A review of acute and chronic peritoneal dialysis in developing countries

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Abstract
Various modalities of renal replacement therapy (RRT) are available for the management of acute kidney injury (AKI) and end-stage renal disease (ESRD). While developed countries mainly use hemodialysis as a form of RRT, peritoneal dialysis (PD) has been increasingly utilized in developing countries. Chronic PD offers various benefits including lower cost, home-based therapy, single access, less requirement of highly trained personnel and major infrastructure, higher number of patients under a single nephrologist with probably improved quality of life and freedom of activities. PD has been found to be lifesaving in the management of AKI in patients in developing countries where facilities for other forms of RRT are not readily available. The International Society of Peritoneal Dialysis has published guidelines regarding the use of PD in AKI, which has helped in ensuring uniformity. PD has also been successfully used in certain special situations of AKI due to snake bite, malaria, febrile illness, following cardiac surgery and in poisoning. Hemodialysis is the most common form of RRT used in ESRD worldwide, but some countries have begun to adopt a ‘PD first’ policy to reduce healthcare costs of RRT and ensure that it reaches the underserved population.

Keywords: acute kidney injury; earthquake; intensive care unit pediatrics; peritoneal dialysis

Illustrative case report

A 16-year-old girl, weighing 40 kg, with body mass index of 15 kg/m2 with idiopathic dilated cardiomyopathy underwent orthotopic allograft heart transplant on 09 August 2014. She was inducted with basiliximab, and immunosuppressants included prednisolone, tacrolimus and mycophenolate mofetil. Her preoperative creatinine was 1 mg/dL, and on post-operative day 3, she developed right heart failure with pulmonary arterial hypertension and prolonged oliguria. Using double-cuffed swan-neck Tenckhoff peritoneal dialysis (PD) catheter, she was initiated on acute PD using Dianeal solution (Baxter healthcare) with a dwell volume of 700 mL and dwell time of 60 min. Her mean dwell volume throughout dialysis was PD in ~7000 mL and PD out ~9000 mL for 24 h. Intermittent manual PD was continued from post-operative days 4 to 13. Serum creatinine was 0.6 mg/dL on Day 21, urine output 1.7 L/day and blood pressure 110/70 mmHg. Current echocardiogram shows adequate left ventricle function with ejection fraction of 60%. She developed ventilator-associated pneumonia due to Klebsiella pneumonia, which responded to intravenous meropenem. PD was a rescue therapy for a cardiac transplant patient with cardiorenal syndrome requiring renal replacement therapy (RRT).

In developing countries, PD has been successfully used to treat both acute kidney injury (AKI) and end-stage renal disease (ESRD). Despite a number of advantages that will be reviewed here, PD still remains underutilized. PD utilization in the intensive care setting varies from no usage at all in some developed nations to ~46% in developing ones [1] where the lack of hemodialysis facilities [2], ease of implementing dialysis and economic considerations make this modality attractive [3, 4]. However, every year several million patients die in developing countries because of the lack of access to RRT to treat AKI or ESRD. Wider availability and use of PD could help mitigate this problem. We now review the current situation and perspective of PD use in the developing world.

Peritoneal dialysis in AKI

AKI is defined as an abrupt decline in glomerular filtration rate (GFR) resulting in progressive elevation of plasma urea and creatinine and is an important cause of morbidity and mortality worldwide [5]. Due to vagaries of nature, overcrowding and poor socioeconomic factors, AKI is common in developing countries but there is no reliable registry data on the incidence, prevalence, causes and recovery from the disease [6, 7]. AKI is a major cause of morbidity and mortality in critically ill patients and aging population in developing countries. About 30% of patients admitted to intensive care unit (ICU) develop
hemodynamic instability, cardiorenal syndrome and sepsis [8, 9].

