


Global costs attributed to chronic kidney disease: a systematic review

 Geraldo Bezerra da Silva Junior^{1,2}
Juliana Gomes Ramalho de Oliveira¹
Marcel Rodrigo Barros de Oliveira³
Luiza Jane Eyre de Souza Vieira¹
Eduardo Rocha Dias⁴

1. Postgraduate Program in Collective Health, Health Sciences Center, University of Fortaleza. Fortaleza (CE), Brasil
2. Department of Epidemiology and Prevention of Renal Disease, Brazilian Society of Nephrology. São Paulo (SP), Brasil
3. Nephrology Service, General Hospital of Fortaleza. Fortaleza (CE), Brasil
4. Postgraduate Program in Constitutional Law, Center for Legal Sciences, University of Fortaleza. Fortaleza (CE), Brasil

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SUMMARY

The aim of this study is to discuss the global costs attributed to chronic kidney disease (CKD) and its impact on healthcare systems of developing countries, such as Brazil. This is a systematic review based on data from PubMed/Medline, using the key words "costs" and "chronic kidney disease", in January 2017. The search was also done in other databases, such as Scielo and Google Scholar, aiming to identify regional studies related to this subject, published in journal not indexed in PubMed. Only papers published from 2012 on were included. Studies on CKD costs and treatment modalities were prioritized. The search resulted in 392 articles, from which 291 were excluded because they were related to other aspects of CKD. From the 101 remaining articles, we have excluded the reviews, comments and study protocols. A total of 37 articles were included, all focusing on global costs related to CKD. Despite methods and analysis were diverse, the results of these studies were unanimous in alerting for the impact (financial and social) of CKD on health systems (public and private) and also on family and society. To massively invest in prevention and measures to slow CKD progression into its end-stages and, then, avoid the requirement for dialysis and transplant, can represent a huge, and not yet calculated, economy for patients and health systems all over the world.

KEYWORDS: Chronic kidney disease. Dialysis. Kidney Transplant. Health care costs.

INTRODUCTION

Chronic kidney disease (CKD) is fast growing in Brazil and worldwide, and is associated with high financial expenditures for patients and healthcare systems. Scaling up its economic repercussions and proposing strategies to minimize the costs involved in its treatment has been configured as a challenge for the scientific community.

Defined as the presence of kidney damage or decreased kidney function for three months or more, with repercussions on the general state of the pa-

tient¹, CKD has as its main causes systemic arterial hypertension (SAH) (35%) and diabetes mellitus (DM) (30%)², both chronic non-communicable diseases (CNCDS) with a high impact on morbidity and mortality and with high prevalence worldwide. In addition, CKD has a strong relationship with aging³ and, based on the Brazilian population, according to projections, by 2050, the estimated number of elderly will be 66 million, while children and adolescents will be 31.8 million, reversing the scenario of 2010,

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CORRESPONDING AUTHOR: Geraldo Bezerra da Silva Junior
Universidade de Fortaleza – Unifor

Av. Washington Soares, 1321, Bloco S, Programa de Pós-Graduação em Saúde Coletiva. Fortaleza, CE, Brasil – CEP 60811-905

E-mail: geraldobezerrajr@yahoo.com.br

when values for these age groups were 19.6 and 49.9 million, respectively.⁴

In general, aging is related to the risk of multi-morbidity, that is, the individual is affected by more than one chronic illness at the same time, which generates greater use of healthcare services and a considerable increase in treatment costs, considering that these are proportional to the number of associated diseases⁵. Population aging, if analysed in isolation, already presents numerous challenges for all sectors of society and imposes the need to rethink the dimension of the supply of services needed to meet the demands of this population group in the long term⁴.

In the more advanced stages of CKD, characterized by a severe decline in the glomerular filtration rate (GFR), the patient must initiate one of the modalities of renal replacement therapy (RRT), whose current options are haemodialysis (HD), peritoneal dialysis (PD) and kidney transplant. Such therapeutic options demand numerous expenses for the healthcare system because, in addition to having a high cost, its users are susceptible to prolonged hospitalizations, continuous treatment and the use of high cost medications. It is known that dialysis and kidney transplant consume disproportionate amounts of healthcare budgets, since about 5% of budgets are consumed by less than 1% of the population¹.

