Nephrology in Bolivia

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General Table

Area[1]	1,098,581 km^2
Population[1]	11,428,245 (2019)
Capital	Sucre (constitutional and judicial) La Paz (executive and legislative)
Three most populated cities[1]	1. Santa Cruz de la Sierra 2. La Paz 3. Cochabamba
Official languages	Spanish and 36 indigenous languages
Gross domestic product (GDP)[2]	40.288 billion USD (2018)
GDP per capita[2]	2559.51 USD (2018)
Human Development Index (HDI)[3]	0.703 (114th)
Official currency	Boliviano (BOB)
Total number of nephrologists[4]	110
National society of nephrology[4]	Bolivian Society of Nephrology and Hypertension www.sobonefro.com
Incidence of end-stage renal disease[5]	2018 – 143 pmp
Prevalence of end-stage renal disease[5] (on dialysis)	2018 – 403 pmp
Total number of patients on dialysis[5]	2018 – 4400; there is no data available for PD
Number of patients on hemodialysis[5]	2018 – 4400
Number of patients on peritoneal dialysis	No data available
Number of renal transplantations per year[5]	2017 – 81 2018 – 76

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3. United Nations Development Program. Human Development Reports. Accessed in January 2020. Available in: http://hdr.undp.org/sites/default/files/2018_human_development_statistical_update.pdf
4. Bolivian Society of Nephrology and Hypertension (SBNeH). Accessed in January 2020. Available in: https://sobonefro.com/
5. National Renal Health Program, Plurinational State of Bolivia Minister of Health. Available in: http://www.saludrenal.minsalud.gob.bo

Introduction

Nephrology is closely linked to other sciences, and it involves major social, ethical, and economic implications that will be set out in this presentation, recalling some of our geography, history, and economic sociology.

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Bolivia, separated from the Pacific Ocean by the Andean Mountain Chain and from the Atlantic Ocean by the Amazon region, has an extension of 1,098,000 km^2 and 11 million inhabitants spread over three well-differentiated geographic areas from the climate, racial, social, and economic viewpoints – the highlands, the valleys, and the tropics (Fig. 9.1). In the past, such a layout prevented the country's integration and the implementation of national health programs.

Historically, Bolivia has stood out because of its convoluted political life. The government of the National Revolution, between 1952 and 1964, created several health insurance institutions to address the needs of salaried workers in urban areas, mineworkers, oil workers, and railroad workers. Unfortunately, the lack of coordination among such institutions was detrimental to the people, who required a more coherent and uniform healthcare, and it prevented a harmonious development of the medical specialties, including nephrology. Since 1964, the political changes prevented the creation of legal instruments to allow a regulated practice of medicine. As a result, there was no transplant law until 1996, and regulation for the provision of dialysis for patients with end-stage renal disease (ESRD) was just approved in 2014. For the same reason, not even moderately serious epidemiological studies concerning arterial hypertension, glomerular diseases, renal stones, acute kidney injury (AKI), or chronic kidney disease (CKD) among our population were carried out until the 1980s.

The drop of international mineral and oil prices in the 1980s jeopardized Bolivia's economy. However, we survived thanks to the growth of the informal economy, which encompassed an increasingly larger mass of individuals, lacking health insurance coverage. On the other hand, the increase in state bureaucracy has prevented the development of hospital laboratories and imaging technologies. In spite of such shortcomings, health insurance institutions were until 3 years ago and are still today the only possible alternative for those patients requiring sophisticated life-sustaining technology.

Fig. 9.1 Different regions in Bolivia; the three main cities are La Paz, Santa Cruz de la Sierra, and Cochabamba

That was the case of ESRD patients who required renal replacement therapies (RRT) until December 2014, when legislation was passed allowing patients without health insurance to receive dialysis.

We can now realize the situation being faced by nephrologists and CKD patients in Bolivia so far.

Brief History of Nephrology in Bolivia

The history of nephrology in Bolivia started with internal medicine doctors and urologists who decided to focus on the study and treatment of kidney diseases as a joint effort. In La Paz, Dr. Guillermo Jáuregui Guachalla, professor of internal medicine, published his *Notes on Nephrology* before passing away around 1970. In the 1940s in Cochabamba, Dr. Ricardo Arze Loureiro, professor of urology, performed kidney decapsulation to restore diuresis in cases of oliguric AKI long before diuretics or dialysis was available. In the 1960s, he ventured into experimental surgery in dogs, as he was convinced of the benefits of renal transplantation as a therapy to replace the chronic loss of kidney function. In Sucre, Dr. Luis Sauma, urologist and devoted to teaching, lighted the way of his son, Alejandro, a great supporter of renal transplantation in Cochabamba (personnel communication).