Dialysis modalities used in AKI are hemodialysis (HD), continuous renal replacement therapy (CRRT) and acute PD either manually or with automated machine in advanced centers. PD is practised for AKI treatment mostly due to its cost effectiveness, minimal infrastructure requirement and in rural areas where access to power, clean water supply and facilities for water treatment are lacking as in many developing countries where renal replacement centers are mainly located in major cities and towns [10, 11]. The availability of safe dialysis fluid in collapsible bags and easy procurement of stylet and flexible catheters has made PD an accessible and effective method for AKI treatment. PD does not require machinery and highly skilled persons for carrying out the procedure. PD can be invaluable at times when a major catastrophe damages the infrastructure such as earthquakes and flash floods [12]. During disasters, crush injuries are the second most common cause of death after direct trauma, and PD can save lives [13, 14]. In the wake of the Haiti earthquake in January 2010, Bartal and colleagues have suggested an algorithm to follow which includes PD [15]. The recent consensus guidelines published by ISPD on PD for AKI are an important step in providing RRT uniformly [16]. PD helps in better preservation of local renal hemodynamics and may be more physiologic and less inflammatory than HD due to the absence of contact between blood and synthetic membrane. PD is still an underutilized modality in developed countries for reasons that are unclear and they resort to CRRT, though doubts have been cast on the superiority of CRRT in multivariate analysis [17]. CRRT requires multiple accesses to blood stream in critically ill patients, which predisposes them to blood borne infections in less ideal situations in developing countries. PD is hemodynamically friendly and requires only a single access to peritoneal cavity, and fluid removal can be smoothly achieved by altering the concentration of glucose in the dialysis fluid. Continuous glucose absorption provides nutritional benefits to the critically ill patient.

Techniques of acute PD

There are five types of acute PD namely acute intermittent peritoneal dialysis (AIPD), continuous flow peritoneal dialysis (CFPD), continuous equilibration peritoneal dialysis (CEPD), tidal peritoneal dialysis (TPD) and high volume peritoneal dialysis (HVPD). These different techniques are used according to patient requirement and facility preference. The urea clearance is 8–12 mL/min for AIPD, 15 mL/min for TPD and 30–35 mL/min for CFPD [18] (Table 1) [19].

Types of PD catheter

There are two types of PD catheter (Figure 1).

(i) Rigid catheter: it is cheap and easier to insert; however, there is a slightly increased risk of peritonitis, catheter dysfunction and poor dialysate flow when compared with a flexible catheter.

(ii) Flexible catheter: it accommodates a higher dialysate flow rate but it has a higher cost; however, locally manufactured in India by the first author has brought down the cost substantially. Swan neck configuration prevents catheter migration from the pelvis. This can be inserted at bedside using a trocar or a peel-away sheath technique.

The approximate cost of PD per day in developing countries includes cost of fluid (US$24 to 27), catheter (Stylet-12 mL/min for AIPD, 15 mL/min for TPD and 30–35 mL/min for CFPD [18] (Table 1) [19].

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<th>Table 1. Techniques of PD for AKI [19]</th>
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<td><strong>Technique</strong></td>
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Fig. 1. (A) Rigid catheter in PD. (B) Flexible swan neck catheter used in PD.
implantation charges. In comparison, cost of CRRT access, fluids, equipment and trained personnel is higher (US$400 to 800) per day. Total cost of intermittent HD including consultation per day comes to around US$104, with access US$66 and daily dialysis cost US$38. Professional reimbursement varies depending on whether it is done under a free scheme or a profit-oriented corporate hospital sector.

**ISPD guidelines for PD in AKI**

ISPD guidelines state that PD should be considered as a suitable method for RRT in AKI [8]. Flexible peritoneal catheters should be preferred over rigid catheters when available. Catheter insertion by a nephrologist is safe and functional results equal that of surgical insertion. The Cochrane systematic review of 2004 indicates that use of preoperative prophylactic antibiotics such as first generation cephalosporins or vancomycin reduces the incidence of peritonitis among PD patients [20].

In multi-organ failure and shock, it is appropriate to insert PD catheter at bedside. ISPD recommends use of PD fluids with bicarbonate as the buffer in patients with shock or liver failure as they are at high risk of accumulation of lactate and worsening metabolic acidosis.

Fluid overload is to be avoided, and ultrafiltration can be increased by raising the concentration of dextrose and shortening the cycle duration. Targeting a weekly Kt/V of 2.1 may be acceptable. CFPD can be considered when an increase in solute clearance and ultrafiltration is desired.

**PD in neonatal and pediatric AKI**

AKI is seen in 3–5% of patients in pediatric and neonatal ICUs and is associated with higher mortality [21]. PD should be the treatment of choice in neonatal and pediatric AKI. The common indications for PD are AKI due to acute diarrheal illness, septicemia and hemolytic uremic syndrome. The peritoneal surface area per unit weight is twice that in rheal illness, septicemia and hemolytic uremic syndrome.

