



## Chronic kidney disease in children of paediatric emergency observation and referral unit admitted in hospital: a study in tertiary care hospital, Dhaka, Bangladesh

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### Abstract

**Introduction:** Chronic Kidney Disease (CKD) for children is a major problem of public health both in poor and developed countries. This study aimed to investigate the diagnosis and the management options of CKD for children.

**Objective:** To find out Chronic Kidney Disease in Children of Paediatric Emergency observation and Referral Unit admitted in Hospital.

**Patients and Methods:** This study retrospectively evaluated patients who had Chronic Kidney Disease (CKD) in the Paediatric Emergency observation and Referral Unit in tertiary Care Hospital, Dhaka, Bangladesh between July 2018 and December 2018.

**Results:** Over 6 month's period, we diagnosed and managed 41 children with CKD. The estimated incidence of CKD is 4.7 new cases per million-child population per year. Parental consanguinity was found in 16 patients (39%). Family history with kidney disease was noted in 6 cases (14.6%). Malformations of the urinary tract were observed in 24 patients (58.5%). Other causes are divided into hereditary kidney disease in 8 patients (19.5%) predominated by primary hyperoxaluria, in vascular nephropathy who were objectified in 5 patients (12%) whereas glomerulopathy were represented in 3 cases (7.5%). No etiology was found in 1 patient. Over the 6 month's 22 patients (54%) had renal replacement therapy (RRT). Peritoneal dialysis (PD) was practiced in over then 90% of patients. A passage from peritoneal dialysis to hemodialysis was done in 8 patients. Only four patients had a kidney transplant. The rate of overall mortality in our series was 40% with median of follow-up in 54 months.

**Conclusion:** In Bangladesh and in all low source country children with CKD must be treated by pediatric nephrologists and the pediatric renal transplantation must be developed.

**Keywords:** chronic, renal failure, children, Bangladesh

### 1. Introduction

Chronic Kidney Disease (CKD) for children is a major problem of public health both in poor and developed countries [1]. Chronic kidney disease (CKD) is now being recognized worldwide as an important problem in children. The overt stage of CKD is the end stage renal disease (ESRD), which is merely the tip of the iceberg of a large number of "covert less severe diseases." CKD represents a developing process that is initiated by various causes, all with the common end result of persistent and usually progressive damage of varying severity to the kidneys. The causes of the child's CRF are mainly the defects of the kidney and urinary tract, hereditary diseases and glomerulopathy [2]. Over 50% of the kidney diseases causing the CRF for the child are hereditary or congenital. Furthermore, diabetes and high blood pressure are about half of cases for the adult [3]. This study aimed to investigate the diagnosis and the management options of CRF for children. These patients have a continuous decline in renal function and hence are said to have progressive renal failure. It is characterized by the common histopathological end point of glomerulosclerosis, tubulointerstitial fibrosis and tubular atrophy, irrespective of the underlying etiology of kidney disease. The mechanisms involved in the

progression of CKD are hemodynamic changes, hypertension and proteinuria, infiltration of inflammatory cells and local release of inflammatory cytokines and profibrogenic growth factors. The aim of this presentation is to identify the clinical and pathological conditions that cause renal damage and suggest measures for its prevention including screening procedures for the early detection of renal disease.

### 2. Literature review

Chronic Kidney Disease (CKD) is an insidious and irreversible condition that eventually progresses to end stage renal failure. It is an important cause of morbidity and mortality in children worldwide. The disease process is better termed as chronic kidney disease (CKD), in order to encompass the entire spectrum and severity of renal disease. In the past various terminologies have been used to describe its severity from chronic renal insufficiency to end stage renal disease (ESRD). This classification did not include the 'at risk' population where intervention could modify the outcome. In order to reduce ambiguity and use more objective terms of reference the new name of CKD was introduced. Chronic kidney disease is defined primarily as an abnormality of kidney function or structure as

