WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 6, 385-395. Review Article ISSN 2277– 7105

AN OVERVIEW ON IMPACT OF PSYCHOLOGICAL FACTORS IN PATIENTS UNDERGOING DIALYSIS

Tahera Mubeen*, Maneesha Annavarapu, Naveen Yaradesi and Padmalatha Kantamneni

Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India, 521108.

Article Received on
26 March 2021,

Revised on 15 April 2021,
Accepted on 06 May 2021

DOI: 10.20959/wjpr20216-20484

***Corresponding Author**
Tahera Mubeen
Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India, 521108.

ABSTRACT

Chronic kidney disease (CKD) also known as End stage renal disease (ESRD) is a commonest, debilitating, long standing public health condition. During the initial stages of CKD, treatment is mainly focused on slowing the progression of kidney damage and treating the complications. In the final stage, dialysis or renal transplantation becomes core responsible to maintain health. The most frequent psychopathological problems among patients undergoing dialysis are depression and anxiety which is still under recognized and misdiagnosed. The dialyzed patients are often subjected to depression and anxiety symptoms due to myriad physical, mental and psychosocial factors. Females are more prone to develop anxiety while males have high tendency to develop depression. The overall prevalence rate of depression and anxiety in dialyzed patients is about 66% and 61% respectively. Moreover, the mechanisms involved between psychological factors and adverse medical outcomes in dialyzed patients are discussed. Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI) are some of the screening tools to diagnose depression and anxiety. Management of dialyzed patients with depression and anxiety is a key role to improve their quality of life. Besides pharmacological treatment, cognitive behavioral therapy and life style modifications have immense fortune on patient's survival. More attention should be given to depression and anxiety care in context to dialyzed patients management. This review provides a selective overview on prevalence rate, etiology, coping mechanisms and treatment in complex patients and also management strategies are appraised and discussed from the relevant literature.

KEYWORDS: Chronic kidney disease (CKD), End stage renal disease (ESRD), Depression, Anxiety, HADS.

INTRODUCTION

Chronic kidney disease (CKD) is initially described as presence of kidney damage which is manifested via atypical excretion of albumin or reduction in kidney function and is quantified by estimated glomerular filtration rate (eGFR). For the assessment of severity of chronic kidney disease, National Kidney Foundation developed a criteria which was divided into 5 different stages.

STAGE 1	Normal estimated GFR $\geq$ 90ml/min per 1.73m^2
STAGE 2	Estimated GFR between 60 to 89ml/min per 1.73m^2
STAGE 3	Estimated GFR between 30 to 59ml/min per 1.73m^2
STAGE 4	Estimated GFR between 15 to 29ml/min per 1.73m^2
STAGE 5	Estimated GFR <15ml/min per 1.73m^2

Stage 5 is often named as End Stage Renal Disease (ESRD).[1]

End stage renal disease (ESRD) or kidney failure is the last stage of chronic kidney disease which is associated with loss of kidney functions where it is necessary for a patient to undergo permanent renal replacement therapy which includes dialysis or renal transplantation. It is a debilitating, severe illness where artificial type of excretion is required for patient's survival.[2] Dialysis (dia = through, lysis = loosening or splitting) is obtained from the Greek word, a process of eliminating excess amount of water, toxins and other solutes from the blood where kidneys fail to function normally. It is a temporary way to restore the normal kidney functions in patients with acute kidney injury (AKI), end stage renal disease (ESRD), awaiting kidney transplantation or in patients where transplantation is not possible. Dialysis is performed in patients whose glomerular filtration rate (GFR) is less than 15ml/min. However, it cannot completely restore the lost kidney function but can manage the normal function through diffusion, filtration, ultrafiltration etc.[3] Patients undergoing dialysis are often associated with changes in their daily activities and lifestyle for themselves as well as their families which significantly has negative impact on their treatment outcomes and quality of life. Depression and Anxiety are most common psychiatric problems occurring among patients undergoing dialysis. Biological imbalances, physiological alterations, neurological and cognitive impairment play a significant role in depression. Unfortunately, depression and anxiety have negative impact on the patients suffering with any chronic illness. The prevalence and association of depression and anxiety in patients

undergoing dialysis varies with type of diagnostic tool employed. So far, the gold standard for diagnosing psychiatric issues is often done using DSM-IV TR criteria. A collaborative team effort is indeed helpful in treating such complex patients.[2] This study gives an overview on psychological factors such as Depression and Anxiety, prevalence, mechanisms involved and management in patients undergoing dialysis.

