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# The Psychological Impact of Hemodialysis on Patients with Chronic Renal Failure

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## 1. Introduction

Renal disease is common throughout the world. In the United States alone, almost 100,000 people began renal replacement therapy (RRT) for end-stage renal disease (ESRD) in 2001 (Kimmel & Peterson, 2005); by 2008, this number had increased to 485,000 patients (Collins et al., 2009). More than 90% of these patients were started on hemodialysis (HD), while only 8.5% began RRT with peritoneal dialysis (PD) (Kimmel & Peterson, 2005). In Korea, the number of dialysis centers and machines has continuously increased, and 62.1% of patients receiving RRT were being treated with HD (Son et al., 2009). An international comparison showed that Taiwan has the greatest incidence and second-greatest prevalence of ESRD (Kuo et al., 2007). Furthermore, renal disease is one of the top 10 causes of death in Taiwan, and roughly 95% of ESRD patients are on HD (Hsieh et al., 2007).

While HD does not cure renal disease, its use does allow patients with ESRD to survive (Weisbord et al., 2007a). Nevertheless, HD is a lifelong treatment that significantly and sometimes adversely affects patients both physically and mentally (Kimmel, 2001). Common psychological effects include depression, anxiety, fatigue, decreased quality of life (QoL) and increased suicide risk (Chen et al., 2010). The global effects of continual treatment lead to changes in patients' family roles and ability to work, with feelings of loss of control and fear of death. These very real psychological consequences of treatment may affect survival in HD patients (Chilcot et al., 2011; Kimmel & Peterson, 2005). Therefore, it is imperative to identify and treat these psychological symptoms among HD patients.

## 2. Depression

### 2.1 Prevalence and influence of depression

Depression is one of the most common psychological problems among HD patients. We still lack reliable data that can be used to directly compare the prevalence of depression between HD patients and the general population. However, extant investigations generally agree that the rate of depression is high among HD patients.

In the general population, the lifetime prevalence of major depressive disorder is about 16.2% (Kessler et al., 2003). However, the rates vary widely across countries, ranging from

Study	Number of patients	Assessment tools	Prevalence	Additional findings
Kurella et al. (2005)	465,563	Medical evidence form in Medicare and Medicaid Services	Withdrew from dialysis: 9.6% Died from suicide: 0.005%	Persons with ESRD significantly higher than in the general population. Independent predictors of suicide: age >75 yr, geographic region, drug dependence, and hospitalization with illness.
Taskapan et al. (2005)	40	HDRS, HARS, PRIME-MD, MMSE, SF-36	Depression: 30% Anxiety: 35% Somatoform disorder: 32.5%	All patients' MMSE scores were within normal range. No relationship between psychiatric disorder and demographic characteristics. Negative correlation between weight gain and QoL on dialysis.
Drayer et al. (2006)	62	PRIME-MD, KDQOL-SF	Depression: 28%	Depressed patients had lower health-related QoL. Depression predicted mortality in a mean follow-up of 29 months.
Kalender et al. (2007a)	HD: 68 PD: 47	BDI, SF-36	Depression in HD: 33.8% Depression in PD: 12.8%	Significant negative correlation between QoL and depression. Significant positive correlation between the QoL and serum albumin value and serum urea nitrogen. Inverse correlation between QoL and the serum urea nitrogen in the HD patients.

