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Risk Factors for Renal Failure: From Infancy to Adulthood

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1. Introduction

Abnormal development of the kidneys and the urinary tract, genetic factors, acquired disease during infancy and childhood, wrong dietary habits and environmental factors may produce renal damage and cause renal insufficiency which may become clinically evident in adulthood. Prevention of renal insufficiency relies on early recognition of risk factors recognizable in childhood.

2. Risk factors for kidney disease

The incidence and progression of renal injury vary substantially among individuals who are at risk for kidney disease. Variability of risk for the occurrence and progression of Chronic Kidney Disease (CKD) suggests that biologically relevant characteristics may influence the occurrence or course of the renal disease. Prediction of increased risk of occurrence or progression of CKD may enable clinicians to identify individuals who may benefit from closer supervision of care or more intensive disease modifying interventions. Risk factors can be used to define at risk population that can be targeted for education and early intervention programs. These factors include familiarity of CKD, genetic factors, nephron number, low birth weight, perinatal programming, nutritional setting, hypertension and congenital abnormalities of the kidney and urinary tract (CAKUT) (Table 1).

Risk factors for Chronic Kidney Disease detectable in childhood
Family history of hypertension and kidney disease
Low birth weight
Perinatal kidney injury
Congenital injury
Hematuria and/or proteinuria
Urinary tract infection
High blood pressure
Overweight

Table 1.

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2.1 Familiarity of CKD

A family history of kidney disease (FAM) has been associated with an increased risk of end stage renal disease (ESRD). In a recent report FAM was identified as an independent risk factor for ESRD **[1]**. In 1998 Lei at al in large population case-control study found a correlation between FAM and ESRD, especially in patients with a strong FAM with an odds ratio of 7.4.**[2].** In the same year Freedman et al. found a high prevalence (20%) of FAM in dialysis patients. The prevalence decreased with age, was higher among African-Americans than Caucasians **[3]**. Satko et al documented a three- to nine-fold greater risk of ESRD in individuals with a FAM of ESRD. He noted a marked racial variation in the familial aggregation of kidney disease, with high rates in African American **[4].** Other authors documented a stronger association in blacks than whites, indicating specific ethnic differences **[5-6].** Recently in USA it has been proposed the ESRD Networks Family History Project as a national CKD surveillance system for patients with stage 5 CKD to identify relatives of incident patients with ESRD who are 2 to 3 times as likely to have ESRD **[7]**.

2.2 Genetic factors

It is well known that genetic factors play a crucial role in CKD and ESRD [8] More recently, genome-wide association studies have yielded highly promising results suggesting a number of potential candidate genes and genomic regions that may contribute to the pathogenesis of CKD **[8].** For example, common variants in the UMOD and PRKAG2 genes are associated with risk of chronic kidney disease **[9].** Genome-wide association studies of CKD are beginning to define the genomic architecture of kidney disease and will impact our understanding of how genetic variation influences susceptibility to this condition.

The expression of genes is defined by their epigenetic state; prenatal factors may produce stable changes in expression of genes as documented in several studies. DNA methylation [10], oxidative stress in response to low protein diet in pregnancy [11], telomere length [12] which is regulated by telomerase enzymatic activity during fetal life have been implicated in fetal renal development and disesase, excess glucocorticoids in early life can permanently alter tissue glucocorticoid signalling. All these studies show that the mechanism involved in developmental programming are likely epigenetic rather than due to DNA sequence mutations. It is important to note that changes produced by epigenetic factors, differently from genetic changes, are potentially reversible.

2.3 Nephron number

The number of nephrons in humans ranges from 250.000 to 2.5 million with an average of about 1 million per kidney; this high variability is due to various causes. Nephrogenesis ends at 36 weeks of gestation, for this reason premature newborns may have a reduced nephron number; the same condition is observed in patients with kidney disease and in older patients due to age–related glomerulosclerosis. In the last 20 years many authors analyzed the association between nephron number and onset of renal disease later in life; most of these studies have been conducted in animals since it is difficult to determinate the number of glomeruli as measure of nephrons' number in humans. Nyengaard and Bendtsen performed in 1992 the first study that calculated the number of glomeruli in the kidneys of 37 Danes obtained at autopsy; they found a significant negative correlation between glomerular number and age **[13].** Successively Keller et al. documented a significant reduced number of

glomeruli in patients with hypertension compared to those who were normotensive **[14].** More recently Zhang et al have documented a wide 4.5-fold variability in the number of glomeruli in children younger than 3 months ranging from 246,181 to 1,106,062 **[15].**

2.4 Prematurity and low birth weight

Low birth weight (LBW) is defined by the World Health Organization as a birth weight of <2500 g. Intrauterine growth retardation (IUGR) is defined as weight below the tenth decile for birth weight.