In 1968, the first Bolivian nephrologist, Dr. Juan Villalba, who was trained in Mexico as a pediatric nephrologist, arrived to Bolivia. At Hospital Obrero #1 in La Paz, he exercised nephrology for the first time. Doctor Villalba is among the founders of the Latin American Society of Nephrology and Hypertension (SLANH), with an outstanding participation in international scientific events. Unfortunately, he met an early death, passing away in 1975. In the late 1970s, the first group of nephrologists arrived from Mexico, and they started the practice of nephrology in La Paz, whereas a second group arrived from Brazil and settled in Santa Cruz de la Sierra. At that time, Dr. Jorge Chávez Chajtur provided prolonged dialysis treatment with a parallel plate dialyzer to a family member affected by a familial renal disease in a small town close to Santa Cruz de la Sierra. For over 5 years, the nurse Martha Chacón offered her uremic husband home hemodialysis (HD) in Cochabamba, at a time in which there were no available nephrologists in that city (personnel communication).

In 1968, the urologist Dr. Néstor Orihuela Montero founded at "Hospital de Clinicas" in La Paz the Institute of Nephrology. He donated the first parallel plate artificial kidney, started experimental surgery in dogs, and organized the first human renal transplantation team at Hospital Obrero #1 together with Dr. Gonzalo Quiroga (nephrologist), Dr. Enrique Zubieta (vascular surgeon), and Dr. Edgar Revollo (immunologist), all of whom performed the first kidney transplant on November 2, 1979. This was the first and only deceased donor renal transplant performed in Bolivia until 1993 and took place as a consequence of a gunshot wound in the head of a curious medical student who was walking around the vicinity of Hospital Obrero #1 in La Paz during one of the many and bloody military coups d'état in such period of our history. A few days later, Dr. Orlando Canedo, also urologist, performed the first living donor kidney transplant in Cochabamba. In the next 7 years, the transplant team of Hospital Obrero #1 in La Paz performed other 24 kidney transplants; it was the most experienced team in the field of transplantation in Bolivia until 1986. One year later the transplant team of Centro Médico Quirúrgico Boliviano Belga and Caja Petrolera de Salud in Cochabamba started their transplant program performing 15 successful transplants over the next 5 years (personnel communication).

In 1982, three renal physicians from the United Kingdom and Mexico arrived in Cochabamba, and they carried out a collective work of spreading knowledge and integration with other medical specialties and with colleagues of other regions of Bolivia. They promoted a comprehensive renal care program for uremic patients in Centro Medico Quirúrgico Boliviano Belga, the Military Hospital, the Oil Workers' Health Insurance, and Hospital Obrero #2. They prospectively studied the epidemiology of AKI, glomerular diseases, lupus nephritis, arterial hypertension, kidney stones, diabetic nephropathy, hyponatremia, and the ethical, social, and economic aspects of CKD and presented the results of such observations in numerous national and international meetings (personnel communication).

The Bolivian Society of Nephrology was established in La Paz in 1978 but remained inactive for several years. The First Bolivian Congress of Nephrology was organized by the nephrologists of Cochabamba in 1984, bringing also together nephrologists from La Paz and Sucre. The society was reorganized in 1987, and Dr. Jorge Nuñez from La Paz was appointed as acting president. The Second Bolivian Congress of Nephrology organized in Cochabamba had numerous participants, with a large number of high-quality presentations from the country's three geographical regions (personnel communication).

Progress has been constant through the organization and promotion of numerous scientific events, education and clinical research has been encouraged, and the level of nephrology practice in Bolivia has increased since 1984. A greater integration occurred, not only among Bolivian colleagues but also with those from Latin American countries, who have shared experiences and similar difficulties to ours. Moreover, active work has been done with national health authorities to show them the importance of CKD as a major public health

problem and to draw up guidelines for peritoneal dialysis (PD) and HD [1] and renal transplantation, as well as the renal transplant guideline and accreditation manuals [1–3].

High-Altitude Polycythemia and Chronic Kidney Disease in Bolivia

More than 140 million people in the world currently live at high altitude, representing 2% of the world's population [4]. The Andean region of South America constitutes a third major high-altitude region, primarily inhabited by two different ethnic groups: Quechua and Aymara. Among the Andean population, the hypoxia-related increase in hemoglobin is observed starting at an altitude of 1600 me above sea level.

An increased prevalence of albuminuria and proteinuria has been reported in subjects living at high altitude [5–7]. The pathogenesis of proteinuria may relate to a variety of factors, including the effects of tissue hypoxia within kidney parenchyma, glomerular capillary hypertension, hyperviscosity, and elevated right heart pressures. Polycythemia might be an independent risk factor for renal and cardiovascular disease in people living at high altitude, which is consistent with our findings that baseline packed cell volume and hemoglobin concentration were positively correlated with arterial blood pressure, serum creatinine, blood urea nitrogen, and proteinuria [8].

In a cross-sectional study of healthy, ethnically similar participants from two regions of different altitude in South America (Bolivia, Peru), we found that individuals living at high altitude had significantly worse renal function than those living near sea level, amounting to a mean difference of estimated glomerular filtration rate (eGFR) of 30%. The worse kidney function and greater proteinuria observed at higher altitude occurred despite similar age and a lower prevalence of metabolic syndrome with respect to sea level dwellers [9].

