

Chronic Kidney Diseases in Children, Management Difficulties and Amelioration in Bangladesh: A Review

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Abstract

Background: Bangladesh is a small country of south Asia with a population of 153 million, among them 66 million are under age of 18years. The exact prevalence of chronic kidney disease (CKD) in children is not well known due to lack of a national registry. But in Bangabandhu sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, the incidence is 7.9% in 2013 and there are approximately thirty five hundred thousand around the country. There are 4.4% of children with renal disease prevalent in the country. But unfortunately, there is diagnostic problem and the treatment facility is very limited. Only few centers provide the renal replacement therapy in this country and only two centers do pediatric renal transplantation. So, to tackle this large burden with very limited resource, it is important to try and reduce the incidence of chronic kidney disease, especially end stage renal disease. We can handle the present situation with our existing resource with some modification of health care delivery system with contribution from government, non government organizations (NGO's) and affluent people. This article highlights chronic kidney disease in children, present treatment modality and some future directive to handle such a crucial problem, thus may help thousands of children from such a devastating situation. [J Shaheed Suhrawardy Med Coll, 2015;7(1): 26-32]

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Introduction

Chronic Kidney disease (CKD) is a devastating disorder with many long term consequences. Epidemiological studies that have been performed provide evidence that end stage renal disease (ESRD) represents the "tip of the iceberg" of CKD and suggest that patients with earlier stages of disease are likely to exceed those reaching ESRD by as much as 50 times¹. Worldwide, the number of patients with CKD is rising markedly, especially in adults, and CKD is now being recognized as a major public health problem that is threatening to reach epidemic proportions over the next decade². The mortality rate for children with ESRD receiving dialysis therapy is between 30 and 150 times that of the general pediatric population³. In this century, we have a good control over infectious disease but non communicable diseases are increasing day by day. But, CKD of these children can be prevented and treated by helping to target key patient populations at risk, by quantifying the extent of the

problem, and by facilitating assessment of the impact of intervention.

Chronic Kidney Disease (CKD)

CKD is defined as abnormalities of kidney structure or function, present for more than three months, with implications for health⁴. It is a devastating medical, social, and economic problem for patients and their families.

Table: GFR stages in CKD2

Stage	GFR	Terms
1	>90	Kidney damage with normal or increased GFR
2	60-89	Kidney damage with mild decrease in GFR
3	30-59	Moderately decreased GFR
4	15-29	Severely decreased GFR
5	<15	Kidney failure

*GFR in ml/min/1.73 m²

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Epidemiology

A number of factors influence incidence and prevalence rate variability of childhood end stage renal disease (ESRD). Factors such as racial and ethnic distribution, type of prevalent renal disease, and quality of medical care available for pre-terminal CKD patients have a significant impact on patient outcome. As the vast majority of treated ESRD patients come from more-developed countries, who can afford the cost of renal replacement therapy, the huge disparity in the management of ESRD between the more-developed and less-developed countries probably seems, in large part, from the inadequacy of health-care resource, centre allocation to programs and experts providing renal replacement therapy in underdeveloped countries⁵⁻⁶. Based on data from the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) chronic renal insufficiency (CRI) database, from 1994-2007, 7037 patients aged 0-20 years were entered into this voluntary listing and had an estimated glomerular filtration rate (eGFR) of less than 75 ml/min per 1.73 m².⁷ In the United States, the incidence and rate of progression to ESRD are equal in both sexes, although obstructive uropathies are more common in males⁸. Globally, the prevalence of chronic kidney disease (CKD) stage III to IV in children is reported to be approximately 18.5-28.3 per million children. Disease prevalence is much lower than that in adults; in a study from India, children constituted 5.3% of all patients with chronic kidney disease seen in a referral hospital⁹. Data from the Italkid study reported a mean incidence of 12.1 cases per year per million in the age-related population (age range, 8.8-13.9 year) and a prevalence of 74.7 per million in this population¹⁰. However, in Bangladesh, 4.4% of children admitted in hospital found to have renal disease¹¹, out of which 7.9% have CKD. There are approximately 35 thousand children with CKD at the moment.

