Invited Review Article

# Home Dialysis is a Viable Option for Treatment of Young Infants with End Stage Renal Disease in Pakistan

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## Abstract

Though renal transplant is preferred mode of renal replacement therapy (RRT), peritoneal dialysis (PD) is an important modality of treatment for children with end stage renal disease (ESRD) but it is underutilized in Pakistan despite several advantages over haemodialysis (HD). The burden of paediatric chronic kidney disease (CKD) and ESRD is under reported, since majority of children (24-63%) present with acute on chronic kidney disease often complicated by multiple co-morbid conditions which may result in death before consideration of long term RRT. In Pakistan, the available care of ESRD/CKD is exclusively hospital based rather than home based dialysis. Manual PD is used as first line option of treatment for acute kidney injury (AKI) or acute on CKD at few centers and long term maintenance PD is not offered at all as first line option of treatment for children with ESRD. Generally, long term PD is less expensive than HD or at least as expensive as HD. This holds true even for most of the developed countries using automated cycler machines but scenario in developing countries like Pakistan is quite different. HD is the only option offered to older children for short period and very few of them become successful to get a renal transplant. Home dialysis or Continuous Ambulatory PD (CAPD) may be the only option to treat young infants to make them free of complications of uraemia and provide adequate nutrition for growth till either HD or transplant become possible. This may be possible once paediatric and adult nephrologists as well as pediatricians recommend and advocate this option for survival of children with ESRD. Furthermore, we need to strengthen the existing RTT facilities and develop more paediatric peritoneal dialysis centers; local production of dialysis fluid and disposables or government should allow free import of PD equipments and solutions. This will not be possible without efforts of all of us including professionals, dialysis nurses or technicians, media persons, pharma industry and community workers as well as parents.


**Keywords:** Chronic kidney disease, end stage renal disease, Continuous Ambulatory Peritoneal Dialysis, home dialysis

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## Introduction

The Non-Communicable Disease (NCD) Child Network has adopted the advanced policies and interventions for prevention and management of NCD including CKD[1]. This has also been incorporated in Sustainable Development Goals (2015) by United Nations with target on reduction of child mortality by 2030[2]. Chronic kidney disease has emerged as a global public health problem and a key determinant of poor health outcomes[3]. CKD is an irreversible and progressive damage initiated by various risk factors which ultimately lead to ESRD[3,4]. Children with CKD are at high risk of morbidity, mortality, and have decreased quality of life[5]. These children die due to either cardiovascular or infectious complications rather than from renal failure itself. Children with early stages of CKD may or may not have symptoms or they may have symp-

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toms and signs of primary disease responsible for CKD[6].

Kidney Disease Improving Global Outcome (KDIGO) recommends classifying severity of CKD in to five stages (based on estimated glomerular filtration rate), with stage 1-2 are considered as mild, stage 3-4 as moderate kidney failure with (symptomatic and requires treatment). CKD stage 5 is known as end stage renal disease (ESRD) which means complete and permanent loss of kidney function and dialysis or renal transplant is the only option for survival[7].

Children with ESRD are usually symptomatic in the form of growth failure, vomiting, loss of appetite, difficulty in respiration, altered level of consciousness and convulsions. They may have symptomatic hypertension, severe anaemia, and bony deformities with walking difficulties[6]. Mostly these children are on restricted diet (low salt, less dairy products, low potassium foods), on multiple medications (bicarbonate, iron preparation, calcium carbonate, vitamin D and water soluble vitamins, antihypertensive or antibiotics) and blood forming or calcium raising injections (synthetic erythropoietin or active vitamin D like Calcitriol)[7,8].

They require frequent follow up for growth and blood pressure (BP) monitoring, blood testing for haemoglobin, urea, creatinine, electrolyte, calcium, phosphorus and alkaline phosphatase. In addition, we need to monitor their iron profile, parathyroid hormone level, vitamin D level and X-ray hand at 6-12 months' interval to exclude iron deficiency and secondary hyperparathyroidism. They often require hospitalization for complications of ESRD. Patients on dialysis need to visit more frequently than those who are on non-dialytic treatment[6,7].