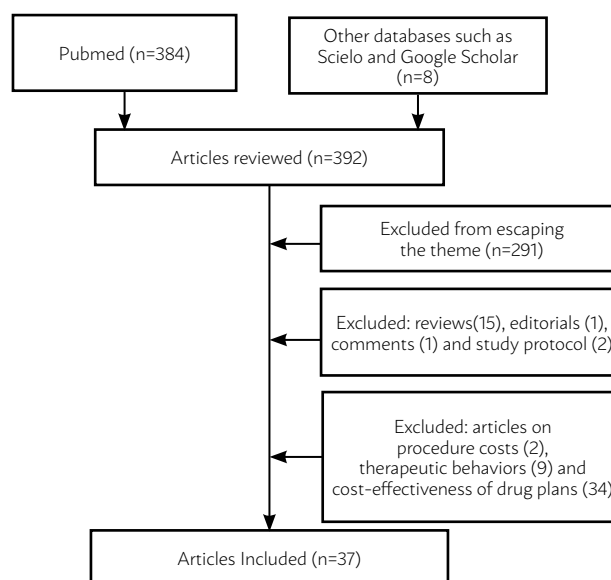
Studies of financial growth suggest that the greatest macroeconomic burden of CKD and other chronic diseases falls on low- and middle-income countries, where high prevalence and high treatment costs create a proportional burden on gross domestic product (GDP)⁶. It is known that the provision of RRT by countries has a directly proportional relation with their GDP, suggesting that poverty is an important disadvantage with respect to the access of individuals to the modalities of CKD treatment⁷. In addition, in the personal sphere, expenditures attributed to healthcare commonly affect the family financial structure, with considerable property loss, in a context of insufficient resources.

Faced with global financial instability, the uncertainties surrounding healthcare financing in developing and underdeveloped countries, the certainty of increasing life expectancy and the consequent increase in chronic health conditions, this review proposes to discuss financial costs attributed to CKD and its repercussions on healthcare systems in developing countries, such as Brazil.

MATERIALS AND METHODS

This is a systematic review carried out in the PubMed/Medline database, using the terms “costs” and “chronic kidney disease”, in January 2017. The search was expanded to other bases, such as Scielo and Google Scholar, with the purpose of identifying local studies related to this matter, published in journals not indexed in PubMed. Only articles published since 2012 have been included, considering the period of the last five years as recent. Studies focused on the costs of CKD and its treatment modalities were prioritized. The studies focused on the cost-effectiveness of drug regimens and therapeutic behaviours were excluded. The detailed selection process of the articles is described in Figure 1.

FIGURE 1: SELECTION PROCESS OF ARTICLES ON THE COSTS OF CHRONIC KIDNEY DISEASE FOUND IN THE SYSTEMATIC REVIEW AND INCLUSION/EXCLUSION CRITERIA.



RESULTS

In total, the search resulted in 392 articles (PubMed and other sources), of which 291 were excluded because they avoided the main theme of this review. Of the remaining 101, 19 articles were excluded because they were reviews, comments and study protocols, and 45 because they deal with costs of procedures, therapeutic behaviours and cost-effectiveness of specific drug regimens. The study included 37 articles focused on the overall costs related to CKD (Table 1).

