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NEPHROLOGY - REVIEW

# A holistic approach to factors affecting depression in haemodialysis patients

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**Abstract**
Depression in dialysis populations is affected by co-morbid diseases, such as cardiovascular disease, diabetes, and immune dysfunction, and it also includes high suicide risk and frequent hospitalizations. Depressive disorders have a close association with malnutrition and chronic inflammation, as well as with cognitive impairment. Impaired cognitive function may be manifested as low adherence to dialysis treatment, leading to malnutrition. Additionally, chronic pain and low quality of sleep lead to high rates of depressive symptoms in haemodialysis patients, while an untreated depression can cause sleep disturbances and increased mortality risk. Depression can also lead to sexual dysfunction and non-adherence, while unemployment can cause depressive disorders, due to patients' feelings of being a financial burden on their family. The present review provides a holistic approach to the factors affecting depression in haemodialysis, offering significant knowledge to renal professionals.

**Keywords** Depression · Haemodialysis · Kidney failure · Pain · Sleep disorders · Unemployment

## Introduction

Depression is the most common psychological disorder in dialysis populations [1–5], ranging from 19 to 60% [2], with higher prevalence in developing and middle-income countries [6]. It is estimated that dialysis patients have about a fourfold higher risk for depression than the whole population and more than doubled possibility of mortality [7]. However, it has been found that physicians make diagnosis for only 16.2% of these people, while only 16–45% of patients with diagnosed depression receive treatment [8].

Depression has a strong association with anxiety, since an untreated anxiety can lead to depressive disorders [9], possibly because anxiety has a negative impact on interpersonal relationships and leads to attachment disruptions and chronic social stress [10, 11]. Additionally, personality traits, such as low extraversion, high neuroticism, and low conscientiousness are major risk factors of depression [12]. Dialysis patients feel anxiety about the outcome of the treatment due to long-term complications [13], while they usually have to wait for a long time for a kidney transplantation and are afraid of returning again to dialysis due to a possible rejection [14].

Depressive disturbances are also affected by co-morbid conditions of haemodialysis and increased hospital admissions [15], chronic pain and sleep disorders [16], chronic inflammation [17] which can lead to malnutrition [18], uraemia, which usually has a negative effect on the central nervous system [19], increased fatigue and decreased sexual functioning [17], and fear of death [19]. Additionally, low family support and return to dialysis after transplantation can lead to symptoms in line with a diagnosis of depression [20], affecting patients' self-care [21]. Transplant failure frequently causes depressive symptoms, feelings of shock, deep sorrow, and anger to dialysis patients and their families [22].

It has been also found that depression is strongly associated with reduced physical performance [23], due to decreased motivation [24]. It is characterized by deterioration in daily activities, increased dependence, high risk of institutionalization and death [25], with patients being

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dependent on dialysis machine [26], as well as on renal staff and their family members [14]. Depression was also found to have a significant association with haemodialysis during morning shift and increased age [27].

Additionally, Liborio et al. [28] found that patients with nephrotic syndrome related to glomerulopathy had high rates of depression. Proteinuria is strongly associated with depression due to patients' concerns about prognosis and disease control, as well as their restrictions in diet and physical activity. Additionally, proteinuria is related with inflammation which in turn is related with depression.

Depression can be viewed in the context of perceived loss [29], since these people experience loss in kidney function [30]. They also have dietary and fluids limitations, financial problems, uncertainty about the future, changes in family roles and limitations in social life [13, 31, 32].

Symptoms of depression include fatigue, reduced appetite, sleep disorders, difficulty in concentration [33], feelings of guilt [34] and thoughts of suicide or death [35]. Patients can also have dialysis inadequacy [33], feelings of tiredness and reduced energy [36], low nutritional status, cognitive impairment, low adherence to medication and body pain [35].

However, the evaluation and early diagnosis of depression is difficult since symptoms of uremia and depression are usually coexisting [37, 38]. More specifically, the somatic symptoms of depression (anorexia, fatigue, sexual and sleep disorders) are also somatic indicators of uremia [31]. Additionally, the lack of a systematic psychiatric evaluation in these people [16] and their denial of their depressive symptoms due to their fear of the stigma of mental illness leads to delayed diagnosis and treatment of depression [3]. Johnson and Dwyer [39] found that $>70\%$ of dialysis patients did not recognize their depression symptoms and they did not perceive the necessity for help.