DISEASE PERCEPTION

Depression and Anxiety

WHO defined Depression as "a common mental disorder characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep, appetite and poor concentration".[4] WHO also notifies Depression as second most chronic and costly illness.[5] It is one of the most challenging psychological disorder and it has significant impact on patients undergoing dialysis affecting financial, social, psychological and physical well-being and involves combination of mechanisms such as inflammation, comorbidities, hormonal imbalances, fatigue, increased hospital stay, low medication adherence and fear of death. Risk factors include increased body mass index, illiteracy, comorbid conditions and financial burden.[4,6] A study revealed that depression and anxiety was identified as under-diagnosed and under-treated among patients undergoing dialysis. Depression is often characterized by presence of both somatic and cognitive functions. There is a close relationship between symptoms of somatic features and uremia such as fatigue, gastrointestinal distress, pain, sleep disorders and anorexia. Moderate to severe Depression is most common with an incidence of 73%. Gender, age, type of dialysis and severity of condition play an important role in association between the psychological factors and depression. However females are effected with higher frequency.[4] One in 500patients attempts a suicide or has decreased acceptancy to dietary food or treatment procedures due to multifaceted conditions such as anxiety, poor self-esteem, depressed mood, pain, far away from their daily activities and family. Assessment of depression severity based on Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Score (HADS). Well validated BDI is often used to separate somatic from cognitive symptoms of depression. Through modifications in immunologic and stress responses, depression is responsible to affect medical outcomes in patients and having its impact on nutritional regimen, decreased compliance for dialysis and medications. Recently, studies concluded that proinflammatory cytokines mediate both neurochemical and behavioral functions of depression and anxiety. There is a close link between increased levels

of depression, anxiety and renal diseases since many of the inflammatory biomarkers are dysregulated in ESRD patients.[4]

Another commonest psychological factor that has impact on ESRD patients is anxiety. Anxiety is defined as a condition which is characterized by dread, fearfulness, disruptive feelings, lethargy and insomnia. When the duration and intensity extend beyond the expectations that is the point where anxiety becomes a disorder. Clinical presentation, severity of condition, treatment in patients undergoing dialysis are the factors considered for diagnosis and management of anxiety. Prevalence of anxiety in ESRD patients is not clearly known, but it was believed that comorbidity conditions usually exist in patients undergoing dialysis which usually include depression and anxiety. Hence it is essential to distinguish between these two disorders so an appropriate management can be provided without overlapping in ESRD patients. The Diagnostic and Statistical Manual defined Anxiety as which persists for at least 6months with symptoms including fatigue, sleep disorders, fatigue and poor concentration. It is also important to consider some of the differential diagnosis such as panic disorders, social phobia, obsessive compulsive disorder, agoraphobia. Anxiety disorders in ESRD patients are measured via scales such as Kidney Disease Quality of Life-Short Form, Health related Quality of Life scale and Medical Outcomes Study-Short Form-36.[4]