determined by laboratory tests, urinalysis or imaging tests, which have been present for three or more months. Importantly, the classification system describes the stages according to level of estimated glomerular filtration rate (GFR), not serum creatinine levels. This staging uses various clinical, laboratory and imaging parameters [20] and is depicted. These stages correspond to the severity of kidney function loss and the prevalence of co-morbidities associated with kidney disease. The identification of low GFR states may allow the implementation of simple measures to prevent worsening. For these reasons, it may be prudent to adopt the system of defining kidney disease according to kidney function, not serum creatinine values. However certain grey areas exist with this classification. The staging takes into consideration normal GFR for a western population. Secondly, correct interpretation of GFR values in children and adolescents, requires a clear understanding that it varies according to age, gender, and body size. The normal GFR in children is 120 to 130 mL/min/1.73 m<sup>2</sup>, whereas in infancy it is much lower. Even when corrected for body surface area it increases in relationship to body size up to two years. Kidney disease is characteristically asymptomatic and is often not diagnosed until it is relatively advanced.

### 3. Objective

To find out Chronic Kidney Disease in Children of Paediatric Emergency observation and Referral unit admitted in Hospital.

### 4. Patients and Methods

This study retrospectively evaluated patients who had Chronic Kidney Disease (CKD) in the Paediatric Emergency observation and Referral Unit in tertiary Care Hospital, Dhaka, Bangladesh between July 2018 and December 2018. Different information concerning sex, age, the circumstances of discovery, the personal history, diagnosis of CRF, treatments and evolution of CRF were collected and analyzed. The clearance of serum creatinine relative to the body surface area was calculated by the Schwartz formula:  $K * \text{Size (cm)} / \text{plasma creatinine (mg/dL)}$ . The constant K was equal to 36.5 irrespective of sex and age of the child outside of prematurity. Blood creatinine was measured by the enzymatic method. In general, CRF is light

for a GFR between 60 and 89 mL/min/1.73 m<sup>2</sup>, moderate between 30 and 59 mL/min/1.73 m<sup>2</sup>, severe between 15 and 29 mL/min /1.73 m<sup>2</sup> and terminal for a GFR of less than 15 mL/min/1.73 m<sup>2</sup>.

### Classification of CKD

There is limited information on the epidemiology of CKD in the pediatric population. This is especially true for less advanced stages of renal impairment that are potentially more susceptible to therapeutic interventions aimed at changing the course of the disease and avoiding ESRD. As CKD is often asymptomatic in its early stages, it is both underdiagnosed and, as expected, underreported. This is in part the result of the historical absence of a common definition of CKD and a well-defined classification of its severity. The current CKD classification system described by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) has helped remedy the situation. According to the K/DOQI scheme, CKD is characterized by stage 1 (mild disease) through stage 5 (ESRD) [22]. By establishing a common nomenclature, staging has been helpful for patients, general health care providers, and nephrologists when discussing CKD and anticipating comorbidities and treatment plans. The classification system has, however, been subject to debate, as it is argued that stages 1 and 2 would be better defined by the associated abnormalities (e.g. proteinuria, Hematuria, structural anomalies) rather being classified as CKD, whereas more advanced stages (3 and 4) should be characterized by the severity of the impaired renal solute clearance [23]. Furthermore, and with particular reference to children, the normal level of glomerular filtration rate (GFR) varies with age, gender, and body size and increases with maturation from infancy, approaching adult mean values at approximately 2 years of age (Table 2). In turn, GFR ranges that define the five CKD stages apply only to children 2 years of age and older. Finally, although the threshold of GFR reduction where chronic renal failure (CRF) and chronic renal insufficiency (CRI) begins is a matter of opinion, many registries have operationally defined this as a GFR below 75 mL/min per 1.73 m<sup>2</sup> [24]. Hence, populations with CRI or CRF are now categorized as those that comprise CKD stages 2-4.