Apparently healthy subjects living at high altitude have a remarkably higher frequency of kidney disease and proteinuria, independent of a history of hypertension or diabetes. This provides some of the strongest evidence to date that long-term living at high altitude carries an increased risk for kidney disease. The characteristics of kidney disease observed at high altitude may be a new form of CKD that might be mediated by chronic hypoxia and its effects.

More than four million Bolivians (38% of total population) currently live at high altitude (2500 m above sea level), and 8–10% of this population develops high-altitude polycythemia [10]. In our study, 40% of total screening polycythemia healthy subjects had some degree of proteinuria [5], so we estimate that roughly more than 300,000 people are at risk for kidney disease.

It is evident that diabetes, hypertension, and glomerular diseases are the leading ESRD causes in the world. However, there are specific regional conditions (e.g., high altitude-polycythemia CKD) that deserve to be studied with the main objective to reduce the exponential increase of patients requiring RRT, inaccessible to large percentage of the population in developing countries. Some of these patients are the dwellers living at high altitude in countries such as Ecuador, Peru, and Bolivia.

Chronic Kidney Disease Epidemiology

The prevalence and incidence of renal diseases in Bolivia are not well known. This lack of knowledge is an obstacle to the adoption of preventive measures, which may be of great value in a social and economic environment where treatment options for ESRD are simply not available. A study coupled with an educational campaign on renal diseases was conducted in 21 centers from three selected areas of Bolivia (plains, tropical, and valleys regions) in 1998 [11]. In this study, urine samples were collected and screened using a dipstick for chemical analysis and microscopic urinalysis. From 14,082 subjects screened, urinary abnormalities were detected in 4261 subjects at first screening. The most common form of urinary abnormality was hematuria, which was found in 2010 (47%). Other renal abnormalities were leukocyturia (41%) and proteinuria (11%). Confirmatory tests and further clinical studies were then carried out in 1019 subjects, and the study found that 35% had no urinary abnormalities. In the remaining subjects, the following diagnoses were made: asymptomatic urinary tract infection (48.4%), isolated benign hematuria (43.9%), chronic kidney disease (1.6%), renal tuberculosis (1.6%), kidney stones (1.3%), diabetic nephropathy (1%), and polycystic kidney diseases (1.9%) [11].

According to the global burden of disease project, CKD stage 3 prevalence in the country was 40%, by 2017, and CKD was the fourth most common cause of death in Bolivia with an increase as a cause of death of 36% from 2007 to 2017 [12]. The main causes of CKD in Bolivia according to the information that the Ministry of Health has through its National Renal Health Program (NRHP) are diabetic nephropathy (47.4%) and unknown causes (13.7%). About 10% had some form of glomerulopathy. Interestingly, chronic rejection or "loss of the graft" was identified in 4% of the patients.

By March 2015 there were 2231 ESRD patients who were receiving HD, 70% (1562) of them were over 60 years old, 3% were children and adolescents, and 27% between 18 and 50 years of age. It is estimated that an increase of 68% will be observed in ESRD patients in the next 5 years [8]. Of the 2231 patients with chronic HD treatment, 44.8% have short-

term health insurance that cover their treatments, 31.3% are covered by the NRHP, and 23.9% of patients pay their sessions from their own pocket [9].

Unfortunately, current policies aimed for the prevention of CKD do not have sufficient support, given that the efforts are regional and supported by local scientific societies without the involvement of the Ministry of Health through its NRHP. Most of the NRHP resources are allocated for providing HD and kidney transplant to patients with ESRD (36 million dollars), and according to the NRHP website, an investment of US$ 34,632 is made every year for providing support to the identification of CKD (creatinine blood samples and urine strips) and for training healthcare workers in the correct identification, diagnosis, treatment, and referral of CKD patients to healthcare centers [10]. Regrettably, there are no official, or up to date, data on the accurate number of CKD patients in Bolivia, and data on mortality is also not available [9].

Renal Replacement Therapy Scenario

Free provision of HD and PD was only contemplated in the National Health Insurance system (the main state-run health insurance provider in the country) and with coverage extensible to intermittent peritoneal dialysis (IPD) until 2014 when the National Renal Health Program (NRHP) was established. After the enactment of Law no. 475 of "Integral Health Services Provision Act of the Plurinational State of Bolivia" (Ley de Prestaciones de Servicios de Salud Integral del Estado Plurinacional de Bolivia) on December 30, 2013, free treatment for patients with ESRD without health insurance started [13]. Upon review of the Ministry of Health's official page and specifically the section pertaining to the National Renal Health Program, it can be seen that all the information is limited to CKD prevention initiatives, HD, and renal transplantation. Currently there are 4400 adult patients and 31 children in Bolivia who are receiving HD treatment. Unfortunately, the NRHP could not provide us information about the number of patients who are currently receiving intermittent peritoneal dialysis (IPD). Until recently, there were no supplies to perform chronic ambulatory peritoneal dialysis (CAPD) or appropriate cyclers to perform APD. To date, the only public institution officially performing CAPD or APD with the twin-bag system, "Y" connector, and flexible 2000–6000 ml PD bags and/or a cycler is the regional National Health Insurance (Caja Nacional de Salud – CNS)'s maternal and child care unit in Santa Cruz (one patient on APD and another two on CAPD). Other patients are also treated with these modalities in private institutions in the city of Santa Cruz (three on APD and three on CAPD). IPD is the prevailing modality in the rest of the country. La Paz and Tarija still have active IPD programs

Fig. 9.2 Local production peritoneal dialysis solution (rigid bottle with 1 L volume and spike connector)

in the National Health Insurance regional units. Cochabamba cancelled a similar program in mid-2018.

