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Correlation between Depression and End-Stage Renal Disease (ESRD): Review Article

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ABSTRACT

Background: Ten percent to fifteen percent of all persons have chronic kidney disease (CKD). The global diabetes epidemic is expected to substantially raise the incidence of this crippling illness. Adjusting to any chronic illness can be difficult. Coping with treatment transitions or failures, learning to use dialysis equipment, incorporating treatment into one's normal life, and accepting the life-threatening diagnosis are all part of the process. Patients with CKD need to make mental adaptations to deal with the disease, its symptoms, and its repercussions. **Objective:** Review of correlation between depression and end-stage renal disease. **Methods:** We scoured scholarly papers and databases including PubMed, Google Scholar, and Science Direct for information on depression and end-stage renal disease. Between August 2003 and March 2020, however, only the latest or most comprehensive study was considered. The authors also assessed the usefulness of references taken from similar books. Documents written in languages other than English have been overlooked because of a lack of funding to translate them. Unpublished articles, oral talks, conference abstracts, and dissertations were all generally agreed upon to not constitute valid scientific investigation.

Conclusion: Depression is common among adults with ESRD and it has been connected to the physiological and psychological changes that take place during dialysis treatment. Recent studies have shown that patients who had CKD being managed by dialysis are at up to three times the risk of developing depression as the general population.

Keywords: Depression, End-stage renal disease.

INTRODUCTION

Depression is common among adults with ESRD, and it has been connected to the physiological and psychological changes that take place during dialysis treatment. Recent studies have shown that the depression rate in cases who had CKD being treated by dialysis is 3 folds more than those of general population. Patients with CKD or ESRD who additionally suffer from depression are more likely to have unfavourable health outcomes [(1)].

Ten percent to fifteen percent of all persons have chronic kidney disease (CKD). The global diabetes epidemic is expected to substantially raise the incidence of this crippling illness. Drug treatment and dietary modifications are used to slow renal disease progression, prevent or treat complications, and manage co-occurring conditions in CKD stages 1 to 4. Stage 5 chronic kidney disease (CKD), often known as end-stage renal disease, leaves patients with no treatment choices outside dialysis or a kidney transplant (ESRD). As more people suffer from chronic kidney disease (CKD), the need for RRT is likely to skyrocket. This could lead to an increase in health care costs [(2)].

Adjusting to any chronic illness can be difficult. Patients with chronic kidney disease (CKD) must make a number of mental adjustments as their disease progresses. With such a large and persistent illness burden, CKD/ESRD management has shifted its focus from purely clinical end points to the preservation of quality of life (QoL) at every stage of the disease's course, from diagnosis to palliative care. Mental health issues arising from kidney disease and its treatment are crucial [(3)].

Numerous studies have shown disturbing correlations between mental health issues such depression and anxiety and end-stage renal disease. Concurrently, it has been shown that mental comorbidities have an impact on care as well. Therefore, it is crucial to comprehend how such mental comorbidities influence CKD outcomes[(4)].

Patients with chronic kidney disease or end-stage renal disease are more likely to suffer from depression. Recent research by **Palmer *et al.*** [(3)], a systematic review and meta-analysis, examined the incidence of depression in these demographics. The researchers looked through 216 studies and counted 55,982 CKD or ESRD individuals. Dialysis patients with ESRD had a screening questionnaire- and clinical interview-assessed depression prevalence of 39.3% and 22.8% respectively. The overall prevalence of depression in CKD patients was 26.5% when analyzing them with screening questionnaires, and 21.4% when assessing them with clinical interviews [(5)].

When depression was diagnosed by a questionnaire, ESRD had a larger frequency than CKD (39% vs. 26.5%), however when depression was identified via clinical interview, the two disorders showed identical prevalence (39%). Uremic symptoms (fatigue, sleeplessness, poor appetite) may share similarities with physical manifestations of depression in ESRD patient populations, which may account for the discrepancy in their measurement [(6)].