Etiologic Considerations and Prevalence Rate

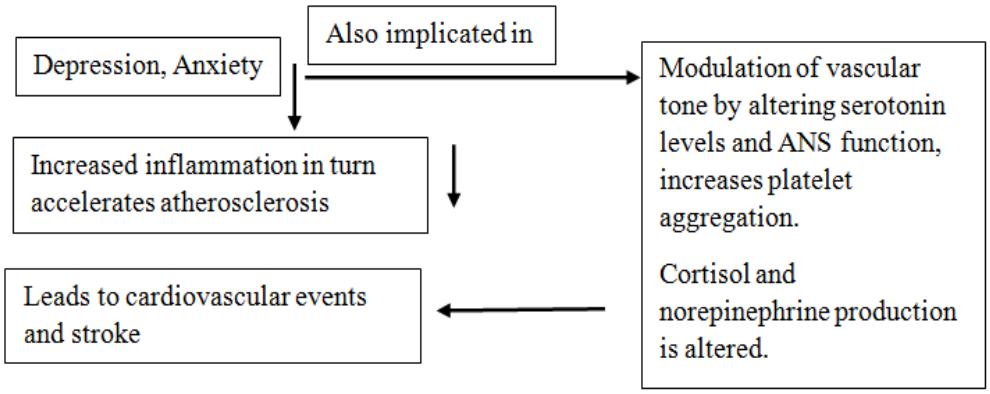
Heavy burden of depression and anxiety in patients undergoing dialysis are usually grouped as primary (medical illness independent) and secondary (medical illness dependent) forms. Etiological factors include younger age, female gender, dialysis duration, comorbidities such as diabetes mellitus, coronary artery disease, cerebrovascular disease and peripheral vascular disease. Hence these risk factors are more common in patients with kidney diseases than in the general population hence more likely to have higher prevalence of depression and anxiety in patients undergoing dialysis than in the general population.[7]

About 10% of adults worldwide have CKD and it is the 5th common cause of death globally by 2040. In India, in a population of >1 billion, the estimated incidence rate of ESRD is 229 per million population and about more than 1,00,000 new patients are engaged in renal replacement therapy annually.[8] Most of the CKD patients have dialysis as predominant mode of treatment and most of them have comorbidities such as hypertension and diabetes. In India, 44.05% patients had major depressive disorder and 46.43% had suicidal ideation

observed in Karnataka state. Depression is initially reported in patients with mean dialysis duration of < 24months. Increased economical cost, monitoring and regular follow ups, psychosocial factors related to disease reveals the association between dialysis and depression.[9] A study conducted in Rajasthan confirmed that the prevalence of depression and anxiety in dialyzed patients was more in unemployed, farmers and service class patients whereas anxiety is more common in nuclear family. Lifelong treatment, diet, recurrent symptoms, regular follow-ups. Treatment cost, limited work capacity, loss of kidney function overtime alter the physical, social and mental functioning of patients undergoing dialysis.[10] As depression and anxiety and other psychological factors are common in dialyzed patients, more attention should be on patients treatment outcomes and quality of life. A study revealed that patients undergoing dialysis have depression three times more than renal transplantation patients, while anxiety affected 1.5times more. Anxiety and depression range from 12-60% and 10-70% respectively in dialyzed patients.[11]

MECHANISM

The association between depression, anxiety with medical outcomes in patients with ESRD can be explained by several potential biologic mechanisms.



Some of the hypothesized mechanisms include

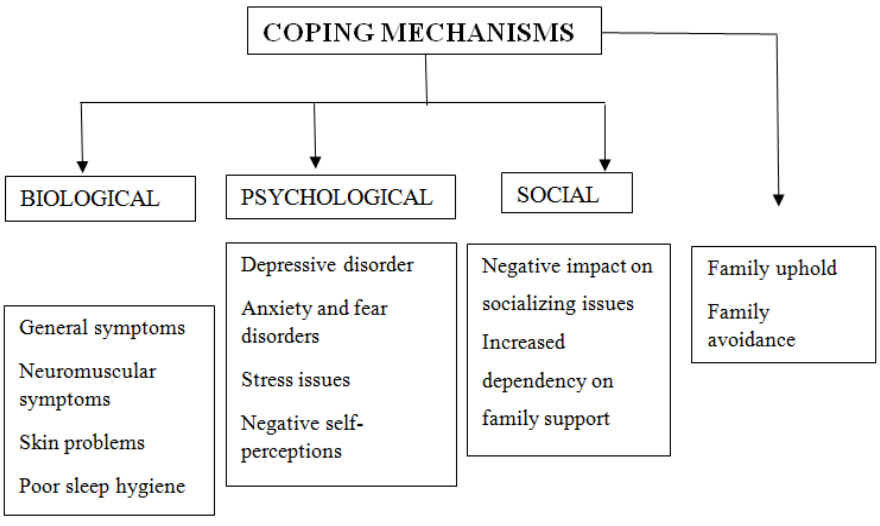
- Biologic, Behavioral, Genetic, Social factors.
- Inflammatory factors (example: C-reactive protein, cytokines)
- Chemical imbalances (example: Increased levels of phosphorus, uremia and decreased hemoglobin, increased cortisol levels)
- Physical inactivity
- Lack of social support

