Chronic kidney disease and dialysis therapy: incidence and prevalence in the world

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Abstract

Chronic kidney disease (CKD) is the important public and medical problem in the world because of a large burden on health care systems. The prevalence of CKD and number of dialysis patients are increasing in the world. The prevalence and incidence of CKD depends on age, race, and gender of patients, region, and the presence of the CKD registry in a country. Diabetes mellitus (DM) and arterial hypertension (AH) are the most common causes of end stage renal disease (ESRD). It is projected that the number of dialysis patients will reach 5.5 million in 2030. Specific strategies and interventions should be urgently aimed at reducing in the burden of CKD by means of the prevention, detection and treatment of DM, AH, and early stages of CKD. One more strategy is the organization of own domestic manufacture of solutions for dialysis therapy.

Keywords

chronic kidney disease, hemodialysis, peritoneal dialysis

Introduction

The prevalence of chronic kidney disease (CKD) has been increased dramatically in the world for the past three decades (Fallahzadeh et al. 2011; Ferguson et al. 2015; Li and Kwong 2017; Carrero et al. 2018; Lv and Zhang 2019; Duan et al. 2020; Li et al. 2020). CKD significantly contributes to mortality, morbidity, reduced quality of life and substantial health care costs (Ayodele and Alebiosu 2010; Levey et al. 2011; Danaei et al. 2014; Murali et al. 2015; Hill et al. 2016; Gaitonde et al. 2017; Lv and Zhang 2019; Ammirati 2020; Matsushita et al. 2020). In general, CKD is a large contributor to chronic non-communicable diseases (NCD) and is widely recognized as an independent major risk factor of cardiovascular diseases (Jha et al. 2012; Jha 2013; Danaei et al. 2014; Brück et al. 2016; Zdrojewski et al. 2016; Glassock et al. 2017; Bouya et al. 2018; Gorostidi et al. 2018; Ammirati 2020; Li et al. 2020).

CKD affects more than 10% of the world population (Duan et al. 2019). Moreover, the prevalence of CKD depends on a country, age and gender of patients, race or ethnicities, presence of the CKD registry in a country, time of the study, and methodology used for the CKD definition, including the choice of biomarker and equation, influence of non-glomerular filtration rate (non-GFR) determinants on biomarker levels, application of ancestry coefficients to estimated glomerular filtration rate (eGFR) equations, etc. (Ayodele and Alebiosu 2010; Chudek et al. 2014; Zdrojewski et al. 2016; Glassock et al. 2017; Carrero et al. 2018; Gorostidi et al. 2018; Thomas 2018; Duan et al. 2019, 2020; Ammirati 2020; Kibria and Crispen 2020).
The prevalence of CKD (stages 3–5 ranges) from 1.3% to 15.7% and 2.2% to 11.7% among men and women, respectively, depending on the country (Carrero et al. 2018). Therefore, the incidence and prevalence of CKD or end stage renal disease (ESRD) could be underestimated as eGFR < 60 mL/min/1.73 m² refers to III–V stages of CKD and does not take albuminuria into consideration (Bikbov et al. 2020).

CKD, diabetes mellitus (DM) and cardiovascular diseases are major regional and global causes of death (Jha 2013; Danaei et al. 2014). Moreover, in 2010 there were 55% of deaths from high blood pressure caused by cardiovascular diseases, CKD and DM in Central Asia, Eastern Europe, and sub-Saharan Africa. Furthermore, the mortality caused by CKD and DM increased twice between 1990 and 2010 (Danaei et al. 2014). Cardiovascular diseases are recognized as the major health and social issue in the world as well (Stepaniuk et al. 2020).

CKD is caused by DM, arterial hypertension (AH), obesity, aging, unhealthy diet and other known and unknown reasons (Fallahzadeh et al. 2011; Danaei et al. 2014; Murali et al. 2015; Zdrojewski et al. 2016; González-Pérez et al. 2020).

The incidence and prevalence of DM increases in the world mainly due to the rise in obesity and other risk factors for type 2 diabetes (González-Pérez et al. 2020). Moreover, obesity induces a faster glomerular filtration rate (GFR) decrement (Sutarka et al. 2012). Overall, the fast increase in the prevalence of DM and AH induces the CKD prevalence growth (Duan et al. 2019). Therefore, the requirement for dialysis and transplantation is increasing constantly in developed and developing countries (Jha 2013; Jha 2015; Chan et al. 2019).

