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Prevalence and association of depression with uremia in dialysis population: a retrospective cohort analysis

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Abstract

Depression may hamper the immune system and nutritional status, which leads to poor outcomes of treatment. It is very common in dialysis patients. There are the numbers of parameters affected by the depression of patients and available studies are not enough to define the association between biological parameters and depression in the dialysis population. The purposes of the study were to find the prevalence of depression and association of it with the biochemical abnormalities in the dialysis patients.

The selected battery of tests (clinician-administered questionnaires) were applied to dialysis patients (test cohort, n = 298) and caregivers (control cohort, n = 202) for establishing depression. The demographic and clinical conditions of participants were also collected. Univariate analysis followed by multiple regression analysis was performed for demographical parameters, clinical conditions, and laboratory results for the detection of association of them with depression. The abnormal test considered as more than 2 SD of mean below the normal value. Out of all tests, at least 2 abnormal tests were considered as mild depression. More than half of abnormal parameters among all tests were considered as moderate depression and all abnormal parameters were considered as severe depression.

There was a significant difference for all the test between dialysis patients and the caregivers ($P < .0001$ for all). The half (153 out of 298) of dialysis patients were depressive and clinically asymptomatic. 70 (23%) dialysis patients were mild depressive, 45 (15%) dialysis patients were moderate depressive, and 38 (13%) dialysis patients were severely depressive. Serum phosphate ($P = .023$), level of parathyroid hormone ($P = .021$), and urea reduction rate ($P = .048$) were directly associated with depression.

Biochemical abnormalities (serum phosphate level, parathyroid hormone, and urea reduction rate) were independent predictors of depression in the dialysis population.

Level of evidence: III.

Abbreviations: RAVLT = Rey Auditory-Verbal Learning Test, STROBE = the strengthening the reporting of observational studies in epidemiology.

Keywords: biochemical abnormalities, caregivers, clinician administered questionnaires, depression, dialysis

1. Introduction

Dialysis may affect 10% of the population.[1] Depression is less (2%–10%) in the general population[2] but common in the dialysis population.[3–6] Depression will lead to poor outcomes of treatment and hamper the immune system and nutritional status.[3] Dialysis may develop depression.[7] Also, depression is the risk parameter for morbidity and mortality.[1] Although evidence for depression and biochemical abnormalities of uremia,[3,7] the depression in the dialysis population is unrecognized and untreated.[2] Because of the high cost of dialysis, there is less evidence of the psychological health of dialysis patients.[5] Patients preferences and improvement of healthcare are necessary particularly for the betterment of the dialysis population.[8] Prevalence and association of depression are important in the understanding of the burden of illness in the dialysis population. In contrast, the cross-sectional studies reported that depression is not associated with dialysis and dialysis only hampered the quality of the life of patients in end-stage renal disease.[9,10] The level of depression is also required to consider for renal replacement therapy in the dialysis population.[11] There is the number of parameters affected by the depression of patients and available studies are not enough to define the association between biological parameters and depression in the dialysis population.[3]

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Determining the bilateral relationship between depression and biological change in the dialysis population is not easy. The evaluation of depression by self-rating scales is convenient[12] but it captures the somatic symptoms only and underestimates the prevalence of depression in the dialysis population.[1]

The purposes of the retrospective study were to find the prevalence of depression through clinician-administered questionnaires and association of it with the biochemical abnormalities, demographical parameters, and clinical conditions in the dialysis patients.

2. Patients and methods

2.1. Ethics approval and consent to participate

The designed protocol (SMU/CL/9/19 dated 25 November 2019) of the established study was approved by the Southwest Medical University review board. The study reporting adheres to the law of China, strengthening the reporting of observational studies in epidemiology (STROBE) statement: Cross-sectional studies, and the V2008 of the Declarations of Helsinki. All enrolled participants have signed informed consent regarding the diagnosis, treatment, and publication of the study during dialysis hospitalization.

2.2. Study population

Between January 21, 2019 and November 12, 2019, a total of 333 patients (history of at least 3-months) were on dialysis (peritoneal dialysis and hemodialysis) at the department of nephrology of the Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan, China, and the referring hospitals. Twenty four patients had age less than 18 years and 3 patients had age greater than 70 years. Therefore, these were excluded from enrollment. Patients who had depressive symptoms (6 patients) and psychiatric illness (2 patients) before the start of the dialysis therapy were excluded from the study. A total of 298 patients who were on dialysis were included in the analyses for the test cohort (Fig. 1).