Though dialysis and kidney transplantation are the effective treatment options for ESRD children, but due to high cost, non-availability of dialysis facility, technical experts and disposables for dialysis in children, lack of transplant facilities and lack of willingness of parents for donating kidneys in the developing countries including Pakistan result in dismissal outcome[8-10]. This form of treatment options (dialysis and transplant) are for those children who are symptomatic and are in advanced stage of CKD/ESRD, which is merely the tip of the iceberg of a large number of asymptomatic diseases in early stages of CKD in the community.

**The Burden of Chronic Kidney Disease and ESRD in Pakistani Children**

Globally 8-12 % of population and 11-16% of US adults are estimated to have chronic kidney disease in 2015[11-13]. In a recent review, it has been estimated that 2.6 million patients were receiving renal replacement therapy with 80% on one or other form of dialysis . A high prevalence of ESRD between 200-300 million age related population has been reported from high income countries[14]. In Pakistan, community based study showed that 11.4-14% of adult population had CKD[15]. In developing countries, the prevalence of ESRD in paediatric population is underestimated and is facility based due to late arrival and multiple co-morbids which leads to early deaths before dialysis[9,10]. The ESRD in paediatric population varies from 12% - 25% in India whereas in Pakistan, the prevalence of Paediatric CKD ranges from 14-30% but exact prevalence of ESRD is not known[16-18]. However, prevalence of dialysis and transplantation in developing countries are 6-12 and less than 5 per million child population respectively[9,10,19].

Since dialysis and kidney transplantation is the only option for survival of children with ESRD. So it is important to know that what options of dialysis are available, their utility, various hurdles and their possible solutions in our circumstances.

**Dialysis**

Broadly dialysis is a form of kidney support therapy in which blood is cleaned from the accumulated waste products (urea, creatinine) in patients with failed kidneys, which otherwise are excreted by the kidneys. Dialysis occurs by transport of solutes and solvents by three important processes, diffusion, ultrafiltration and absorption Fig. 1 (b).

Renal Support Therapies (RST) is of either intermittent or continuous based on duration of therapy. The duration of intermittent therapy is less than 24 hours whereas continuous therapy runs for 24hours. Intermittent therapies include intermittent haemodialysis (HD) and continuous therapies are all forms of peritoneal dialysis (PD) and continuous renal replacement therapy (CRRT) which is a form of extracorporeal blood purification used for acute kidney injury over 24 hours per day[8]. Renal support therapies are used as either acute treatment in temporary kidney failure or as maintenance therapy (long term) in patients with ESRD awaiting for kidney transplantation. Here, a brief introduction of HD, followed by more details of PD used both in children and adults is given.

**Haemodialysis**

Haemodialysis (Fig. 2) is form of dialysis in which a machine, vascular access (either double lumen catheter or arteriovenous fistula), extracorporeal circuit (blood tubing and dialyzer), dialysis solutions (Bicarbonate) and purified water are required to accomplish the job of kidneys when they fail to work. In this mode, blood from the patient is taken through the extracorporeal circuit to the dialyzer (artificial kidney) with the help of blood pump where exchange of solutes (urea, creatinine) and solvent (body water) taked place by the process of diffusion and osmosis to clean the blood and after cleaning it is returned to patient (Fig 2).[20] We need a Reverse Osmosis System (ROS) of water purification by which toxic chemicals (like aluminum) and bacteria are removed before water is mixed with dialysate in 32:1 to make a final form of dialysis solution[20,21].

Haemodialysis is commonly performed in hospitals or dialysis centers and it is scheduled as 3 days per week and each session of 4 hours duration depending upon need of patient and availability of machine. It also requires trained dialysis technician and availability of water and electricity. HD is not suitable for too sick children with hypotension and in young infants it is technically difficult to accomplish due to difficult vascular access as well as non-availability of small sized dialyzers and tubing. HD in infants need experienced dialysis nurse/technicians[20-22].

**Peritoneal Dialysis**

Another mode of renal support therapy used for both either temporary or permanent kidney failure in adults and children is peritoneal dialysis (Fig 3). For peritoneal dialysis, we need three major components; the peritoneal membrane (anatomic structure) along with the peritoneal microcirculation, peritoneal access (peritoneal catheter) and the dialysis fluid (dialysate). First and foremost is the intact and functioning peritoneal membrane and peritoneal cavity. Peritoneal cavity has a large surface area equal to body surface area of child and 30-60% of its surface remains in contact with dialysis fluid during dwell period of peritoneal dialysis exchange.