The number of people receiving renal replacement therapy (RRT) was more than 2.5 million in 2010 and was projected to reach 5.439 million (3.899–7.640) in 2030 (Li and Kwong 2017; Chan et al. 2019; Bikbov et al. 2020). There were 3.37 million ESRD patients in the world in 2014 compared to 2.3 million in 2008, while the number of patients undergoing RRT increased only from 1.77 million to 2.67 million from 2008 to 2014 (Li and Kwong 2017). Among reasons of such an increase in patients receiving RRT are widening acceptance criteria for RRT, an improved survival of the general population, reduction in the mortality of dialysis patients, larger access to dialysis therapy in low- and middle-income countries, an increase in the incidence of CKD, etc. (Chan et al. 2019).

The aim of this paper is to generalize data on the prevalence and incidence of CKD, end-stage renal disease (ESRD), hemodialysis (HD) and peritoneal dialysis (PD) as well. Reliable data about the prevalence of NCD is essential for the elaboration of health policies for their prevention, treatment and control (Kearney et al. 2005).

### Incidence and prevalence of CKD and ESRD

The 2012 KDIGO guidelines contain the advanced classification. CKD was defined as eGFR less than 60 mL/min per 1.73 m² or the presence of albuminuria. CKD is classified into 5 stages depending on eGFR (Levey et al. 2011; Webster et al. 2016; Gaitonde et al. 2017; Ammirati 2020). This classification of CKD is provided in Table 1.

| Stage | eGFR (mL/min/1.73 m²) |
|-------|----------------------|
| 1     | <30                  |
| 2     | 30–60                |
| 3     | 60–89                |
| 4     | 89–15                |
| 5     | >15                  |

CKD induces the profound challenge for health care systems related to the consumption of significant social and financial recourses (Fallahzadeh et al. 2011; Glassock et al. 2017; Li and Kwong 2017).

ESRD is a consequence of the CKD progress (Jha 2013; Gaitonde et al. 2017; Li et al. 2020). The prevalence of CKD and ESRD increases rapidly in the world (Duan et al. 2020). Moreover, the prevalence of CKD increased with age regardless of gender (Duan et al. 2019, 2020). In general, the prevalence of CKD fluctuates from country to country that could be explained by the prevalence of obesity, AH and DM in the populations, and demographic, socioeconomic, genetic, climate, environmental and other factors. Among these factors are age, age distribution in a population, gender, income, urban or rural residence, working, living and climate conditions, prevalent diet, including alcohol consumption, communicable disease, dehydration episodes in specific climate of South Asia, etc. (Chudek et al. 2014; Jha 2015; Glassock et al. 2017; Kibria and Crispen 2020). One more significant factor is a way of the GFR estimation (measured GFR or eGFR) (Glassock et al. 2017).

The issue of the connection between GFR and age is disputed as there is a natural decline in GFR in the elderly with aging. This controversial issue raises a question about what is normal aging and what is disease (Glassock et al. 2017). Nevertheless, aging of the world’s population will probably increase in the occurrence of CKD for the next decades (Chudek et al. 2014).

In 2017 there were 649.2–752.1 million people with CKD in the world. Thus, the prevalence of CKD was estimated as 9.1%. Patients with 1–2 stages of CKD accounted for 4.5–5.5%, 3 stage – 3.5–4.3%, 4 stage – 0.13–0.19%, 5 stage – 0.06–0.08%, dialysis patients – 0.037–0.044% and patients with kidney transplantation – 0.010–0.012% (Bikbov et al. 2020). The age-standardized prevalence was in the range of 8.8% to 10.2% for women and 6.8 to 7.9% for men (Hill et al. 2016).

Asia is considered to be the region with the biggest ESRD population (Li and Kwong 2017). One third of patients with CKD in the world lives in China and India. Among other countries with a large CKD population are Bangladesh, Brazil, Indonesia, Japan, Mexico, Nigeria,
Pakistan, the Russian Federation, the USA, and Vietnam. In 2017 each of these countries had more than 10 million people with CKD (Bikbov et al. 2020).

It is worthy of attention that the epidemiology of CKD and ESRD in South Asia had been not well defined by 2012, despite being one of the most populous region (Jha 2015; Kumar and Jha 2016).