TABLE 1: STUDY ON THE OVERALL COSTS RELATED TO CKD

Main Author	Year	Country	Study Model	Study Object	Primary Conclusion
Small (8)	2017	United States	Cross-sectional	Costs of CKD treatment	The costs of patients with CKD who do not go through dialysis are high and may be equal to or higher than those of cancer or CVA patients.
Damien (9)	2016	United States	Cross-sectional	Costs of CKD treatment	Therapeutic follow-up before and after the beginning of dialysis and the managing of comorbidities are potential sources of savings in CKD care.
Eriksson (10)	2016	Sweden	Cohort	Costs of CKD treatment	In comparison with the general population, the average yearly costs for CKD treatment are higher in all its modalities.
Anutrakulchai (11)	2016	Thailand	Cross-sectional	Clinical outcomes and treatment costs for CKD	The group of hospitalized CKD patients who presented the fewest benefits and highest mortality was composed of farmers, low-income, and unemployed individuals.
Silva (12)	2016	Brazil	Environmental	Socioeconomic and mortality aspects for patients with CKD	Men and the elderly presented the highest mortality. Associated with a high prevalence, kidney transplant (deceased donor) and HD presented the highest costs.
Turchetti (13)	2016	Italy	Cross-sectional	Social cost per CKD patient stages 4-5 pre-dialysis	The indirect and non-medical direct costs from CKD treatment were similar to the direct costs.
Kerr (14)	2016	England	Cross-sectional	Cause, site, and hospital costs related to the death of CKD patients	The primary causes for the death of CKD patients were not kidney related. Deaths at home are associated with a reduction of hospital costs.
Roggeri (15)	2016	Italy	Retrospective cohort	Costs of CKD treatment	CKD is associated with a high economic burden and the beginning of dialysis with an increase in direct costs with health care.
Mendu (16)	2016	United States	Retrospective cohort	Rational clinical criteria for the diagnosis of CKD.	Some clinical criteria can guide the diagnosis of CKD and reduce its costs.
Silva (17)	2016	Brazil	Cost analysis/Literature review	Costs of CKD treatment	Kidney transplant stood out as the best alternative from a financial and clinical point of view, under the perspective of the Unified Health System (SUS).
Kulkarni (18)	2015	India	Cross-sectional	Costs of CKD treatment	The costs of HD in India are high when compared with the per capita income in the country.
Atapour (19)	2015	Iran	Cross-sectional	Costs of CKD treatment	PD presents a lower cost lower than HD.
Ferguson (20)	2015	Canada	Cost models	Operation costs for dialysis units	HD units in remote areas are more expensive, per patient, than hospital HD in urban areas.
Francis (21)	2015	Peru	Cross-sectional	CKD demographics	The high prevalence rates of CKD in Lima and Tumbes are compatible with high-income countries.
Takura (22)	2015	Japan	Cost-effectiveness analysis	Cost-effectiveness of CKD treatment.	Hemodiafiltration is a cost-effective therapy.
Wyld (23)	2015	Australia	Cohort	Costs of CKD treatment	CKD patients spend 85% more on health treatments and 50% more government subsidies than individuals with no CKD, and costs rise as the disease progresses.
Ozieh (24)	2015	United States	Cross-sectional	The costs for CKD treatment on DM patients	CKD significantly contributes to the treatment costs for individuals with DM.
Kent (25)	2015	England	Cohort	Costs of CKD treatment	RRT and vascular events are the leading causes of the rising costs in CKD treatment.
Brunelli (26)	2015	United States	Retrospective cohort	Costs for CKD treatment in individuals with autosomal dominant polycystic kidney disease.	The use and costs of health care for patients with autosomal dominant polycystic kidney disease and CKD in the terminal stage in dialysis are high.
Blanchette (27)	2015	United States	Cross-sectional	Costs for CKD treatment in individuals with autosomal dominant polycystic kidney disease.	Patients with autosomal dominant polycystic kidney disease presented higher rates of renal procedures, which can contribute to the rising costs of treatment.