Study	Number of patients	Assessment tools	Prevalence	Add
Cukor et al. (2008)	70	SCID, HADS, KDQOL-SF	Depression: 29% Anxiety: 45.7%	Patients with per... marked decreases... health status, com... and intermittently
Hedayati et al. (2008)	98	SCID, BDI, CDI, CESD	Depression: 26.7% Major depression: 17.3%	There were no dif... hospitalization fo... depressed. Patien... increased risk of o... year.
Ibrahim & Salamony (2008)	60	BDI, SF-36, DSI, MIS	Depression: 33.3%	Depression was a... marital status. DS... correlations with... correlations with
Hsu et al. (2009)	51	HADS	Depression: 35%	Depression was le... used polysulfone... who used cellulose... Depression was a... albumin, and nur...
Kao et al. (2009)	861	SF-36, BDI	Depression: 60.5% Insomnia: 31.0% Fatigue: 30.6%	Depression scores... with QoL. Higher... increased social a... better health-rela...
Son et al. (2009)	146	BDI, PHQ-9, KDQOL	Depression: 25.3%	There were more... reported in depre... depressed ones.
Bossola et al. (2010)	80	BDI, HARS, SF-36, SCL-90-R, CCI; MMSE	Depression: 52.5% Mild anxiety: 47.5% Moderate to severe anxiety: 48.7%	BDI score correlat... CCI, SF-36 Vitalit... albumin, plasma... 6 levels.

Study	Number of patients	Assessment tools	Prevalence	Additional outcomes
Chen et al. (2010)	200	MINI, HADS, CFS, SF-36	Depression: 35% Anxiety: 21%	In the previous month, 21.5% patients had suicidal ideation. Depressed patients had higher rates of fatigue, and lower QoL. Suicide risk was strongly related to depression and anxiety.
Montinaro et al. (2010)	HD: 30 Control (patients with CKD stage 1-2): 20	HADS, KDQOL	Depression: HD = 50%, controls = 20% Anxiety: HD = 43%, controls = 45%.	Cytokine production (IL-1, IL-6 and TNF- $\alpha$ ) was significantly higher in HD patients than controls. KDQOL correlated inversely with levels of IL-6, TNF- $\alpha$ and IL-10. IL-6 was associated with anxiety.
Keskin & Engin (2011)	92	BDI, SBQ, COPE	Depression: 40.2%	Suicidal ideation increased as the severity of depression increased. Depression and suicidal ideation were increasing with age and lower education status.
Araujo et al. (2011)	400	BDI	Depression: 19.3%	Depression was associated with female gender, poor sleep quality, unemployment, diabetes, hypoalbuminemia, low education, and pruritus.

KEY: BDI: Beck Depression Inventory; CCI: Charlson Comorbidity Index; CESD: Center of Epidemiological Studies Depression Scale; CFS: Chalder Fatigue Scale; CKD: chronic kidney disease; COPE: Coping Orientation to Problems Experienced Inventory; CRP: C-reactive protein; DSI: Dialysis Symptom Index; HADS: Hospital Anxiety and Depression Rating Scale; ESRD: end-stage renal disease; HARS: Hamilton Anxiety Rating Scale; HD: hemodialysis; HDRS: Hamilton Depression Rating Scale; IL: interleukin; KDQoL: Kidney Disease Quality of Life; KDQoL-SF: Kidney Disease and Quality of Life Short Form; MINI: Mini International Neuropsychiatric Interview; MIS: Malnutrition-Inflammation Score; MMSE: Mini Mental State Examination; PD: peritoneal dialysis; PHQ-9: Patient Health Questionnaire; PRIME-MD: Primary Care Evaluation of Mental Disorders; SBQ: Suicide Behaviours Questionnaire; SCID: Structured Clinical Interview for DSM; SCL-90-R: Hopkins Symptom Checklist 90 Revised; SF-36: The Short-form Health-related Quality of Life; TNF: tumor necrosis factor

Table 1. Psychological impacts in hemodialysis patients demonstrated in recent studies

The variation in prevalence rates of depression might be accounted for by differences in sample sizes and assessment tools (Watnick et al., 2005). Despite such discrepancies, depression is unquestionably one of the most important mental illnesses among HD patients. Strong correlations have been noted between depression and longitudinal outcome among HD patients, including poor treatment adherence and higher mortality rates (Drayer et al., 2006; Kimmel et al., 1993). In addition, depression in HD patients is associated with higher rates of hospital admission, and a greater likelihood of emergency department visits (Abbas Tavallai et al., 2009; Hedayati et al., 2008).