The prevalence of dialysis patients is increasing in China. For example, there were 33.2 persons per million people (p.m.p) in 1999, 51.7 p.m.p in 2008, 92.3 p.m.p in 2009, while the prevalence of CKD was in the range of 10.2–11.3% in 2012 in a cross-sectional survey of Chinese adults (Jha et al. 2012; Zhang et al. 2012). The adjusted prevalence of patients with eGFR less than 60 mL/min per 1.73 m² and albuminuria was 1.7% and 9.4%, respectively (Zhang et al. 2012).

Duan et al. (2020) revealed that the overall adjusted prevalence of CKD was 16.8% (15.8–17.8%) in a central Chinese urban population in 2018 and people with 1 stage of CKD accounted for 5.3–6.6%, 2 stage – 7.1–8.5%, 3 stage – 2.2–3.1%, 4 stage – 0.1–0.4%, 5 stage – 0.1–0.2%. Moreover, urban patients with both AH and DM show the highest prevalence of reduced eGFR (4.0–10.5%) and albuminuria (48.6–61.1%) compared to those with either AH or DM (Duan et al. 2020).

Similar situation was determined in a cross-sectional survey of Chinese rural residents in 2015–2017. The prevalence of CKD was in the range of 15.9–16.8% (16.4%). However, the division between stages was not analogous. The patients with 1 stage of CKD accounted for 10.6–11.4%, 2 stage for 2.9–3.3%, 3 stage – 1.1–1.4%, 4 stage – 0.3–0.5%, 5 stage – 0.3–0.5% (Duan et al. 2019). Therefore, the total prevalence of CKD in China was higher in these two studies compared to the average prevalence in the world (9.1% in 2017) (Duan et al. 2019, 2020; Bikbov et al. 2020).

The prevalence of CKD among urban diabetic patients is 48%, while its prevalence among rural diabetic patients was 35.5% (Duan et al. 2020). Therefore, CKD and diabetic kidney disease (DKD) is a major burden of the public health care in China (Duan et al. 2019).

Developed countries spend 2–3% of their annual health care budget to treat patients with ESRD, but their number is only 0.02–0.03% of the total population (Jha 2015; Li and Kwong 2017; Li et al. 2020).

There are fluctuations in the prevalence of CKD between European populations. The results of the NATPOL 2011 survey demonstrated that the prevalence of CKD was estimated at 5.8% in Poland (95% confidence interval (95% CI) 4.6–7.2%). An eGFR less than 60 mL/min/1.73 m² and albuminuria were revealed in 1.9% (95% CI 1.5–2.5%) and 4.5% (95% CI 3.4–5.9) of the studied population, respectively. AH and DM were more frequent in the patients with diagnosed CKD compared with those without CKD (67.8% versus 29.0% (P < 0.001) and 18.5% versus 4.5% (P < 0.001), respectively). DM and AH were, apart from increasing in age, the greatest risk factors of CKD (Zdrojewski et al. 2016; Li et al. 2020). In one more study conducted in 2007–2011 (the PolSenior study) it was established that CKD affects almost one third of the elderly Polish population. In this study the elderly were divided into six groups: 65–69, 70–74, 75–79, 80–84, 85–89, 90 years and above. The PolSenior study confirmed the opinion that the prevalence of CKD grew with aging (Chudek et al. 2014). One more report provided the prevalence 11.6% in Poland in 2011 (Bart and Malik 2015).

Okparavero et al. (2016) studied the prevalence and complications of CKD among older Icelandic adults at the age of 80 ± 5. These authors examined the distribution of eGFR from creatinine and cystatin C, the albumin-to-creatinine ratio (ACR). They established that the prevalence of a reduced eGFR (<60 mL/min/1.73 m²), albuminuria (ACR >30 mg/g) and CKD (either reduced eGFR or albuminuria) was 40%, 14% and 45%, respectively (Okparavero et al. 2016).