2.3. The modified mini-mental state examination

All the enrolled participants were subjected to the modified mini-mental state examination by psychiatrists (with the minimum of 3-years of experience) of the institute. The score of less than 75 was considered as a cut-off of depression for those who had primitive education and 80 for those who had higher education.[13]

2.4. Auditory-verbal learning test

The learning speed, learning techniques, short-term auditory-verbal memories, proactive interference, retroactive interference, a confabulation of information, and retention of information were evaluated by psychiatrists (with the minimum of 3-years of experience) of the institute using the RAVLT (Rey Auditory-Verbal Learning Test) Adult calculator.[14] RAVLT value 23 or less was considered as normal value.[15]

2.5. Trail making test

In Trail A test, participants had to draw a line between a Chinese word and a Chinese number (1–25). In Trial B, participants had to draw a line between pictures and Chinese zodiacs. The score of 150 or less (in an individual trial) was considered as normal

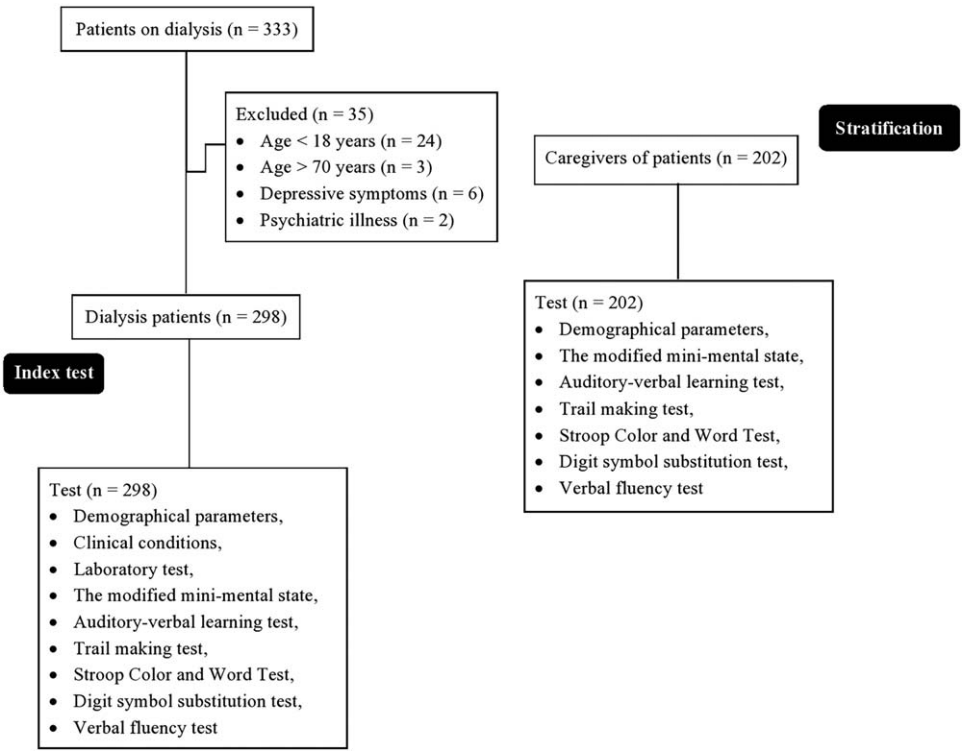

Figure 1. Flow chart of the study.

value.[16] Trained instructors (a minimum of 3-years of experience) were performed the tests.

2.6. Stroop color and word test

The test had 2 parts congruous and incongruous. In the congruous test, the name of colors (green, pink, orange, and black) was written randomly but written in the same color (e.g., word green was printed in green color). In the incongruous tests, the name of the color was written in a different color (e.g., word green was written with orange ink). The participants had to speak the color of ink in both parts. The time taken to complete part by participants was the score of that part. Time of 200 s or less was considered as normal value for each part.[16] Trained instructors (a minimum of 3-years of experience) performed the tests.

2.7. Digit symbol substitution test

In this test, the digit was changed with the symbol (¥ was written for "Yuan"). Total, 133 digits were replaced with symbols. The answer to each one was considered as 1 score. A score of 80 or more considered normal value.[17] Trained instructors (a minimum of 3-years of experience) were performed the tests.

2.8. Verbal fluency test

Trained instructors (a minimum of 3-years of experience) were asked participants to name animals as many as within minutes. The names of 15 and more animals within a minute was considered as normal value.[18]

The abnormal test considered as more than 2 SD of mean below the normal value.[15] Out of all tests, at least 2 abnormal tests were considered as mild depression. More than half of abnormal parameters among all tests were considered as moderate depression and all abnormal parameters were considered as severe depression.