Substance abuse, alcohol intake, increased suicidal tendency are usually more prone in depressive illness. Recent meta-analysis demonstrated that patients undergoing dialysis have higher rates of depression and anxiety and higher risk of hospitalization whereas patients with both CKD and major depression episode have twice the risk of hospitalization.[12] Prominent features of depression among dialysis patients are hopelessness and distress. Loss of somatic and psychological level are seen in patients with ESRD. Pathogenesis of depression in dialysis patients involves cytokine induced depression due to increased levels of cytokines and acute phase reactants in ESRD patients.[13] Some studies revealed that depression is mostly caused due to uremia which effects synthesis and metabolism of certain neurotransmitters in the CNS. Hence uremic control can reduce the depression and anxiety to some extent.[13]

The association between depression and adverse renal outcomes has been suggested by two mechanisms although not well characterized.

Firstly, biological factors are core responsible. Depression has higher likelihood to cause allostatic dysregulation which in turn leads to hypothalamic-pituitary axis hyperactivity which therefore results in excretion of cortisol and norepinephrine. Alteration in malnutrition, immunity, inflammation states are also observed in patients undergoing dialysis.

Secondly, behavioral pathways are implicated. Patients undergoing dialysis have increased risk of suicide attempts, self violation due to many restrictions to themselves such as diet, alcohol, smoking, dialysis frequency, stress, pain, less physical activity, feeling abandoned by family which usually has its impact on clinical outcomes.[14]



Coping mechanisms and Bio psychosocial impact on patients undergoing dialysis[15]

Screening and Management Care

An immediate necessary to establish appropriate procedures and tools for screening depression and anxiety is required.

When to screen- At initiation of dialysis, ESRD patients should be screened for every 6months and then continue annually. Rescreening should be considered in case of change of treatment plan, major life stressors, disturbed behavior and mental health.

How to screen- Firstly, a two question approach modified from Patient Health Questionnaire is usually recommended:

1. In past 2week, have you been bothered by having little interest in doing things?
2. Have you felt depressed?

More specific depression/anxiety symptoms should be screened if any positive response to either of the question is obtained.

Some of the screening methods include Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory, Patient Health Questionaire-9 and Generalized Anxiety Disorder-7. Limited sensitivity and specificity are shown by most of the screening tools. Diagnostic and Statistical Manual of Mental Disorders diagnostic criteria is recommended for its consistency and accuracy.[16]

Impression on Neuroimaging- Patients undergoing dialysis have higher prevalence of more severe white matter disease and cerebral atrophy, small and large vessel infarcts. White matter hyper intensities (WMHs) are more commonly seen in elderly patients and late onset depression. WMHs include arteriolar ectasia areas, perivascular spaces enlargement, myelin pallor due to arteriosclerotic changes of perforating arteries, basal ganglia lesions. CNS complications are more common in patients on long term dialysis which include white matter changes, cerebral atrophy, hypertensive encephalopathy, sinus thrombosis, hemorrhage. Generally endothelial damage leads to lesion formation and giving rise to pathological hemodynamic and cerebrovascular regulation in turn unable to regulate stable blood flow causing impaired protein synthesis which is necessary in both affective and cognitive processing and regulation.[12]