Fetal growth is conditioned by multiple factors which include the composition of maternal body, alimentary habits during pregnancy, transport of nutrients through the placenta and others. The final consequence of the alteration of this factors determinate a fetal-growth reduction. The IUGR can be related to maternal undernutrition and/or placental insufficiency **[16].** Placental insufficiency, usually associated with preeclampsia and maternal cardiovascular risk factors, is due to poor placentation. Maternal malnutrition is often related to wromg dietaty composition more than total calorie intake. In rats Langley-Evans et al have demonstrated that even short periods of maternal protein restriction during gestation in rats are associated with LBW and subsequent hypertension **[17].** In humans, increased protein turnover at 18 weeks of gestation is associated with increased length of babies at birth [18**].**

In humans, the causes of LBW are multifactorial: demographic factors, socio-economics status, poor maternal weight especially during pregnancy, shorter maternal height, maternal gestational weight gain below 7 kg, maternal hypertension, chronic infections, glucose intolerance or DM during pregnancy, maternal smoking or alcohol abuse, genetics, etc. Irving et al demonstrated that premature children, independently of birth weight, have an high risk of cardiovascular disease in adult age, thus making it very difficult to separate the effects of gestational age and birth weight **[19].** However, the growth retardation for a given gestational age has greater relevance than the effect of prematurity on subsequent cardiovascular disease in adult age, as was demonstrated by Whincup et al **[20].** The correlation between low birth weight and number of nephrons was reported by Ma˜ nalich et al.; they observed a mean reduction of 20% of the nephrons in children with LBW. **[21].** The same observations was obtained by Hughson et al who documented that LBW is accompanied by fewer large-volume nephrons than in individuals with normal birth weights **[22].**

Multiple animal models have demonstrated the association of LBW with later development of hypertension. The link between adult hypertension and LBW in these animal models appears to be mediated by a congenital nephron deficit showed by Vehaskari et al **[23].** In humans many studies have reported higher blood pressures in those who had been of LBW. Barker et al first reported the association between hypertension in adult life and birth weight **[24].** A study in Swedish children by Nilsson et al found a significant relation between birth weight and systolic arterial pressure **[25].** Similar observations was done by Huxley et al **[26]**. In several studies, the relationship was more significant in girls than boys **[27]** and in woman than man **[28].** The relationship between birth weight and blood pressure is also increased by accelerated postnatal growth **[29] .** Hoy et al in 1999 reported an association between low birth weight and CKD, observing increased rates of microalbuminuria in Australian Aborigines, a population with high rates of low birth weight **[30].** In the last years many studies have documented that low birth weights contribute to high rates of early-onset chronic renal failure in United States patients, in

ducth adolescents, and in young and adult Norwegians **[31-34].** In a meta-analysis, White et al. found that the combined odds ratio (OR) for risk of albuminuria associated with low birth weight was 1.81 (1.19–2.77) and for ESRD 1.58 (1.33-1.88). They concluded that existing data indicate that low birth weight is associated with subsequent risk of CKD **[35].** Recently, Hodgin et al. described an association between focal segmental glomerular sclerosis (FSGS) and prematurity and very low birth weight **[36].**

2.5 Perinatal programming

The processes of development and maturation of organs occur continuously throughout the pre- and postnatal periods. Intrauterine growth is generally regulated by intrinsic growth potential, genetic endowment, and support of nutrients from the materno-uteroplacental unit. However, during the postnatal period growth may be affected by environmental conditions and genetic background. The environmental impact on a genetic program determine the renal perinatal programming of each individual. The term "fetal programming" describes the structural and functional adaptive phenomena in response to critical periods during fetal life and early postnatal growth. Perinatal programming may produce a reduced nephron number leading to the development of chronic kidney disease **[37].** Several environmental stressors may act on specific genetic programming of low nephron number. The time at which an adverse factor is involved during gestation before completion of nephrogenesis may affect kidney growth **[38].** A history of LBW and IUGR, vitamin A deficiency, urinary tract malformations, administration of nephrotoxic drugs may interact to increase potential nephron damage. Maternal nutrition may have an important influence on renal programming **[39].** In rats, a restricted supply of nutrients to the mother during nephrogenesis contributed to a reduced number of glomeruli per kidney, activation of the renin-angiotensin system, glomerular enlargement, and hypertension in adult life **[40].**