2.9. Statistical analysis

SPSS 25.0 (IBM Corporation, New York, USA) was used for statistical analyses purpose. Fischer exact test[3] was performed for constant data and Mann–Whitney *U* test[19] was performed for continuous data. Univariate analysis followed by multiple regression analysis was performed for demographical parameters, clinical conditions, and laboratory results to predict the association of them with depression.[20] The results were considered significant at a 95% confidence level.

3. Results

3.1. Characteristics of participants

All enrolled patients were on dialysis at least twice a week. Caregivers of patients were also enrolled in the study for purposes of normal participants (control group). Caregivers were younger ($P < .0001$) and mostly male ($P < .0001$). The demographical parameters, clinical conditions, and laboratory test results of the participants are reported in Table 1.

3.2. Perceived deficits questionnaire

There was a significant difference for all the test between dialysis patients and the caregivers ($P < .0001$ for all, Table 2).

Table 1

Characteristics of participants.

Parameters	Cohorts	
Nature	Test Person on dialysis	Control Caregivers
Numbers	298	202
Minimum	18	18
Maximum	70	55
*Age (years)		
Mean ± SD	51.22 ± 10.32	35.45 ± 8.11
*Gender		
Male	174 (58)	155 (77)
Female	124 (42)	47 (23)
Ethnicity		
Han Chinese	272 (91)	184 (91)
Mongolian	23 (8)	16 (8)
Tibetan	3 (1)	2 (1)
Health insurance		
Yes	17 (6)	12 (6)
No	281 (94)	190 (94)
Education status		
Primitive	204 (68)	135 (67)
Below graduate	61 (21)	45 (22)
Above graduate	33 (11)	22 (11)
Diabetes	45 (15)	19 (9)
*Cardiac disease	43 (14)	12 (6)
*Body weight (kg)	51.12 ± 8.13	55.42 ± 7.45
*Systolic blood pressure (mmHg)	138 ± 15	128 ± 12
*Diastolic blood pressure (mmHg)	85 ± 12	81 ± 8
*Hemoglobin (g/dl)	9.45 ± 1.58	10.01 ± 0.65
Serum potassium (mM/L)	4.75 ± 0.71	N/E
Serum sodium (mM/L)	131 ± 8	N/E
Serum calcium (mg/dl)	8.6 ± 0.6	N/E
Serum phosphate (mg/dl)	4.4 ± 0.6	N/E
Parathyroid hormone (pg/ml)	441 ± 52	N/E
Serum albumin (g/dl)	3.55 ± 0.6	N/E
Serum ferritin (μG/L)	298 ± 44	N/E
Urea reduction rate	81 ± 15	N/E
*Hearing loss (impaired hearing)	15 (5)	2 (1)

Continuous data are shown mean ± SD and constant data are shown as frequency (percentage).
*Significant difference.
N/E = not evaluated.

3.3. Prevalence of depression

70 (23%) of dialysis patients were mild depressive, 45 (15%) dialysis patients were moderate depressive, and 38 (13%) of dialysis patients were severely depressive. While 2 (1%) caregivers were mild depressive (Fig. 2).

3.4. Association of depression

Univariate analysis showed age ($P < .0001$), gender ($P < .0001$), diabetes ($P < .0001$), cardiac disease ($P < .0001$), serum sodium level ($P = .034$), serum phosphate level ($P < .0001$), parathyroid hormone ($P < .0001$), urea reduction rate ($P < .0001$), and hearing loss (impaired hearing, $P < .0001$) were directly associated with depression (Table 3). Multivariate regression analysis showed serum phosphate ($P = .023$), level of parathyroid hormone ($P = .021$), and urea reduction rate ($P = .048$) were directly associated with depression (Table 4).

4. Discussion

The study reported about half (153 out of 298) of dialysis patients with depressive and clinically asymptomatic in clinician-

Table 2

Perceived deficits questionnaire results.

Parameters	Cohorts		Comparisons between both cohorts
Nature	Test Person on dialysis	Control Caregivers	
Numbers	298	202	*P* value
The modified mini-mental state examination	70 ± 11	88 ± 9	<.0001
Auditory-verbal learning test	21 ± 4	17 ± 4	<.0001
Trail making test			
A	120 ± 30	161 ± 11	<.0001
B	135 ± 25	165 ± 15	<.0001
Stroop Color and Word Test			
Congruous	225 ± 31	158 ± 25	<.0001
Incongruous	230 ± 38	165 ± 27	<.0001
Digit symbol substitution test	58 ± 25	85 ± 6	<.0001
Verbal fluency test	11 ± 5	21 ± 6	<.0001

Data are shown at mean ± SD.