## Association of depression with morbidity and mortality

Depression displays high rates of morbidity [40–44], while mortality is 20 times higher in patients on haemodialysis than in the whole population [45]. It is related with poor survival [17] and leads to increased hospital admissions [19]. Moreover, 45% higher risk of death in dialysis patients with depression [8] and 30% more risk of hospitalizations in these patients [46] have been reported.

Depression increases the mortality risk, particularly due to cardiovascular disease [17], which is the largest cause of death among dialysis population [19]. Saeed et al. [38] also found that anaemia had a significant association with depression, possibly due to increased fatigue and weakness caused by that.

Additionally, patients with diabetes were found to have high rates of depression [47], possibly due to its complications, such as vision and cardiac disorders, cerebrovascular events, and peripheral vascular disease [48]. Patients with diabetes have frequent amputations, reduced physical health, and are incapable of getting involved with daily activities [49]. Jong et al. [50] found that dialysis people with diabetes had double risk of depression than those without diabetes.

Moreover, depressive disorders have a strong relation with immune dysfunction, which is the second largest cause of death among dialysis population, due to infections [19]. Depression increases inflammation, which is a risk factor for cardiovascular disease, diabetes, and all age-related diseases [51].

### Depression and hospitalizations

Lacson et al. [52] found that dialysis patients with increased depressive symptoms had significantly more hospitalizations, while Chan et al. [53] found an important increase in depression rates in hospitalized patients on dialysis. Nowak et al. [54] found that the time spent on hospital admissions and the use of central catheters had significant association with depression in dialysis patients, since it reflects the overall patient's health status, the seriousness of co-morbid diseases, and the need for longer treatment.

It has been found that patients have higher rates of depression during the first year of haemodialysis [54], possibly due to frequent patients' hospital admissions [52]. Central catheters are widely used in this period of time and may lead to infections and inflammation, implicating more intensive treatment at hospital [54]. Dijk et al. [17] found that patients who were depressed the first period after the beginning of dialysis had high risk of mortality and more co-morbidities. Thus, depression has a significant association with the number of co-morbid diseases in haemodialysis [36], due to the severity of complications, the disability caused by them, and the high risk of death [3].

### Depression and suicide risk

Depression also includes high risks to commit suicide, since about 20% of patients on dialysis choose to withdraw from dialysis. A suicidal behaviour may include refusal of dialysis treatment and lack of adherence to dietary restrictions [55]. In the USA, withdrawal from dialysis and suicides are the third most common cause of death among these patients [56]. Patel et al. [36] found that suicide ideation had a strong association with depression in dialysis patients.

### Depression and falls

It has been found that falls have an annual possibility of occurrence among 25% of dialysis patients and are more likely to occur in those patients with increased rates of depressive symptoms [57].

## Association of depression with malnutrition

Depression has a close association with low nutritional status in dialysis patients [19], since it leads to reduced appetite and gastrointestinal disorders [58]. Teles et al. [27] found that depression had a significant correlation with low levels of phosphorus and serum albumin, possibly due to poor nutritional status.

Malnutrition can be due to inadequate food intake, hormonal disturbances, restrictions in diet, use of drugs, insufficient dialysis, and co-morbid diseases. The use of large quantities of drugs may cause a decrease in appetite and food intake, due to nausea and vomiting [59].

Malnutrition can be also due to chronic inflammation [50], since stress and depression increase inflammation, while inflammation raises depressive symptoms [51]. Patients' inflammatory status significantly affects the development of depression due to increased proinflammatory cytokines [54].

Malnutrition causes a variety of emotional symptoms [60], leading to increased fatigue, exhaustion, and more infections due to low proteins and fat in patients' body [32]. The elderly patients have higher risk for malnutrition due to their difficulty in preparing meals, decreased appetite, more chronic and acute illnesses, reduced mobility, and low food intake. Malnutrition is regarded as a factor of poor prognosis in Chronic Kidney Disease and is related with high rates of mortality and hospital admissions [59].