Main Author	Year	Country	Study Model	Study Object	Primary Conclusion
Medway (28)	2015	Australia	Qualitative	Financial impact of CKD in children	For parents, the impossibility of keeping their jobs combined with medical and non-medical expenses where the primary factors with a financial impact.
Menezes (29)	2015	Brazil	Cross-sectional/retrospective cohort	Costs of CKD treatment	A considerable increase in the number of HD sessions and their cost was found, from 2008 to 2012.
Nassir (30)	2015	United States	Cohort	Costs of CKD treatment	No association was found between the relative costs of the treatment and the failure of the kidney grafts.
Villarreal-Rios (31)	2014	Mexico	Cross-sectional	Costs of CKD treatment	The high costs of CKD pose a serious problem for healthcare services and families. CAPD is the most cost-efficient option for both.
Satyavani (32)	2014	India	Cross-sectional	The costs for CKD treatment on DM patients	The direct costs of hospital admissions for treating CKD are considerably higher than those of the patients who suffer from the complication.
Lorenzo-Sellares (33)	2014	Spain	Cohort	Costs of CKD treatment	HD is five times more expensive than the treatment for advanced stages of CKD and three times the costs for kidney transplantation.
Moura (34)	2014	Brazil	Environmental	Incidence and prevalence of patients on dialysis who rely on public financing	During the time of the study, there was a constant increase in incidence, and prevalence rose, especially amongst the elderly.
Gador-Whyte (35)	2014	Australia	Cross-sectional	Costs for implementing protocols for CKD and DM treatment	Adherence to best practices for DM and CKD treatment was compromised by inadequate financing and matters related to the workforce.
Karopadi (36)	2014	Italy	Meta-analysis	Costs of CKD treatment	Even in the absence of a market for the local production of PD equipment, it is possible for a country to save with the provision of PD.
Vupputuri (37)	2014	United States	Retrospective cohort	The costs for CKD treatment on DM patients	The progression of CKD in DM type 2 patients substantially increases treatment costs.
Kadam (38)	2013	England	Cross-sectional	Treatment costs for chronic diseases	Multimorbidity is associated with a broad variety of treatments and different costs. CKD is one of the diseases with the highest and most expensive impact in healthcare.
Coentrão (39)	2013	Portugal	Retrospective cohort	Costs of CKD treatment	Compared with HD, PD requires fewer resources over the first year of treatment.
Essue (40)	2013	Australia	Cross-sectional	Costs of CKD treatment	A considerable proportion of the patients face difficulties due to the high costs associated with the treatment and managing of CKD.
Erdem (41)	2013	United States	Cross-sectional	Treatment costs for chronic diseases	People with chronic diseases represent a disproportionate share of Medicare payments, both for Part A and for Part B, over a period of two years. CKD is among the most expensive chronic diseases, in both parts.
Ramachandran (42)	2013	India	Cohort	Costs of CKD treatment	Kidney transplant is associated with catastrophic spendings and leads most patients who are treated in a public hospital to a serious financial crisis, as well as to school evasion and loss of employment.
Chiroli (43)	2012	Multicenter (Europe)	Retrospective cohort	Costs of CKD treatment	Secondary hyperparathyroidism increases the financial burden of CKD in Europe.
Kerr (44)	2012	England	Cross-sectional	Costs of CKD treatment	The financial impact of CKD is high, with high costs related to RRT and cardiovascular complications.

Research has warned that CKD is one of the most costly diseases in healthcare (38), and that its economic burden is already considerably high in the early stages, and can be equal to or greater than the costs attributed to cancer or cerebrovascular accident in adults⁸. With the progression of the disease and the need to initiate dialysis, there is a significant increase in direct costs related to health maintenance¹⁵.

When comparing the financial expenditures related to the modalities of RRT, patients who are not on dialysis and kidney transplant patients are considered less costly to healthcare systems than those on dialysis⁹. Among dialysis, hemodiafiltration, a form of HD, is considered as a cost-effective therapeutic option²². In contrast to HD, PD stood out as a lower cost option^{10,19}. In Spain, HD is five times more expensive than the treatment of the more advanced stages of CKD and three times more expensive than transplantat³³. Continuous ambulatory peritoneal dialysis was mentioned as the most efficient use of institutional and family resources³¹.

In Sweden, in relation to the healthcare costs of the general population, patients on HD, PD and kidney transplant present a 45, 29 and 11 times higher cost, respectively¹⁴. In Australia, CKD patients represent an 85% higher healthcare cost and require 50%

more government subsidies than the general population²³.