2.6 Hypertension

Maternal hypertension is a significant risk factor for LBW and is more prevalent among black than white women, making the population-attributable risk of LBW highest among babies of hypertensive black mothers **[41].** Taittonen et al found that a history of mother's high blood pressure during pregnancy predicted future blood pressure more eminently than birth weight **[42].**

Hypertension is one of the major causes of renal insufficiency in adults. It has been proven that children with higher blood pressure develop hypertension, cardiovascular diseases and renal failure as adults. The first study that found a correlation of adult blood pressure with childhood blood pressure was the Muscatine study in 1989 **[43].** Successively the Bogalusa Heart study documented that childhood blood pressure predicts adult microalbuminuria in African Americans, but not in whites **[44].** In the same group of patients it was found that diastolic blood pressure in children and increased blood pressure variability in children are significantly correlated with adult hypertension **[45-47].**

2.7 Obesity

Obesity is a recognized risk factor for end-stage renal disease (ESRD) [48]. The increased blood pressure associated with obesity is accompanied by impaired pressure natriuresis.

The volume expansion is related to activation of the sympathetic nervous system and renin-angiotensin system. Obesity also causes renal vasodilation and glomerular hyperfiltration as compensatory mechanisms. In the long-term, these changes, along with the increased systemic arterial pressure, causes glomerular injury. Moreover obesity causes an increase of urinary protein excretion and gradual loss of nephron function that worsens with time and exacerbates hypertension. Overweight and obesity are associated with the metabolic syndrome and type II diabetes, a major cause of kidney disease; in obese patients renal failure progresses much more rapidly [49].

2.8 CAKUT

Congenital abnormalities of the kidney and urinary tract in most cases apparently are not associated with a reduced glomerular filtration rate (GFR) but the renal reserve may be reduced to the point that an increased demand by a growing body produces a drop in GFR. A recent review of Sanna-Cherchi et al evaluated the renal outcome in patients with CAKUT [50]. They found that patients with solitar kidney, usually considered to have good prognosis, have a higher risk for dialysis with an HR of 2.43 compared to patients with hypodysplasia or multicystic kidney. These data are in contrast to precedent studies that found a good prognosis of renal function in patients with unilateral agenesis [51]. In the last years many authors have looked for a correlation of CAKUT with genetic disorders [52].

2.9 Hematuria and proteinuria

Iseki et al in 1996 in a community mass screening found that proteinuria was the most useful predictor of ESRD (adjusted odds ratio 14.9, 95% confidence interval 10.9 to 20.2), and the next most potent predictor was hematuria (adjusted odds ratio 2.30, 95% confidence interval 1.62 to 3.28) [53]. In a recent paper Vivante A et Al found an increase of incidence of ESRD in patients (aged 16 to 25 year) with persistent asymptomatic isolated microscopic hematuria [54]. In 2011 a meta-analysis found that albuminuria is a risk factor for all-cause and cardiovascular mortality in high-risk populations [55].

2.10 Urinary tract infections and vesico-ureteral reflux

Vesicoureteral reflux (VUR) is a frequent condition in pediatric patients. Approximately 1/3 of patients who have had a urinary tract infection (UTI) have VUR and 9–20% of patients with prenatal hydronephrosis have VUR [56]. Children affected by VUR may develop reflux nephropathy (RN) and some of them chronic kidney disease (CKD). In a recent review Brakeman identifies the principal risk factors of progression of VUR to CKD: reduced glomerular filtration rate (GFR), bilateral VUR and/or renal scarring, grade V VUR, proteinuria, and hypertension. [57]. Ardissino et al found an estimated risk of end stage renal disease (ESRD) of 56% in italian children by age 20 years [58]