The adjusted prevalence of CKD stages 1–5 was in the range of 3.30% to 3.33% in Norway, 9.0% to 10.6% in Spain, 16.5% to 18.1% in Germany, and 4.8% in the Netherlands (ages 20–74). Thus, the total prevalence of CKD in some European countries was lower compared to the prevalence in the world. The regional variations in CKD could be explained by the prevalence of DM, AH, and obesity in the general population and other factors. Among these factors are dietary habits, healthcare policies, gene factors, differences in the time period of a study. All estimations were performed considering the same definition of CKD stages 1–5: eGFR <60 mL/min per 1.73 m² calculated by the CKD-Epidemiology Collaboration equation and/or ACR >30 mg/g (Brück et al. 2016). According to Gorostidi et al. (2018), the prevalence of CKD was 15.1% in Spain, while this prevalence was higher in men (23.1% vs 7.3% in women) (Gorostidi et al. 2018).

One more report provided the following prevalence for Spain, Portugal and the Netherlands in 2014: 9.2%, 6.1–10% and 10.4%, respectively (Bart and Malik 2015).

Bikbov et al. 2020 state about the following age-standardized rate per 100000 in the countries of Central Europe in 2017: Albania – 7259, Bulgaria – 8000, Croatia – 7779, Czech Republic – 7998, Poland – 7271, Slovakia – 7736, namely, the prevalence of CKD in Central Europe was approximately 8% (Bikbov et al. 2020).

In the USA the prevalence of CKD increased from 10.0% in 1988–1994 to 13.1% in 1999–2004 (Coresh et al. 2007). The age-adjusted prevalence for CKD was 14.1%, 13.0%, 14.0% and 13.3% in 2003–2006, 2007–2010, 2011–2014 and 2015–2018, respectively. In these periods the prevalence of 5 stage of CKD was in the range of 0.1% to 0.3%. It is worthy of attention that women had a higher prevalence of CKD compared to men. Among different races non-Hispanic blacks showed a higher prevalence of CKD compared to non-Hispanic white people and Hispanic (Thomas 2018; Kibria and Crispen 2020).

Pakistan and India are the biggest and most populous countries in South Asia (Jha 2013). The burden of NCD has increased in recent years and it was evaluated that over 40% of all deaths were due to NCD. The exact burden of CKD or ESRD had not been known by 2013. A population-based study calculated the ESRD incidence rate at 152 per million in India and 100 per million in Pakistan (Jha 2015; Kumar and Jha 2016).
Chronic kidney disease (CKD) is a complication of long poorly controlled diabetes (González-Pérez et al. 2020). Among the risk factors of CKD and DKD are cardiovascular diseases, including AH, DM, obesity, overweight, smoking, age and high social deprivation, gender, alcohol consumption, dyslipidemia and hyperuricemia, nutrition and indigenous medicines (Fallahzadeh et al. 2011; Jha et al. 2012; Danaei et al. 2014; Jha 2015; Hill et al. 2016; Duan et al. 2020; González-Pérez et al. 2020). Therefore, González-Pérez et al. (2020) state about the importance of good glycemic control at an early stage of DM for reducing or delaying diabetic vascular complications (González-Pérez et al. 2020).

In 1997, the number of deaths from high blood pressure (HBP) caused by cardiovascular diseases, CKD and DM in Central Asia, Eastern Europe, and sub-Saharan Africa (Danaei et al. 2014).

Overall, AH is a cause of CKD in Eastern Asia, Eastern Europe, tropical Latin America, and Western sub-Saharan Africa, while DM is a cause in other regions (Hill et al. 2016; Yang et al. 2020).

According to Carreo et al. (2018), the number of women with predialysis CKD is larger compared to that of men that could be explained by the longer life expectancy and overestimation of eGFR (Carreo et al. 2018). However, this issue is controversial and depends on region and age. For example, the prevalence of reduced eGFR and albuminuria were much higher in men at the age of 18–39 (3.0% versus (vs) 0.7% and 13.8% vs 12.9%) and 40–59 (1.5% vs 0.9% and 15.5% vs 14.5%), while that there was an opposite situation in men at the age of 60–69 (1.9% vs 2.3% and 14.9% vs 18.8%) and ≥70 (6.9% vs 10.5% and 18.6% vs 25.8%) (Duan et al. 2019). Nevertheless, the prevalence of CKD increased with age in both men and women (Gorostidi et al. 2018; Duan et al. 2019; Duan et al. 2020).