The Mann–Whitney *U* test was performed for statistical analysis.

A $P < .05$ was considered significant.

administered questionnaires. The results of the study were consistent with cross-sectional studies.[3,6,13,20,21] Multiple drug therapies, frequent dialysis, and hospitalization in low-income Chinese people may lead to developing depression and worse mental health.[6] The study reported a higher percentage of dialysis patients with depression than cross-sectional[5,9,22] and retrospective[23] studies because of enrollment of comparatively older population in the test cohort than control cohort ($P < .0001$),[13] clinician-administered questionnaires,[3] and not self-reported mental health.[5] Chronic illness is emotionally challenging.[5] Clinician administered questionnaires are necessary for the diagnosis of depression in dialysis patients rather than the clinical interviews of patients.

The study reported that the level of parathyroid hormone and urea reduction rate was associated with depression. The results of the study were in line with cross-sectional studies[3,6] but not in line with a cross-sectional study.[24] These discriminations in the results were due to different stages of chronic renal diseases of patients and different approaches used for evaluation purposes.[3] Patients approach to dietary restriction can contribute to depression.[25] The mental health of the dialysis patients is not only associated with the blood urea concentration but also associated with the other biochemical parameters of the blood.

The study reported that serum phosphate was associated with depression. The results of the study were in line with cross-sectional studies.[3,6] Higher serum phosphate level is responsible for endothelial dysfunction, which causes depression.[26] A serum phosphate level is a common indicator of depression in any person.

The results of the study are limited with a cross-sectional study and the absence of randomized controlled trial or longitudinal

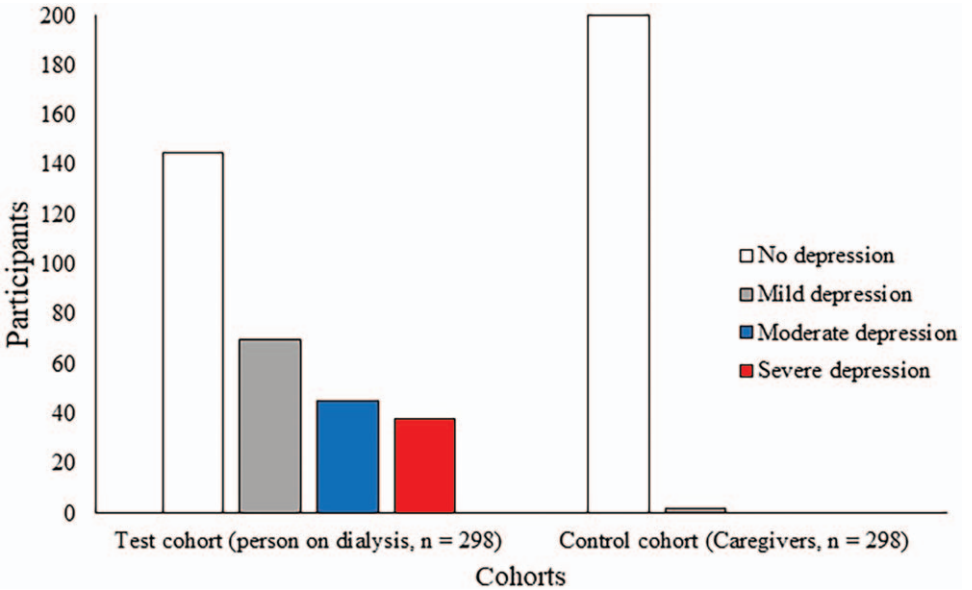

Figure 2. Prevalence of depression. Data shown presented as frequency. The abnormal test considered as more than 2 SD of mean below the normal value. Out of all tests, at least 2 abnormal tests were considered as mild depression. More than half of abnormal parameters were considered as moderate depression and all abnormal parameters were considered as severe depression.

Table 3

Depression and parameters of person.