3. Evolution of renal damage

The pathogenesis of progressive renal functional deterioration is certainly multifactorial, and the decline in glomerular filtration rate varies in groups of patients with different nephropathies, but also in patients with the same disease. Some of these factors may be modifiable, particularly in children, and therapeutic interventions may result in a reduced

rate of deterioration of renal function. The persistent deterioration of renal function may be a result of repeated and chronic insults to the renal parenchyma leading to permanent damage and/or to the adaptive hyperfiltration response of the kidney. The reduced glomerular filtration area due to congenital or acquired nephron deficit, according with the Brenner's hypothesis of "glomerular hyperfiltration", could expose to a higher risk of cardiovascular and renal disease in adulthood since the increased workload produces proteinuria with glomerulosclerosis, tubulointerstitial inflammation and fibrosis [59]. In addition to hyperfiltration and proteinuria, there is evidence that chronic renal hypoxia could be directly involved in the progression of CKD, particularly in progression of tubulointerstitial fibrosis. Chronic renal hypoxia could be elicited by several factors such as loss of peritubular capillaries (PTCs), decreased PTC flow, decreased nitric oxide production and/or bioavailability and activation of the renin-angiotensin system. With regard to this, Kang et al previously demonstrated that the inhibition of NOS accelerated renal damage in a remnant kidney model by eliciting PTC loss [60]. Recent evidence suggests that overweight and obesity play a role in renal-pressure natriuresis. Excessive weight gain increases renal tubular reabsorption and impairs pressure natriuresis, in part, through activation of the sympathetic and renin-angiotensin system as well as physical compression of the kidney. With prolonged obesity, there are also structural changes in the kidney (including enlargement of Bowman's space, increased glomerular cell proliferation, increased mesangial matrix, and thicker basement membranes, increased expression of glomerular transforming growth factor) that eventually cause loss of nephron function, further impairment of pressure natriuresis, and further increases in arterial pressure [61]. Finally, a number of genetic factors (eg, single nucleotide polymorphisms and modifier genes) may influence the immune response, inflammation, fibrosis, and atherosclerosis, possibly contributing to accelerated progression of CKD [62]. With respect to specific genes, apolipoprotein E (ApoE) polymorphisms may alter the risk of atherosclerotic disease, and therefore progression of CKD. The ApoE epsilon-2 allele is associated with elevated lipoprotein and triglyceride levels, whereas the ApoE epsilon-4 allele is associated with elevated levels of high density lipoprotein and lower triglycerides. In a secondary analysis of the Atherosclerosis Risk in Communities Study of 14,520 patients with a median follow-up of 14 years, individuals with an ApoE epsilon-4 allele (present in 30 percent) had a 15 percent reduction in risk of progression of CKD compared to individuals with ApoE epsilon-3 allele (present in 90 percent). The risk with the ApoE epsilon-2 allele was not significantly different compared with ApoE epsilon-3 [63]. Gene expression profiles within the kidney may help identify molecular prognostic factors in chronic renal disease. In the future, genetic testing and molecular analysis of renal biopsy specimens (and/or urine) may provide useful prognostic information.

The rate of progression to ESRD in childhood is inversely proportional to the baseline CrCl at presentation. In addition, genetic, familial, or ethnic predisposition may influence the rate of renal decline. As an example, African-Americans are more susceptible to CKD, and the rate of progression of CKD is higher among African-American males than other ethnic groups. The rate of progression of CKD is usually greatest during the two periods of rapid growth, infancy and puberty, when the sudden increase in body mass results in a rise in the filtration demands of the remaining nephrons [64]. Therefore children may have a normal glomerular filtration rate which sharply reduces in young adulthood. These events place increased demands upon the preexistent compromised kidney function. As a result, children with CKD should be closely monitored during these two periods for an accelerated

progression of CKD. In addition to the increase in body mass, hormonal changes during puberty may also contribute to the rapid decline in renal function seen in adolescence.

4. Causes of renal injury and renal failure in children

Genetic and environmental factors are traditionally considered causes of human disease. Many genetic disorders may cause renal disease in childhood or in adults (Table 2) but also prenatal factors may produce stable changes in expression of genes. Studies from diverse populations suggest that fetal programming may be the origin of several intrauterine events that ultimately manifests as overt disease such as hypertension, type 2 diabetes, obesity, and chronic kidney disease (CKD) [65].