The emphasis in performing IPD is stated textually in the regulations, noting, "PD must be performed in second and third level hospitals." The regulations recommend a ratio of 1 nephrologist and 1 nurse for every 40 patients. Other guidelines provided for in such a document include a solutions' instillation time of 10–15 min, using dwell time of 30–40 min, 20 exchanges per session, 2 weekly sessions, and an exchange volume of 1000–1200 ml/m^2 of body surface area.

The hospitals performing IPD use locally produced solutions, sold in rigid plastic containers of 1000 ml, in 1.5%, 2.5%, and 4.25% glucose concentrations and with spike-type connectors (Fig. 9.2).

As for regulations of RRT for ESRD patients in Bolivia, there is a document entitled "Hemodialysis and Peritoneal Dialysis Regulations," which can be accessed on the Web [1]. Such regulations describe briefly HD and PD techniques, their different modalities, prescriptions, and technical aspects of each technique, like the reuse of filters which is allowed to be done up to 15 times. Most of the document is focused on administrative and technical requirements of implementing an HD unit; for example, in the case of a PD unit, the document states that for every 40 patients, the PD unit needs 1 nephrologist, 1 nurse with training and experience in PD,

and 2 PD technicians for every 15 patients. The PD unit also needs to have one social worker, dietitian, psychologist, surgeon, and administrative personnel. In the case of an HD unit, it is required to have 1 nephrologist for each 40 patients and 1 nurse with training and experience in HD for no more than 4 patients, whereas the number of HD technicians is not well defined on the document, and it will depend on each HD unit workload; it also needs to have one social worker, nutritionist, psychologist, surgeon, and administrative personnel.

Convective therapies like hemodiafiltration (HDF) and hemofiltration (HF) are available in Bolivia, usually in private centers. However, the number of patients who are receiving such therapies is not known, and the number of patients placed on such therapies could be low due to the high cost of these types of therapies not reimbursed by the government.

Peritoneal Dialysis

According to Arze's data, introduction of chronic peritoneal dialysis (PD) catheters in our country took place in the early 1980s [14]. In Bolivia, PD has always played a marginal role in relation to HD. As described by Pecoits-Filho [15], there is great variability across Latin America in the proportion of patients who receive RRT with this technique. Only Mexico provides care to a larger percentage of its ESRD population using PD (86%). Brazil has a total number of patients higher than Colombia, but proportionally Colombia ranks second in the region (46%). As mentioned by D'Achiardi [16], insufficient training in PD could be one of the causes for which such a technique is used with less frequency. An additional factor for PD not to be more widely used is the delay in the implementation of technologies that represent milestones in the provision of this type of RRT (such as the double or twin-bag system and "Y" set or the cycler machines for automated peritoneal dialysis (APD)).

An important source of information about some characteristics, particularly epidemiologic and clinical, is available through the "National Peritoneal Dialysis, Hemodialysis, and Renal Transplantation Registry," which provides information from 18 hospitals and data of 334 patients monitored until June 2007 (30.92% of all patients with RRT surveyed) [17].

Information related to PD was collected in a "National Peritoneal Dialysis Registration Form." Most of the patients on PD were elderly over 60 years old (27.4% between 61 and 70 years old and 22.3% ≥71 years old). Moreover, 49.7% were women. By ethnicity, 70.9% were mestizos, 28% white, and 1.1% Afro-Bolivian.

Almost half of the patients had completed high school (49.7%) and 32% elementary school. Only 3.4% were illiterate, and 14.3% had some university degree.

The registry also mentions some employment aspects: 44% of the patients were unemployed, 36.6% were retired, and only 14.9% were actively employed.

The eastern region of Santa Cruz had most of the patients on PD (61.1%), and when compared with the rest of the regions in the country, it had at that time one of the lowest HD percentages (17.7%).

In terms of other conditions and care received by such patients, the majority (81.7%) had high blood pressure or was on antihypertensive medication; 55.9% received erythropoietin, and 14.3% received intravenous iron. Because of the voluntary nature of the registry, it is worth mentioning that in most cases there were no data related to such prescriptions.

