INTRODUCTION

Chronic kidney disease (CKD) is a global public health problem of immense proportions. underdiagnosed and undertreated CKD in children has important implications for kidney transplantation. ESRD is defined as permanent loss of the kidneys' ability to filter wastes from the circulatory system ***(Hansen M, 1998).***

Once the GFR decreases to < 10 mL/min/m^2 (normal = 80-125 ml/min/m^2), normal homeostatic function of the kidney cannot be sustained. Regardless of the cause, if ESRD is untreated, renal failure leads to severe illness and death ***(Ray T , 2008).*** Thus, once kidney function declines to < 12% to 15%, patient survival is dependent on renal replacement therapy ***(Ardissino G et al., 2003).***

Currently, lot of children receive treatment for ESRD via in-center hemodialysis, peritoneal dialysis, or kidney transplantation ***(Kiberd BA et al., 2002).***

Although there are multiple approaches to management of ESRD, kidney transplantation offers the greatest potential for return to near-normal renal function, increased longevity, enhanced quality of life, and lower healthcare costs ***(Jofre R et al., 1998).***

Clinical kidney transplantation has become the treatment option of choice for most patients with ESRD. Over the past 40 years, numerous advances have been made in this field that have contributed not only to dramatic improvements in short-term outcomes, but also to substantial gains in medium-term outcomes. ***(Ardissino G et al., 2003).***

There are guidelines designed for use by physicians and other transplant professionals to facilitate the evaluation of potential kidney transplant candidates, with the acknowledgment that each candidate is different and faces a unique set of biopsychosocial challenges ***(Kasiske PL et al., 2001).***

Kidney transplant recipients have unique medical and nursing care requirements, care of the immunocompromised patient in acute and chronic care settings, and the psychosocial and sociopolitical aspects of ESRD and kidney transplantation ***(Ray T, 2008).***

The current status of kidney transplantation, types of kidney transplantation procedures, the evaluation of the patient with ESRD for transplantation, complications associated with kidney transplantation, factors that affect short and long term outcome of renal transplantation. these issues will be discussed in this essay.

Aim of the Work

To highlight on updated knowledge of short and long-term surgical complications and their management after pediatric renal transplantation

ETIOLOGY AND PATHOPHYSIOLOGY OF END STAGE RENAL FAILURE IN CHILDREN

Chronic kidney disease (CKD) and renal failure (RF) have been recognized as significant medical problems for most of the last 2 centuries and, until relatively recently, were uniformly fatal. Scientific and technologic improvements during the second half of the 20th century provided renal replacement therapy as a life-sustaining option for many individuals who otherwise may have died. The impact of these medical advancements has been remarkable.

Chronic kidney disease is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Chronic kidney disease has emerged as a serious public health problem. Moreover, in the past 2 decades, the incidence of the chronic kidney disease in children has steadily increased, with poor and ethnic minority children disproportionately affected ***(Ardissino G et al., 2003)***

Definition of chronic renal disease

The definition and classification of chronic renal disease may help identify affected individuals, possibly resulting in the early institution of effective therapy. To achieve this goal, the Kidney Disease Outcomes Quality Initiative (KDOQI) working

group of the National Kidney Foundation (NKF) defined chronic kidney disease as "evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min per 1.73 m^2."

Note, however, that the above definition is not applicable to children younger than 2 years, because they normally have a low GFR, even when corrected for body surface area. In these patients, calculated GFR based on serum creatinine can be compared with normative age-appropriate values **(table 1)** to detect renal impairment ***(Way AF et al., 1994).***

Table (1): Normal glomerular filtration rate values for children ***(Way AF et al., 1994).***

Age	GFR (mL/min/1.73 m^2)	Range (mL/min/1.73 m^2)
Preterm neonates (<34 wk GA)		
2 to 8 d	11	11 to 15
4 to 28 d	20	15 to 28
30 to 90 d	50	40 to 65
Term neonates (>34 wk GA)		
2 to 8 d	39	17 to 60
4 to 28 d	47	26 to 68
30 to 90 d	58	30 to 86
1 to 6 mo	77	39 to 114
6 to 12 mo	103	49 to 157
12 to 19 mo	127	62 to 191
2 to 12 years	127	89 to 165

GA = gestational age.

End-stage renal disease is diagnosed when a person's glomerular filtration rate (GFR) drops to less than 15 mL/min, according to the National Kidney Foundation.