Aetiology and common risk factors for the development of CKD

In children, CKD may be the result of congenital, acquired, inherited, or metabolic renal disease and the underlying cause correlates closely with the age of the patient at the time when the CKD is first detected. The risk factors which are responsible for the development of CKD are family history of renal disease, antenatal detected renal anomalies, neonatal acute renal failure, low birth weight babies, history of urinary tract infection with reflux, history of nephritis or nephrotic syndrome and lower urinary tract obstruction¹². Common cause of CKD includes renal hypoplasia and dysplasia, obstructive uropathy and various forms of glomerulonephritis (GN) including lupus nephritis, hereditary nephropathy and reflux nephropathy. The chief cause of chronic kidney disease stage 4 and 5 in 46 patients admitted to Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during 2013, were glomerulonephritis and nephrotic syndrome (26.08%), obstructive uropathy (17.39%), hypoplastic kidney (19.56%), acute renal failure (6.52%), neurogenic bladder

and reflux (8.68%), other and unknown (21.73%). Other parts of the south Asia have similar type of etiology⁴. In the United States Renal Data System (URDS) Registry, congenital disorders; Congenital Anomalies of kidneys and Urinary Tract (CAKUT) and hereditary nephropathies were the most common etiologies in the youngest ESRD group, whereas the proportion of acquired diseases increased progressively with age⁶. Overall, CAKUT are the main causes, accounting for 34-43% of pediatric ESRD cases in Europe, Australia, and New Zealand¹³. In 2008, the proportion of ESRD caused by glomerulonephritis was lower in Europe according to the (European Society of Pediatric Nephrology/ European Registry for Children on Renal Replacement Therapy) ESPN/ERA-EDTA registry (15%) compared with a Japanese study (22%) and the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA; 29%). The ANZDATA Registry showed a decline in glomerulonephritis as a cause of ESRD over time. Data from Japanese registry has revealed that 34% of their pediatric CKD causes were secondary to glomerulonephritis¹⁴.

Factors hastening the progression of CKD8

There are certain factors which hasten the progression CKD and these include, obstruction to the urinary tract, ongoing active glomerular disease, hypertension, proteinuria, infections of the urinary tract, hyperlipidemia and use of nephrotoxic medications.

Presenting features of CKD and pitfalls in diagnosis and investigation

In stage 1 and 2 most of the patients are asymptomatic; usually some are detected by incidental investigations. Clinical features of stage 3 to 5 include anorexia, failure to thrive, growth retardation, hypertension, fatigue, anemia, and bone disease (renal rickets). The late features are itching, severe acidosis, hyperkalemia, left ventricular failure, pulmonary edema, pericarditis, pericardial effusion, increase sleep, poor school performance, reduced immunity, neurological abnormalities like encephalopathy, hypotonia, delayed motor development, seizure (due to hypertension, hypocalcemia, hyponatremia, azotemia and sepsis), truncal ataxia and other cerebellar dysfunction, uremic neuropathy and severe proximal myopathy and pale renal facies¹⁴⁻¹⁵. Common clinical presentations among the children with CKD are regarded as vague symptom, pallor, failure to thrive and growth retardation are attributed to widespread malnutrition prevalent in this country, 43% are wasted and 48% are stunted¹⁶, urinary symptoms (poor stream, incontinence and enuresis) are ignored by many physicians. Urinary tract infection which is often undiagnosed because of poor diagnostic facility and poor urine collection system, and hence remains misdiagnosed leading to CKD, nephritic and nephrotic syndrome are not handled properly at times. Hypertension found in 60-80% of cases and causing progression of renal damage and most of the time physicians or caregivers do not measure blood pressure in children routinely. Polyuria,

polydipsia and symptoms pointing towards urinary system are rarely found in children with CKD. Lastly rickets (Renal osteodystrophy), is regarded as nutritional cause or ignored as normal variant. Some children are diagnosed by incidental investigation but majority are not diagnosed early because of the above reason and we get most of the children at the end stage renal disease.