*Dialysis solution* is composed of high concentration of glucose to create osmotic gradient required for ultrafiltration and a buffer (bicarbonate ) for correction of metabolic acidosis and electrolytes (Na, Cl, lactate) to maintain electrolyte homeostasis[8,20,21]. Third component of PD is the well functioning peritoneal access which may be temporary or permanent one. Temporary peritoneal access is used for acute kidney injury for emergency dialysis or short term PD. In developing countries like our center at National Institute of Child Health (NICH), a rigid disposable catheter is inserted into peritoneal cavity at bed side by doctor and PD exchanges are done for 3-5 days using rapid exchanges (hourly cycles). This is associated wtih high risk of infections, leakage and drainage failure[21-23].

For long term PD, the permanent access is placement of PD catheter. This catheter implantation is made by either surgical (Fig. 4b) or laproscopic technique or subcutaneous insertion of a soft silicone tube, commonly known as Tenckhoff Catheter (Fig 4a)[20,24,25].

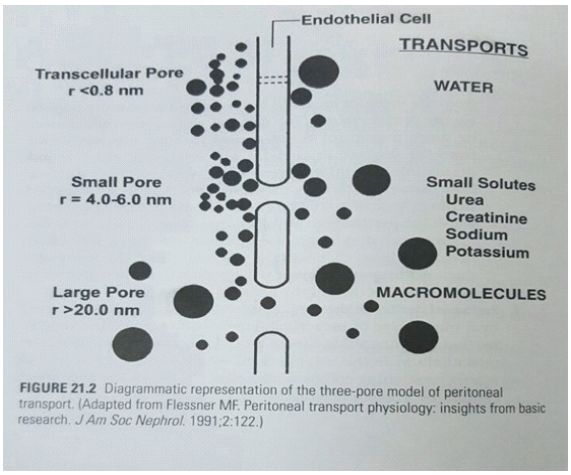


**Fig 1(a).** Three -pore model of peritoneal transport

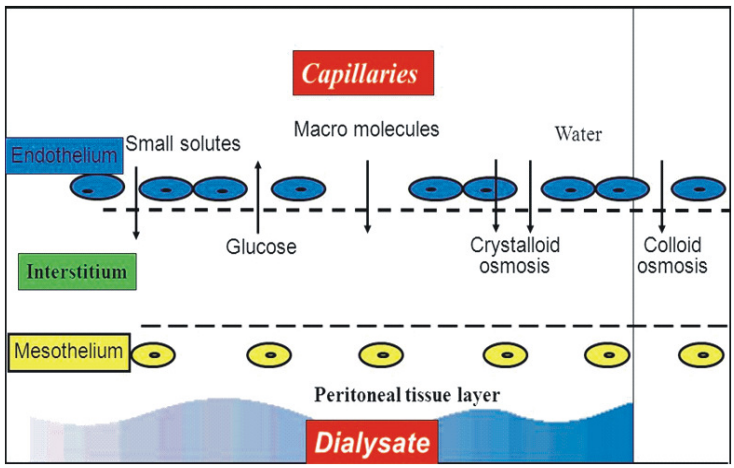


**Fig 1(b).** Peritoneal Transport physiology (modified from www.baxter.org)

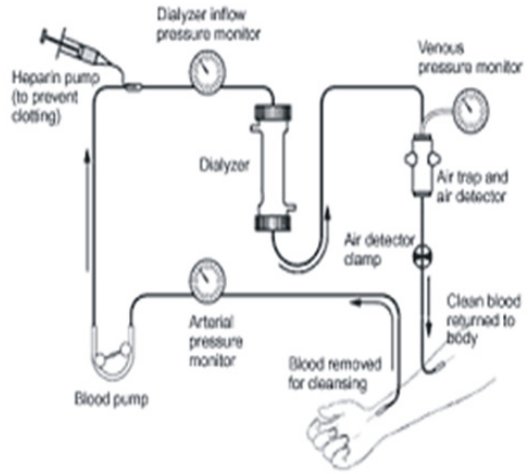


**Fig 2.** Hemodialysis circuit

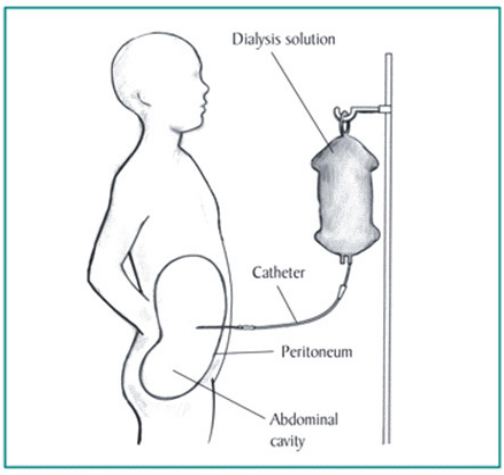


**Fig 3(a).** Peritoneal Dialysis

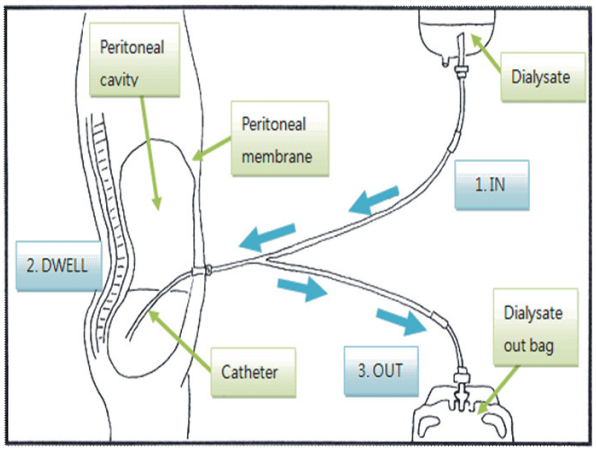


**Fig 3(b).** Diagrammatic Representation of PD system .From www.childrenkidneyfund.org

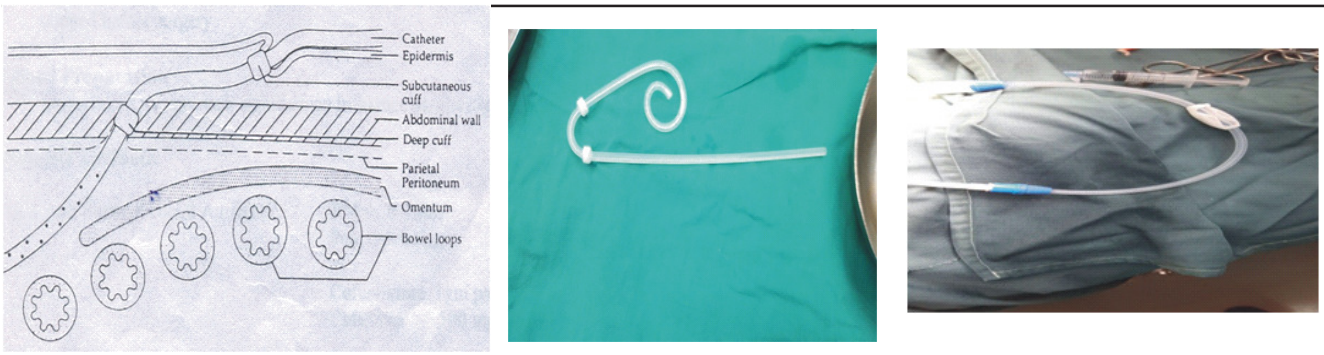


**Fig 4(a).** Diagram of straight PD catheter, Swan neck double cuff curved catheter & catheter extension tube

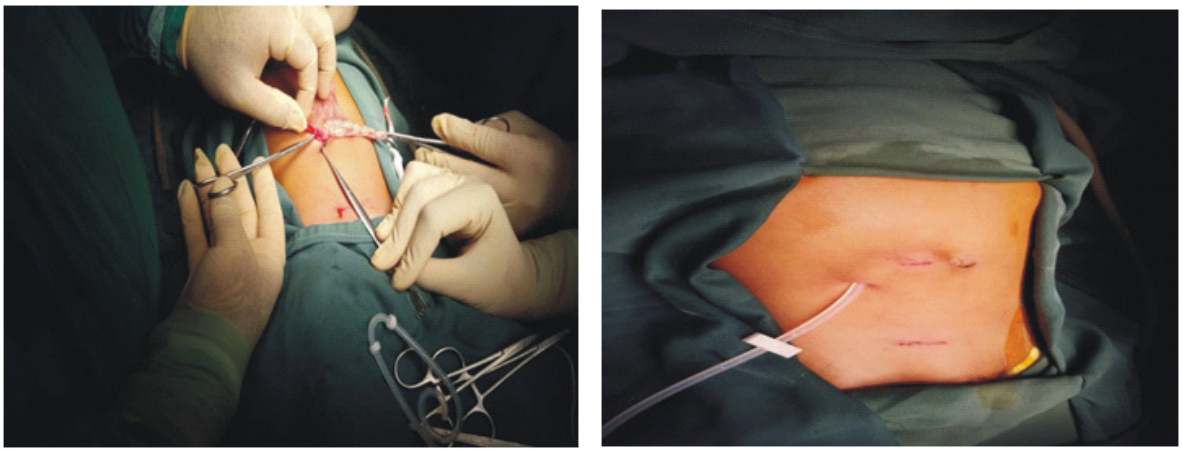

**Fig 4(b).** Peritoneal Catheter Implantation( 1)Removal of omentum (2) Exit site and catheter insertion site

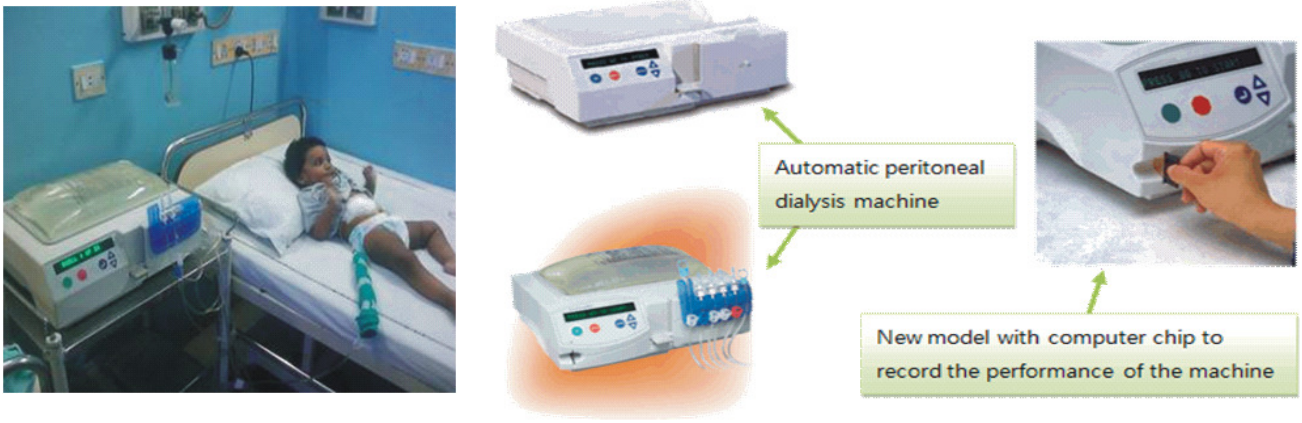


**Fig 5**. Automated Peritoneal Dialysis machine/PD Cycler

(a): Child on Automated P D Cycler (Baxter) (b) Types of cycler machines

**Table 1.** Factors to be considered for Peritoneal Dialysis in Children

| Acute or short term PD | Long term Peritoneal dialysis |
|---|---|
| *Clinical Indications* | *Clinical Indications* |
| Encephalopathy | Contraindication to anticoagulation |
| Pulmonary edema/Congestive Cardiac Failure | Cardiovascular instability |
| Severe metabolic acidosis | Hypertensive cardiomyopathy |
| Anuria for more than 24 hours | No vascular access for HD |
| *Laboratory parameters* | *Socio-economical Conditions* |
| Severe hyperkalemia(7.5 meq/L | Parental education and choice |
| Urea (>250mg/dl)/ Cr (>3 mg/dl) | Parental commitment |
| Acidosis(Ph(<7.2,HCO3<10 meq/L) | Young age and growth failure |
| *Technical consideration* | Developmental status and schooling |
| Experienced technical staff | Liberal water and dietary intake |
| Dialysis disposables | Financial Support -Public, Non-Government Organization |
| Dialysis solution | *Technical Consideration* |
| Elective/ Emergency procedure | Dialysis facility and trained staff |
| | Peritoneal access/ Arteriovenous Fistula |
| | Contradictions: Diaphragmatic or inguinal hernia, omphalocele, gastroshisis and bladder extrophy |