## 2.2 Biological factors underlying depression

The etiology of dialysis-related depression is multifactorial, and is related to biological, psychological, and social mechanisms (Chilcot et al., 2008). Some of the biological mechanisms include increased cytokine levels, possible genetic predisposition, and neurotransmitters affected by uremia (Kimmel, 2001; Smogorzewski et al., 1995).

For decades it's been known that immunologic factors have potent influences on neurotransmitter metabolism and neuroendocrine function (Irwin & Miller, 2007; Wichers & Maes, 2002). A growing number of studies have investigated the relationships between cytokines and depression (Howren et al., 2009; Loftis et al., 2010; Sonikian et al., 2010). During hemodialysis, the blood-dialyzer interaction has the potential to activate mononuclear and dendritic cells, leading to production of inflammatory cytokines (Agrawal et al., 2010; Pertosa et al., 2000). Several researchers support the supposition that pro-inflammatory cytokines are involved with depression in renal patients. In particular, there is evidence that depression is associated with interleukin (IL)-1, IL-6, tumor necrosis factor-alpha (TNF- $\alpha$ ), and C-reactive protein (CRP) in both the general and ESRD populations (Gill et al., 2010; Simic Ogrizovic et al., 2009; Sonikian et al., 2010). These pro-inflammatory cytokines also appear to be associated with survival rate in HD patients (Kimmel et al., 1998). The underlying biological mechanisms have been proposed as a defect in serotonergic function and hypercortisolemia associated with stimulation of the hypothalamic-pituitary-adrenal (HPA) axis (Capuron & Miller, 2011; Leonard, 2010), thus leading to depression and affecting mortality.

Malnutrition, which is commonly observed in dialysis patients, is related to chronic inflammation (Pertosa et al., 2000). It has also been reported that malnutrition is associated with emotional symptoms among HD patients (Bossola et al., 2009; Czira et al., 2011; Huang & Lee, 2007; Ibrahim & El Salamony, 2008; Koo et al., 2003). These authors also determined that patients with depression had lower-than-normal body mass indices (BMI) (Chen et al., 2010).

There is evidence of an association between malnutrition, inflammation, and atherosclerosis (MIA) in ESRD patients, and some researchers have suggested that depression might be involved in the MIA syndrome (Simic Ogrizovic et al., 2009). Others have demonstrated frequent and close relationships between serum albumin levels and depression (Huang & Lee, 2007; Hung et al., 2011; Koo et al., 2003). However, a correlation between hemoglobin, ferritin, and emotional symptoms is less clear-cut (Bossola et al., 2009; Czira et al., 2011; Huang & Lee, 2007). Hopefully the causal relationships in the complexity of psychoneuroimmune mechanisms will be further elucidated in future studies.

Racial effects on depression and anxiety have been studied in HD patients, once again with conflicting results (Feroze et al., 2010). Higher prevalence rates of major depressive disorders have been noted among Caucasians than among African-Americans or Mexican-Americans (Riolo et al., 2005). In contrast, the results of some studies revealed no differences in the prevalence of depression among races (Chen et al., 2011; Weisbord et al., 2007b). Balakrishnan et al. (2004) demonstrated that single nucleotide polymorphisms in the promoter region of the proinflammatory cytokines appear to have a strong association with indices of comorbidity, biological and nutritional markers. Whether depression is associated with a genetic predisposition for racial differences or cytokine gene polymorphisms warrants further investigation.

Other studies have evaluated the possible effects of dialysis materials on depression. Peritoneal dialysis (PD) patients have been noted to have less severe anxiety, insomnia, and depression than do HD patients (Ginieri-Coccosis et al., 2008; Noshad et al., 2009). It has been suggested that the rate of depression is greater among patients using cellulose-derivative dialyzers than among those using polysulfone dialyzers (Hsu et al., 2009). Using PD or more biocompatible dialyzers thus might be associated with better mental health in HD patients.

### 2.3 Psychological and social factors for depression

A number of studies have focused upon the effects of HD patients, including feelings of hopelessness, perceptions of loss and lack of control, job loss, and altered family and social relationships (Kimmel, 2001). Because ESRD is a lifelong disease, feelings of lack of control and perceptions of overwhelming illness might be inevitable. The intrusiveness of these thoughts is related to depression (Christensen & Ehlers, 2002; Devins et al., 1997).