Treatment for depression and anxiety in patients undergoing dialysis is complicated and hard to treat if comorbidities are also implicated.[13] Early identification and remission or improvement of symptoms related to depression, anxiety is the treatment goal recognized by Nephrology community. Some studies revealed that antidepressants were used by only 34.9% patients undergoing dialysis who are diagnosed with depression and many patients are left undertreated and underdiagnosed for depression and anxiety.[14] Most commonly used antidepressants such as Selective serotonin receptor inhibitors (SSRI) and Selective norepinephrine reuptake inhibitors (SNRI) are advisable initially given in low dose and thereby increasing overtime. Tricyclic antidepressants are usually avoided due to risk of cardiac events. A double blind placebo controlled study was conducted in dialyzed patients where fluoxetine (20mg/d) found to be effective in alleviating symptoms with no adverse events.[13] Benzodiazepines and beta-blockers are useful for short trails in case of episodic anxiety with more attention towards dose adjustments, adverse events, drug-drug interactions. SSRI particularly sertraline is advantageous which is safer in cardiovascular diseases and requires no dose adjustments in ESRD patients whereas fluoxetine, citalopram, citalopram, paroxetine, Non-SNRIs such as mirtazapine, venlafaxine, bupropion have limited data existed.[16] Additional attention should be given to avoid medical interactions with already prescribed renal medications in patients with depression receiving pharmacological treatment.[14]

The evidence reveals that cognitive behavioral therapy is more effective in dialyzed patients to relieve depression and anxiety symptoms.[13] The main goal is to decrease the symptoms and improve the overall physical functioning. The non-pharmacological treatments include cognitive behavior therapy (CBT) and exercise programs. Depression scores and quality of life are improved due to chair side CBT. Limiting tobacco and caffeine use, relaxation, meditation, psychodynamic therapy, sleep patterns and hygiene education are suggested for patients with anxiety disorder.[16] CBT is most advanced, accepted method of treatment and effective in dialyzed patients. Novel developments in telehealth or e-health are practiced for distressed patients through online found to be successful. Other mental health services include communicating with nurses, doctors, caregivers, stress management procedures supports the patients.[14]

Impact On Caregivers

The caregivers of the patients undergoing dialysis commonly have extraordinary poor effect on their emotional state. Moreover, anxiety and depression, mental fatigue, physical stress, social quarantine, collapse of family relationships are experienced by the caregivers. Anxiety which is untreated further leads to depression which may have contrary effect on mutual relationships leading to failure of treatment adherence. Increased patients mortality is based on caregivers impoverished psychological status for which the common needs of their loved ones are generally ignored by the depressed caregivers thus decreases the survival rate. Hence the valuable source for dialyzed patients to improve their quality of life are healthy, emotionally strong and supportive caregivers with better understanding on treatment strategies to maintain physical and mental health. Periodic counselling to dialyzed patients as well as caregivers helps to restore mental health and increases treatment compliance.[17]

CONCLUSION

Patients undergoing dialysis usually deal with varied stressors of their illness and cope with multiple demands from family, society and occupation. The most common psychological problems encountered by dialyzed patients are depression and anxiety. A collaborative and hospitality approach by kidney care team along with nurses is necessary to identify, screen and treat the complex patients. Even the pharmacy team and clinical pharmacist can play a tremendous role in educating patient and their caregivers regarding medication use, suspected adverse drug reactions and report to them, if any, immediately. Also Palliative care specialists along with kidney care team can help to reach diagnosing and management goals and improve patient's survival rate by counselling them to withhold their thoughts on dialysis withdrawal and changeover to hospice.

ACKNOWLEDGEMENT

We are gratefully acknowledged Dr. Padmalatha Kantamneni, Principal, Vijaya Institute of Pharmaceutical Sciences for Women for support and valuable guidance.