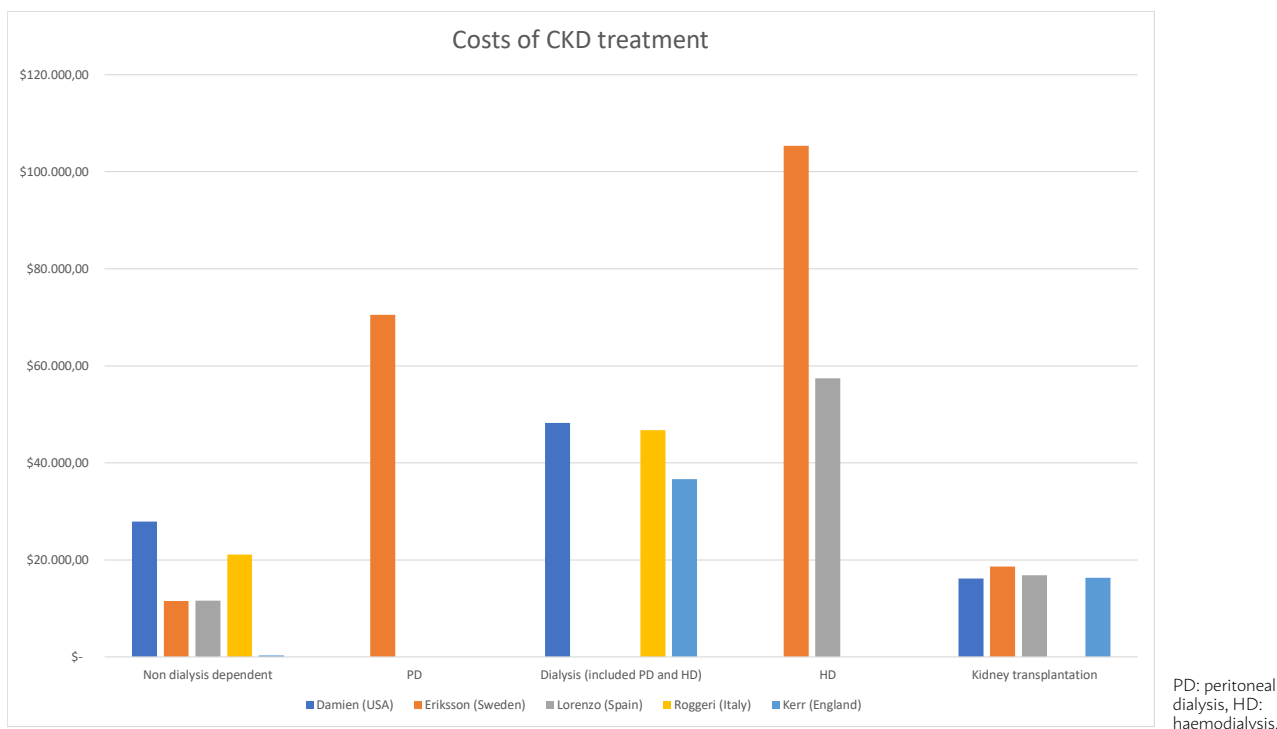
In Brazil, HD and kidney transplant stand out because of the high costs, which may be related to the high prevalence of the two modalities in the country¹². In India, costs associated with transplant are considered catastrophic and are responsible for a serious financial crisis⁴².

The socioeconomic profile of chronic kidney disease patients was highlighted in several articles as a relevant factor in the outcomes. Higher mortality was found among those with low income, unemployed¹¹, males and the elderly¹². In addition, evidence shows that the prevalence of CKD increases considerably in the elderly³⁴.

A study carried out in England showed that the main causes of death in chronic kidney patients were not related to kidney problems but to heart disease, and that despite this, CKD added to hospital costs high values in the last 12 months of life¹⁴. In India, hospital costs of CKD patients were found to be substantially higher than those without CKD³².

In diabetic patients, progression of CKD makes treatment more costly³⁷ and the direct costs of hospital admissions of patients with kidney complications are considerably higher than those without this complication³². In addition, CKD is responsible for the

FIGURE 2: ANNUAL COSTS (IN US DOLLARS) OF THE TREATMENT OF CHRONIC KIDNEY DISEASE (CKD) IN ITS DIFFERENT MODALITIES.



increase in expenses borne by DM patients, which strengthens the finding that it is the most expensive complication²⁴. Other clinical conditions that, when associated with CKD, further increase their financial burden are autosomal polycystic kidney disease^{26,27} and secondary hyperparathyroidism⁴³.

The financial repercussions of CKD treatment also have a strong impact on the economic structure of families^{18,40}. A study points out that, for parents with chronic kidney disease children, the main culprits are the impossibility of maintaining employment and high expenses related to treatment²⁸. Other research also highlights school drop-out as one of the consequences of treating the disease⁴².

With a view to reducing CKD financial expenditures, studies suggest that clinical follow-up before and after initiation of dialysis and management of comorbidities are potential sources of savings in CKD care⁹. In specific cases, home death is associated with reduced hospital costs¹⁴ and that some clinical criteria may guide the diagnosis of CKD and reduce its costs¹⁶.