Etiologies for end stage renal disease

The largest single disease group causing ESRD in children is primary glomerulonephritis (GN) (approximately 30%), followed by cystic/ hereditary/congenital diseases (26 %). The next most common causes for pediatric ESRD are interstitial nephritis (9 %) and collagen vascular disorders (secondary GN; 9 %). Some other disease categories of interest include Hypertension (4.5%) diabetes (extremely rare) & polycystic kidney disease ***(Warady BA et al., 1997).***

All these uropathies manifest as hydronephrosis or ureterohydronephrosis. The obstruction to the urine flow, if not corrected, eventually produces irreversible reduction of the renal function ***(Podestá M & Bertolotti G 2008).***

Pathophysiology of ESRD

The damaged kidney responds by increasing filtration, which masks the dysfunction until only 10-15% of kidney function remains. The kidneys lose their ability to balance water and solutes, acids and basis, retain nutrients and excrete waste in the form of urine. This loss of regulatory

and excretory function results in uremic syndrome (uremia), which can be diagnosed via high levels of serum creatinine, high levels of urea and reduced glomerular filtration rate. High creatinine levels reflects a high glomurelar filtration rate which is an important measure of renal function. Almost any substance that is found in abnormal quantities in the blood can cause uremia including increased phosphate and parathyroid hormone. Uremic syndrome also has a negative impact on the kidneys ability to excrete and produce the hormones rennin, calcitriol and erythropoietin resulting in poor regulation of blood pressure, calcium metabolism and reduced erythrocyte production respectively ***(Ardissino G et al., 2003).***

Effects of ESRD

Cardiac Disturbances

Such as congestive heart failure, coronary artery disease, arrhythmias and hypertension. The most common morphological change in ESRD patients is left ventricular hypertrophy resulting in systolic and diastolic dysfunction including a decrease in left diastolic dispensability. This is caused by an increase in blood volume/edema due to a build up of uraemic toxins. Other factors contribute to the build up of pressure including ischemia, fibrosis and other biochemical abnormalities. Moreover, uraemic toxins also

decrease myocardial contractility. Decreased left ventricular diastolic dispensability and decreased myocardial contractility result in an increase in blood pressure and an increased risk of CVD such as congestive heart failure. Cardiovascular and Autonomic Disturbances such as Chronic uraemia leads to ischemia, inflammation, and scarring of the myocardium causing uremic neuropathy. Uremic neuropathy causes electrical instability and reduced vagal activity resulting in a decrease in autonomic control and an increase in sympathetic stimulation. This overstimulation puts pressure on the heart causing hypertension and arrhythmias such as tachycardia increasing the risk of heart failure. In addition to this, psychological tension disrupts the functioning of the pacemaker cells, further contributing to heart failure **(Salusky IB & Goodman WG, 2002).**

Muscular Disturbances

Uremic myopathy is associated with changes in muscular structure and function including azotamia (high levels of calcium), academia (low levels of carnitine), abnormal activity of enzymes that produce energy, an increase in connective tissue, fibre grouping, atrophy of both fibre types and an increase in necrotic fibres due to phagocytosis. These abnormalities cause muscular weakness and fatigue in patients with ESRD. Uraemic

neuropathy causes the degeneration of axons and myelin sheath resulting in a loss of sensation, decreased nerve conduction velocity, loss of or a decrease in deep tendon reflexes and muscular weakness. Muscle weakness and wasting can also result from the debilitating nature of the disease (patients simply do not have the energy or strength to move) ***(Soares CM et al, 2003).***

Fluid and Electrolyte Imbalance

Individuals with ESRD also display electrolyte imbalances such as: Hyperkalemia – high potassium levels in the blood. Potassium is involved in regulating muscle tissue, metabolism and homeostasis. Hypocalcaemia – low calcium levels in the blood caused by a decrease in the release of calcitirol from the kidneys. Symptoms include: - Increased tendon reflex sensitivity, uncontrollable muscle contraction in the hands, tingling pins and needles around the mouth and or neck, life threatening conditions such as heart arrhythmias can also develop. Hypophosphatemia – high levels of phosphate in the blood. Hypomagnesaemia – low levels of magnesium in the blood causes increased irritability of the nervous system resulting in tremors, muscle weakness and an increased risk of arrhythmia ***(Soares CM et al., 2003).***

Metabolic acidosis

Caused by the inability of the kidneys to excrete ammonia from metabolised protein causing a build up of hydrogen thus making the blood more acidic. Blood Ph is stabilised however, through the release of calcium phosphate from the bones. This contributes to renal osteodystophy increasing the risk of bone pain, deformation and or fracture. Sodium bicarbonate supplementation is required to maintain a blood Ph of greater than 7.35 (serum bicarbonate levels should remain at20meq/L) ***(Franch HA & Mitch ME., 1998).***

Endocrine/Metabolic Abnormalities

Hyperparathyroidism : The kidneys take vitamin D and convert it to its active form calcitriol. Calcitriol regulates calcium in the blood, increasing absorption from the intestines and resorbtion from the bones when calcium levels are low and increasing bone formation when calcium levels are high. Calcitriol also regulates the activity of the parathyroid gland which helps to maintain serum calcium levels in a similar manner. If the kidneys are not functioning properly calcitriol production reduces resulting in abnormal regulation of calcium, low serum calcium levels, high phosphate levels, resistance to calcitriol develops and there is also a decreased response to

parathyroid hormone (resulting in an increase in release). All these factors lead to the development hyperparathyroidism (there is too much parathyroid hormone in the blood) resulting in osteodystrophy including osteomelacia and osteoporosis. Treatment includes dietary phosphate restriction, vitamin D supplements combined with strict monitoring of calcium and phosphate levels in the blood ***(Salusky IB et al., 2005).***