Table: Investigations for CKD in children¹⁴⁻¹⁵

To assess severity and duration

- Complete blood with peripheral blood film
- Glomerular filtration rate (GFR)
- Serum creatinine
- Blood urea and BUN
- Serum electrolyte
- Blood PH and bicarbonate
- Serum calcium
- Inorganic phosphate
- Alkaline phosphatase
- Serum albumin
- albumin creatinine ratio (ACR)
- Parathormone
- Iron profile
- Serum uric acid
- X-ray hand and wrist (left)
- X-ray chest
- Electrocardiogram
- Echocardiography
- Urine creatinine

To assess etiology

- Ultrasonography of kidney ureter and bladder
- Micturating cystourethrogram
- Intravenous urogram
- Radio-isotope scan: di ethyl triamine penta acitic acid (DTPA)
- Dimercapto succinic acid (DMSA)
- Urodynamic study
- Urine analysis- microscopy and culture
- C3, C4
- Anti nuclear antibody
- Anti double strand DNA
- Anti GBM antibody
- pANCA & cANCA
- HBsAg
- Anti HCV
- Renal biopsy
- WBC cystin level
- Oxalate excretion
- Purine excretion

Management of Chronic Kidney disease¹⁴⁻¹⁵

Management of CKD include the following aspects,

1. Specific therapy, directed to underlying treatable cause like obstructive uropathy, reflux, GN and congenital anomalies
2. Measure to retard the progression of the disease by controlling hypertension, correcting anemia (by food, oral iron, zinc, folic acid, subcutaneous erythropoietin), control of proteinuria by angiotensin converting

enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), control of hyperlipidemia, correction of acidosis, restriction of phosphate rich diet (milk, milk product and chocolate), mineral bone disease (MBD) correction by vit D and calcium and vitamin supplementations (A, B₁, B₂, B₆, B₁₂, C, E, K), fluid and electrolyte balance and finally control of infection are essential. Growth hormone is considered in selective cases. Erythropoietin is frequently used but expensive so, many patients cannot afford to maintain. Erythropoietin stimulator proteins like darbopoitin alpha and continuous erythropoietin receptor activator such as Mirsera are promising but costly and not readily available. In severe anemia (Hb <6gm/dl) leucocyte depleted packed cell should be given but it can cause subsequent graft rejection by prior antibody production

3. Evaluation and management of co-morbid condition
4. In end stage renal disease patients need renal replacement therapy in the form of dialysis and renal transplantation

Renal Replacement Therapy and Bangladesh scenario

Once a child develops CKD Stage V, some form of renal replacement therapy (RRT) is required. The choice is limited to a chronic dialysis or renal transplant. A preemptive transplant is possibly the best option. Besides providing a good renal replacement therapy it ensures better growth and does not drain the family resources. The facilities for providing renal replacement therapy to children with CKD Stage 5 are grossly inadequate in Bangladesh. The lack of a health insurance scheme or a national ESRD program makes RRT beyond the reach of the majority of the people. The options for RRT other than a transplant include chronic hemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD). For successful dialysis appropriate sizes of catheters, tubings, dialyzers, small volume dialysis bags, etc, are required. These are now available but in limited number of places in our country. The cost of continuous ambulatory peritoneal dialysis (CAPD) is two times higher than hemodialysis if infrastructure and manpower costs are not taken into consideration. The goal of treatment in children with ESRD is renal transplantation. Children on long-term hemodialysis show subnormal growth, poor quality of life and delayed sexual maturation. Hemodialysis is performed, 2-3 days in a week, in the hospital as a daycare procedure with each session lasting for 3-4 hours. In developed countries home nocturnal hemodialysis is becoming a feasible option¹⁷. In comparison to adults, the procedure of hemodialysis is technically more difficult in children and requires close monitoring to prevent complications. Dedicated pediatric hemodialysis units with skilled nursing and technical staff are necessary to provide safe and effective hemodialysis for children. The high cost of hemodialysis in relation to per capita income is a constraint for long-term dialysis and the maintenance of a satisfactory vascular access is a major technical problem faced by pediatric hemodialysis units. In adult