GENETIC KIDNEY DISEASE
Cystic disease
Polycistic Disease (ARPKD, ADPKD) Tuberous Sclerosis Von Hippel Lindau Syndrome Glomerulocystic Disease Medullary Cystic Disease (Nephronophthisis)
Glomerular Disease
Alport Syndrome Family Focal Glomerulosclerosis Congenital Nephrotic Syndrome Nail-Patella Syndrome Denys-Dash Syndrome
Tubular Disease
Dent Syndrome Distal tubular acidosis Lowe's syndrome Fanconi Syndrome Gitelman syndrome Bartter syndrome

Table 2.

In addition to prenatal conditions, adverse postnatal events must be taken in consideration: infections, drugs, trauma, systemic diseases etc. In fact, CKD in children, which has a much lower prevalence than in adults, is the result of a heterogeneous group of disorders (Figure 1). Congenital disease accounts for almost 60 percent of CKD cases and includes obstructive uropathy, renal hypoplasia, and renal dysplasia. Glomerular disorders are the second largest cause of childhood CKD and are present in 7 to 17 percent of children with CKD.

Glomerular disease is more common in children greater than 12 years of age. Focal segmental glomerulosclerosis (FSGS) is the most common glomerular disorder occurring in 9 percent of all CKD cases. Other causes account for approximately 25 percent of cases. In 18 percent of all cases of CKD, the underlying primary diagnosis is not identified (15 percent) or is unknown (3 percent). Other more uncommon causes of CKD in children include hemolytic-uremic syndrome, genetic disorders (eg, cystinosis, oxalosis, and hereditary nephritis), and interstitial nephritis.

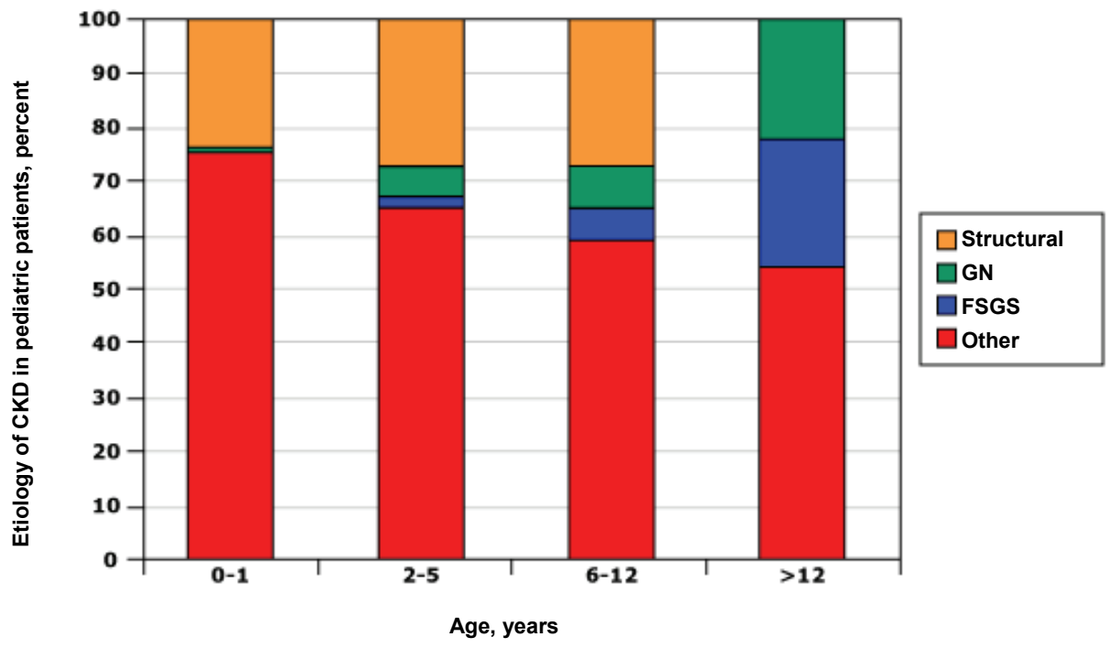


Fig. 1. FSGS: focal segmental glomerulosclerosis; GN: glomerulonephritis; Structural: structural anomalies of the kidney and urinary tract.
Adapted from: NAPRTCS: 2007 Annual Report, Rockville, MD, EMMES, 2007. Available at https://web.emmes.com/study/ped/announce.htm.