More recent work has focused upon the possible effects of underlying illness upon depressive symptoms among ESRD patients (Guzman & Nicassio, 2003). Perception of loss has been regarded as a strong predictor of depression (Chan et al., 2009), which in turn predicts mortality (Chilcot et al., 2011). In terms of the risk by demographic characteristics, results have been inconsistent (Taskapan et al., 2005). It was reported that depression among dialysis patients increased with increasing age and lower educational levels (Keskin & Engin, 2011). In some studies, depressive symptoms were more common among women, and increased with unemployment and also rose among patients with higher comorbidity of physical diseases (Araujo et al., 2011; Chen et al., 2010; Ibrahim & El Salamony, 2008). Thus, negative cognition and lack of social support might exacerbate patients' negative feelings, and thus further contribute to depression.

## 3. Anxiety

Anxiety is also commonly seen in HD patients (Kring & Crane, 2009). Cukor et al. demonstrated a 27% incidence of anxiety among 70 urban HD patients, which was somewhat higher than the 18% incidence reported in a national survey (Kessler et al., 2005). During a 16-month follow-up study, 9% of patients had both anxiety and depression at baseline; the incidence of both conditions rose to 13% by the end of the study. At the end of the study, two-thirds of individuals with comorbid depression and anxiety at baseline had both diagnoses (Cukor et al., 2008b). Furthermore, Cukor et al. (2008a) reported that 45.7%

of a group of dialysis patients recruited from a single center met criteria for an anxiety disorder. The most prevalent disorders were specific phobias (26.6%) and panic disorder (21.0%). Bossola et al. (2010) indicated that 47.5% of 80 HD patients had mild symptoms of anxiety, while 48.7% had moderate or severe symptoms of anxiety. In addition, the anxiety scores correlated significantly with age and comorbidities, and anxiety were commonly noted in patients with poor appetite (Bossola et al., 2011). A review of 55 studies that investigated symptoms of anxiety in ESRD patients found that 12% to 52% of patients with ESRD had substantial anxiety (Murtagh et al., 2007).

In one of our previous studies, 21% of dialysis patients had symptoms of anxiety. In addition, 15.5% of these subjects had comorbid depression and anxiety, and 44.3% of depressed patients had comorbid anxiety (Chen et al., 2010). Furthermore, suicide risk was not only attributed to depression, but also to anxiety.

The call for depression screening in HD patients is growing, but screening for anxiety in patients with ESRD population is relatively disregarded. This is an indication that many clinicians underestimate the importance of anxiety among HD patients. O'Donovan et al. (2010) reported that clinically anxious participants exhibited significantly lower levels of morning cortisol and significantly higher levels of IL-6, compared with non-anxious participants. Uncertainty about the future and fear of losing control of one's life are important factors associated with anxiety that adversely impact emotional stability (Haenel et al., 1980). Notably, anxiety is a common psychological problem that may emerge during the initial course of dialysis (Cukor et al., 2008b), and is a reminder to clinicians to pay close attention to this issue.

#### **4. Fatigue**

Fatigue is a subjective symptom characterized by tiredness, weakness, and lack of energy. (Lee et al., 1991) Fatigue is also one of the most debilitating symptoms reported by HD patients, and roughly 60% to 97% of patients on HD experience some degree of it (Jhamb et al., 2008). People with chronic renal disease, regardless of whether they are pre-dialysis or receiving either HD or PD, are reported having high levels of fatigue and are often unable to engage in normal daily activities (Bonner et al., 2010). In addition, fatigue is positively correlated with depression (Chen et al., 2010; Sklar et al., 1996), and negatively correlated with QoL (Lee et al., 2007). In one study, researchers noted a significant relationship between the duration of treatment and the level of fatigue. The experience of fatigue was more commonly reported in respondents who had been receiving treatment for more than 2 years, compared to those treated for less than 2 years (Letchmi et al., 2011). In a longitudinal analysis of 917 incident HD and PD patients, those with lower levels of fatigue at baseline survived longer (Jhamb et al., 2009).