Insulin resistance : ESRD patients experience insulin resistance and the problem is exacerbated by hyperparathyroidism and metabolic acidosis causing impaired insulin release. However, ESRD patients have poor insulin clearance therefore diabetic patients may not need insulin or may need to make a reduction to their insulin intake. **(Salusky IB et al., 2005.)**

Thyroid disease

Thyroid disease may be difficult to diagnose however findings show a low conversion rate of thyroxine to triiodothyronine in patients with ERSD resulting in reduced metabolic rate. Some patients will also experience goiter. **(Lim VS., 2001.)**

Neurological Abnormalities

Uremic encephalopathy is a brain disorder in patients with ESRD. Toxin build up is a likely cause especially the

build up of parathyroid hormone (hyperparathyroidism). Parathyroid hormone causes increased calcium deposition disturbing neurological function however dialysis reduces the risk of encephalopathy therefore build up of parathyroid hormone is not thought to be the main cause. There has also been mention of changes in neurotransmitters within the brain causing myoclonus and seizures as a result of uremia. ***(Salusky IB et al., 2005).***

Haematological Dysfunctions

Anemia The production of erythropoietin is markedly reduced in ESRD patients attributing to anaemia. Other factors can cause anaemia such as reduced vitamin B12, iron deficiency, hemolysis of red blood cells (RBC's) and a short RBC life span therefore proper investigation is essential to determine the appropriate treatment. Anaemia decreases aerobic capacity, quality of life (QOL) and also exacerbates the symptoms of angina increasing the risk of coronary heart disease. Treatment includes subcutaneous or parental erythropoietin drugs with a dosage of 80-120U/kg per week. Serum ferritin levels may also be low which can be remedied through ferrous sulphate intake (325mg once to three times daily). ***(Warady BA & Ho M., 2003)***

Coagulation and Platelet Dysfunction

Patients with ESRD also experience uremic bleeding (increased bleeding time) due to poor platelet function and abnormal factor VIII. Platelets aggregate more aggressively during circulation and are not able to clot the blood when needed. Discolouration of the skin due to bleeding under the skin can occur (purpura), as well as broken blood vessels causing small red marks (petechiae), increased bruising and an increased risk of bleeding. Uraemic bleeding can usually be controlled by cryoprecipitate (frozen plasma containing factor VII) and dialysis. **(Collins AG et al., 2000).**

Abnormal Blood Lipid Profile

ESRD patients often experience abnormalities in blood lipid levels including high triglycerides and low HDL levels which lead to in conjunction with other endothelial disorders a high incidence of accelerated arthrosclerosis increasing the risk of CVD ***(Muntner P et al., 2004).***

The Immune system

Immune function is depressed as total immunoglobulin's and complement levels are decreased in ERSD patients rendering the patient less able to cope with pathogens including bacterial, fungal and viral infections. The immune

system can be maintained through good nutrition, moderate intensity aerobic exercise, proper education concerning the importance of hand washing and immunization. **(van der Heijden BJ et al., 2004.)**

The Gastrointestinal System

The retention of urea and other metabolic waste products result in gastrointestinal problems. Initial symptoms include a metallic taste, loss of appetite followed by nausea, vomiting and weight loss. Increased ammonia causes ulcerations in the mouth and GI tract. Treatment involves decreasing protein intake and once dialysis begins most GI problems generally resolve **(Mitch WE., 2005)**

The Reproductive System

ERSD patients also have reduced levels of estrogen, progesterone, testosterone and normal or increased levels of follicle-stimulating hormone and luteinizing hormone. Women experience amenorrhea, menorrhagia, decreased libido and infertility. Men experience decreased libido and impotence ***(Hogg RG et al., 2003).***

MEDICAL EFFECT OF CHRONIC RENAL FAILURE IN CHILDREN

Prior to 2002, the term chronic renal insufficiency was used to characterize patients who had progressive decline in renal function, defined as a glomerular filtration rate (GFR) of less than 75 mL/min per 1.73 m2 body surface area. Chronic kidney disease (CKD) is the new term defined by the National Kidney Foundation Kidney Disease and Outcome Quality Initiative (KDOQI) Group to classify any patient who has kidney damage lasting for at least 3 months with or without a decreased GFR or any patient who has a GFR of lessthan 60 mL/min per 1.73 m2 lasting for 3 months with or without kidney damage. The KDOQI Group also classified CKD into five stages:

- Stage 1: Kidney damage with a normal or increased GFR (90 mL/min per 1.73 m 2)
- Stage 2: Mild reduction in the GFR (60 to 89 mL/min per 1.73 m2)
- Stage 3: Moderate reduction in the GFR (30 to 59 mL/min per 1.73 m2)
- Stage 4: Severe reduction in the GFR (15 to 29 mL/min per 1.73 m2)