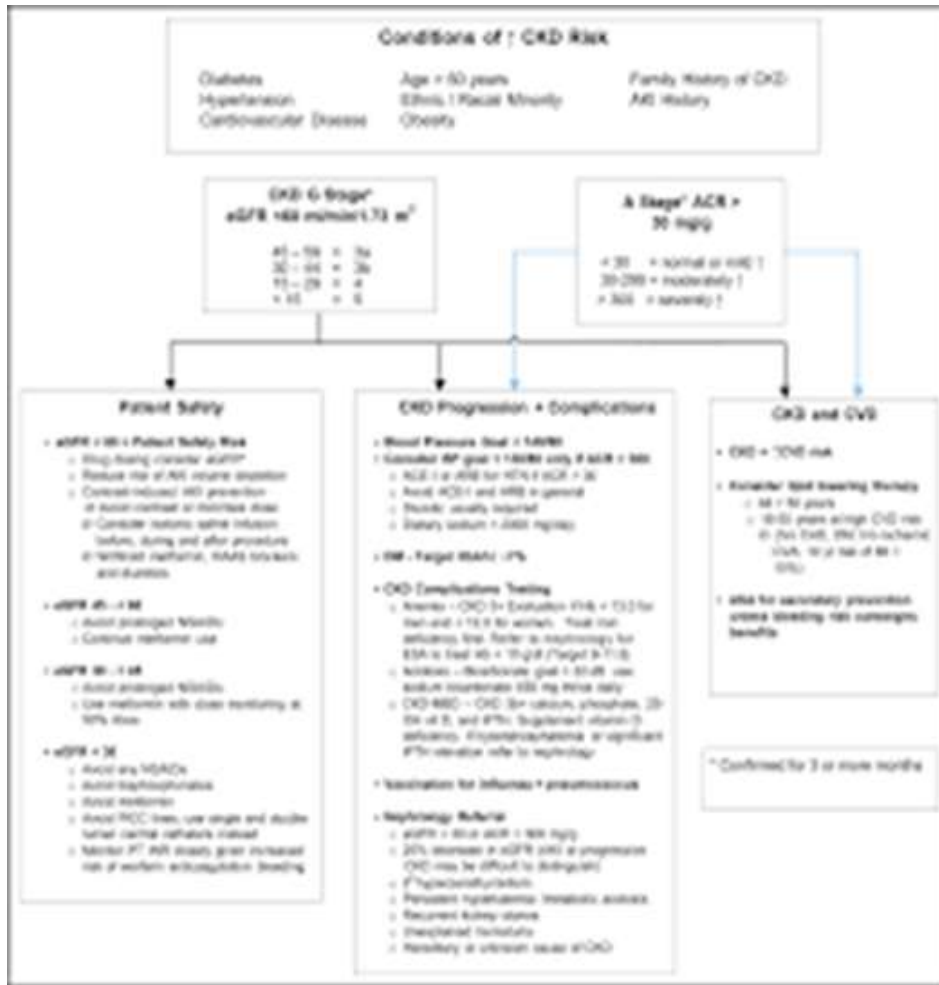


Fig 1: Management of as chronic kidney disease (CKD), Source: Google

**5. Results**

This study over 6 months period, we diagnosed and managed 41 children with CKD. 25 were male (61%) and 16 were female (39%). the average age was 4.9 years (60 months-12 years). CRF represented 6.8% pathologies of children hospitalized in our department during this period. The estimated incidence of CRF is 4.7 new cases per million-child population per year. The history of urinary tract infection was found in 13 patients (32%). Parental consanguinity was found in 16 patients (39%). Family history with kidney disease was noted in 6 cases (14.6%). Renal failure was discovered on the occasion of clinical symptoms in 29 patients (71%). Digestive disorders were found in 19 patients (46%), anorexia in all children and vomiting in 13 patients (32%) while osteodystrophy clinical signs were observed in 15 patients (36.6%). In biology exploration, anemia was found in 34 patients (83%), hypocalcemia was seen in 20 children (49%), hyperphosphataemia is seen in 20 children (49%), the average value of the urea at diagnosis is equal to 27 mmol/l +/- 15 mmol/l, with a range of 7-63 mmol/l. Thirteen patients (32%) had uremia > 30 mmol/l at diagnosis. Creatinine at diagnosis ranged from 79 mg/dL to 1000