Factors that may contribute to fatigue in dialysis patients include anemia, malnutrition, inflammation, depression and/or sleep disorders (Jhamb et al., 2008). Anemia resulting from reduced erythropoietin production has been cited as an important cause of fatigue in this population (Singh et al., 2006). Additionally, patients undergoing chronic HD show evidence of accelerated protein catabolism, which might be due to the significant loss of amino acids induced by dialysis (Pertosa et al., 2000). Thus, it is reasonable to presume that lower levels of albumin can be significantly correlated with greater levels of fatigue (Bonner



et al., 2010). Malnutrition in dialysis patients might also be related to poor intake, or the result of chronic inflammation (Stenvinkel et al., 1999). Cytokines productions, particularly IL-6, might induce protein catabolism and lipolysis (Memoli et al., 2002), and cytokines have a strong negative correlation with serum albumin levels in HD patients (Montinaro et al., 2010). Thus, chronic inflammation and malnutrition might result in fatigue by either directly activating the central nervous system through adrenal axis or by indirectly triggering multisystem deregulation (Jhamb et al., 2008).

## 5. Decreased Quality of Life (QoL)

Health-related QoL is an important measure of how a disease affects the lives of patients. The QoL domains include physical, psychological, and social functioning and general satisfaction with life (Tsay & Healstead, 2002). Once patients with ESRD start to receive HD, they must face the chronic stress related to restrictions on their time, the economical and vocational costs related to treatment, functional limitations, dietary constraints, and possible adverse effects of medications (Son et al., 2009). Numerous studies have demonstrated that these patients have a lower QoL than that of healthy populations (Kao et al., 2009; Perlman et al., 2005; Wolcott et al., 1988). Depression is strongly correlated with decreased health-related QoL, especially in mental dimensions (Chen et al., 2010; Kao et al., 2009). Furthermore, several studies have shown that patients with poorer QoL had a higher incidence of anxiety and fatigue (Kring & Crane, 2009), and longitudinal follow-up showed increased mortality (Drayer et al., 2006; Wolcott et al., 1988).

Biological function, mental illnesses, general health perception, and characteristics of the individual and environment may contribute to the variability in patients' QoL (Kring & Crane, 2009). Biological factors that have been associated with QoL include altered hemoglobin, albumin, ferritin, CRP, IL-6, IL-8, and TNF- $\alpha$  levels (Farag et al., 2011; Kalender et al., 2007a; Montinaro et al., 2010; Perlman et al., 2005). Poor exercise tolerance and muscle weakness may limit daily activity, again causing poor QoL (Hsieh et al., 2007; Sakkas et al., 2003). However, Barros et al. (2011) suggested there was no association of nutritional status with malnutrition-inflammation, QoL, or depressive symptoms. There is still debate about whether patients' QoL can be directly correlated to malnutrition-inflammation markers.

Among psychological issues, uncertainty about the future and lack of energy emerged as the major contributors to poor QoL (Tsay & Healstead, 2002). A patient's dependency on treatment may negatively impact his or her QoL and exacerbate feelings of a loss of control (Chilcot et al., 2008). Improved QoL is correlated with higher self-esteem and lower levels of mood disturbances (Wolcott et al., 1988). Furthermore, time of diagnosis of chronic renal failure may be an important factor related to the QoL of patients receiving dialysis. Late diagnosis of renal failure and the consequent lack of predialysis care adversely affect QoL among these patients (Sesso & Yoshihiro, 1997). Therefore, early detection of renal failure and identification of underlying mental illnesses might be important issues for establishing better QoL in HD patients.