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PD use should be adjusted according to the patient’s needs [21]. It is recommended to use frequent, continuous low volume (10–20 mL/kg body weight, 300–600 mL/m²) exchanges with adequate ultrafiltration rate [21]. This recommended approach has been beneficial in preventing dialysate leakage and lung compression. Short dwell times of ∼20 min have been effective in infants, but there is a risk of sodium sieving. ICU nurses can be taught by a PD nurse specialist to perform manual exchanges quickly. However, patients in ICU frequently experience multi-organ failure, hypercatabolism and shifts in volume status, and hence, dialysis adequacy must be cautiously monitored and defined [21]. As in patients with cirrhosis, neonates and infants should also preferably be dialyzed with PD fluids with bicarbonate buffer only as the metabolism of lactate is impaired in this population.

**PD in AKI in adults**

PD has been found to be an adequate form of treatment for AKI occurring as a result of snake bites especially the Russell’s viper, malaria, leptospirosis, gastroenteritis, febrile illness, sepsis, acute pancreatitis, rhabdomyolysis, hepato-renal syndrome, following cardiac surgery and poisoning such as barbiturates, lithium, ethylene glycol and boric acid [22–25], more so when hemodialysis facilities are not immediately available though the two modalities have never been compared.

Dr. Sergio et al. compared the use of PD for AKI in ICU and ward settings in Europe, Asia and North America by administering an anonymous self-administered questionnaire distributed to attendees at three dialysis meetings in 2009 [26]. Though half of the respondents felt that PD was a suitable modality for most AKI patients admitted in the ward, there was a marked discrepancy in opinion and reality as only 22% were actually using the modality. Both in the ICU setting and in the wards, PD was used in ∼46% in Asia-Pacific/Australasia regions and to a far lesser extent in Europe and North America, 18.9 and 12.2%, respectively. In addition, most of the physicians irrespective of their respective continent were unsure about the adequate PD dosing for AKI.

In our tertiary care center, we prefer PD over HD in acute settings such as heart failure, hemodynamic instability, bleeding diathesis and cholesterol atheroembolic disease. Extra-corporeal therapies in patients with significant cardiac disease can lead to electrolyte disturbances, hypotension and poor myocardial function, which are less likely while using PD. Those patients may also require thrombolysis and other interventions which are hurdles while contemplating extra-corporeal therapies. We retrospectively analyzed the outcome of AKI using PD as a cost-effective modality for AKI patients with myocardial infarction, cardiogenic shock and cardiac dyssrhythmias. PD was provided for 84 patients with cardiorenal syndrome type 1 among 6687 patients admitted to the coronary care unit (CCU) over a period of 36 months. Males were 64% and mean age 59 ± 11 years. The mortality rate was 14%. Of the remaining 72 patients, we observed functional recovery in 68 patients (81%) and 4 (5%) patients were transferred to temporary HD because of exit site leak. Complications were exit-site leak in eight patients (9.5%) that was less frequent with a swan neck double-cuff Lenckhoff catheter (1 of 43, 0.023% versus 7 of 41, 0.17%; P = 0.021). None developed peritonitis. We observed a decrease in serum creatinine by 47% (P < 0.0001).

Advanced age, poor cardiac function, hypercatabolic stage, hemodynamic instability and diabetes mellitus are associated with poor outcome in AKI patients. Appropriate volume control by monitoring ultrafiltration with minimal hemodynamic disturbance and using aseptic techniques with use of dialysis fluid in collapsible bags can favorably influence the outcome of AKI in the CCU setting. Management of reversible AKI by early detection and use of PD is feasible, effective and affordable [27].