Parameters	Cohorts		Comparisons between both cohorts
Nature	Person with depression	Person without depression	
Numbers	155	345	*P* value
*Age (years)			
Minimum	18	18	
Maximum	70	55	<.0001
Mean ± SD	48.42 ± 8.92	41.52 ± 9.52	
*Gender			
Male	26 (17)	303 (88)	<.0001
Female	129 (83)	42 (12)	
Ethnicity			
Han Chinese	136 (88)	308 (89)	.881
Mongolian	17 (11)	33 (10)	
Tibetan	2 (1)	4 (1)	
Health insurance			
Yes	9 (6)	20 (6)	.999
No	146 (94)	325 (94)	
Education status			
Primitive	105 (68)	234 (68)	.104
Below graduate	27 (17)	79 (23)	
Above graduate	23 (15)	32 (9)	
*Diabetes	43 (28)	21 (6)	<.0001
*Cardiac disease	33 (21)	22 (6)	<.0001
Body weight (kg)	52.45 ± 7.95	53.15 ± 8.15	.371
Systolic blood pressure (mm Hg)	132 ± 14	131 ± 13	.438
Diastolic blood pressure (mm Hg)	83 ± 8	82 ± 9	.235
Hemoglobin (g/dl)	9.89 ± 1.51	10.01 ± 0.09	.142
Serum potassium (mM/L)	4.76 ± 0.73	4.71 ± 0.75	.487
*Serum sodium (mM/L)	131 ± 10	129 ± 9	.034
Serum calcium (mg/dL)	8.5 ± 0.8	8.6 ± 0.9	.235
*Serum phosphate (mg/dl)	5.3 ± 0.5	4.5 ± 0.7	<.0001
*Parathyroid hormone (pg/ml)	425 ± 48	401 ± 39	<.0001
Serum albumin (g/dl)	3.51 ± 0.5	3.52 ± 0.6	.856
Serum ferritin (μG/L)	295 ± 41	296 ± 42	.804
*Urea reduction rate	82 ± 7	77 ± 3	<.0001
*Hearing loss (impaired hearing)	10 (6)	7 (2)	.016

Continuous data are shown mean ± SD and constant data are shown as frequency (percentage).

Fischer exact test was performed for constant data and Mann–Whitney *U* test was performed for continuous data.

A $P < .05$ was considered significant.

*Significant difference.

Table 4

Association of depression.

Numbers patients evaluated	153		
Parameters	Odd ratio	CI	*P* value
Age (years)	1.01	0.55–0.95	.089
Gender			
Male	1.02	0.57–0.91	.075
Female	1.09	0.56–0.89	.071
Diabetes	1.07	0.55–0.87	.081
Cardiac disease	1.06	0.54–0.88	.082
Serum sodium (mM/L)	1.11	0.25–0.75	.062
*Serum phosphate (mg/dl)	2.11	0.12–1.89	.023
*Parathyroid hormone (pg/ml)	1.85	0.15–1.55	.021
*Urea reduction rate	1.57	0.35–0.95	.048
Hearing loss (impaired hearing)	1.01	0.61–0.72	.152

Results of the person without depression were considered as the reference standard.

Multivariate regression analysis.

Odd ratio > 1 and $P < .05$ were considered significant.

*Significant parameter associated with depression.

CI = confidence limit.

study. Therefore, the effects of parameters over time were not evaluated.[5] Also, socioeconomic, employment, marital status,[6] dialysis modality,[3] and levels of pro-inflammatory cytokines[24] have an impact on the depression level of the dialysis patients but the study did not evaluate such parameters. There were significant differences in age, gender, and the other demographical characters between the test cohort and the control cohort ($P < .0001$). The control cohort included patients were caregivers but were not normal individuals. Caregivers have also felt depression due to chronic illness of dialysis patients.[10] It could be more optimal to create a control group with less variance in demographic features compared to the test group, such as chronic kidney disease patients who are not having dialysis treatment yet. Nevertheless, the time spent on dialysis has a direct effect on quality of life and anxiety/ depression to be due to clinical problems arising from chronic renal failure and long-term dialysis. The influence of time (both in terms of treatment sessions and dialysis vintage) in treatment with dialysis in depression, has not been taken into account. The study selected a battery of tests for establishing depression, however it is not clear of any of these tests have been validated for screening dialysis patients.

5. Conclusions

The study reported that about half of the dialysis patients with depressive and clinically asymptomatic. Serum phosphate level, parathyroid hormone, and urea reduction rate were independent predictors of depression in the dialysis population. The study may help nephrologists to understand the burden of illness in the dialysis population. A prospective, longitudinal study using clinician-administered questionnaires is required to evaluate variables for depression in dialysis patients for the better mate of mental health of the dialysis population.

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