## 6. Suicide

Suicide may be the most serious result of mental illness among HD patients. Kurella et al. (2005) reported the death rate from suicide was 0.24% per 1000 dialysis patients-years at

risk. Patients with ESRD had a significantly higher rate of suicide compared with the general population in the United States. Chen et al. (2010) demonstrated that among 200 patients with HD, 21.5% had suicidal ideation; 3.5% had planned a suicide attempt in prior months; and 3.5% had attempted suicide during their lifetime. It is noteworthy that an increased number of patients with ESRD had withdrawn from dialysis before their death. Nevertheless, only a small proportion (12%) of the respondents were unsure or believed that discontinuing dialysis was the equivalent of suicide (Cohen et al., 2002). If the data on withdrawal from dialysis were factored into current epidemiologic investigations, the suicide rate among HD patients might be much greater.

Suicide was associated with several demographic characteristics among HD patients. Independent predictors of suicide included old age, male gender, lower educational status, alcohol or drug dependence, and recent hospitalization for mental illness (Keskin & Engin, 2011; Kurella et al., 2005). Having strong religious beliefs has been suggested as one protective factor of suicide risk among HD patients (Martiny et al., 2011). Preexisting depression and anxiety disorders have been identified as independent risk factors for subsequent onset of suicidal ideation and attempts in the general population (Martiny et al., 2011; Sareen et al., 2005). Specific for HD patients, suicide risk was also significantly predicted by anxiety and depression. On the other hand, fatigue and QoL may not directly affect suicide risk (Chen et al., 2010). Because suicide might be preventable via early detection of warning signs, it is crucial to identify the psychological impact and possible risk of suicide among dialysis patients.

## **7. Managing the psychological impact on dialysis patients**

Numerous studies investigated the managements for mental illness in HD patients, including pharmacological and non-pharmacological interventions (Table 2).

### **7.1 Pharmacological interventions**

Today, selective serotonin reuptake inhibitors (SSRIs) are the treatment of choice for HD patients with depression or anxiety (Raymond et al., 2008). Fluoxetine has been effective and safe in HD patients, although trials have thus far involved only small numbers of patients (Blumenfeld et al., 1997). Citalpram, which is similar to fluoxetine in treatment effects, is thought to be safe (Cohen et al., 2004), and it has been beneficial for improving QoL in HD patients (Kalender et al., 2007b). Paroxetine, combined with supportive psychotherapy, has been shown to be not only successful for treating depression, but also for improving nutritional status in chronic HD patients with depression (Koo et al., 2005). Sertraline has safe pharmacokinetics in patients with ESRD, and treatment with sertraline in PD patients is associated with improved QoL and fewer symptoms of depression (Atalay et al., 2010). Duloxetine and venlafaxine, which are categorized as serotonin-norepinephrine reuptake inhibitors, are beneficial for patients with major depressive disorder (Ye et al., 2011). However, these agents' safety and efficacy have not been specifically established for HD patients. Bupropion, a dopamine-norepinephrine reuptake inhibitor, and mirtazapine, a noradrenergic and specific serotonergic, have also been widely used for patients with depression. However, once again, it is not clear whether the beneficial effects of these agents can be generalized to dialysis patients. Generally, older tricyclic medications have an adverse cardiac profile and anticholinergic effects, which limits their use for HD patients

Treatment	Target Symptoms	Side Effects	Clinical
<b>Pharmacological interventions</b>			
Selective serotonin reuptake inhibitors (fluoxetine, citalopram, paroxetine, sertraline)	Depression Anxiety	Gastrointestinal symptoms, sexual dysfunction, risk of bleeding, suicidal ideation	Fluoxetine Citalopram severe renal patients. Paroxetine
Serotonin-norepinephrine reuptake inhibitors (venlafaxine, duloxetine)	Depression	Accumulation of toxic metabolites, sexual dysfunction, hypertension	Decrease in mild-to impairme
Dopamine-norepinephrine reuptake inhibitors (bupropion)	Depression Fatigue	Insomnia, agitation, seizure, accumulation of toxic metabolites	Use with reduction impairme
Noradrenergic and specific serotonergics (mirtazapine)	Depression	Sedation, somnolence, weight gain	Reduce do
Tricyclics and tetracyclics (amitriptyline, desipramine, doxepin, nortriptyline)	Depression	Anticholinergic effects, sedation, QTc prolongation, cardiac arrhythmias, orthostatic hypotension	Avoid if p side effect
Serotonin modulators (netazodone, trazodone)	Depression	Accumulation of toxic metabolites, liver failure (for nefazodone), sedation, hypotension, cardiac arrhythmias	Avoid use cardiac di
Erythropoietin	Fatigue Quality of life	Seizures, increased clotting, and influenza-like syndromes	No signifi between c thrice-wee administr

