unit of the hospital. Convenient sampling technique was used for patient selection and inclusion criteria were age of 30 and above, and for stage 5D patients they had to receive hemodialysis treatment for at least 3 months. Ethical clearance was taken from the respected authority before and informed written consent was taken from each participant. 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 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 MDRD formula.

Bangla version of the Patient Health Questionnaire-9 (PHQ-9)^{11,12} was used in the study to assess the frequency of depressive thoughts or feelings over the previous 2 weeks. Each question rates symptom severity from 0 to 3 with total scores ranging from 0 to 27. Scores ≤ 4 or ranging from 5 to 9, from 10 to 14, from 15 to 19 and ≥ 20 points correspond to minimal, mild, moderate, moderately severe and severe grade respectively. This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of “not at all,” “several days,” “more than half the days,” and “nearly every day.” 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 | CKD |
|---|------------------|-----------------|
| | stage 3-5 (n=53) | dialysis (n=50) |
| Age (mean±SD, year) | 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 (thousand BDT) | | |
| 5-10 | 19 (18.4) | 10 (9.7) |
| 11-30 | 22 (21) | 22 (21) |
| 31-50 | 12 (11.6) | 18 (17.4) |
| Profession | | |
| Service | 6 (5.8) | - |
| Business | 6 (5.8) | 14 (13.5) |
| Cultivator | 8 (7.7) | 2 (1.9) |
| Dependent | 21 (20.3) | 20 (19.4) |
| Others | 12 (11.6) | 14 (13.5) |
| Comorbidity | | |
| None | 8 (7.7) | - |
| Diabetes | 25 (24.2) | 38 (36.8) |
| Hypertension | 45 (43.6) | 50 (48.5) |
| Serum creatinine (mg/dl) | 3.14±1.77 | - |
| URR (%) | | 65±7.00 |
| eGFR (ml/min/1.73 m ²) | 24.07±9.67 | - |
| hsCRP (mg/L) | 28.8±46.5 | 16.4±10.1 |
| Serum albumin (g/L) | 3.48±1.05 | 3.08±0.79 |
| Hemoglobin (g/dl) | 9.99±2.17 | 8.86±1.44 |
| iPTH (pg/ml) | 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 depression severity falls in the moderate range. A significant number of patients (35%) had moderately severe to severe depression severity. Table 2 shows the severity of depressive symptoms in CKD patients. T tests and ANOVA was used to see the differences in depression severity between various sociodemographic variables. No significant difference was observed between CKD stage 3-5 and hemodialysis patients (Table 3). Those with education level below SSC, rural residents, monthly expenditure below 10 thousand and above 31 thousand BDT, businessmen and dependent on other's income showed higher depression levels. No significant difference was observed between males and females and married and widow/widower individuals (Table 3).

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

| Depression state | CKD stage 3-5 (n=53) | CKD dialysis (n=50) | Total (N=103) |
|------------------------------|----------------------|---------------------|---------------|
| PHQ-9 score (mean±SD) | 12.32±7.19 | 13.80±6.32 | 13.04±6.79 |
| Depression severity | | | |
| Minimal | 8 (15.1) | 4 (8) | 12 (11.7) |
| Mild | 15 (28.3) | 10 (20) | 25 (24.3) |
| Moderate | 14 (26.4) | 16 (32) | 30 (29.1) |
| Moderately severe | 4 (7.5) | 8 (16) | 12 (11.7) |
| Severe | 12 (22.6) | 12 (24) | 24 (23.3) |

PHQ-9, Patient Health Questionnaire-9

Table 3: Differences in depression severity between various sociodemographic variables of CKD patients (N=103)