REFERENCES

1. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Prim Care, 2008; 35(2): 329-vii.
2. Finnegan-John J, Thomas VJ. The Psychosocial Experience of patients with End Stage Renal Disease and its impact on Quality of Life: Findings from a needs assessment to shape a service. ISRN Nephrology, Oct 21, 2012; 2013: 308986.

3. Vadakedath S, Kandi V. Dialysis: A review of the Mechanisms Underlying Complications in the Management of Chronic Renal Failure. Cureus, 2017; 9(8): e1603.
4. Stavroula K. Gerogianni, Fotoula P. Babatsikou. Psychological aspects in chronic renal failure. Health Science Journal, 2014; 8(2): 205-214.
5. Paul L. Kimmel. Psychosocial factors in dialysis patients. Nephrology Forum, 2001; 59(4): 1599-1613.
6. Muthukumaran A, Natarajan G, Thanigachalam D, Alavudeen Sultan S, Jeyachandran D, Ramanathan S- The role of psychosocial factors in depression and mortality among urban hemodialysis patients, Kidney International Reports, 2021.
7. Shirazian S, Grant CD, Aina O, Mattana J, Khorassani F, Ricardo AC. Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management. Kidney International Reports, Sep 20, 2016; 2(1): 94-107.
8. Gadia P, Awasthi A, Jain S, Koolwal GD. Depression and anxiety in patients of chronic kidney disease undergoing haemodialysis: A study from western Rajasthan. Journal of Family Medicine and Primary Care, Aug 25, 2020; 9(8): 4282-4286.
9. Gupta S, Patil NM, Karishetti M, Tekkalaki BV. Prevalence and clinical correlates of depression in chronic kidney disease patients in a tertiary care hospital. Indian Journal of Psychiatry, 2018; 60(4): 485-488.
10. Ahlawat R, Tiwari P, D'Cruz S. Prevalence of depression and its associated factors among patients of chronic kidney disease in a public tertiary care hospital in India: A cross-sectional study. Saudi Journal of Kidney Diseases and Transplantation, 2018; 29(5): 1165-1173.
11. Daniela Cristina Sampaio de Brito, Elaine Leandro Machado, Ilka Afonso Reis, Lilian Pires de Freitas do Carmo, Mariangela Leal Cherchiglia. Depression and anxiety among patients undergoing dialysis and kidney transplantation: a cross-sectional study. Sao Paulo Medical Journal, 2019; 137(2): 137-147.
12. Talkers US, Anayet HTB, Mandal S, Ahmed F, Ibrahim MA, Depression in Dialysis: A Poor Prognostic Factor and the Mechanism behind It. International Journal of Depression and Anxiety, 2020; 3: 019.
13. Joseph Chilcot, David Wellsted, Maria Da Silva-Gane, Ken Farrington. Depression on Dialysis. Nephron Clinical Practise, 2008; 108: c256-c264.

14. Zhong Sheng Goh, Konstadina Griva. Anxiety and Depression in patients with end stage renal disease: impact and management challenges- a narrative review. International Journal of Nephrology and Renovascular Disease, 2018; 11: 93-102.
15. Han E, Shiraz F, Haldane V, Koh JJK, Quek RYC, Ozdemir S, Finkelstein EA, Jafar TH, Choong HL, Gan S, Lim LWW, Legido-Quigley H. Biopsychosocial experiences and coping strategies of elderly ESRD patients: a qualitative study to inform the development of more holistic and person-centred health services in Singapore. BMC Public Health, Aug 14, 2019; 19(1): 1107.
16. Bates N, Schell J, Jordan A. Depression and anxiety in ESRD: a practical guide for nephrologists. ASN Kidney News, 2017: 1-2.
17. Georgia Gerogianni, Maria Polikandrioti, Fotoula Babatsikou, Sofia Zyga, Victoria Alikari, George Vasilopoulos, Stavroula Georgianni, Eirini Grapsa. Anxiety- Depression of dialysis patients and their caregivers. Medicina (Kaunas), 2019; 55(5): 168.