population, 5year survival by hemodialysis is 55%¹². The number of hemodialysis center is 86 for adults¹⁸ and only 8-10 for children, unfortunately 5-6 of them running regularly. In our institution, in 2013, out of a total of 46 children with ESRD, only 35% enrolled for maintenance HD and rest refused to take due to financial problem. Among them only 10% continued HD regularly and rest of them either died due to complications related to inadequate and irregular dialysis or opted out due to financial constraints. It is felt that more pediatric hemodialysis units with trained personnel are required for meeting the unique needs of children. CAPD provides near steady-state of biochemical control with no risk of disequilibrium syndrome, minimal need for dietary and fluid restrictions and freedom from repeated dialysis needle puncture. CAPD exchanges are carried out 4-5 times a day with very meticulous attention for maintaining asepsis. Parents need to be explained and trained about the techniques for performing exchanges and trouble shooting. Despite adequate precautions, such patients are at significant risk for peritonitis. Smaller dialysate bags are not freely available in our country resulting in wastage of dialysis fluid and increased cost with the use of larger bags. However it is a viable option for a successful bridge between ESRD and renal transplantation¹⁹. Renal transplantation is undoubtedly the best option. In Bangladesh, the number of institution which provides transplant facility is only 8 for adults and only 2 for children¹². The first renal transplantation in children was performed in BSMMU in 2006. Unfortunately, in last seven years only 4 patients had transplantations and last one in 2013. Though we have a very qualified and skilled team for transplantation and outcome is very much similar to the developed countries, the number of transplant is only 4% of ESRD in adult and in children only 0.2%. Now country needs pediatric transplant surgeon and skilled urologist with the logistic which is quite possible²⁰.

Current situation and challenges as health care of Bangladesh concerns

Bangladesh is a small land of 147570 m² and has a population of 153million and is the eighth most populated country of the world²¹. Sixty six million of people are children who are under 18year of age. Bangladesh has had exceptional health achievements especially in reducing infant mortality rate and maternal mortality rate. In 2010, the United Nation recognized the country for exemplary progress towards Millennium Developmental Goal (MDG)- 4 in child mortality²²⁻²³. Bangladesh was praised as an example of 'Good health at low cost'. Thirty two percent of its people were facing poverty¹⁶ which has been decreased in to 25.6%²⁴ in last year. The cause is very much unequally distributed economy of this country. Infant mortality rate is 37.3 per thousand live birth²⁵, under 5 mortality is 42 per thousand live-births and life expectancy at birth is 68.3 years¹⁶. A major provider of the health services is Government which has hospitals at different levels starting from union, sub-district, district and tertiary level medical colleges and frontline workers plus health care providers in villages¹⁶. Registered private

for profit hospitals and clinics are situated in divisional as well as district level. Now some small private clinics are also situated in sub-district level. The country also has non profitable NGOs (Non government organizations) which provide maternal, fertility and child related problems. Like many countries of the world, Bangladesh has had decline in infectious disease but rapid rise of non communicable and chronic disease related to aging¹⁶. Bangladesh Diabetic Association is doing a great job by serving for the diabetic patients and also providing training in different corner of the country. Similarly, coronary heart diseases are being treated at international standard by government and non government hospitals with a cost which the majority people of country can afford which was not possible few years ago. International Diarrhoeal Disease and Research, Bangladesh (ICDDR,B) is inventor of oral rehydration saline (ORS), center is treating thousands of patients and one of the pioneer institute of research. Bangladesh Rural Advancement Committee (BRAC) is working on tuberculosis, gender issue and other field at low cost. Recently some private profitable hospitals are started dealing with all sorts of critical diseases including renal disease but at high cost.