mg/dL with a median equal to 232 mg/dL. The creatinine clearance calculated using the Schwartz formula was between 3 and 49.6 ml/min/1.73 m<sup>2</sup> with a mean of 18.6 ± 13 ml/min/1.73 m<sup>2</sup>. Renal ultrasonography was performed in all patients. Malformations of the urinary tract were observed in 24 patients (58.5%). The most frequent malformations were represented by a neurological bladder in 8 cases, hypoplasia/renal dysplasia in 5 cases. Vesicoureteral Reflux and congenital posterior urethral valves were found in 7 cases, a megaureter in 2 cases and a pyelo-ureteral junction syndrome in 2 cases. The ureteral reimplanation was made for patient who had Vesicoureteral Reflux and megaureter. The congenital posterior urethral valves had a resection in the 1st year of life. Medical treatment was prescribed in all patients with neurological bladder, of which 3 were operated on later and had a vesical enlargement. Other causes are divided into hereditary kidney disease in 8 patients (19.5%) predominated by primary hyperoxaluria, in vascular nephropathy who were objectified in 5 patients (12%) whereas glomerulopathy were represented in 3 cases (7.5%). No etiology was found in 1 patient (Table 1). Over the 11 years, 34 children were terminally CRF (83%).

Table 1: Etiology of CKD children (n=41).

| Primary Kidney disease              |    | Percentage |
|-------------------------------------|----|------------|
| Congenital urological malformation: | 24 | (58.5%)    |
| -neurogenic bladder                 |    | 8          |
| - hypoplasia / renal dysplasia      |    | 5          |

|  |   |         |
|--|---|---------|
| - Vesicoureteral Reflux                |   | 3       |
| - congenital posterior urethral valves |   | 4       |
| - Megaureter                           |   | 2       |
| -pyelo-ureteral junction syndrome      |   | 3       |
| hereditary kidney disease              | 8 | (19.5%) |
| vascular nephropathy                   | 5 | (12%)   |
| Glomerulopathy                         | 3 | (7.5%)  |
| No etiology                            | 1 | (2.5%)  |

**Table 2:** Stages of chronic kidney disease (n=41).

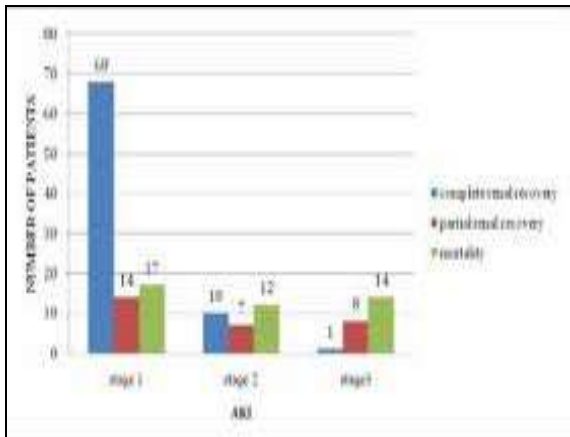
| Stage | Description                              | GFR (mL/min/1.73m <sup>2</sup> ) |
|-------|--|----------------------------------|
| 1     | Kidney damage with or increased GFR      | 12>                              |
| 2     | Kidney damage with mild decreased in GFR | 10-11                            |
| 3     | Moderate decrease in GFR                 | 7-10                             |
| 4     | Severe decrease in GFR                   | 5-7                              |
| 5     | Kidney failure                           | <5 or dialysis                   |

GFR glomerular filtration rate

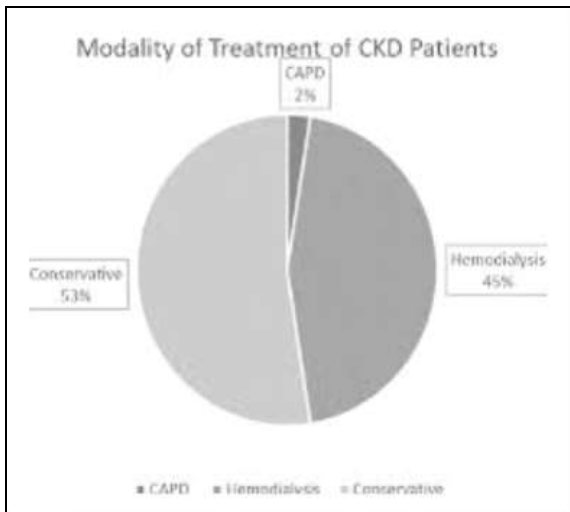
**Table 3:** Normal glomerular filtration rate (GFR) in children and adolescents (n=41).

