

INTRODUCTION

Chronic renal failure (CRF) during childhood is a significant stressor with a psychological and social impact on the children and their family.⁽¹⁾ It is becoming a major public health concern ⁽²⁾, with increasing incidence and prevalence, use of health services and associated costs of health care .CRF causes enormous economic losses, also triggers major challenges as regards to health. ⁽³⁾ CRF is defined according to Kidney Disease: Improving Global Outcomes Guideline for the Evaluation and Management of Chronic Kidney Disease (KDIGO) 2012 ⁽⁴⁾ as abnormalities of kidney structure or function, present for >3 months, with implications for Health (table1).

Table (1): Criteria for CRF. ⁽⁴⁾

| |
|--|
| Criteria for CKD (either of the following present for >3 months): |
| 1-Markers of kidney damage (one or more) |
| - Albuminuria (AER \geq30 mg/24 hours; ACR \geq30 mg/g [\geq3mg/mmol]) |
| - Urine sediment abnormalities |
| - Electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology |
| - Structural abnormalities detected by imaging. |
| - History of kidney transplantation |
| 2-Decreased GFR |
| - GFR <60 ml/min/1.73 m2. |

AER= Albumin excretion rate.

ACR=Albumin-to-creatinine ratio.

GFR= glomerular filtration rate.

Children with CRF suffer from an illness that requires daily life-style modification. They often experience growth retardation and altered body image and frequently miss school and other normative activities, thereby affecting their psychosocial development ⁽⁵⁾. Consequently, the World Health Organization (WHO) makes CRF the medical condition with the fourth highest loss of life years due to premature death or years living with a severe and chronic incapacity. ⁽⁶⁾These obstacles likely affect the psychological well-being of these children. ⁽⁷⁻¹²⁾.

Complications of pediatric chronic renal failure :

Chronic renal failure may also be identified when it leads to one of its recognized complications, such as cardiovascular disease, anemia or pericarditis. (4, 13)

Table (2): Complications of pediatric chronic renal failure. (14)

| Complication | Etiology | Sequelae |
|-----------------------------|--|---|
| Electrolyte Abnormalities | -Renal tubular wasting -Decreased glomerular filtration rate -Impaired gastrointestinal absorption | Poor feeding, emesis, decreased energy, growth retardation, dehydration |
| Inadequate Nutrition | -Uremia -Increased metabolic rate - Early satiety in peritoneal dialysis patients | Cachexia, anorexia |
| Growth Impairment | -Impaired growth hormone and insulin-like growth factor -Anemia -Secondary hyperparathyroidism | Short stature |
| Anemia | Reduced erythropoietin synthesis, iron deficiency | Fatigue, poor school performance |
| Bone and mineral Metabolism | Impaired production of 1,25 dihydroxycholecalciferol | Renal osteodystrophy |

Planning for dialysis:

Planning for renal replacement therapy should begin with progression of CKD to stage 4 (GFR is <30 ml/min/1,73 m²) (Table 3).Frequent multidisciplinary assessments must be made to determine the appropriate timing to initiate dialysis based on the Child’s health and metabolic status. Family support services and intervention from child psychiatrist/therapist may also become necessary in order to enhance coping mechanisms within the family unit and the patient. It is generally recommended that renal replacement therapy should begin with decline of GFR<15 ml/min/1, 73m². (14)

Table (3): Standardized Terminology for Stages of Chronic Kidney Disease (15)

| STAGE | DESCRIPTION | GFR (mL/min/1.73 m²) |
|--------------|--|--|
| 1 | Kidney damage with normal or increased GFR | >90 |
| 2 | Kidney damage with mild decrease in GFR | 60-89 |
| 3 | Moderate decrease in GFR | 30-59 |
| 4 | Severe decrease in GFR | 5-29 |
| 5 | Kidney failure | <15 or on dialysis |

Psychiatric challenges in patients starting maintenance dialysis

Any chronic medical illness is a significant risk factor for the development of psychiatric disorders. ^(16, 17) Psychiatric disorders can increase the severity of the preexisting physical illness by disturbing cardiac and nervous system, decreasing immune function or modulating nutritional conditions. ^(18, 8) Patients with CRF will cope with the anger, fear, anxiety, frustration, and sadness of having a chronic illness, accept the disruption of their activities and confront their own mortality and shortened life span. Also medical management of their end-stage renal disease requires adjustment to dietary prescription and reduced fluid intake. They must accept recurrent hospitalizations, placement and repair of vascular or peritoneal access and the discomfort of dialysis and other medical treatment that they were in need of therapy for their mental health condition. ⁽¹⁹⁾