The majority of studies have identified an association between depression and poor psychosocial and medical outcomes for ESRD patients, although a few have not. Eighteen studies exclusively included patients undergoing hemodialysis, four included patients undergoing peritoneal dialysis, and nine included patients undergoing both modalities. Independent of all confounding factors, the authors

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observed that dialysis patients with depressed symptoms had a mortality risk 1.5 times higher. They also noticed that the correlation between depression and death increased in proportion to the severity of the condition [7].

Hedayati *et al.* [6] conducted the only study that looked at how a clinical interview diagnosis of depression affected patients' clinical outcomes after dialysis for ESRD**.** However, because it reported a composite outcome, this research was not included in the meta-analysis. Participants included 98 ESRD patients on continuous hemodialysis; 26 of them had been diagnosed with depression (MDD, dysthymia, or minor depression). The study followed patients for an average of a year where 52 were successful (a composite of death or first hospitalization). After taking into account potential confounders, the risk of the primary outcome occurring was 2.07 times higher in depressed patients.

Patients with ESRD who are depressed are more likely to experience a wide range of other negative health outcomes, such as increased use of emergency rooms and hospitals, longer stays in hospitals, cardiovascular events, peritonitis, dialysis discontinuation, and even death. They showed that a BDI score of 11 or lower was substantially linked with Gram-positive peritonitis in an analysis of 162 peritoneal dialysis patients tested at 6-month intervals [5]. In addition, **Kurella *et al.*** [8] found that the suicide incidence for ESRD patients on long-term dialysis was much higher than the general population, and that a history of mental health hospitalization in the previous 12 months was significantly linked to dialysis discontinuation and suicide.

Patients with ESRD who additionally suffer from depression have worse psychosocial outcomes. Higher levels of depression were associated with poorer quality of life in the AASK cohort study in a way that was both statistically significant and independent of other factors. Depression is also linked to issues like low energy, soreness, itching, trouble sleeping, and erectile dysfunction [9].

Recent investigations of people with CKD who are not on dialysis have connected depression to hospitalisation, acute kidney damage, as well as loss of kidney function. One of the most comprehensive analyses of health outcomes for people with significant depression and CKD was conducted by **Hedayati *et al.*** [6]**.** A total of 267 individuals with CKD stages 2-5 were enrolled in this study and were given a MINI interview; 56 of these patients were experiencing a major depressive episode at the time of the interview. For the purpose of tracking the emergence of the primary outcome composite, all participants were followed for a full year.

Why ESRD patients feel down:

There are two types of depression that could account for the elevated rates seen in people with CKD and ESRD: primary depression (not caused by a medical condition) and secondary depression (caused by a medical condition). Mechanisms driving primary depression in people with kidney illness are likely comparable to those outlined for the general population but are outside the focus of this review. Unfortunately, little research has focused on the causes of secondary depression in CKD and ESRD patients. Research of depression risk factors in these groups, as well as studies of depression mechanisms in other chronic disorders, can provide clues as to possible mechanisms [10].

Patients with ESRD are more likely to have depression if they are younger, female, white and being on dialysis for a longer period of time, or have comorbid conditions including diabetes, coronary artery disease, cerebrovascular disease, or peripheral vascular disease. Depressive symptoms are also more common in people with CKD if they are younger, female, black, Hispanic, uneducated, poor, unemployed, hypertensive and smokers, or have diabetes or coronary artery disease [11]. It has been found that depression is more prevalent in those with lower socioeconomic level and the prevalence of comorbid conditions. However, this link is increased in this patient population due to the higher prevalence of these risk factors in people with kidney disease., They may contribute to the explanation for why people with kidney illness are more likely to experience depression than the general population [12].