## Association of depression with cognitive impairment

Cognitive impairment has increased in prevalence in dialysis patients, particularly in those of an old age [24], ranging from 30 to 60% [61]. Jung et al. [61] found that deterioration in cognition was closely associated with depression, while cognitive symptoms represent the basic characteristics of depressive disturbances [62]. A decline in cognitive function negatively affects patients' interference with daily activities [63], while a mild decline cannot be easily detected by health professionals [61].

Cognitive deterioration affects patients' attention, language, memory, learning, decision making, and problem solving [63]. Dialysis patients usually have memory disorders and decreased attention due to low metabolic rates and the accumulation of toxic substances in their brain, affecting the function of the central nervous system and leading to a decline in cognition [61].

However, impaired cognitive function may be manifested as low adherence to medications and dietary issues, leading to malnutrition [52]. Patients usually ignore their dietary restrictions and do not comply with dialysis schedule. Thus, it is significant to early detect cognitive impairment and depression because it can lead to dementia, which is related with low quality of life and increased mortality [61].

### Factors associated with cognitive impairment

Cognitive impairment is negatively affected by hypertension, diabetes mellitus, stroke [62], old age [64], cerebrovascular disease [65], inflammation, atherosclerosis, anaemia, uremic toxins [63], and frailty [66]. A low sleep quality is also a possible risk factor for decreased cognitive function [67], while excessive daytime sleepiness was related with impaired verbal memory in dialysis patients [64]. Additionally, Oliveira et al. [68] found that reduced cognitive function was related to increased numbers of missed haemodialysis sessions.

## Depression and pain

Gerogianni et al. [32] found that pain is a frequent problem among patients on haemodialysis, with its prevalence ranging from 8 to 82% [69]. It has been found that patients with chronic pain have more depressive symptoms than those without pain [70].

Pain is associated with increased hospitalizations [71], poor quality of life, high rates of mortality, increased stress, and high levels of proinflammatory cytokines [72]. It is mostly caused by venipuncture, muscle cramps, and headaches occurring during haemodialysis, as well as painful syndromes including ischemic limbs and musculoskeletal and neuropathic syndromes. However, musculoskeletal is the most troublesome pain, leading to sleep disorders [70]. Harris et al. [72] found that a significant number of patients experienced high levels of pain, both during dialysis and non-dialysis days.

## Depression and sleep disorders

Sleep disorders range from 41 to 83% in dialysis patients [73] and are regarded as a risk factor for depressive disturbances [74]. The prevalence of insomnia in ESRD patients was found to be at 54.3% [75], while patients with low quality of sleep were found to have high rates of depression

[67, 73]. Additionally, patients with sleep disturbances were three times more likely to have depression than those without sleep disorders [7]. Depression was found to be the main factor for poor quality of sleep [76], while an untreated depression can cause sleep disturbances, increasing mortality risk [35].

Dialysis patients often complain about insomnia, irregularity in sleeping hours, difficulty in falling asleep, awakening early in the morning or at night, sleep apnoea, nightmares, morning headaches, daytime sleepiness, decreased functional capability, and restless leg syndrome They also suffer from increased fatigue, deterioration in memory, and increased anxiety [77].

### Factors associated with sleep disorders

The quality of sleep is mostly affected by uraemia and itching due to uremic pruritus [78, 79], coronary disease, heart failure, respiratory disorders, stress, depression, and anxiety [80]. Anxiety and depression were found to directly affect sleep disorders in dialysis patients [81].

Poor sleep quality is also affected by malnutrition, increased age, disabilities, muscle cramps, peripheral neuropathy, somatic disorders, pruritus, bone pain [82, 83], diabetes [73], and long duration on haemodialysis [84]. The long time on haemodialysis may be related with a progressive appearance of symptoms and co-morbid diseases which lead to low quality of sleep [84].

### Restless leg syndrome

A large number of patients with restless leg syndrome were found to have anxiety and depression [85]. Restless leg syndrome is a disorder of the central nervous system, where patients want to move their legs or other parts of their body during their sleep. It is mostly caused by uraemia, iron deficiency, and diabetes [75], while it can cause discomfort, pain, tingling, and numbness, making patients unable to rest and negatively affect their psychological well-being [77]. The prevalence of restless leg syndrome in dialysis patients is threefold to fourfold higher than in the whole population [86].