| Age                            | Mean GFR±SD (mL/min/1.73 m <sup>2</sup> ) |
|--------------------------------|---|
| 1 week (males and females)     | 41 ± 15                                   |
| 2-8 weeks (males and females)  | 66 ± 25                                   |
| >8 weeks (males and females)   | 96 ± 22                                   |
| 5-12 years (males and females) | 133 ± 27                                  |

Sources: Of pediatric data



**Fig 1:** Chronic kidney disease in Bangladesh.



**Fig 2:** Treatment of chronic kidney disease.

Large population-based studies, such as the Third National Health and Nutrition Examination Survey (NHANES III), have made it possible to estimate the incidence and prevalence of CKD in the adult population [22]. According to this report, the prevalence of patients with early stages of CKD (stages 1–4; 10.8%) is approximately 50 times greater than the prevalence of ESRD (stage 5; 0.2%). There is no comparable information available in the United States on the prevalence of the earlier stages of CKD in children and its relationship to ESRD. This is, in large part, due to differences in disease etiology for children and adults. Furthermore, the relationship between the prevalence of earlier stages of CKD and the subsequent development of more severe CKD/ESRD is determined in part by factors unrelated to disease etiology, as was recently shown in a comparison between adult patients in Norway and the United States [23]. Data that do exist on the epidemiology of CKD in children come from a variety of sources. Population-based data from Italy (ItaKid Project) has reported a mean incidence of preterminal CKD ( $C_{Cr} < 75$  mL/min per  $1.73$  m<sup>2</sup>) of 12.1 cases per year per million of the age-related population (MARF), with a point prevalence of 74.7 per MARF in children younger than 20 years of age [49]. The national survey performed in Sweden from 1986 until 1994 included children (ages 6 months to 16 years) with more severe preterminal CKD ( $C_{Cr} < 30$  mL/min per  $1.73$  m<sup>2</sup>) and reported a median annual incidence and prevalence of 7.7 and 21 per MARF, respectively [16]. Similarly, the incidence rate of severe pre-terminal CKD in Lorraine (France) has been estimated as 7.5 per MARF in children younger than 16 years; the prevalence rate ranged from 29.4 to 54 per MARF [35]. In Latin America, the Chilean survey from 1996 reported incidence and prevalence rates of 5.7 and 42.5 per MARF, respectively, in children younger than 18 years of age with  $C_{Cr} < 30$  mL/min/ $1.73$  m<sup>2</sup>, including patients with ESRD [12]. As alluded to above, there are 81.2 million children in the United States younger than 20 years of age [25], but no data on the incidence or prevalence of preterminal CKD is available. Due to a lack of national registries, any semblance of incidence and prevalence data from developing countries primarily originates as reports from major tertiary care referral centers [37-39]. The nature of the data depends on local referral practices and accessibility to hospital care. The Jordan University Hospital has estimated the annual incidence and prevalence of severe CKD ( $C_{Cr} < 30$  mL/min per  $1.73$  m<sup>2</sup>) to be 10.7 and 51 per MARF, respectively, based on their hospital admission rate [26]. A 15-year review of admissions from a university teaching hospital in Nigeria estimated the median annual incidence of severe CKD ( $C_{Cr} < 30$  mL/min per  $1.73$  m<sup>2</sup>) to be 3.0 per MARF, with a prevalence of 15 patients per million children [27]. In a recent report, data from a major tertiary hospital in Bangladesh revealed that approximately 12% of patients ( $n = 305$ ) seen by the pediatric nephrology service over a 7-year period had moderate to severe CKD