What causes depression and how:

There is a two-way relationship between diabetes and CAD and depression in these people. Depressive symptoms, for instance, have been linked to the onset of diabetes, and those with clinically diagnosed diabetes are more likely to have these symptoms than those who do not have diabetes. It is unclear which way the association runs between depressed symptoms and CKD, but it is likely to go both ways. Several behavioural and molecular factors have been proposed to explain the similarities between CKD and depression caused by other chronic diseases. Figure (1) depicts biological and behavioural explanations for the association between depression and CKD, as well as the association between depression and adverse outcomes in this cohort [13].

Behavioral:

Self-care difficulties associated with CKD and ESRD, such as increased clinic and hospital visits, dietary restrictions, drug loads, and home monitoring of glucose, blood pressure, and weight, are a potential cause of depression. This adds another layer of difficulty to the already challenging process of dialysis, whether it be thrice-weekly clinic visits for hemodialysis, once-daily home hemodialysis, or once-weekly peritoneal dialysis. Adults who have just started dialysis may feel particularly overwhelmed by these difficulties. Anxiety and depression were found to be independently linked with death in a study of 160 incident dialysis users [14].

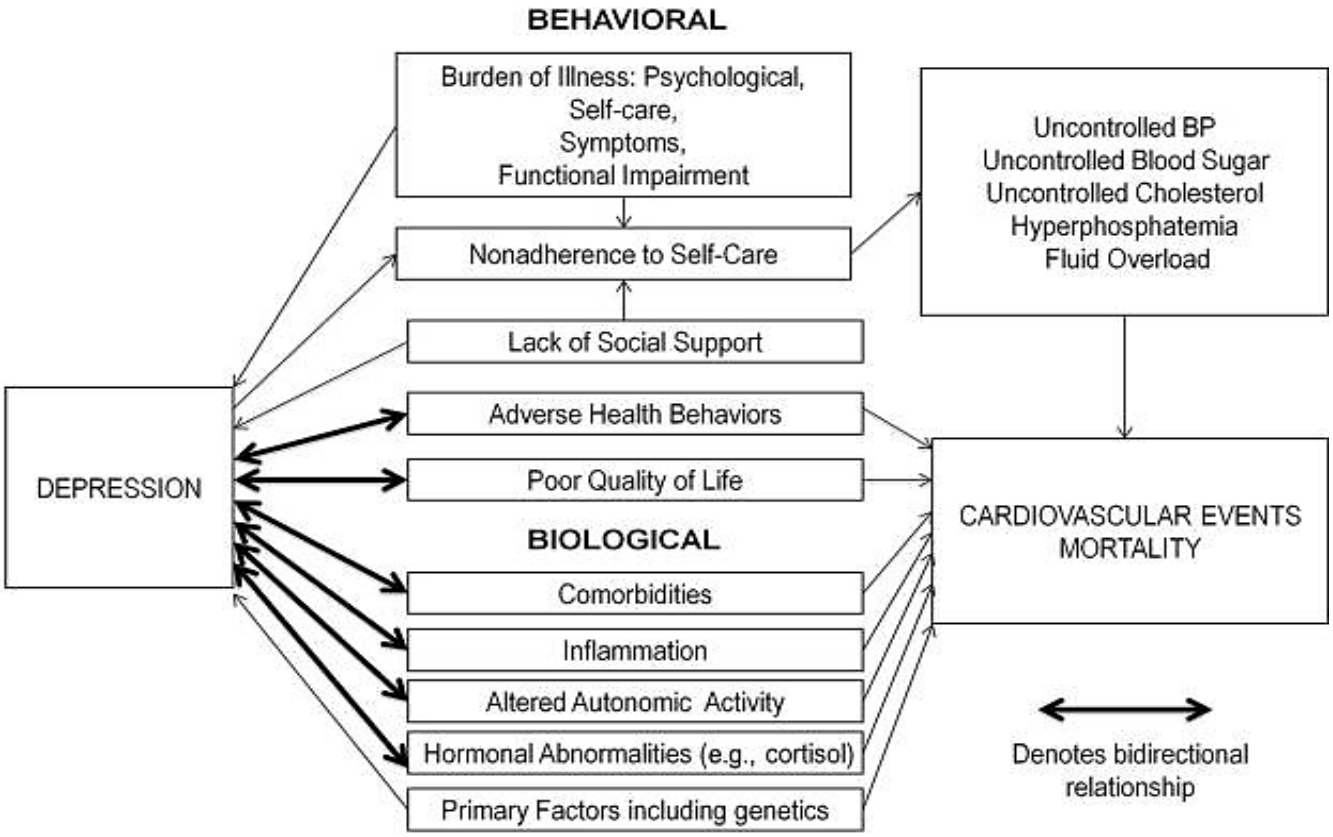

Fig. (1): How depression develops and how it impacts health[5]

A chronic illness's mix of functional impairment with physical symptoms may increase depression. Patients with CKD and ESRD may have difficulty doing daily tasks due to concomitant diseases such as dementia and a history of stroke, or heart failure. Orthostasis, headaches, and weariness during hemodialysis can impair daily functioning in patients with end-stage renal disease. As mentioned before, the physical symptoms these people experience as a result of uremia, dialysis treatment, and/or medicines (such as gastrointestinal distress from phosphate binders) have been associated to depression. It is still not known if depression causes these symptoms or whether somatic symptoms induce depression [9].

Patients with CKD and ESRD are at an increased risk of developing depression due to the emotional toll of dealing with a chronic condition that poses a threat to their long-term health and survival. Patients with CKD who are also dealing with the prospect of dialysis or a transplant may find this to be of particular importance [13].