Psychiatric illness in patients with CRF

Levy introduced the term “**psychonephrology**,” to refer to psychiatric problems of people suffering from kidney disease, and particularly those with kidney failure who undergo maintenance dialysis or who are transplanted. ⁽²⁰⁾ The patient with known or unknown renal disease is informed that he needs to undergo weekly sessions for renal function support, causes a variety of psychological reactions like denial of the illness, irritability, despair, feelings of helplessness, fear of death, aggressiveness, anxiety symptoms, depressive symptoms, and even suicidal tendencies. ⁽²¹⁾

- The dialytic stage has several periods:

The patient initially develops feelings of fear of either the machine or the medical staff that may lead to anxiety, aggressive behavior, and emotional instability. Later, in advanced stages, the chronic patients who undergo haemodialysis (HD) develop doctor/medical team-patient-machine relationships with new rejection and attachment facets. Apart from the problems caused by the organ’s disease, before the introduction of renal function replacement therapies, patients undergo external pressure comparable to that affecting other chronic patients (dietary and hydro-electrolytic restrictions, drug intake, the effects of the illness itself, multiple loss – of independence, life expectancy, social role, the altering of future plan, uncertainty, damaged self-image and self-esteem). ⁽²²⁾

They confront many stresses that may affect health status in the chronically ill by reducing compliance behaviors. ⁽²³⁾ Learning problems and physical consequences of the illness contribute to a lower self-esteem. They could feel depressed and powerless. They often have poor self-esteem and a pervasive sense of losing their identity, body integrity, control, independence and opportunity. ⁽²⁴⁾

In addition to the stress inherent to CRF and its treatment, studies have pointed out to other factors that contribute to the predisposition to psychiatric disorders in this group:

1. An organic base, such as autoimmune diseases or secondary hyperparathyroidism, contributes to the occurrence of secondary depressive symptomatology.
2. Also, medications that patients take may be involved in the pathogenesis of depression, as illustrated by corticosteroids.

3. The existence of previous history of depression before the onset of CRF is an important risk factor.⁽²⁵⁾
4. CRF patients face multiple casualties during the disease, also reported as risk factors. However, the emotional response of patients to various losses is individual and does not always lead to the emergence of depressive disorder.⁽²⁶⁾ We have found that there is higher correlation of depression with convictions of patients regarding their disease, despite the severity of the disease. Great importance is the way of stress management.⁽²⁷⁾
5. Depressive symptoms also are associated with lower serum albumin Levels.⁽²⁸⁾
6. We can mention also the decrease in the levels of the brain -derived neurotrophic factor and the low serum levels of serotonin in CRF patients, also uremia can be associated with irritability, restlessness, insomnia and delayed development of secondary sexual features.^(9, 29)
7. Also during HD, the blood –dialyser interaction has the potential to activate mononuclear and dendritic cells leading to production of inflammatory cytokines.⁽³⁰⁾ 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 IL1,IL-6,tumour necrosis factor alpha (TNF, alpha) and c-reactive protein in both general and ESRD population.⁽³¹⁻³³⁾ Seventy-five patients were enrolled in a cross-sectional study from September to November 2011 in Pelotas, Rio Grande do Sul revealed that HD patients with depression showed higher levels of IL-6 but the severity of depressive symptoms was not correlated with levels of this cytokine.⁽³⁴⁾

Anxiety and mood disorders occur frequently in patients with advanced chronic disease⁽³⁵⁻³⁹⁾ with the observed prevalence fluctuating between 17 and 46% for anxiety disorders⁽⁴⁰⁾ and between 5% and 26% for mood disorders.⁽⁴¹⁾ In patients on dialysis, the prevalence rate for anxiety is about 30 to 45% .⁽⁴²⁻⁴⁴⁾ Regarding depression,Lopes and colleagues found a 20% prevalence of depression in 5256 patients and 13.9% in 9382 patients, both undergoing chronic HD⁽⁴⁵⁾ Bakr and coworkers compared children undergoing chronic HD with children not undergoing chronic HD, finding that 52.6% of the HD patients had psychiatric alterations, anxiety and depression have been reported in 5.1%,10.3% respectively. The prevalence of depression changes according to the studied population and the diagnostic method.^(9, 1)