5HT: 5-hydroxytryptamine; QTc: corrected QT interval  
 Table 2. Treatment options for psychological impact on hemodialysis patients

Treatment	Target Symptoms	Side Effects
<b>Pharmacological interventions</b>		
Partial Serotonin 5HT(1A) receptor agonists (buspirone)	Anxiety	Dizziness, nausea, headache, insomnia, tremor
Benzodiazepines (alprazolam, lorazepam, diazepam, midazolam, chlordiazepoxide)	Anxiety Insomnia	Prolong sedation, physical and psychological dependence, cognition impairment, withdrawal symptoms
<b>Non-pharmacological interventions</b>		
Cognitive behavior therapy (CBT)	Depression Quality of life	Takes longer time to reach effects than pharmacological treatment
Exercise training	Depression Quality of life	No serious adverse effects were reported
Acupuncture	Quality of life	No serious adverse effects were reported
Social support, marital, family counseling	Depression Spousal depression	No serious adverse effects were reported.

In summary, with the exception of the SSRIs, the efficacy and safety of antidepressant drug therapy in dialysis patients have not been clearly established, although these medications are believed to improve depression empirically. Notably, the relative activity and mode of excretion of metabolites of antidepressants in dialysis patients are as yet unknown and may complicate the use of these drugs if adverse events occur. It also remains unclear whether there are potential drug-drug interactions between antidepressants and other drugs commonly used in HD patients. Therefore, the general rule for prescribing antidepressants among HD patients is to start at a lower dose and increase the dosage gradually (Cohen et al., 2004).

There is evidence that the use of erythropoietin-stimulating agents might reduce fatigue and improve QoL among ESRD patients (Jones et al., 2004). Benzodiazepines (BZD), such as diazepam, alprazolam, and lorazepam, have been successfully used to relieve acute episodes of panic and anxiety. In addition, BZD are also widely prescribed for HD patients with insomnia (Wyne et al., 2011). In recent years, the use of non-BZD drugs such as zolpidem, zopiclone, and zaleplon for insomnia patients has rapidly increased. However, it is noteworthy that the liability for abuse and dependence exist in both BZD and non-BZD drugs, especially with long-term use (Victorri-Vigneau et al., 2007). Buspirone, a partial serotonin agonist that acts on the 5HT(1A) receptor, is often recommended for patients with anxiety, and it is generally considered to have fewer unfavorable side effects than does BZD. Generally, it is not necessary to adjust the dosage of most of the erythropoietin-stimulating agents we have mentioned for the level of the glomerular filtration rate, for these agents are metabolized in the liver (Hedayati & Finkelstein, 2009). However, buspirone and lorazepam may take longer to be eliminated in ESRD patients, and thus the dosage of these two drugs should be carefully titrated. Notably, Winkelmayr et al. (2007) reported that BZD or zolpidem are commonly used for incident dialysis patients and may be associated with greater mortality in this group. Although the causal reference to this effect warrants further investigation, it is also a warning that clinicians need to consider the necessity of long-term use of BZD in dialysis patients.