Increased rates of smoking, inactivity, and obesity are all risk factors for chronic kidney disease, and depression may play a role in this. These actions are widespread among CKD patients and have been linked to a worsening of preexisting conditions such diabetes, hypertension, and coronary artery disease. Alcohol consumption is widespread among depressed people, and surprisingly, there appears to be a protective link between alcohol consumption and the risk of getting CKD [15].

To sum up, depression has been connected to people with ESRD isolating themselves from their social networks and struggling financially. One hundred and ten of 210 dialysis patients in a study had experienced clinical depression before, and among those patients, 12.8% cited personal or family troubles and 10.7% cited financial difficulties as causes of their sadness [14].

Biological:

Multiple studies have shown that there is a two-way connection between chronic inflammation and depression. Patients with CKD and ESRD are at a higher risk for adverse health outcomes like CKD progression and mortality if they have high levels of inflammation [16].

Patients with CKD and ESRD may be more prone to depression because comorbid cerebrovascular illness, which is quite frequent among these patients, has a direct effect on the brain's mood control processes. For instance, depression has been linked to damage in the frontal lobe and the left anterior and left basal ganglia after a stroke. Mood may be indirectly affected by cerebrovascular disease due to its effect on inflammation[17].

How depression causes harm, biologically speaking:

Patients with CKD and ESRD are more likely to experience negative medical outcomes, and this correlation has been linked to depression. Atherosclerosis and cardiovascular events may be hastened by the increased inflammation brought on by depression. Stress hormones like cortisol and

norepinephrine, as well as the neurotransmitters serotonin and the autonomic nervous system, all have a role in elevating the risk of cardiovascular disease and stroke [6].

Medical outcomes may be hampered by the fact that depression also has behavioural repercussions. Patients with ESRD who are depressed are more likely to fail to take their medications as prescribed, make poor food choices, gain weight between dialysis treatments, and skip sessions. In a sample of 65 hemodialysis patients and 94 kidney transplant patients, researchers found that depressive symptoms were a significant independent predictor of lower adherence among psychological factors and self-reported medication adherence [18].

A study including 295 hemodialysis patients found that patients who did not adhere to their prescribed dialysis schedules also experienced an increase in depressive symptoms. If patients with CKD and ESRD do not follow self-care instructions, they may experience a deterioration in their blood pressure, blood sugar, cholesterol, bone metabolism, anaemia, phosphorus, and volume status [5].