Causes of CKD

Among the main causes of CKD are DM, AH, chronic pyelonephritis, chronic glomerulonephritis, autoimmune diseases, prolonged acute renal disease, etc. (Hill et al. 2016; Vučak et al. 2016; Webster et al. 2016; Ammirati 2020), however, inflammatory diseases are less frequent (Vučak et al. 2016). It is worthy of mentioning that glomerulonephritis is a main cause of CKD in China (Jha et al. 2012; Yang et al. 2020).

DM is the most common cause of ESRD in the whole world (Fallahzadeh et al. 2011; Hill et al. 2016; Li and Kwong 2017). For example, the ESRD caused by DM ranged from 27% to 64% in the countries of Asia, South America and the USA (Brazil 27%, India 31.2–41%, Australia 35%, Japan 43–44%, Taiwan 45%, Philippines 45%, Republic of Korea 48%, Hong Kong 49%, Malaysia 64%, and the USA 43–44%) (Jha et al. 2012; Murali et al. 2015; Li and Kwong 2017). In addition, China and India had the biggest quantity of patients with DM (Jha et al. 2012). Moreover, DM is expected to rise to 439 million by 2030. In 2010 the world prevalence of DM among the adults at the age of 20–79 years was 6.4%, affecting 285 million people, and will increase to 7.7% and 439 million adults, respectively, by 2030. In 2010 India, China, the USA, the Russian Federation, Brazil, Germany, Pakistan, Japan, Indonesia, and Mexico were the top ten countries for the number of people at the age of 20–79 suffering from DM. It is expected that in 2030 among the ten top countries will be India, China, the USA, Pakistan, Brazil, Indonesia, Mexico, Bangladesh, the Russian Federation, and Egypt (Shaw et al. 2010).

The second cause of CKD is AH. In 2010 there were 55% of deaths from high blood pressure (HBP) caused by cardiovascular diseases, CKD and DM in Central Asia, Eastern Europe, and sub-Saharan Africa (Danaei et al. 2014).

According to Carreo et al. (2018), in 2000 there were 26.4% (972 million) people suffering from AH and that number was predicted to reach 29.2% in 2025 (1.56 billion) (Kearney et al. 2005). However, obesity is preventable (World Health Organization). An increase in people with obesity is explained by changing lifestyles, especially a reduced physical activity (Shaw et al. 2010).

According to the World Health Organization (2020), obesity has increased nearly by 3 times since 1975. In 2016, there were more than 1.9 billion overweight adults at the age of 18 and older, including over 650 million were obese that accounted for 39% and 13% of the world’s population, respectively. However, obesity is preventable (World Health Organization). An increase in people with obesity is explained by changing lifestyles, especially a reduced physical activity (Shaw et al. 2010).

RRT is recommended to patients at GFR less than 20 ml/min (Ammirati 2020).
The incidence of all the RRT forms grows as well. For instance, the incidence of HD and PD annually increases by 6–7% and 8%, respectively (Li and Kwong 2017). There was 1.1 million of dialysis patients in 2002 and 1.3 million at the end of 2003 in the world (Lameire et al. 2005; Jha et al. 2012), while there were 2.376 million HD patients and 0.289 million PD patients in 2014. It is predicted that the number of patients undergoing RRT will reach 1.571–3.014 million in Asia by 2030 (Li and Kwong 2017). Moreover, Lv and Zhang state that the number of patients with ESKD needing RRT ranged from 4.902 to 7.083 million in the world at the prevalence of CKD of 13.4% in 2019 (Lv and Zhang 2019).

In 2002 the prevalence of RRT was 79, 273, 405, 488, 636, 658, 918, 895–1081, 1097 p.m.p, respectively, in the Russian Federation, Estonia, Poland, Slovakia, Finland, the Netherlands, Germany, Spain (depending on region), Portugal (Lameire et al. 2005). One more publication stated about the following prevalence of RRT in Spain, Poland, Portugal and the Netherlands in 2014: 1078, 747.5, 1670, 925.8 p.m.p (Bart and Malik 2015). A significant increase in the prevalence of RRT patients in Poland, Portugal and the Netherlands was observed. One more report provided the following unadjusted prevalence of V stage of CKD in Portugal, Spain, the Netherlands, Poland, Bulgaria and Ukraine: 1906, 1234, 1047, 812, 610 and 188 patients per million population, respectively, in 2016 (Kolesnyk et al. 2019).