Studies in pediatric patients with chronic illnesses have shown that this patient population has a higher prevalence of depression than healthy populations and that depression has a negative effect on the underlying medical condition.^(7, 10,46-50) Studies of adults with CRF indicate a high risk of depression, with prevalence between 20–40 %⁽⁵¹⁻⁵⁴⁾. In recent years the prevalence of depression has increased worldwide, and, at the same time, the presentation age has decreased.⁽²⁷⁾ One study found that CRF patients have a nearly 4-fold higher risk for depression than the general population.⁽⁵⁵⁾ One cause of concern was that depression, not only elevated the length of hospitalization by 30%⁽⁵⁶⁾, but also more than doubled the likelihood of mortality in CRF patients with depression compared to those with CRF only.⁽⁵⁵⁾ Another study demonstrated that there was a statistically significant correlation between the existence of organic co-morbidities and the presence of symptoms of depression and suicidal ideation⁽⁵⁷⁾

Estimates of the actual prevalence of psychiatric illness in patients with CRF estimates may be erroneously low, because patients often fail to seek mental healthcare. Johnson and Dwyer reported that over 70% of patients on maintenance HD that had symptoms of depression or anxiety and described barriers to mental health treatment did not recognize their symptoms.⁽⁵⁸⁾ Dialysis physicians and nurses who are not psychiatrists may pay less attention to somatic complaints of psychiatric illnesses, and therefore, leave these co-morbidities undiagnosed.⁽¹⁹⁾

In patients with CRF, the symptoms of depression or anxiety may be similar to those that occur with kidney failure or uremia. Therefore, the diagnosis and treatment of depression and anxiety in these patients is often delayed or missed altogether because the symptoms are attributed to uremia⁽⁵⁹⁻⁶⁰⁾, this is especially true for the symptoms of depression. Insomnia is commonly reported in patients with either depression or uremia⁽⁶¹⁾ and drug-induced symptoms (eg, glucocorticoids) may also present in ways that overlap with the symptoms of anxiety, depression, or uremia. Therefore it is important that the diagnosis of depression is based especially in psychological symptoms such as anhedonia, decreased self-esteem, guilt and suicidal ideation.⁽⁶²⁾

Anxiety disorders

Anxiety, a part of emotional status, is perceived as one of very important aspects of health-related quality of life ^(35, 63, 29). The prevalence of anxiety disorders among children and adolescents with chronic medical illness are higher compared to their healthy counterpart. ^(16, 17, 64) It influences the quality of the patient’s life and mainly related to emotional upset and social relationships. ⁽⁴³⁻⁴⁵⁾ It shares features of excessive fear and anxiety and related behavioral disturbances.

Fear is the emotional response to real or perceived imminent threat, whereas **anxiety** is anticipation of future threat. Obviously, these two states overlap, but they also differ, with **fear** more often associated with surges of autonomic arousal necessary for fight or flight, thoughts of immediate danger, and escape behaviors, and **anxiety** more often associated with muscle tension and vigilance in preparation for future danger and cautious or avoidant behaviors. ⁽⁶⁵⁾

The DSM-5 classifies anxiety disorders into several groups of disorders including⁽⁶⁵⁾: Generalized anxiety disorder (GAD) ,separation anxiety disorder (SepAD),selective mutism, Phobias, social anxiety disorder (also known as social phobia) ,panic disorders, agoraphobia ,substance/medication-induced anxiety disorder

Generalized anxiety disorder (GAD) is a common chronic disorder characterized by long-lasting anxiety that is not focused on one object or situation. Those suffering from generalized anxiety, experience non-specific persistent fear, worry and become overly concerned with everyday matter for duration of at least six months. ⁽⁶⁵⁾

Table (4): Diagnostic criteria for generalized anxiety disorder (GAD)

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|----------|---|
| | |
| B | The individual finds it difficult to control the worry. |
| C | The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months); Note: Only one item is required in children. |
| | 1. Restlessness or feeling keyed up or on edge. 2. Being easily fatigued. 3. Difficulty concentrating or mind going blank. 4. Irritability. 5. Muscle tension. 6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep). |
| D | The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| E | The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism). |
| F | The disturbance is not better explained by another mental disorder |

Separation anxiety disorder (SepAD): ⁽⁶⁵⁾

Is the feeling of excessive and inappropriate levels of anxiety over being separated from attachment figures and events that could lead to loss of attachment figures, as well as nightmares and physical symptoms of distress, to a degree that is developmentally inappropriate. ⁽⁶⁵⁾

Selective mutism: ⁽⁶⁵⁾

Is characterized by failure to speak in social situations in which there is an expectation to speak (e.g., school) even though the individual speaks in other situations which have significant consequences on achievement in academic settings.