The adoption of this renal replacement modality was slow in the decade of the 2000s. By 2001–2002, there were records of three active patients only; by 2005, other two patients had been treated with PD. It was only in 2006 and 2007 that a significant increase in the number of patients treated with this dialysis modality was noticed (60 and 104, respectively). Most of them had short-term health insurance (59.5%) in public institutions. The main institutions that provide PD were the National Health Insurance (Caja Nacional de Salud – CNS) with 34.9% of the patients and the Oil Workers' Health Insurance (Caja Petrolera de Salud – CPS) with 18.9% of the patients. It is also noteworthy that 34.5% were private patients. Until June 2007, the two regions in the country with the most reported new cases were Santa Cruz (75 cases, 58.1%) and Oruro (30 cases, 23.5%). It is important to mention that the latter region ranks seventh in the country's GDP and that its PD patients were treated in a public institution. The latter region also contrasts with Santa Cruz, which has the most thriving economy in Bolivia. This means that the election of PD over HD was related to aspects other than economic ones, such as probably the healthcare provision (physicians and nurses), knowledge of the technique, and logistical aspects (availability or not of technology for HD, the overcrowding of HD units, etc.). Also, 77% of the patients did not exceed a year with PD. Only 61.7% had a period of less than 5 days between the IPD sessions, 22.3% had a period of 6–10 days between sessions, and 16% were treated with a latency period greater than 10 days between each session.

Physical capacity was very limited in 34.9% of the cases, 46.9% had normal activity with some limitations, only 9.1% had unrestricted normal activity, and 9.1% were unable to take care of themselves. At that time, three patients with hepatitis B (1.7% of those surveyed) and one with hepatitis C (0.57% of those surveyed) were treated in the country. No patient with HIV was treated with PD during this period. The main causes for ceasing treatment were death (31.4%) and dropping out of the technique; 6.3% were transplanted and 4% switched to HD. Here we must also take into account the

considerable underreporting of mortality, which led the authors to speculate that the actual mortality figure was around 45.7%. The main causes of mortality were cardiovascular (30.9%) and multi-organ failure (29.1%). The direct percentage of mortality attributable to infectious complications related to the technique is not specified.

Colleagues from La Paz and Cochabamba (who work for the Caja Nacional de Salud – CNS) contributed data on their respective IPD programs. In La Paz, Dr. Abel Lucero is responsible for a cohort of patients receiving PD due to a formal contraindication to perform HD or the loss of vascular access. They have occasionally treated patients positive for hepatitis B. In Cochabamba, an analysis with data kindly provided by Dr. Rolando Claure-Del Granado was performed and found a total of 33 patients treated between 2014 and 2018; 48.5% were women, with a median follow-up of 21.9 months (over a period of 0.4–67.6 months). The patients received an average of 8.2 ± 1.46 sessions (or IPD days) per month and were treated for a median of 66 sessions (range, 2–145). Mortality during the follow-up was 27.3%, and the average survival with the technique was 50.1 months (CI 95% 39.9–60.3, median of 67.6 months). Survival at 12 and 48 months was 93.6% and 64.8%, respectively (Fig. 9.3); 54.5% of the patients required a switch to HD with a median follow-up of 35.6 months (CI 95% 20.6–60) until the switch (Fig. 9.4).

Dialysis Reimbursement Policies

Until 2005, short-term health insurance companies like Caja Nacional de Salud (CNS) provided healthcare benefits to patients receiving HD up to 52 weeks; thereafter, the patient was transferred to public HD units of the Ministry of Health. In that year, the NRHP was established, and after the enactment of Law no. 475 of "Integral Health Services Provision Act of the Plurinational State of Bolivia" (Ley de Prestaciones de Servicios de Salud Integral del Estado Plurinacional de Bolivia) on December 30, 2013, free treatment for ESRD patients without health insurance started [18].

In 2008, it was estimated that 800 new cases of ESRD patients were being identified each year. The cost per HD session was estimated to be US$ 70, making a total of US$ 10,920 the cost of HD for one patient per year. Patients who did not have any type of short-term insurance like the Caja Nacional de Salud (CNS) needed to pay for their sessions. As of September 2008, 1080 HD patients were registered nationally; 40.7% corresponded to the CNS, 21.8% to private centers, and 18.6% to public hospitals. The cost per HD session at public institutions for patients who did not had any type of health insurance was approximately US$ 34.6 per session (US$ 5402 per patient per year) and was subsidized in part (around 80%) by the Minister of Health NRHP that provided some supplies for each HD treatment (i.e., filters and lines),