Figure 2 summarizes the annual costs of treating CKD in different modalities in different countries. Despite the characteristics of the analyses of the articles of this review, such as the variability of the factors included in the total expenditure and year of the study, when presented graphically, the costs of the CKD treatment show a significant difference between the different modalities of treatment, with haemodialysis having the highest cost.

DISCUSSION

Chronic kidney disease (CKD) has been gaining major repercussion due to its increasing incidence and prevalence worldwide, becoming a serious public health problem. The treatment of CKD is costly and, therefore, it is necessary to discuss possible cost reduction solutions, especially in Brasil, where political and economic crises are repeatedly faced. Although the methods and analyses are diverse, the results of the studies incorporated in this review are unanimous in alerting about the strong financial and social impact of CKD that affects the public and private healthcare systems, patients with the disease, family members and society as a whole. It is noted that the costs of CKD, compared to data from several countries, are higher in the long term for renal replacement therapies, especially in the haemodialysis modality. Transplant, despite being a high-cost surgi-

cal procedure, has become more cost-effective over the years, not to mention improving patient survival and quality of life.

Although the economic repercussions of CKD in developing countries are even more serious in the face of the economic difficulties faced in various sectors, it is observed that these are not different in developed countries. A study carried out in Italy concluded that annual costs for patients undergoing CKD treatment before dialysis were set at EUR 11,123 (approximately USD 13,668) versus EUR 53,764 (approximately USD 66,067) for dialysis patients, proving that prevention, early diagnosis and the consequent delay in starting dialysis could considerably reduce healthcare sector expenditures¹⁵ also in countries with a more stable economy.

In the United States, considering the population served by Medicare, aged 65 or over, the total costs for parties A (Hospital Insurance, or HI) and B (Supplementary Medical Insurance, or SMI) increased by 11.5% to USD 227.100 million between 2008 and 2012, while such costs rose 53.6% to USD 44.6 billion among patients with CKD. The costs for patients with CKD and DM increased 70.2% between 2008 and 2012, while similar costs for patients without CKD, DM or congestive heart disease increased by only 4.1%⁴⁵.

In India, the average monthly cost of HD in the city of Mumbai, for example, was INR 6,142.33 (approximately USD 92), while the per capita income in the country was INR 5,130 (approximately USD 77), according to data from 2011-2012, that is, the majority of patients were not able to pay for the treatment of CKD, since there are no state HD programs in the country¹⁸, and this cost in India is significantly lower than in others countries analysed in our study, even lower than in Brasil. However, there is insufficient data to explain the reasons for this lower cost. It is estimated that in 2010 there were 2.6 million people on dialysis and 93% lived in countries with middle-high or high incomes, but the estimated number of people around the world who needed RRT was 4.9 to 9 million, indicating that approximately 2.3 million people died due to lack of access to adequate CKD care⁶.

In Brasil, most of the specialized services (secondary and tertiary care) that have the treatment modalities of CKD are linked to the Brazilian Healthcare System (SUS), representing one of the biggest bottlenecks in the system, which currently faces serious management and transfer of resources prob-

lems. According to an article of the *Folha de S.Paulo* newspaper, on March 29, 2014, for every BRL 100 (approximately USD 30) invested in healthcare, BRL 54 (approximately USD 15) come from the families and corporate investment, and only BRL 46 (approximately USD 13) come from the public sector. According to experts, among the countries that adopt the universal healthcare system, Brasil is the only one where government healthcare spending is lower than private investment. It should be remembered that Brasil is the country with the largest public and universal healthcare system, and therefore should invest a much larger amount of public capital in the healthcare sector. In the United Kingdom, public sector spending accounts for 83% of the total; in Canada, 70.4% and in Argentina, 61%⁴⁶.

Regarding the Human Development Index (HDI), in the comparison between different countries, there is a proportional association with the transplant rate⁴⁷. In 2014, Norway ranked first in the global HDI ranking (0.944) and performed 53.5 kidney transplants per million population (pmp), while in the same period, Brasil ranked 75th in the HDI (0.755) and performed 29.6 transplants pmp^{48,49}. It is emphasized that the goal for the country is to reach 50 kidney transplants pmp by 2018⁴⁹.