5. Prevention of renal diseases and kidney injury

Preventing renal impairment is an urgent challenge for medical practitioners. Several studies indicate that earlier stages of CKD can be detected through laboratory testing, and that early therapeutic interventions in the course of CKD are effective in slowing or preventing the progression toward ESRD and its associated complications [66]. Pediatricians and General Practioners should closely follow these infants, Health Care and Education providers should prioritize programs to stress the importance of preventive care and continuity of care especially for children of mothers with evidence of low propensity toward health promotion.

The NKF-K/DOQI guidelines for CKD, reviewed in Kidney Disease Improving Global Outcomes (KDIGO), recommend that all individuals should be assessed, as routine health examinations, to determine the increased risk for developing CKD. Patients who are at risk

for developing CKD should be screened for hematuria with a urinalysis and with a urine test for proteinuria and a blood test for creatinine to estimate GFR. Depending upon the presence of particular risk factors, additional testing such as renal ultrasonography may be required, for example in patients with a family history of polycystic kidney disease. A formidable task for paediatricians is to prevent renal diseases that may develop in adult life. In order to achieve such goal, they should identify children at risk, counsel families to minimize any further renal risk factors such as smoking, obesity, and hypertension, and, in some cases together with a nephrologist, to institute pharmacologic therapy **[67].**

Strict blood pressure control has been shown to slow the progression of kidney disease and reduce the risk of cardiovascular disease. The National High Blood Pressure Education Program Working Group (NHBPEP) established guidelines for the definition of normal and elevated blood pressures (BP) in children by developing blood pressure percentiles based on gender, age, and height **[68].** Hypertension (HTN) is defined as either systolic and/or diastolic BP ≥95th percentile measured upon three or more occasions. Therapy includes both nonpharmacologic and pharmacologic interventions. Treatment should be initiated with conservative measures such as weight reduction, exercise, and dietary salt reduction. Pharmacologic therapy may be started in non responders; ACE inhibitors or angiotensin II receptor blockers (ARBs), that are the preferred antihypertensive agents as they reduce proteinuria and appear to be more beneficial in slowing the progression of CKD compared to other agents in patients with CKD [69-70].

Additional interventions that have been studied in adults with CKD include dietary protein restriction, lipid lowering therapy, and correction of anemia. However, results are inconclusive with respect to the impact of these interventions upon delaying the progression of CKD. In children, data have not shown a benefit of a low protein diet upon the progression of kidney disease CKD [71]. The current consensus by pediatric nephrology experts is to provide children with CKD the age appropriate recommended daily allowance for protein.

6. Treatment

The management of patients with CKD varies upon the severity of CKD. In the early stage it is important to treat reversible kidney dysfunction and prevent or slow the progression of kidney disease. In advanced stages (Stage 3 to 5) the management is focused on preventing and treating the complications of CKD, that include disorders of fluid and electrolytes, renal osteodystrophy, anemia, hypertension, dyslipidemia, growth impairment. The most common conditions with potentially recoverable kidney function are primarily due to decreased kidney perfusion or to the administration of nephrotoxic agents. Kidney hypoperfusion is produced by systemic hypotension, volume depletion from vomiting, diarrhea, diuretic use, or bleeding, and the administration of drugs that lower the kidney perfusion (such as nonsteroidal anti-inflammatory drugs, angiotensin converting enzyme [ACE] inhibitors, angiotensin II receptor blockers [ARBs]). Common nephrotoxic drugs include nonsteroidal anti-inflammatory agents, diagnostic agents (eg, radiographic contrast materials), and others (eg, aminoglycosides, amphotericin B, cyclosporine, and tacrolimus). The administration of such drugs, therefore, should be avoided or used with caution in patients with underlying CKD, with the assistance of therapeutic drug level monitoring. [72]

6.1 CKD complications

Major Problems in children with CKD
• Water and sodium retection • Hyperkalemia • Metabolic acidosis • Mineral metabolism and bone disease • Anemia • Nutrition • Growth

Table 3.

6.1.1 Water and sodium retention

It's present as GFR becomes severely decreased (ie, stages 4 and 5 disease), and it may result in volume overload. In general, a combination of dietary sodium restriction and diuretic therapy may correct the increased water balance. Dietary sodium intake should be decreased to 2 to 3 g/day and diuretic therapy includes loop diuretics such as furosemide given at a dose of 0.5 to 2 mg/kg per day [73].