HD penetration is much larger than PD worldwide. HD is more prevalent RRT modality in the world (Li and Kwong 2017). In 2016 all the forms of RRT were available in India, Pakistan, Sri Lanka, Bangladesh, and Nepal. Their penetration, however, is mainly limited to urban areas (Jha 2013; Kumar and Jha 2016). Patients were maintained on long-term HD in increasing numbers. In general, the dialysis prescription was unsatisfactory, with a majority getting not more than two 4-hour sessions per week. Dialyzers were reemployed multiple times usually after manual cleaning in order to cut costs. Most patients were poorly rehabilitated. The absence of government regulations prevented dialysis treatment standardization (Jha 2013). In South Asia there is a shortage of renal replacement services (Jha 2013; Jha 2015). In general, it was supposed that approximately 66% of all ESRD patients in South Asia did not receive RRT in 2016 (Kumar and Jha 2016).

Up to 2013 data from Pakistan had suggested that about 30% of dialysis units did not have any water treatment facilities. In India and Pakistan the penetration of chronic PD was weak as less than 20% of all long-term dialysis patients were on PD. Cost and high infection rates interfered with increasing in the penetration of chronic PD. The Indian government had included the care for CKD in its 12th 5-year plan cycle and developed a framework for dialysis and transplantation. It was planned to set up dialysis centers across the country and manage by the private sector, however, the government was going to reimburse these centers costs at a predetermined rate (Jha 2013; Kumar and Jha 2016).

In 2013 the RRT expenditures were less in India and Pakistan than in developed countries, however, they were out of the reach for most people. The monthly cost of the common prescriptions (2 HD procedures per week and 3 PD exchanges per day) was 609 and 585 US dollars, respectively. These expenditures were paid by most patients (Jha 2013). Generally, out-of-pocket expenses formed approximately 50–70% of total healthcare cost in 2015 (Jha 2015). Kumar and Jha stated about the same cost of 3 HD and PD exchanges per day. The average cost of a single hemodialysis session was almost 20–40 US dollars, whereas the average monthly expense of PD was approximately 300–400 US dollars. The overall cost of renal-transplant surgery was over 5000 US dollars (Kumar and Jha 2016).

The nephrological care with HD is growing in Ukraine. There were 724–866 HD apparatuses in 2012. This number grew to 1164 in 2016 (Pyrih 2020).

The presence of the CKD register indicates the CKD surveillance in a country and, thus, gives a real possibility to evaluate the number of people suffering from CKD and patients needing RRT (Jha et al. 2012; Venuthurupalli et al. 2012; Jha 2013). Renal registries in Europe provide even the information on the number of HD sessions per week and weekly duration of HD. In 2005 more than 90% HD patients in Belgium, Macedonia, Finland, France and Slovenia received three HD sessions (Couchoud et al. 2009).

The CKD Registry started to recruit all CKD patients in 2011 in Australia (Venuthurupalli et al. 2012). The Ukrainian registry was included into the European registry ERA-EDTA in 2006 (Kolesnyk et al. 2019). Despite decline in the Ukrainian population, the number of people suffering from CKD is growing in Ukraine (Pyrih 2020).

The availability of RRT is limited in many countries with a high burden of CKD (Hill et al. 2016; Hudz et al. 2018a; Lv and Zhang 2019). The development and manufacture of solutions for dialysis therapy (concentrates for HD and solutions for PD) in a country will permit to reduce their cost mainly because of the absence of international deliveries. It is worthy of mentioning that there are only few publications with open access related to the pharmaceutical development of solutions for dialysis therapy (Hudz et al. 2018a, b; Hudz et al. 2019).

Conclusions

This article summarizes the information on the epidemiology of CKD in some countries of the world. CKD is the important public and medical problem in the world because of a growing number of patients suffering from CKD and a large burden on health care systems. Providing CKD and ESRD care is a social, economic and medical challenge. On the one hand, revealing risk factors of the development of CKD is likely to reduce its prevalence, but on the other, an increased availability of RRT and the projected growth in DM, AH and cardiovascular diseases will enlarge the prevalence of CKD in the future. The review shows that it is necessary to develop strategies in order to prevent...
or reduce the burden of CKD and manage CKD and ESRD. Among the strategies are the prevention, detection and treatment of DM, AH, and early stages of CKD. One more strategy in each country is the organization of own manufacture of solutions for dialysis therapy in order to reduce their cost by the elimination of international delivery.

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