Based on the evidence that kidney transplant is the mode of treatment for CKD with better clinical and quality of life outcomes, these data show that, although developed countries feel the financial repercussions of the CKD, their citizens are in a privileged position, in terms of access to the best therapeutic options. The HDI ratio and number of transplants also reveals the intrinsic association between CKD and financial support, because although the magnitude of the disease is transcultural, clinical outcomes are irremediably dependent on adequate funding.

Using Brasil as a reference, it was observed that in an analysis of the years 2008 and 2013 (last report available), about BRL 61.8 and BRL 189 million (approximately USD 17 and 55 million) were spent, respectively, in kidney transplants, that is, in the five-year period, the increase in expenditures was 300%⁵⁰. However, in the same period, kidney transplants increased only 67.6%⁴⁹. This disparity may be related to the improvement of surgical techniques, the incorporation of new less invasive technologies; to the use of new, more potent and more reliable immunosuppressive drugs, both in induction and

maintenance therapy after transplant, and in the treatment of rejections; to the growth of transplant teams in number and staff; and greater longevity of patients and grafts, which generate a greater prevalence of outpatient visits in post-transplant follow-up. However, if this trend of rising charges continues, funding for the healthcare system will be seriously compromised in the future.

Given the high costs and complexity of treatments, the trend is for greater visibility to healthcare at the secondary and tertiary levels, but the results of this review point to the urgency of investing in primary care as a viable alternative for containment of expenses related to CKD.

Therapeutic interventions in the early stages of CKD are proven effective in slowing its progression. Considering that CKD, in general, is based on diseases such as hypertension and DM, continuous follow-up of patients and their families, screening new cases in the population, increasing the chances of early diagnosis, and implementing treatment for preserving kidney function are actions that need to be firmly incorporated into healthcare service practices, with emphasis on those offering basic care.

Increasing numbers of CKD and the high material and immaterial values involved in treatment modalities in a context of scarce resources have alerted to the need to develop tools and implement policies to control disease progression, aiming to reduce need for dialysis, transplant and complications.

CONCLUSIONS

It can be seen that the economic impact of CKD is global. It reaches all countries, regardless of the level of development and the model of healthcare. The studies analysed warn of the importance of primary and secondary prevention of CKD as a healthcare economy strategy. The association between population aging and the expansion of NCDs requires countries to reformulate care strategies and target their healthcare systems. The magnitude of the situation can be verified through the high incidence rates and prevalence of CKD, which is a complication of chronic diseases such as hypertension and DM. Massively investing in prevention and measures to slow the progression of CKD to the final stages, and hence avoid the need for dialysis and transplant, can represent a huge, not yet calculated, economy for patients and healthcare systems worldwide.

RESUMO

O objetivo deste estudo é discutir os custos financeiros mundiais atribuídos à doença renal crônica (DRC) e suas repercussões sobre os sistemas de saúde em países em desenvolvimento, como o Brasil. Trata-se de uma revisão sistemática realizada na base de dados do PubMed/Medline, utilizando os termos em inglês "costs" e "chronic kidney disease", em janeiro de 2017. A busca foi ampliada a outros bancos, como o Scielo e o Google Acadêmico, com o objetivo de identificar estudos locais relacionados ao assunto, publicados em revistas não indexadas no PubMed. Foram incluídos apenas artigos publicados a partir de 2012. Priorizaram-se estudos que abordavam os custos da DRC e das modalidades de tratamento. A busca resultou em 392 artigos, dos quais foram excluídos 291 por fugirem da temática principal desta revisão. Dos 101 restantes, foram excluídos revisões, comentários e protocolos. Foram incluídos 37 artigos cujo foco eram os custos globais relacionados à DRC. Apesar de os métodos e análises serem diversos, os resultados dos estudos são unânimes em alertar sobre o forte impacto, financeiro e social, da DRC que atinge os sistemas de saúde, públicos e privados, portadores da doença, familiares e a sociedade. Investir maciçamente em prevenção e nas medidas para retardar a progressão da DRC para os estágios finais e, conseqüentemente, evitar a necessidade de diálise e transplante, podem representar uma enorme, e ainda não calculada, economia para pacientes e sistemas de saúde do mundo todo.

PALAVRAS-CHAVE: Insuficiência renal crônica. Diálise. Transplante de rim. Custos de cuidados de saúde.

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