The major question raised regarding PD in AKI was in 2002 by an open–labeled, randomized study from Vietnam, which showed a higher mortality rate in AKI patients treated with PD than that in patients treated with continuous venovenous hemofiltration (CVVH) (47 versus 15%, P = 0.005) [3]. Another prospective, randomized crossover study showed acceptable outcome of both TPD and CEPD in treating hypercatabolic AKI in developing countries although concerns were expressed about the use of PD in hypercatabolic AKI patients [28] since only TPD achieved adequacy as per guidelines but there was excess protein removal. Gabriel et al. [29] in a prospective, randomized, controlled trial showed there is no significant difference in the rate of infectious complications observed between HVPD group and intermittent daily HD group. HVPD group patients received two-liter exchanges (36–44 L per day over 18–22 exchanges) adjusted to prescribe a Kt/V of 0.65 per day. Both HVPD and intermittent daily HD lead to low serum albumin and declined equally in both modalities. The mortality rate was not significantly different (58% for HVPD versus 53% for intermittent HD), nor was the rate of renal recovery [20].
George et al. in an open-labeled, randomized trial compared PD with continuous venovenous hemodiafiltration (CVVHDF) by emphasizing uremia correction, electrolyte and acid base disorders and correction of fluid overload [30]. Urea and creatinine clearance was higher with CVVHDF than PD. PD showed better control of acid-base balance as compared with CVVHDF. Fluid correction was faster with CVVHDF. Both modalities showed a similar result with respect to correction of hyperkalemia and hemodynamic instability. PD was extremely cost-effective as compared with CVVHDF with no difference in mortality (84% in CVVHDF group versus 72% in PD group (P = 0.49).

Limitations of PD in AKI

Though cheap, easy and reliable, PD has limitations in the treatment of AKI [31], the most important being its need for an intact peritoneal cavity with adequate peritoneal clearance capacity and its less efficacy for severe acute pulmonary edema and in life threatening hyperkalemia. Unlike HD, ultrafiltration and clearance cannot be exactly predicted in PD and its adequacy is of some concern in hypercatabolic patients. In CCU settings where patients are on ventilation, PD using high volume may impair diaphragmatic movement and this should be taken into consideration while profiling the patient. The buffer used is rarely bicarbonate, and there is concern about protein loss and hyperglycemia. The effective peritoneal blood flow in uremic patients during dialysis is 100 mL/min [32] and cannot be increased as in the case of CRRT and HD. However, it must be emphasized that in nearly all the above-mentioned situations, PD may be tried as the initial RRT modality and prescription adjusted to get optimum dialysis and ultrafiltration.

Contraindications to PD in AKI

The contraindications of PD in AKI are similar to those in CKD, namely, a large pleuroperitoneal communication, recent abdominal surgery and a history of multiple previous abdominal surgeries leading to peritoneal adhesions

Peritoneal dialysis for chronic kidney disease

In 1894, Starling from Guy’s Hospital, London, first documented the principles of PD when he observed that concentrated saline in the peritoneum withdrew fluid from capillaries, dilute saline did the opposite and isotonic saline did neither [33]. It is a lesser known fact that PD was the earliest modality of RRT to be attempted for chronic kidney disease (CKD) when 33-year-old Ms. Mae Stewart was kept on PD for 7 months [34]. PD has come a long way since then being used for about four decades with >250,000 ESRD patients worldwide [35]. Due to increasing life expectancy, risk factors and screening, there has been an increasing prevalence of CKD and ESRD [36].

PD as ‘first choice’ for ESRD patients

Unfortunately, PD and HD are often contrasted rather than their complementary roles understood. Use of PD as ‘initial’ RRT modality is probably advantageous for more patients than utilizing this modality presently, probably because of better survival in initial 2 years. Flexibility of schedule, freedom from mandatory hospital visits thus saving time and convenience of doing dialysis at one’s own home are compelling reasons to start PD [37]. Patients on PD are free to pursue careers, travel around and engage in social activities without illness intrusion. With improvements in technique, PD-related infections are declining whereas they are increasing in HD patients. The risk of septicemia, hospitalization and death thereby are higher in HD patients [38]. Transplant recipients previously on PD are likely to have faster decline in plasma creatinine, less likely to develop delayed graft function [39] and are at lower risk of death and graft failure [40], making PD the preferred modality in prospective recipients. In most patients, PD permits initial preservation of residual renal function (RRF) with the native kidneys’ contribution to improved middle molecular clearance, fluid status, cardiac function, nutrition, hemoglobin levels, bone-mineral metabolism and quality of life [41].

Survival of ESRD in patients on PD

Survival on PD was believed to be superior in initial 2 years and HD scoring thereafter [42], but the data had residual confounding [43] and survival is similar when elective, outpatient, incident dialysis patients are compared. When data of Canadian Organ Replacement Register and United States Renal Data System [44] were properly analyzed, survival was similar. After stratifying for age, gender and diabetic status, survival on PD was better in younger non-diabetic patients, survival of older diabetics was better on HD and similar in all the rest. Similar data from developing countries are lacking and may be different. The Chinese randomized control trial (NCT 01413074) comparing survival between the two modalities is complete, and the results may finally end the debate [45].