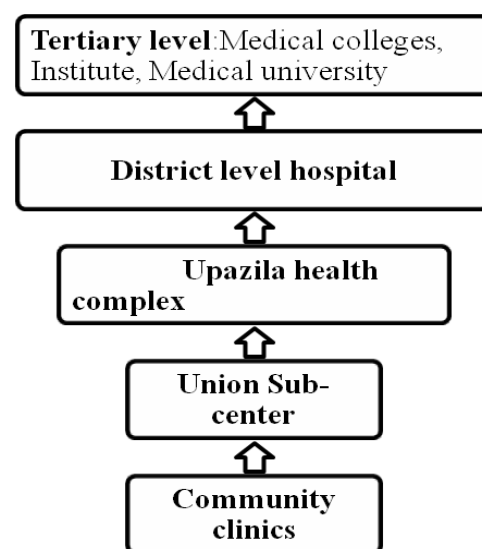


Figure: Health care delivery system in Bangladesh

However, impressive health progress has been imbalanced. Despite progress in human survival and health indicator some other health indicators have lagged behind. One of the important aspects is non communicable diseases in children. As a part of the society we, health professionals are drawing attention to the government, NGOs as well as private sectors and international agencies and affluent people. The exact incidence and burden of CKD in children in Bangladesh is not known. But from a study in 2006¹¹ showed male were more than female which shows similarities worldwide with regards to gender^{14, 26-28} and common age of presentation was 8-12 yrs. In 2005-2007, the number of CKD patients admitted in pediatric nephrology ward, BSMMU was 6%²⁹.

From government point of view

Maternal and child health, Prevention of communicable diseases and Family planning are the priority of health in Bangladesh¹⁸. The physicians could not inform to the authority about the magnitude of the problem and the consequences of ESRD and death of these children. Health professional should raise the issue and explain the health delivery in terms of manpower service, logistics and fund for these CKD children which seem to be quite feasible. Bangladesh needs a comprehensive health policy with a vision for the totality of the health sector. As a steward for the health systems, the Ministry of Health and Family Welfare should come up with an overarching strategic direction for the health sector as a whole encompassing both the public and the private sector. Recently, government has created 43 posts in paediatric nephrology in eight medical colleges all over country and posted all existing qualified and trained pediatric nephrologist. However, more trained personnel and equipments are needed. Further expansion of full range of treatment of CKD will be needed.

Socio-economic point of view

Bangladesh is a developing country with about 43% (66 million) children. The literacy is 60%¹⁶. Moreover, people are not health conscious and don't have a separate budget for health expenditure and the insurance system is not well developed. So, there are high levels of out-of-pocket and informal payments for health services and medicines that are impoverishing millions of households¹⁶. Most of the people do not visit a registered physician for their health problem. Untrained traditional healers, drug sellers, village doctors are their primary physicians. The government expenditure for health is 3.7%¹⁶. Therefore,, economic constrain is an important issue. In spite of that 43 new post are created in pediatric nephrology and so newer experts are posted. More experts are to be created to fill these posts. In near future more post and more experts will be required to tackle the burden of CKD. But there is ignorance and lack of information among the population about the disease as well as knowledge about the availability of the treatment. Patients and there is delay in diagnosis and treatment. Most of the patients we get in the end stage. So, RRT is the choice of treatment. We have limited centers for providing treatment care to the ESRD As per the country concerns about the cost of maintenance hemodialysis US \$ 6000.00/ patient/ year, renal transplant US \$ 6000.00/patient, CAPD- US \$ 8000.00/ patient/ year²⁰. So patients are unable to maintain the treatment cost and give up in the middle. In BSMMU only 10% take regular treatment and drop-out rate is almost 80%. On maintenance hemodialysis one year survival is 80% and rest follow up is not available due to drop out or lost follow up. Another important aspect is the travelling hazard and the distance of the specialized center from the every corner of the country and also cost of travelling and loss of daily earning.