Treatment results as affected by depressive and anxious symptoms:

Patients with CKD who also suffer from a psychological disorder have a higher risk of experiencing a worse clinical outcome. Longitudinal studies of HD patients have shown that individuals who were diagnosed with depression have worse clinical endpoints, increased likelihood of hospitalisation, length of stay, withdrawal from dialysis, death, and use of other medical services [2].

Patients on HD had a higher risk of death and hospitalisation, as shown by **Mapes *et al.*** [19]. The predictive connection of depression with overall mortality has been verified by a number of other original investigations and systematic reviews. Using data from nearly 67,000 patients on dialysis, **Farrokhi *et al.*** [7] did a meta-analysis of 31 studies and found that patients with depressive symptoms have a 50% higher risk of dying. Regardless of the method used to assess depression, a strong association was shown to exist with mortality.

Persistent depressive symptoms are more important from a therapeutic standpoint. In a study of 917 incident patients on dialysis for 2 years, researchers found that depression that lasted more than 6 months or returned was related with death from cardiovascular causes, although depression diagnosed more than 6 months beforehand or at baseline was not. This shows that depressive symptoms over a long period of time are associated with an increased risk of death, however the prognostic impact of depression that has been successfully treated is less certain [20].

Depression has been linked to a quicker rate of ESRD progression in patients with CKD who do not yet need dialysis. Depressive symptoms in CKD were associated with a higher risk of developing ESRD, starting dialysis sooner, dying, or being hospitalised, according to one prospective observational study. This study confirms the findings of another study by **Hedayati *et al.*** [6], which found that those with CKD and a clinical diagnostic of depression are more than three times as likely to develop ESRD and require dialysis as those without CKD and a clinical diagnostic of depression. This association was unaffected by illness severity or the presence of co-morbidities like diabetes [21].

The success rate of kidney transplants may also be affected by the presence of depressive symptoms. Patients with depressive symptoms following a kidney transplant had a higher mortality rate than those without depressive symptoms. Patients with depression had a greater mortality rate than those without depression among 840 transplant recipients studied over a 5-year period (21% vs. 13%; p = 0.004) [22]. Patients' likelihood of being placed on the kidney transplant waiting list may also be affected by psychiatric disorders. According to the research of **Bayat *et al.*** [23] having a diagnosable mental illness is a major, independent determinant in whether or not a patient is allowed to join the transplant waiting list. Patients with lower CES-D depression scores were more likely to be added to the renal transplant waiting list, as discovered by **Szeifert *et al.*** [24] for those on the kidney transplant waiting list, however, this correlation was not observed.

Depression and anxiety have been linked to poor outcomes for people with PD. Depressed PD patients are more likely to have inflammation, cardiovascular illness, and death than their non-depressed counterparts. Peritonitis is more common in patients with depression who use PD, and it is a potentially lethal infection of the peritoneum if left untreated. Anxiety and depression enhanced the likelihood of developing peritonitis during the course of the subsequent year [25]. Similarly, **Troidle *et al.*** [26] showed that patients with a BDI 11 at baseline were 2.7 times more likely to develop peritonitis compared to patients without depression in their prospective trial of 162 patients on peritoneal dialysis.

There has been significantly less research into the clinical outcomes of anxiety compared to depression. Quality of life (QoL) is significantly diminished in HD patients with anxiety disorders compared to those with no psychopathology and even further diminished compared to those with only a depressed condition [18]. Small-scale investigations have not identified a consistent association between anxiety and negative clinical outcomes. Patients with CKD who did not require dialysis at first may be adversely affected by the presence of anxiety symptoms. Among CKD patients who are not yet receiving dialysis, for example, anxiety symptoms have been associated with an increased risk of death or a delay in starting the treatment [27].

CONCLUSION

Depression is common among adults with ESRD, and it has been connected to the physiological and

psychological changes that take place during dialysis treatment. Recent studies have shown that patients who had CKD being managed by dialysis are at up to three times the risk of developing depression as the general population.

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