### Fatigue and sleep disorders

Fatigue is a reduced ability of physical and mental work [14], with over 70% of renal patients having severe fatigue due to the high levels of endotoxins and inflammatory cytokines in blood circulation [87]. Symptoms of fatigue are tiredness, weakness, and lack of energy [1], while a significant number of patients feel tired after dialysis therapy and are incapable of getting involved in daily activities [88].

The major factors responsible for fatigue are sleep disturbances due to excessive daytime sleepiness [89], bone and muscle pain, repeated dialysis therapy, stress, anxiety and depression [14], anaemia, malnutrition, and inflammation [1]. It has been found that fatigue, sleep disorders, and depression lead to reduced quality of life in renal patients [87].

## Depression and sexual dysfunction

Depression can lead to sexual dysfunction and negatively affect the quality of life in dialysis patients [90]. Enzlin et al. [91] found that depression was the major factor of sexual disorders in 625 patients with Type I diabetes on haemodialysis, while 55.4% of the sexually active patients were found not to be satisfied with their sexual life, with depression score being 80.5% [92]. Sexual disorders are also affected by diabetic nephropathy [93].

The most frequent sexual dysfunctions in men were loss or reduced sexual needs, erectile dysfunction, and inhibited or lack of ejaculation, while women were troubled by arousal dysfunction and anorgasmia [92].

### Factors associated with sexual dysfunction

Saglimbene et al. [94] found that depressive symptoms among women on dialysis were related with reduced lubrication and high rates of pain, while those of childbearing age have decreased fertility and poor infant survival [95], with half of pregnancies being not successful [96, 97].

Erectile dysfunction affects about 80% of men undergoing haemodialysis and is associated with high rates of depression, anxiety, loss of self-esteem, and marital disruption. It is mostly caused by increased patients' age, hypertension, diabetes mellitus, and anaemia, while only a small proportion of men follow a pharmacological therapy [98].

## Depression and non-adherence

Depression is a major factor of non-adherence in dialysis populations and is associated with increased mortality [99]. Renal patients with depression are three times more likely to have reduced compliance to the treatment than those without depression [55], with non-compliance ranging from 14.4 to 67% among these people [100]. Cukor et al. [99] found that among 86 patients on haemodialysis who were candidates for kidney transplantation, 49 were non-adherent.

Depression usually leads to low adherence to food and fluid restrictions, leading to increased morbidity and mortality [101]. Thus, fluid overload is a very common condition among these patients, requiring frequent hospitalizations

[52]. Non-adherence can be also manifested as missing or shortening dialysis sessions, gaining interdialytic weight, and increasing the level of potassium and phosphorous before dialysis [99]. It has been also found that non-compliance to fluid restrictions and medications ranges from 30 to 70% and 19 to 99%, respectively, while non-adherence through missing dialysis sessions varies from 7 to 32% [101].

### Factors associated with non-adherence

Low adherence can be affected by the increasing number of elderly dialysis people, their co-morbid diseases, such as cognitive impairment and psychiatric diseases [61], as well as by low income, family problems, frequent hospital admissions, and long time of medication [32]. It can be also affected by reduced social support, low knowledge, and negative perceptions about dialysis [65]. However, depression can be a possible problem even after renal transplantation due to patients' non-compliance with medications which can lead to loss of graft [20].

Asher et al. [102] found that depression is a risk factor for mortality due to non-adherence, while Ibrahim et al. [101] found high rates of non-compliance among haemodialysis patients with a close association to malnutrition. They also found that depression rates were increased and quality of life was reduced among non-adherent patients.

## Depression and unemployment

Depression is strongly affected by unemployment [103], since patients have a feeling of being a financial burden on their family, which leads to high rates of depressive symptoms [35]. Andrade and Sesso [23] found high rates of depression among unemployed patients and those without monthly income. Similarly, Andrade et al. [45] found that patients who had no job had more depression than those who had. Changes in the level of employment status are frequent among dialysis populations, with unemployment affecting > 75% of them [104].

### Factors associated with unemployment in haemodialysis

Unemployment is strongly associated with low level of education, increased age, female gender, and co-morbid disorders [104], as well as the place of patients' residence, the hours of dialysis regimen, patients' inability to choose their dialysis shift, and their job before the initiation of dialysis [105]. Patients with primary and secondary school education are particularly worried about their working status, since they usually have manual jobs and are unable to continue them after the beginning of haemodialysis [105].