Physician point of view

The number of specialist physicians in pediatric nephrology is very limited. Most of the specialists reside in urban area and it is out of reach for poor village population. There are also some pitfalls in diagnosis of CKD in early stage and most patients come to a late stage as mentioned earlier. As per we concern about diagnostic facility round the country, there are very few reliable center for diagnostic facility and very limited center where all the investigations are available. Private sectors are expensive in comparison to government hospitals in all countries of this region except in Malaysia³⁰. The ratio is most lopsided even in India, with private sector spending being almost 4.5 times than of public sector³¹⁻³². In Bangladesh, the picture is almost same or more. As the rate of investigation is high the common people cannot afford to do investigations which they need. As a result the physicians are also in dilemma to advice an investigation which is mandatory to evaluate the cause and the outcome. Many patients go home or leave without knowing the exact etiology or even the diagnosis. Therefore, economic issue is again a predictor for healthcare delivery.

Future directive and plan

It is unquestionably true that chronic non-communicable diseases are increasing burden on developing countries and also in Bangladesh. Most developing countries lack the resources to prevent and treat chronic disease including CKD. In order to do battle against CKD in our country, the establishment of cost-effective prevention programs is going to be a key strategy. The cost of treatment per annum all CKD children will be only 21hundred million dollars (1680 crore taka) which is manageable by collaboration of government and private sectors and affluent people. It is only less than one percent of our national budget. Economy is progressing and there are good numbers of generous rich people. Of the several hurdles that prevent the implementation of such programs in the country, is the lack of trained manpower. Capacity building therefore should be a priority. Raising public awareness by educating people in CKD prevention and early detection is another key factor to improve outcomes. In developed countries, people can freely access disease information via the Internet and mass media. However, access to these modalities is still limited in the country. Therefore, mass media with the collaboration of the government should play a crucial role to disseminate the information throughout the country. It has been badly needed to share educational tools and support implementation according to the specific requirements of each local region, at least district level. In order to accomplish this mission, developing and implementing evidence-based clinical practice guidelines is the key to success. Furthermore, raising fund from local donors as well as international agencies, training strategy, increase centers, removal of social obstacles and awareness and campaign are the steps that can lead us to the good future for the children suffering from chronic kidney disease in the country. Moreover, we can manage this dreadful

condition by our own economy and own resource, we just need proper planning and utilization of the resource. Strengthening the health system through better management and organization and effective use of resources can improve health conditions and enhance the quality of health care delivery in Bangladesh.

At last there are few suggestions to improve care for these thirty five hundred thousand children and save their lives.

1. Form a national registry for non communicable diseases in the children across the country which can easily be made by the policy of current government 'Digital Bangladesh Program'. Birth registration number or national identification number can be used for the purpose.
2. Establish a national health insurance system which can provide the expenditure in emergency for health care.
3. The government should come forward to import tax free medication so that the poor people can get the drugs at cheapest cost for these CKD patients.
4. The government, NGOs and private (low profit) organizations should increase reliable diagnostic facility, dialysis facility, make the equipment available, train the physician as well as nurses and auxiliary stuffs, decrease the cost of dialysis and establish the facility at least in the every district level government hospitals which is feasible at present economic condition.
5. Create awareness through mass media and electronic media to inform about the disease, available treatment modalities across the country.
6. Encourage people for organ donation.
7. In collaboration with international organizations and NGOs technical advancement can also be made.
8. There are approximately 5-10% people who are very rich in this country. Many of them are generous and can come forward to help by establishing such facilities and extend their hand to prevent and treat such life threatening condition.
9. Small fund allocation in each national budget (taka one thousand crore)

Conclusion

It is not dream but little effort from government, private-public sectors, remodeling of some health policies, focus on need of people, small social involvement, heartily efforts from the professionals and the contributions from the rich, developing some system can save lives of thousands children and make them smile in future.

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