( $C_{Cr} < 50$  mL/min per  $1.73 \text{ m}^2$ ), and one quarter of these patients had already developed ESRD, highlighting the late diagnosis and referral pattern [23]. Similar data was reported from another tertiary hospital in Bangladesh where 50% of 48 patients presenting with CRF over a 1-year period had ESRD [22]. Finally, data from a major Iranian hospital collected over 7 years (1991–1998) reported that 11% of pediatric nephrology admissions ( $n = 298$ ) were due to severe CKD ( $C_{Cr} < 30$  mL/min per  $1.73 \text{ m}^2$ ), and one half of the patients advanced to ESRD [25]. The incidence rate of ESRD, adjusted for race and gender, is much higher among adults than among children. Data from the USRDS revealed that in pediatric patients younger than 20 years of age, the annual incidence of ESRD increased marginally from 13 per MARP in the 1988 cohort to 15 per MARP in the 2003 cohort [22]. This is in contrast to the adult incidence rate of 119 per MARP for patients 20–44 years of age and 518 per MARP for those 45–64 years old in the 2003 cohort [5]. As in children, a higher incidence rate with older patients was also found across the 5-year age groups within the pediatric cohort. The incidence rate was nearly twice as high among children 15–19 years of age (28 per MARP) compared with children 10–12 years of age (14 per MARP), and nearly three times higher than the rate for children 0–5 years of age (9 per MARP). The point prevalence for pediatric patients (adjusted for age, race, and gender) was 82 per million population during 2002–2017 [22]. The EDTA registry recently reported its cumulative data on 2000 patients (<5 years of age) with ESRD who initiated RRT between 1980 and 2000 in 12 European countries [20]. With a total of 18.8 million children between 0–12 years in the countries surveyed, data revealed that the incidence of ESRD rose modestly from 7.1 per MARP in the 1980–1984 cohort to 9.9 per MARP over the next 15 years. In contrast, the prevalence of patients receiving RRT increased from 22.9 per MARP in 1980 to 62.1 per MARP in 2000, providing evidence of improved long-term survival.

### Outcome for children with CKD

The outcome of children with severe CKD is highly dependent upon the economy and availability of health care resources. Approximately 90% of treated ESRD patients come from developed countries that can afford the cost of RRT [29]. Despite comparable incidence rates, high mortality in countries that lack resources for RRT results in a low prevalence of CKD patients in those countries. In one of the tertiary care hospitals in Bangladesh, for example, up to 40% of the ESRD patients opted out of further therapy because of a lack of financial resources [22], and of the 91 patients with ESRD in another hospital, only 15 underwent renal transplantation, 63 received hemodialysis, and the remainder opted out of dialysis or transplantation care secondary to financial constraints [23]. Similar results were recently published from South Africa where only 62% of children (<20 years of age) with ESRD were accepted by an “Assessment Committee” for RRT as part of a rationing program [30]. In countries where RRT is readily available, the most favored renal replacement modality is transplantation in all pediatric age groups. Sixteen percent of children newly diagnosed with ESRD in North America receive a preemptive transplant, and three fourth of children receive a transplant within 3 years of RRT initiation [5]. Similar figures are reported by the ANZDATA registry [21]. Among Western countries, Spain/Catalonia has the highest

pediatric transplant rate, reaching 15 patients per million population, followed by a rate of 12 patients per million population in the United States and Finland (Fig. 2) [5]. In the United States, white pediatric patients are more likely to receive a renal transplant than are patients from other racial groups. (54%) had renal replacement therapy (RRT). 5 patients (12%) were died before starting dialysis. Peritoneal dialysis (PD) was the most used technique. It was practiced in over then 90% of patients. It was the dialysis method of choice for patients under the age of 2 years. Hemodialysis was initially performed in only two patients. A passage from peritoneal dialysis to hemodialysis was done in 8 patients. Only four patients had a kidney transplant; they were 2 girls and 2 boys aged between 11 and 16 years. The rate of overall mortality in our series was 40% with median of follow-up in 54 months.