Additionally, co-morbid disturbances have a negative impact on employment due to frequent hospitalizations, with more frequent co-morbidities being diabetes, cerebrovascular, and neurological and psychiatric diseases [104]. Muehrer et al. [103] found that patients with more co-morbid diseases had less possibility to keep their job. Anaemia is also associated with increased fatigue and weakness, being a significant factor affecting patients' capability to maintain their job. Carayanni et al. [106] found that women of an increased age, with co-morbid diseases and low economic status, had high rates of depression.

Moreover, the long duration of haemodialysis negatively affects employment status since patients have to undergo haemodialysis three times per week, usually during the working days, with each regimen lasting 3–4 h. Thus, there is an increase in retired patients after the initiation of haemodialysis due to their difficulty in their work capability, while a large proportion of them resign from their jobs or reduce their working hours after the beginning of haemodialysis [105].

## Depression and duration of haemodialysis

Radwan et al. [3] found that the long duration on haemodialysis had a significant correlation with patients' depressive symptoms, possibly due to the higher occurrence of complications and co-morbidities [54]. The time spent on dialysis is a high-rated stressor, since they usually receive therapy three times a week, each lasting 3–4 h, while they spend enough time on transportation to and from the renal unit, to rest at home after dialysis, and at hospital due to frequent hospitalizations [14], which limits their independent living [107]. It has been also found that there is a decrease in mental health, social interaction, and quality of life among patients undergoing haemodialysis for > 4 years [108].

## Interventions for reducing depression in haemodialysis patients

There are a variety of interventions for reducing depression in dialysis patients, which include pharmacological therapy with antidepressants, cognitive behavioural therapy, as well as physical activity and exercise programs during haemodialysis [109].

### Pharmacological therapy

Medication with antidepressants is an effective therapy for depression and is widely used in dialysis patients [110],

since it usually has rapid therapeutic effects [56]. However, it is difficult for these people to follow the multiple drug therapy due to its side effects, such as arrhythmias [33] sleepiness, dry mouth, and tachycardia [100].

### Cognitive behavioural therapy

Cognitive behavioural therapy is a psychotherapeutic approach that manages dysfunctional emotions, behaviours, and knowledge through a systematic procedure [73]. It was found that after receiving cognitive behavioural therapy, dialysis patients had an improvement in their symptoms of depression and their suicidal thoughts [111].

### Physical activity

A systematic physical activity can lead to reduction of depressive symptoms in dialysis patients [7], since it improves cardiovascular function and joints flexibility, it also reduces musculoskeletal pain, improves the quality of appetite and nutrition, increases the blood supply in brain, and acts as an antidepressant drug [56]. It was found that aerobic physical activity was related to reduced symptoms of depression, while patients who were exercising for 1 or more times a week had improved quality of sleep and reduced mortality [112].

### Intradialytic exercise programs

Exercise during haemodialysis regimens results in increased muscle blood flow and improved dialysis adequacy, blood pressure, anaemia, and phosphorous clearance [113]. It was found that a 6-month exercise training program reduced symptoms of restless legs syndrome and improved depression in patients with uremia [114]. Moreover, it was found that a 6-month regular physical training had an association with a decrease in depression and anxiety symptoms in dialysis patients, and especially in those of an older age [56].

Thus, all the above interventions can be incorporated as a part of haemodialysis treatment in order to reduce depression in patients undergoing haemodialysis.

## Conclusion

This review offers important information to renal professionals about the factors affecting depression in haemodialysis. More specifically, depression is affected by co-morbid diseases, such as cardiovascular disease, diabetes, immune and dysfunction, and it also includes high suicide risk and frequent hospitalizations. Additionally, malnutrition, cognitive impairment, pain, sleep disorders, sexual dysfunction, and unemployment are significant risk factors for depressive disorders in these patients.

This implies the necessity for the development of effective interventions in the renal setting, in order to help these people reduce their depressive disorders and improve their health status. There is also a need for a formal screening of patients when they first begin haemodialysis treatment in order to make early diagnosis of depression and reduce the levels of depressive symptoms. Finally, there is a necessity for further research in the dialysis setting, which can be derived from this review, for an in-depth investigation of risk factors of depression in dialysis population.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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