Phobias: ⁽⁶⁵⁾

It includes all cases in which individuals with specific phobia are fearful or anxious about or avoidant of circumscribed objects or situations. There are various types of specific phobias: animal; natural environment; blood-injection-injury and situational.

Social anxiety disorder: (SAD; also known as social phobia):

Describes an intense fear and avoidance of negative public scrutiny, public embarrassment, humiliation, or social interaction.

Panic disorders:

Panic attacks are abrupt surges of intense fear or intense discomfort that reach a peak within minutes, accompanied by physical and/or cognitive symptoms. the individual experiences recurrent unexpected panic attacks and is persistently concerned or worried about having more panic attacks or changes his or her behavior in maladaptive ways because of the panic attacks

Agoraphobia: ⁽⁶⁵⁾

Individuals are fearful and anxious about two or more of the following situations: using public transportation; being in open spaces; being in enclosed places; standing in line or being in a crowd; or being outside of the home alone in other situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms.

Depressive disorders: ⁽⁶⁶⁾

Depressive disorders are public mental health problem that affect children, adolescents, and adults, negatively impacting their personal, academic, social, and family lives. ⁽⁶⁾ A key question is whether depression itself has a direct mechanistic role in the development of morbidity and mortality in patients with CRF or whether depressive symptoms are merely a surrogate marker for increased co morbidity and disease severity. ^(52, 67, 68)

Depressive disorders include disruptive mood dysregulation disorder, major depressive disorder, persistent depressive disorder (dysthymia), substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder.

The clinical recognition of childhood depression has developed over the past decade. Multiple studies ⁽⁶⁹⁻⁷¹⁾ have demonstrated that depression in children and adolescents may present with different symptoms than adult depression. Symptoms that differentiate childhood depression from the classic clinical picture of adult depression include; irritable mood, anger, decline in academic performance, psychomotor agitation, anxiety symptoms, phobias, and regressing behaviors including separation anxiety. Vegetative and somatic complaints can also be associated with depression in children. ⁽⁷²⁾

During adolescence, psychomotor retardation, anhedonia, hypersomnia, hopelessness, weight changes, and drug abuse are more prominent. Suicidal ideation occurs at about the same rate in children and adolescents, but there is a dramatic increase in suicide attempts and completion of suicide with the onset of puberty. ⁽⁷³⁾

DSM-V criteria of major depressive disorder (MDD).⁽⁶⁶⁾

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.(Table 5)

Table (5): DSM-V criteria of major depressive disorder (MDD).⁽⁶⁶⁾

| | |
|---|---|
| 1 | Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note: In children and adolescents, can be irritable mood.) |
| 2 | Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation). |
| 3 | 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.) |
| 4 | Insomnia or hypersomnia nearly every day. |
| 5 | Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down). |
| 6 | Fatigue or loss of energy nearly every day. |
| 7 | Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick). |
| 8 | Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others). |
| 9 | Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. |

- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or to another medical condition.
- D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
- E. There has never been a manic episode or a hypomanic episode.

Chronic physical illness like CRF appears to be a significant risk factor for emotional, behavioral and family difficulties that can negatively affecting the course of physical disease.⁽⁷⁴⁾First and foremost, it is important to recognize risk factors for CRF. Second, it is important to include in the clinical history questions aimed at obtaining specific information of the more common psychiatric disorders and not limit the evaluation to information about the renal condition.

Although a clinical history remains the best diagnostic tool, the use of screening instruments has gained much acceptance, as they alert the clinician to the possible existence of a psychiatric disorder and provide a quantification of signs and symptoms. Different types of instruments are used to measure psychological variables in children and adolescents. Scales and questionnaires, self-reports of attitudes and behavior are the most simple and frequently used in research in this field. ⁽⁷⁵⁾0