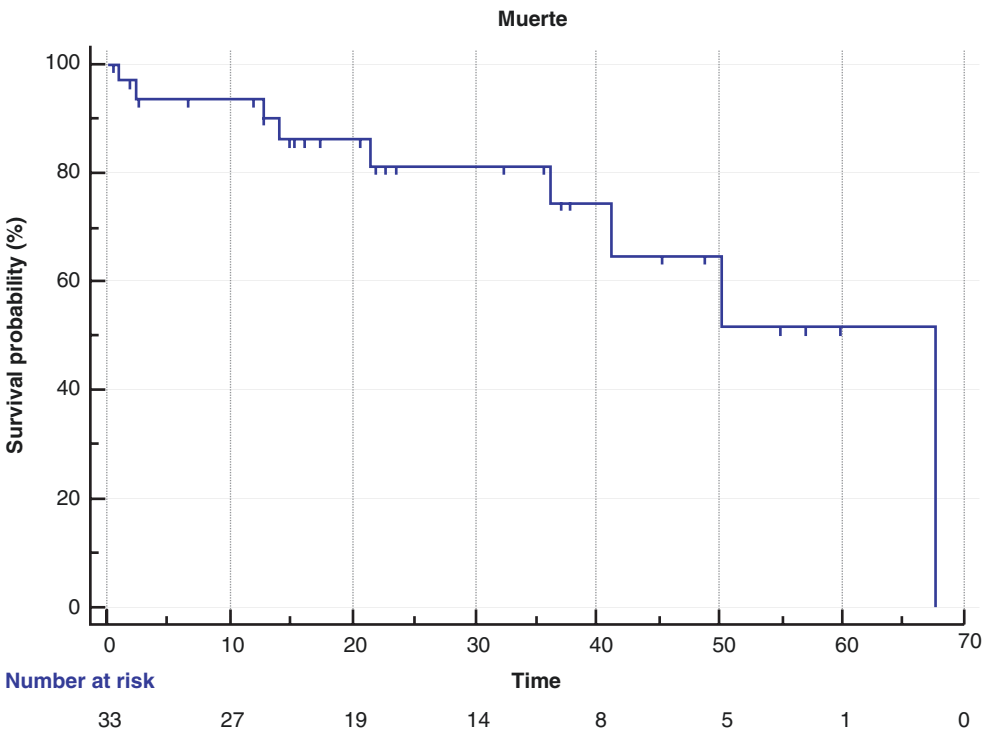

Fig. 9.3 Survival of patients who are on the intermittent peritoneal dialysis program at Hospital Obrero #2, CNS, in Cochabamba, Bolivia

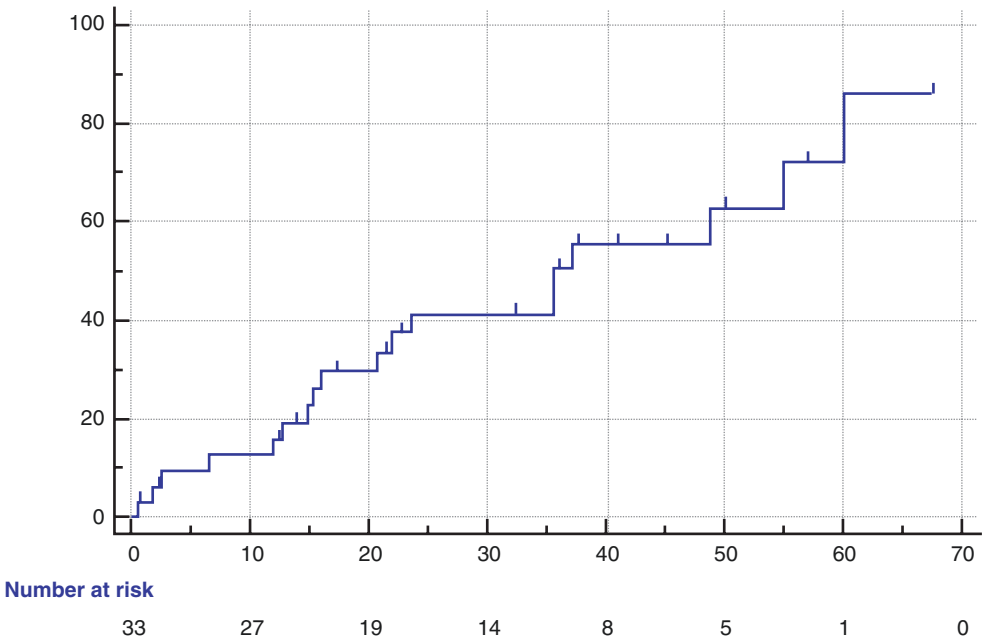

Fig. 9.4 Cumulative incidence of technique failure and transfer to hemodialysis of patients on the intermittent peritoneal dialysis program

and the patient needs to pay US$ 6 per session (US$ 936 per year). However, not all patients had the capacity to pay this amount, besides the costs of transportation, medication, and monthly laboratory analyses. Since 2014, the municipal governments of each province in Bolivia pay each HD session for all patients who do not have any type of health insurance [18]. Since 2016, municipal governments have started the purchase of HD services from private units due to the saturation of the public units. The reimbursement that each HD center receives should include the cost of medications (i.e., antihypertensive, phosphate binders, vitamins, etc.), erythropoietin, and IV iron. Currently the cost per HD session is US$ 173 in the short-term health insurance system (i.e., CNS) HD centers, and the amount per HD session subject to reimbursement is US$ 103 for patients who benefit from Law no. 475; however, there is no data about the cost per IPD session, given that this modality of dialysis is only done in limited places.

Until March 2019, there were 4400 patients on HD, with a total of 686,400 sessions per year, representing a total cost for the NRHP of US$ 16,050 per patient/year (US$ 103/session) and a total expense of more than 70 million dollars a year [17]. The cost of HD per patients per year in Bolivia is lower as compared with other countries with similar GDP per capita (US$ 16,050 vs. US$ 18,720) [13]. Finally, we want to highlight that current reimbursement policies are focused on intermittent HD, with no peritoneal dialysis (IPD, CAPD, or APD) or home HD reimbursement policies available, except for anecdotal cases.