| Variable | Frequency (n) | PHQ-9 score* | t/F | P Value |
|---|---------------|--------------|-------|---------|
| CKD group | | | | |
| CKD stage 3-5 | 53 | 12.3±7.1 | -1.01 | 0.272 |
| CKD dialysis | 50 | 13.8±6.3 | | |
| Gender | | | | |
| Male | 55 | 14.1±6.5 | 1.81 | 0.072 |
| Female | 48 | 11.7±6.9 | | |
| Education | | | | |
| Below SSC | 53 | 15.4±5.7 | 6.68 | 0.000 |
| SSC | 40 | 10.4±7.2 | | |
| HSC and above | 10 | 12.2±4.6 | | |
| Residence | | | | |
| Urban | 62 | 11.7±6.5 | -2.50 | 0.014 |
| Rural | 41 | 15±6.8 | | |
| Marital status | | | | |
| Married | 79 | 13±7.4 | 0.03 | 0.975 |
| Widow/widower | 24 | 13±4 | | |
| Monthly expenditure (thousand BDT) | | | | |
| 5-10 | 29 | 14.4±7.3 | 3.46 | 0.035 |
| 11-30 | 44 | 11±6.5 | | |
| 31-50 | 30 | 14.6±5.9 | | |
| Profession | | | | |
| Service | 6 | 3.6±1 | 4.98 | 0.001 |
| Business | 20 | 15.7±5 | | |
| Cultivator | 10 | 10.8±5.6 | | |
| Dependent | 41 | 14.2±6.2 | | |
| Others | 26 | 12.1±7.9 | | |

*Mean±SD

There were strong negative correlations between urea reduction ratio in hemodialysis patients and moderate positive correlation between age, serum creatinine level, serum parathyroid hormone level in all stages of CKD patients with depression severity. Strong negative correlations were found between serum albumin and hemoglobin levels with depression severity. Also, CKD stage 3-5 patients there was moderate negative correlation between GFR and depression severity.

Table 4: Correlation of depression severity with age and biochemical profile of the CKD patients (N=103)

| Variable | Pearson's correlation coefficient (r) | P value |
|------------------------------------|---------------------------------------|---------|
| Age (year) | 0.348 | 0.000 |
| URR (%) | -0.800 | 0.001 |
| Serum creatinine (mg/dl) | 0.644 | 0.000 |
| eGFR (ml/min/1.73 m ²) | -0.529 | 0.008 |
| hsCRP (mg/L) | 0.245 | 0.017 |
| Serum albumin (g/L) | -0.718 | 0.000 |
| Hemoglobin (g/dl) | -0.719 | 0.000 |
| iPTH (pg/ml) | 0.521 | 0.000 |

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

Discussion

Amira estimated that 23.7% of patients with CKD have depression and CKD patients on dialysis are more likely to develop depression (34.5%).¹³ Through the administration of PHQ-9 questionnaire, we found that most of the patient falls in the moderate range of depression severity. A significant number of patients had moderately severe to severe depression severity. Similar findings were observed in some of the previous studies.^{14,15} The meta-analysis of Palmer et al. confirms the estimated high prevalence of depression in patients with CKD and highlights that it varies according to the stage of CKD and the tools used for diagnosis.¹⁵ But our study showed no significant difference between severity of depression in predialysis patients and patients on hemodialysis. Comorbidities in CKD patients along with underdiagnosed and

undertreated depression might have been related with this finding.

Low socio-economic status and dependency tend to be associated with a higher prevalence of depression. Moreover, education and income of people correlate with each other¹⁶ and there could be an inverse association between the prevalence of depression and level of education.¹⁷ Worldwide, depression is more common in women, however in cases of chronic illnesses men have been reported to have higher prevalence of depression, anxiety and stress symptoms.¹⁸

Inverse relationship between serum albumin and hemoglobin levels with depression can be interpreted as that patient's mental health perception is not only related to the renal function, but also to other conditions – like anemia, malnutrition commonly seen in patients of CKD.¹⁹ We found a direct correlation between increasing severity of depressive symptoms and hs CRP, PTH. Elevated CRP is found in patients with depression and more so in treatment-resistant patients, in those with childhood adversity and specific depressive and anxious symptoms.²⁰ An association of depression status and severity with decreased serum 25-hydroxyvitamin D levels and increased serum PTH levels in older individuals have been found.²¹ Increasing serum creatinine level, blood urea level and decreasing eGFR suggest increasing CKD severity and consequent poor quality of life.

We acknowledge several limitations of 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 severe depressive symptoms and the symptoms showed association with several routinely measured biochemical parameters.

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