*Peritoneal Dialysis Exchange:* In PD, a selected volume (10-40 ml/kg) of PD solution is instilled into the peritoneal cavity through catheter connected with extracorporeal dialysis system and after dwell (hours) it is drained. This is called PD exchange or PD cycle[8,20].

*Physiology:* PD is a process of exchange of solute and fluid between peritoneal capillary blood and dialysis solution in the peritoneal cavity across the peritoneal membrane. In this process solute movement occurs by diffusion and convective transport whereas fluid moves by osmosis created by an osmotic agent (glucose) in PD solution.This removal of fluid from the body is called ultrafiltration[20]. Peritoneal membrane act as a barrier across which transport occurs and is made up of *capillaries, interstitial and meothelial layers*. The process of diffusion and osmosis uses three-pore models for transport of solute and water mediated by pores of different sizes (Fig 1a). According to this model, the peritoneum is characterized as a three-pore membrane with few water-exclusive ultra small pores (aquaporins, ~1-2 % radius 2-4 Å), small pores (90-95 %, radius 40-60 Å), and a large pores (~5 %, radius 200-300 Å)[20,21].

*Long term Peritoneal Dialysis:* The long term maintenance PD is commonly called Home Dialysis, though now a day's hemodialysis is also performed at home with portable ROS and HD machine. Home dialysis can be performed by two methods, one advanced form in developed countries using automated PD Cycler (a computerized hydraulic machine) which performs dialysis after feeding a prescription of particular patient over a specified period usually 8-12 hours at night during sleep (Fig 5 a,b) or another more simplified performed manually at home by the parents/patient himself known as CAPD[24,26]. The latter form of dialysis consists of 4 standard exchanges (cycles) per day, at early morning (before school time), afternoon/mid day (after school), evening and at bed time. This form is called continuous since it works for 24 hours a day, ambulatory because patient can move around and can do routine activities and schooling[20-23].

*When to initiate long term dialysis?* National Kidney Foundation-Kidney Disease Outcome Quality Initiative (NKF-KDOQI) and KDIGO guidelines recommend to consider long term dialysis in a patient with CKD-stage 5 (GFR<30ml/min/

1.73m$^2$)[8,20,26]. Preparation for RST includes counseling of parents regarding modality selection, dialysis access preparation and advantages and disadvantages of modality, social and financial support and close follow up with nephrology and dialysis team[27-29]. It may be initiated earlier in any patient who is symptomatic or when residual GFR declines to <15ml/min/1.73m$^2$. Early dialysis in children may prevent malnutrition, growth retardation and better long term out come[21]. Factors to be considered for selection of dialysis modality are listed in Table 1[30-33]. There are certain conditions like cardiovascular instability, in which HD may not be possible and in certain surgical conditions like bladder extrophy PD will not be possible.

*Home Dialysis in children:* Home dialysis is a standard mode of treatment for infants, children and adults with end stage kidney failure in many developed and developing countries including India and Pakistan[28-31]. In this method of treatment, either patient or one of parents of children with kidney failure does peritoneal dialysis at home after training by dialysis team. Parents are trained to do safe, exchanges, modify prescription and take care of exit site as well as how to take care of common problem[30-32].

**Peritoneal Dialysis Facility in Pakistan:** There are very few centers which offer dialysis in children but occasional in young infants. Some public sector hospitals are dialyzing children above 3 years of age or above 15 kg by haemodialysis including Sindh Institute of Urology and transplantation (SIUT), National Institute of Child Health (NICH) in Karachi and Institute of Child Health and Children Hospital, Lahore. Few private centers are also dialyzing older children for acute kidney failure and for ESRD on long-term basis. In case of emergency, acute manual PD is performed at many teaching hospitals of Punjab, Sindh and Khyber Pukhtonkhuwa[34].