### 6. Discussion

Chronic Kidney Disease (CKD) is an important cause of morbidity and mortality in children worldwide. The disease process is better termed as chronic kidney disease (CKD), in order to encompass the entire spectrum and severity of renal disease [4]. The incidence of CRF varies in different parts of the world. In most developed countries the incidence varies between 10 per million-children below 12 years of age. The etiology of CRF varies in different parts of the world. Hereditary disorders are more common in regions, where the frequency of consanguineous marriages is high [6]. In our study parental consanguinity was found in 39% of patients and family history with kidney disease was noted in 14.6% of cases. The detecting of CKD is important for pediatricians, family physicians, pediatric nephrologists, urologists and other health care providers who have the opportunity to detect CKD in children and adolescents during its early stages [7]. In our work the majority of patients with CRF were detected on the occasion of clinical symptoms. The CRF was discovered at a very advanced stage, these results can be explained by the CRF is made that a condition that remains long few symptoms but also by inadequate management and sometimes late renal pathologies likely to progress to the CRF. These results are close to those of the Bangladesh series and the Egyptian series who report frequent ESRD at diagnosis respectively about 54% and 57.6% [8, 9]. But these values are considerably high compared to European data records [10, 11]. All attempts should be made to determine the aggravating factors for worsening renal functions in any given child [7]. Anemia, renal osteodystrophy and acidosis are often the presenting features and have a variety of deleterious consequences [4]. In our patients anemia was present in 83% of patients and osteodystrophy was noted in almost the half of patients. An understanding of the important causes of CRF in any country is important as it may guide the distribution of limited resources towards its prevention [4]. According to the data of our series, uropathies malformations represented the most common of the child's CRF (58.5%). Hereditary kidney diseases were the second etiology of childhood CKD (19.5%) represented mainly by primary hyperoxaluria followed by vascular nephropathy (12%). Glomerular renal disease accounted for only 7.5% of the causes of the CRF when they were about 23% of the causes of CKD in the series. Our results are close to those of European studies where uropathies malformations are the leading cause of chronic renal failure in children (more than

55% of etiologies) followed hereditary kidney disease (between 15% and 19%) and glomerular renal disease (between 5% and 11.5%) [12-14]. In America, the distribution of etiologies reported by various US registers is a little different [15]. Indeed, urinary malformations remain the leading cause of CKD in children (48%), however, the second cause is represented by glomerulonephritis (14%) followed by hereditary kidney disease (10%). This distribution is also found in neighboring Mediterranean countries such as Egypt and Algeria [17]. Significant advances have been made in the understanding of various renal replacement measures, which have enabled provision of better care. Both chronic peritoneal dialysis and hemodialysis along with other supportive measures can ensure longevity and improved quality of life in patients with CRF [4]. Management of children with CKD aims at possible interventions to retard progression of disease and the treatment of co-morbid conditions in the early stages [4]. In our study, majority of our patients required extra renal purification. 90% of dialysis children were initially purified by the peritoneal dialysis. Only 4 patients received a kidney transplant [18, 19]. Most of the existing data on the epidemiology of CKD during childhood concentrates on the late and more severe stages of renal impairment [25, 26] and are not population based in nature [27]. In addition, some methodologically well-designed childhood CKD registries are limited by being restricted to small reference populations [27-29]. Finally, direct comparisons of the incidence and prevalence rate of childhood CKD in different geographical areas around the world is difficult due to methodological differences in study age group, characterization of the degree of renal insufficiency, and disease classification. NAPRTCS was established as a transplant registry in 1987 with a goal of gathering data from the majority of pediatric renal transplant centers in the United States, Canada, Mexico, and Costa Rica. Its registry was expanded in 1992 to include data from patients receiving maintenance dialysis, and in 1994, data was first collected from patients with CRI characterized by a Schwartz estimated creatinine clearance of  $\leq 75$  mL/min per  $1.73 \text{ m}^2$  [29]. Participation in this registry is voluntary and mandates the involvement of a pediatric nephrologist in the provision of care to those patients entered into the registry. As of December 2015, information had been collected on more than 6,400 patients who entered the registry with a diagnosis of CRI [25]. In contrast to the European Dialysis and Transplant Association (EDTA) was established in 1964 to record demographic data and treatment details of patients receiving renal replacement therapy (RRT), including dialysis and renal transplantation. Historically, the EDTA registry gathered data on RRT in children from individual renal units by means of center and patient questionnaires, a process that was subject to underreporting. At the turn of the century, the EDTA office moved to Amsterdam and began collecting data on RRT entirely through national and regional registries and recently reported data on RRT in children from 12 registries located in Europe (*vide infra*) [41]. Other regional societies, such as the Japanese Society for Pediatric Nephrology (JSPN), have also provided useful epidemiological information. In contrast, epidemiological information from Asia, where 57% of the world's population resides and a geographic region characterized by a very high proportion of children, is very scant and is primarily based on patients referred to tertiary medical

centers [44, 45]. The situation in central and southern Africa or in the Arab countries of North Africa and the Middle East is even more unfortunate, as there are no regional pediatric nephrology societies in place to collect and publish any valid epidemiological data.