Reimbursement policies also cover some medications like antihypertensive medications (i.e., B-blockers, ACEIs, ARBs, and calcium channel blockers), ESAs (alpha-EPO), calcium-based phosphate binders, IV iron, and vitamins.

Acute Kidney Injury in Bolivia

AKI is a global healthcare issue with high morbidity and mortality and caused by multiple and diverse etiologies. It can develop both in the community and in the hospital setting. A recent observational study has shown that the incidence of hospital-acquired AKI in Latin America is 45% and predominately affects a much younger population [19]. While cardiac failure, postoperative AKI, and nephrotoxins are the main etiological risk factors in high- and upper-middle-income countries in the region, in low- and low-middle-income countries (LLMIC), dehydration, infections, animal envenomation, use of herbal medicines, and complicated pregnancy are the most important drivers of AKI. Unfortunately, there is not much published data about the incidence, risk factors, etiology, and outcomes of AKI in Bolivia. Ramirez Torrejon JN and Arze RS published one of the first studies of AKI in Bolivia in 1993; it was a single-center study that described the incidence, etiology, treatment, and outcomes of patients with hospital-acquired AKI (HA-AKI) [20]. During a period of 2 years, they found 41 cases of HA-AKI (defined as a doubling of the baseline serum creatinine) and divided AKI into oliguric and non-oliguric. The first group was defined by a urinary volume <5 ml/kg/h or <400 ml in 24 h in adults and <1 ml/kg/h in children, most of the patients were male (51%), and the mean age was 54 ± 17 years. Common risk factors were

hypotensive episodes, most commonly due to cardiogenic shock, sepsis, and hypovolemia, exposure to nephrotoxins (NSAIDs and aminoglycosides), use of contrast media, and rhabdomyolysis. Prerenal AKI was the most common presentation with and incidence of 59%, with oliguria being found in 76% of patients at the time of diagnosis. Ten patients required RRT, PD was used in five of them and intermittent HD in three, and two patients were treated with continuous arteriovenous HF. The mortality rate was 49%, and nine patients died due to sepsis and eight to cardiac failure. In a more recent study, Carpio-Deheza et al. described the incidence of AKI in a single third level center [21]. Using Acute Dialysis Quality Initiative (ADQI) RIFLE criteria and Acute Kidney Injury Network (AKIN) diagnostic criteria, the authors found 65 patients with HA-AKI during 2010; most patients were male (58.3%) and older than 60 years (25%). The three most frequent causes and/or risk factors for HA-AKI described in this study were hypovolemia (41.6%), hypertension (30.5%), and congestive cardiac failure (11.1%). Unfortunately, this study fails to describe what type of medical treatment patients received, RRT requirements, or short-term and long-term outcomes like renal recovery, mortality, and progression to CKD.

In low-income countries like Bolivia, most people who develop AKI continue to die as a consequence of this disorder and are not fortunate to have an early diagnosis or receive adequate treatment [22]. In Bolivia, like in other LLMIC, AKI commonly occurs in the community (CA-AKI) and is a disease of the young, and it is frequently developed as a complication of a single, potentially preventable, treatable, and reversible disease [23]. Community-acquired AKI is often preventable with simple measures like hydration or treatment of an acute infection. In those patients who progress to a stage where RRT is needed, dialysis is usually provided in nephrology units located in third level healthcare centers with ≤5 machines devoted to AKI treatment [24]. Intermittent HD is usually available in 100% of the units and is the most frequent form of RRT employed, while other techniques like prolonged intermittent HD, continuous renal replacement therapies, and PD are less frequently used. In areas with poor infrastructure, most of the patients present to the healthcare system late and often in advance disease stages and where RRT is not available.

Following the example of the 3 by 5 initiative by UNAIDS and WHO to provide three million people with HIV/AIDS living in low-income countries with antiretroviral therapy by 2005, the International Society of Nephrology (ISN) launched the 0by25 initiative with the goal to achieve zero preventable deaths from AKI by 2025 in low-income and low-middle-income countries where lack of early identification and resources for treatment may impact patient outcomes, and Bolivia is one of the three pilot centers of this initiative. Preliminary data from the 0by25 Pilot Feasibility Project, designed to evaluate an education and training program coupled with a point of care (POC) test and teleconsultation to improve detection and management of AKI in low-resource settings, has shown that the incidence of CA-AKI is 30% with a mortality rate at discharge of 3.1% and at 6 months 13.7%; 26% of patients developed CKD at day 90. The 0by25 initiative has shown that the use a POC test could identify a significant number of patients with CA-AKI who might otherwise not be recognized, allowing an early diagnosis and the implementation of an adequate treatment.