**What is the outcome of young infants with ESRD in Pakistan?** There is no definite data to give the estimate of outcome of young infants who either arrive late or die on way to hospital during initial visits or who has been dialysis once or twice as acute manual PD. But it is very sad and unfortunate scenario in Pakistan that we are losing almost all children either early in the hospitals or after discharge from hospital after counseling that we (doctors/hospitals) can give hope to parents for their loved ones without long term dialysis which is not available in public sector hospital and not affordable by parents. This type of counseling is mostly done in all public or private centers after one or two-time acute manual peritoneal dialysis. These children usually die of infection, cardiovascular or metabolic complication.

**What are the hurdles in growth of CAPD in Pakistan?** Currently dialysis disposables including PD catheters and dialysis solution for long term CAPD are not available in Pakistan, not only in public sector hospitals but also in private centers. CAPD disposables are only available for adults by Lahore based company, Fresenius Medical Care. This is the only company working in dialysis for more than two decades but still struggling for its survival. This is due to multiple factors[28-30]. Disposables are costly, made in Germany, dialysis solutions are also not made locally and not approval by the government and are imported. Also medical professional community is not well known to CAPD mode of renal replacement therapy and its utility. This is because of major complication of repeated episodes of peritonitis and ultimately catheter removal and thus failure of treatment. Children may die after attempts of CAPD so why such futile exercise should be done. This is a general view of not recommending CAPD or no interest of nephrology and urology community. Majority of haemodialysis centers are either government funded or running with philanthropist support and officials involved do recommend hemodialysis rather than CAPD (home dialysis). Another major hurdle is lack of trained dialysis staff in pediatric dialysis care which needs urgent attention of policy makers and involved medical community. Other hindering factors for home dialysis in addition to non-availability of dialysis solution, dialysis disposables are sociodemographic characteristic of community[9,10].

Majority of children are from far distant areas (difficult to follow up and travel), with lack of education specially mothers (for training of home dialysis), water supply(essential for hand washing to prevent infection) and electric supply, and a separate room in house with electric supply.

**Is there any hope of survival for children with ESRD in near future?** This depends upon priorities of government officials and policy makers. No doubt our priorities are treatment and prevention of infectious diseases by vaccination and treatment of cases, maternal and child nutrition and neonatal mortality. We know that though new methods and new technologies are difficult to understand and handle but not impossible if we change ourselves for good outcome.

This year 11th World Kidney Day, march 2016 was celebrated with special focus on childhood kidney disease and kidney diseases have been decleared as antecedent of adult kidney disease particulary ESRD.

Following are the suggested solutions to promote CAPD and improve survival and growth of young infants, till they get kidney transplant or put on long term haemodialysis after certain period of CAPD.

1. Creating awareness and training of medical personals including nurses, technicians.

2. Development of CAPD centers in different cities with mobile teams for coordination between dialysis center and parents doing home PD.

3. Local preparation of dialysis solution and disposables at low cost.

4. Provision of dialysis facility at all tertiary care centers

5. More companies should be registered for provision of CAPD disposable like Baxter and Fresenius Medical Care in India

6. Most important is motivation of our philanthropists to support home dialysis programs and in establishing dialysis facility, provision of dialysis solution, disposables, medications and laboratory tests.

**Peritoneal Dialysis Facility at National Institute of Child Health, Karachi**

*Acute Peritoneal Dialysis:* Acute manual PD is performed 24 hours a day in emergency cases in all children except new borns. This is a simple live saving procedure, done at bed side by even junior doctor. This is a common initial treatment of acute or acute on chronic kidney failure practiced at the institute for the last 20 years.

*CAPD in Children:* We have performed CAPD in about 10 selected children and now we are planning to enroll more children below 3 years for CAPD till they grow enough for transplantation, with the help of philanthropists/donors from this community. Currently we have two kids on CAPD.

## Conclusion

Despite many hurdles like dialysis facilities and trained technical staff, availability of dialysis disposables and solutions, risk of peritonitis and catheter associated infections, sociodemographic conditions like rural and far distance living, poor financial capacity and lack of education among parents, CAPD is still a viable option for young infants with ESRD and should be promoted by all of us.

## Conflict of Interest

Author has no conflict of interests and no grant/ funding from any organization for this review.

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