### Progression of CKD

Although the stages of CKD are now reasonably well defined, the natural history of the early stages is variable and often unpredictable. However, most available data demonstrates a slower progression toward ESRD in patients with congenital renal disorders compared with patients with glomerular disease. For this reason, and as alluded to previously, the relative proportion of glomerular diseases increases in groups of patients with more advanced stages of CKD. The progression of established CKD is also influenced by a variety of risk factors, some of which (e.g., obesity, hypertension, and proteinuria) may be modifiable [35-37], whereas others, including genetics, race, age, and gender, are not. Obesity is associated with hypertension, albuminuria, and dyslipidemia, all of which can potentially influence the progression of CKD. The incidence of certain glomerulonephritis's, such as FSGS, is higher in obese than in lean individuals [38, 39]. Hypertension together with proteinuria has been shown to be an important risk factor for progression of primary renal disease in children and adults [40, 41], and the Reno protective efficacy of renin angiotensin system (RAS) antagonists, which is in part independent of blood pressure, has been clearly demonstrated in animal models and adults with acquired nephropathies [42-46]. Whereas both angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers have been shown to reduce proteinuria in children with CKD, the Reno protective efficacy of these medications in children and their potential impact on the epidemiology of CKD still needs to be better delineated, as is currently being addressed by the Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of Chronic Renal Failure in Pediatric Patients (ESCAPE) trial [47, 48]. The clustering of CKD in families is strongly suggestive of a genetic or familial predisposition in some cases [49]. Studies have suggested the presence of links between CKD and various alterations or polymorphisms of candidate genes encoding putative mediators, including the renin-angiotensin system. Additionally, racial factors may play a role in susceptibility to CKD, as there is a strong concordance of renal disease in the families of African Americans with hypertensive ESRD [49]. Not only may there be an increased susceptibility to disease, but there is evidence that the rate of progression of CKD is faster among African American males [50]. Low birth weight in some ethnic communities might be associated with a reduction in the number of nephrons and a subsequent predisposition to hypertension and renal disease in later life [51]. Irrespective of the underlying kidney disease or presence of additional risk factors, it is clear that the risk of progression to ESRD in childhood is inversely proportional to the baseline creatinine clearance [10, 19]. Additionally, regardless of the initial level of renal insufficiency, puberty seems to be a critical stage for patients with renal impairment, as a steep decline in renal function often occurs during puberty and the early post puberty period [19]. Whereas the specific reasons are yet to be determined, it is speculated that this pattern of progression may be attributable to an adolescent-specific

pathophysiological mechanism, possibly related to sex hormones and/or the imbalance between residual nephron mass and the rapidly growing body size. Data collected by NAPRTCS has also revealed that patients whose baseline serum albumin was below 4 g/dl, inorganic phosphorus above 5.5 mg/dl, calcium below 9.5 mg/dl, blood urea nitrogen (BUN) above 20 mg/dl, or hematocrit below 33% had a significantly higher risk of reaching ESRD ( $p < 0.001$ )<sup>[10]</sup>. Data pertaining to a variety of risk factors potentially associated with the progression of CKD, including those noted above, is being collected by the Chronic Kidney Disease in Children Study (CKD), a prospective, multicenter initiative funded by the National Institutes of Health designed to follow the course of 540 children with CKD for 2–4 years<sup>[52]</sup>.

## 7. Conclusion

Studies in developed countries have shown that children with CKD cared for by pediatric nephrologists fare better in the long run than those managed at adult nephrology units. So in Bangladesh and in all low source country children must be treated by pediatric nephrologists and the pediatric renal transplantation must be developed. A large number of clinic pathological conditions can produce renal damage in children. Anticipation, early recognition and institution of preventive measures can reduce the morbidity, mortality and the economic burden due to CKD. In a country like Bangladesh, where dialysis and transplantation care is not within the reach of many children, steps should be taken to prevent the onset and progression of CKD in childhood.

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