PD for ESRD across the globe: the impact of socioeconomic and policy factors

Of all ESRD patients on PD, 41% are in developed countries. Of the entire chronic dialysis population, only 11% are on PD with Mexico, USA and China having the largest absolute number of patients. Apart from Mexico, Hong Kong, El Salvador and Guatemala, HD is the predominant RRT modality worldwide [46]. The proportion of PD patients among prevalent dialysis patients varies widely from <1% to ~80% (Figure 2), the latter in countries with ‘PD first’ policy. PD has been growing exponentially in Thailand because of recently introduced ‘PD first’ policy [46]. Although the nephrology community generally agrees that PD utilization should be ~25–30% [47], current rates are far lower. Within certain countries such as France, Spain and Italy, utilization rates vary tremendously, suggesting that some are ‘believers’ and many are ‘nonbelievers’ in PD [46].

In Australia, Canada, Netherlands, New Zealand, most of Scandinavia and United Kingdom, where dialysis is provided by the government, utilization of PD is higher (20–30%) and is propagated as the cheaper modality [48]. HD predominates in Japan, USA, Germany, Belgium and most south European countries where dialysis is provided by private sector, reimbursement being a strong incentive for HD utilization [49] relegating PD utilization to <10%. Japan’s fee-for-service remuneration policy caused 96% of ESRD patients to receive in-center HD [50].

In Hong Kong, cost effectiveness of CAPD led to the establishment of ‘PD first’ policy by the Central Renal Committee in 1985 and PD has grown [51] to ~80% prevalence [35, 46]. Renal physicians and specialist nurses introduce
CKD concepts and various RRT modalities with emphasis on independent RRT via CAPD with its inherent procedural simplicity, flexibility, continuous nature and importance of RRF preservation. Interactive patient groups are formed in each dialysis center with patient rehabilitation using sports, games and other competitions. These help patients to adapt to their illness easily and live relatively normal lives [52, 53].

In developing countries, more than half the patients present with CKD stage 5 as the initial presentation of renal illness [54]. It becomes imperative that RRT is planned at the time of diagnosis. PD should become the default modality for the largely non-urban population. A case in point is the very high PD utilization in Mexico [55], because of the presence of few certified nephrologists, governmental ‘PD first’ policy combined with public institutions being major dialysis providers, absence of a reimbursement system (all doctors are salaried), increased experience with PD during nephrology training and local production of PD fluid, the latter forcing multinational competitors to lower prices. HD centers in Mexico are only situated in large cities and thus are inaccessible for most [56]. Home PD thus is an excellent RRT modality for ESRD patients in the developing world who live in remote villages with poor access to HD facilities [56, 57]. The Thailand government reduced the fluid import duty while implementing a ‘PD first’ policy. This made PD cheaper [58] while increasing utilization [59].

Cost of doing PD is less than HD in most countries, especially in the developed world [60]. The governmental ‘PD first’ policy of Hong Kong has resulted in PD costs being less than half of HD [52] whereas greater remuneration for HD results in enlisting more patients on HD in facilities, thus reducing actual per-patient cost of providing care [61]. Similar remuneration for both HD and PD as implemented in the USA recently [62] should allow more utilization of PD. In south Asian countries like India, most PD patients do not have health insurance and have to pay for their monthly fluid supplies. The one-time payment for life-long fluid supplies has been available for the past decade improving PD utilization [63]. Poor accessibility of remote villages to PD fluid suppliers, especially across mountainous terrains remains a challenge in some areas. Problems of space constraints for doing PD exchanges, availability of running water for hand-washing and poor hygienic living conditions still pose a challenge in many but are slowly being successfully addressed.