6.1.2 Hyperkalemia

Hyperkalemia develops primarily because of inadequate potassium excretion due to a reduced GFR. Other factors that can contribute to elevated potassium levels include a high dietary potassium intake, metabolic acidosis, hypoaldosteronism (due in some cases to administration of an ACE inhibitor or an ARB), or an impaired cellular uptake of potassium. Management to prevent hyperkalemia in children with CKD consists in low potassium diet, administration of a loop diuretic (eg, furosemide) to increase urinary potassium loss, correction of acidosis with oral sodium bicarbonate [73].

6.1.3 Metabolic acidosis

Metabolic acidosis is characteristically present when the estimated GFR is less than 30 mL/min per 1.73 m2 (ie, stage 4 disease). Acidosis is associated with growth impairment because the body utilizes bone buffering to bind some of the excess hydrogen ions. Current guidelines by the K/DOQI working group are to maintain the serum bicarbonate level at or above 22 mEq/L . Sodium bicarbonate therapy is started at 1 to 2 mEq/kg per day in two to three divided doses, and the dose is titrated to the clinical target **[74].**

6.1.4 Mineral metabolism and bone disease

Alterations of mineral metabolism are an almost universal finding with progressive CKD due to abnormalities in the metabolism of calcium, phosphate, vitamin D, and parathyroid hormone (PTH) levels. If these abnormalities are not addressed, these changes result in kidney bone disease, referred to as renal osteodystrophy. The management and prevention of secondary hyperparathyroidism is complex and requires frequent monitoring and adjustment of therapy. The initial step is to correct phosphate retention by dietary restriction

usually combined with either calcium-containing phosphate binders and/or sevelamer. The KDOQI guidelines recommend that treatment with calcitriol should be started when the serum 25-hydroxyvitamin D is <30 ng/mL (75 nmol/L), or when serum PTH is above the target range [75]. In adults, calcimimetics have been increasingly used to suppress PTH secretion and decrease the risk of hypercalcemia associated with calcitriol. These agents, which increase the sensitivity of the calcium-sensing receptor (CaSR) in the parathyroid gland to calcium, have not been adequately studied in the pediatric population.

6.1.5 Anemia

Anemia in CKD is due to reduced kidney erythropoietin production and generally develops when the GFR is below 30 mL/min per 1.73 m2. The treatment of anemia in children with CKD often includes iron supplementation and erythropoiesis stimulating agent (ESA). The K/DOQI guidelines recommend a target Hgb between 11 and 12 g/dL based upon consensus expert opinion. The initial ESA dose in older children not receiving dialysis is 80 to 120 u/kg per week, administered in two to three divided doses. Children younger than five years of age or children receiving dialysis frequently require higher doses (300 u/kg per week) [76-77].

6.1.6 Nutrition

Malnutrition is common in children with CKD because of poor appetite, decreased intestinal absorption of nutrients, and metabolic acidosis. Attention to nutrition is critical as it affects both the physical growth and neurocognitive development of children [78].

6.1.7 Growth

Growth failure has been long recognized in children with CKD. While the institution of recombinant human growth hormone (rHuGH) therapy can have a profound effect on the height velocity of children with CKD who are growing poorly, early recognition and management of malnutrition, renal osteodystrophy, acid-base abnormalities and electrolyte disturbances should take place prior to considering the institution of rHuGH. [79].

6.1.8 Renal replacement therapy

Once the estimated GFR declines to less than 30 mL/min per 1.73 m^2 (stage 4 CKD), it is time to start preparing the child and the family for renal replacement therapy. The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. As in adults, some form of renal replacement therapy will generally be needed when the GFR falls below 15 mL/min per 1.73 m2 (stage 5 CKD). However, renal replacement therapy is often initiated before children reach these levels.

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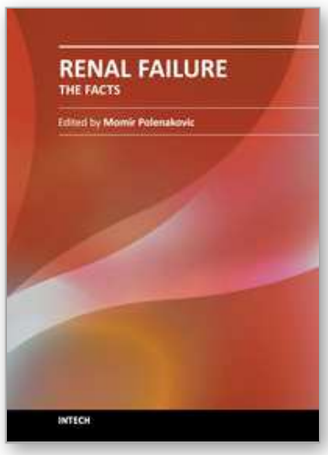
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The book "Renal Failure - The Facts" consists of some facts about diagnosis, etiopathogenis and treatment of acute and chronic renal failure. Acute, as well as chronic renal failure is great medical problems and their treatment is a burden for the 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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