## 7.2 Non-pharmacological interventions

Psychotherapy has been used for a wide range of chronic illnesses, including patients with HD (Hedayati & Finkelstein, 2009). Of these approaches, cognitive behavioral therapy (CBT), a well-documented evidence-based therapy for depression, has been shown to be effective (Chen et al., 2011; Duarte et al., 2009). CBT is based on the assumption that one's dysfunctional "automatic thoughts" in response to a situation can result in strong negative feelings/emotions, and thus lead to depression. Correction of those faulty dysfunctional constructs can lead to clinical improvement. Duarte et al. (2009) demonstrated that CBT performed during 3-month-long group therapy is effective for improving depression and many dimensions of QoL in chronic HD patients. Chen et al. (2011) conducted a randomized controlled interventional study of 72 sleep-disturbed HD patients. Compared with the control group (who received sleep health education), patients who received CBT had significant improvements in sleep quality, fatigue, depression, and anxiety. Interestingly, CRP, IL-18, and oxidized low-density lipoprotein levels also significantly declined among those receiving CBT in comparison to those in the control group (Chen et al., 2011). Thus,

these studies suggest that CBT might be effective for improving mental health, and for reducing inflammation and oxidative stress in HD patients.

Exercise programs may have a beneficial effect on depressive symptoms in patients with ESRD. Ouzouni et al. (2009) reported that 10-month intradialytic exercise training improved QoL in both physical functioning and psychological status in HD patients, and decreased in self-reported depression. In another study, a 1-year exercise training program reduced emotional distress and concomitantly improved cardiac autonomic modulation measured by heart rate variability (HRV) indices (Kouidi et al., 2010). For alternative therapy, Kim et al. (2011) reported that 24 HD patients who received individualized acupuncture treatments over 6 consecutive weeks showed significant improvements in some QoL subscales.

Social support has been shown to help improve emotional disturbances in a variety of chronic illnesses. Support and education, either individually to patients or including their caregivers and family members, may be helpful (Symister & Friend, 2003). A patient's depression could be influenced by the psychosocial status of his or her spouse, and the spouse might be amenable to interventions that could improve patient outcome (Daneker et al., 2001). Social support has been shown to decrease depression by improving the self-esteem of patients with ESRD, which led to increased optimism (Symister & Friend, 2003). Treatment programs that address problems with social interactions of patients need to be comprehensive, and should explore use of family and marital counseling, and involvement of the community, along with consideration of the patient's social life (Cohen et al., 2007).

## 8. Conclusion

HD is a life-sustaining treatment for patients with ESRD; however, it adversely affects patients' mental status. Increasingly, depression is being recognized as a substantial comorbid illness in these patients. Anxiety, feelings of fatigue, and decreasing QoL are also significant psychological symptoms, and they may be interrelated. Depression and anxiety particularly increase patients' suicide risk. Mental illnesses may have underlying biological and psychological causes. There is considerable evidence that these psychological effects are associated with adverse outcomes in HD patients with ESRD. It is important, therefore, to develop systematic approaches to screening patients for mental illness, and then planning treatment strategies. To improve treatment outcome and patient QoL, a comprehensive management plan that includes pharmacological and psychosocial interventions, is essential.

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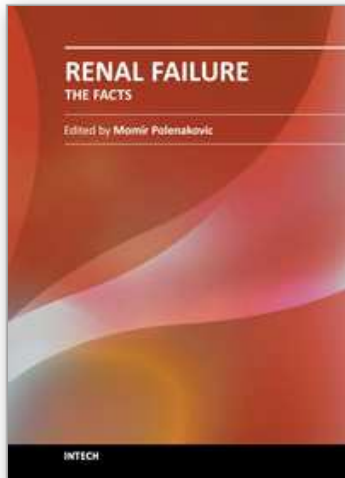
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### **Renal Failure - The Facts**

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The book "Renal Failure - The Facts" consists of some facts about diagnosis, etiopathogenesis and treatment of acute and chronic renal failure. Acute, as well as chronic renal failure is great medical problems and their treatment is a burden for the budget of each government. The purpose of the chapters is to present some important issues of diagnosis and causes of AKI, as well as caused by snakes and arthropods, after cardiac surgery, as well as some therapeutic achievements in AKI. Well presented are the psychological condition in patients on haemodialysis, as well as the treatment of diabetic uremics. The book is aimed at clinicians with a special interest in nephrology, but it should also prove to be a valuable resource for any generalists who encounter a nephrological problems in their day-to-day practice.

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