Chronic PD in children
Children with ESRD are best managed with transplantation with better quality of life and superior long-term survival. When transplantation is delayed, PD is the preferred RRT modality in children allowing them flexibility of therapy in concordance with their educational and other lifestyle requirements [64]. PD is the ideal modality of RRT in children, and especially so when the weight is <5 kg for those who, have a difficult vascular access and where anticoagulation is contraindicated. Since the number of children on PD is relatively small globally, pooled clinical data from the North American Pediatric Renal Trials and Collaborative Studies, International Pediatric Peritonitis Registry and pediatric
ESRD registries of European Society for Pediatric Nephrology/European Renal Association-European Dialysis and Transplant Association (ESPN/ERA-EDTA) and the International Pediatric Peritoneal Dialysis Network are collated to obtain more generalizable information. The 5-year technique survival appears to have been improving from 64% in the pre-1992 era to 78% thereafter in the Japanese registry [65] with peritonitis and ultrafiltration, together contributing to two-thirds of the reasons for technique failure. Patient survival is better in those older than 5 years of age [66]. Similar data are lacking from developing countries.

The problems of hypertension in more than two-thirds of the children (contributing to left ventricular hypertrophy in 50%) [67], severe hyperphosphatemia and hyperparathyroidism in half [68], growth impairment and malnutrition especially in infants [69] are somewhat unresolved with no clear recommendations for treatment. Unique to the developing world is poor availability of small dialysate bags restricting utilization of PD. Unavailability of specialized HD units makes children to be dialyzed in adult HD units making PD on an attractive option.

**PD for chronic dialysis ‘crash starts’**

Worldwide, most patients who start on dialysis without predialysis education (‘crash starts’) are started on HD via a temporary central venous catheter in the internal jugular vein. These are associated with high mortality in the first 3 months [70]. The available literature on similar unplanned PD initiation suggests similar mortality between PD and HD [71]. Between planned and ‘crash start’ patients on PD, the latter group is likely to have a higher mortality and risk of hospitalization related to more comorbidities, poorer biochemistry profile [72] and older age [73].

Infections (including bacteremia) occur more in patients who ‘crash start’ HD than PD. The latter group’s peritonitis rates are similar to those on planned PD but have a greater risk of mechanical complications [73]. Except in patients with severely uncontrolled hypertension, pulmonary edema, severe hyperkalemia or uremic pericarditis/colitis, most may be suitable candidates for a PD ‘crash start’ and this should be offered to all eligible patients.

Bedside percutaneous PD catheter insertion by nephrologists obviating the requirement of a long break-in period, acute start of chronic PD can be done successfully with the added advantages of short hospital stay, non-requirement of operation room facilities and personnel (including surgeons and anesthetists) and reduced costs [74]. This can be successfully employed even in patients with past abdominal surgeries with low likelihood of peritoneal adhesions [75].

**Glucose-based fluids and ‘biocompatible fluids’**

The high glucose concentration of conventional PD fluid creates an osmotic gradient for ultrafiltration. The low PD fluid pH reduces formation of glucose degradation products (GDPs). The substantial carbohydrate load from PD fluid can lead to high blood sugars and a potentially atherogenic lipoprotein profile. Locally, PD fluid glucose, low pH, lactate and GDPs [76] cause long-term unfavorable effects on the membrane. Systemic absorption of GDPs may decrease RRF by their action on renal tubules [77]. The ‘biocompatible’ PD solutions are associated with lower peritonitis rates in most series. In the randomized, controlled trial, baANZ study, peritonitis rate was 0.49 in the conventional group and 0.30 episodes per patient-year in the biocompatible fluid group (P = 0.01) [78]. There may be increased RRF as evidenced by increased GFR and urine output possibly due to renoprotective effect of reduced GDPs in these fluids [79]. However, newer solutions may change the patient’s transport status and decrease ultrafiltration by 30%, volume expansion thus caused possibly increasing urinary volume [78]. Although two trials showed a mortality advantage, the baANZ study did not [78]. Of the newer solutions, only icodextrin is freely available in most developing countries and is ~45% costlier.

**Conclusion**

Looking globally, the majority of the population lives in developing countries and two-thirds are living at or below the poverty line. AKI is common in such populations due to a variety of causes. Dialysis modality should be simple, cost-effective to save lives. Hence, PD is the treatment of choice. Chronic PD including CAPD, which is a home-based therapeutic modality, is expanding in developing countries. Manufacturing catheter and dialysis fluid in developing countries will bring down the cost of PD, thereby making a PD first policy in different parts of the world.

Conflict of interest statement. None declared. The results presented in this paper have not been published previously in whole or part, except in abstract format.

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