Pediatric Nephrology

The interest on pediatric nephrology as a subspecialty has increased in our country; in the past 10 years the number of pediatric nephrologists has increased from two to ten practitioners. Pediatric nephrologists in Bolivia have helped to increase early diagnosis and improve treatment of glomerular diseases in children, as well as to improve diagnosis and treatment of AKI like improving and expanding the use of PD to patients under 10 kg and especially to critically ill neonates and toddlers [25]. Certain aspects of pediatric nephrology like ongoing patient care needs and its technical aspects (renal biopsy, dialysis, and transplantation) guarantee its continuing future growth as a major pediatric discipline in our country. CKD management by pediatric nephrologists has made us gain a space within pediatric specialties, and our colleagues now refer their patients for treating this condition properly. But if we look to improve outcomes, CKD treatment needs to be provided by a multidisciplinary team. On the other hand, we have an intense work in the diagnosis and routing of the treatment of congenital abnormalities of the kidneys and the urinary tract (CAKUT) since the number of pediatric urologists is insufficient in Bolivia. Pediatric nephrologists have become a fundamental part of the screening and diagnosis of CAKUT. However, some patients have to travel to the main cities of Bolivia or even to border countries like Chile, due to the lack of pediatric urologists.

Nephrocalcinosis and urolithiasis are other important medical conditions in our country. We have been surprised by the amount of kidney stone episodes in children, due to dietary factors, lack of proper fluid intake, increase in sodium load from daily diet (i.e., instant soups, broths, and energy drinks), and from obesity and metabolic syndrome in adolescents. Genetic and/or metabolic disorders are usually involved when the recurrence is the rule in young children [26].

Before the enactment of the Law no. 475 in our country, treatment of CKD in children meant a catastrophic expense for their families [18]. Dialysis and kidney transplantation coverage is now provided to all patients with AKI and ESRD who need acute or chronic RRT. On February 20, 2019, this

law was subject to an amendment, which has increased the coverage to children over 5 years of age who had earlier been without health insurance. To benefit from this law, ESRD patients are considered to have a visceral disability (a wrong concept from our point of view). This definition leaves many children with AKI, pre-dialysis CKD, and other kidney diseases without health coverage and treatment. Although these policies are changing and extending health coverage to the pediatric population, it is still not clear how much of the pediatric population this law covers, but these are the first important first taken in order to improve the care of CKD children.

The number of pediatric nephrologists in Bolivia is still low. Currently there are ten distributed in the three main cities of Bolivia (La Paz, Cochabamba, and Santa Cruz de la Sierra) as follows: four in La Paz, four in Cochabamba, and two in Santa Cruz de la Sierra. Pediatric nephrologists do not have their own scientific society, and most of them are affiliated to the Bolivian Society of Nephrology and Hypertension; however, pediatric nephrologists actively communicate among themselves through social media networks and have an active participation in some academic and special events of pediatric nephrology in the region.

Among future perspectives of pediatric nephrologists in Bolivia are to organize an independent scientific society, review the national practice standards of pediatric HD, PD, and renal transplantation, and develop an initiative so that PD could become a sustainable form of RRT in Bolivia.

Renal Transplantation: Living Donor and Deceased Donor

Even though the dialysis and renal transplantation records in Bolivia are mandatory, compliance with such requirements barely reaches 32% [27], which provides only partial information of living deceased donors transplant in Bolivia. The number of transplants performed in Bolivia the past 3 years has remained above 70 per year according to the information provided by the National Kidney Health Program registry (2016, $n = 89$; 2017, $n = 82$; and 2018, $n = 76$).

In the past 4 years, there has been an increase in the number of nephrologists (5–11 pmp) [28], but we are still below the average as compared to other countries in our region. Moreover, the prevalence of patients living with a functioning transplant totals 31.6 pmp, five times below the average in Latin America (159 pmp) [27]. Some of the causes for this low prevalence are explained on Fig. 9.5. This also explains why our deceased donor transplantation activity is 0.8 pmp, only exceeding the Dominican Republic according to the 2015 registry of the Latin America and the Caribbean Society

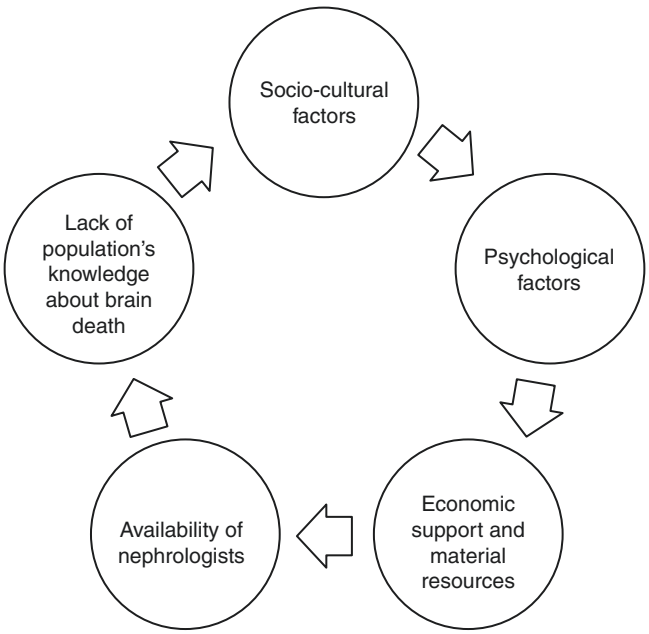

Fig. 9.5 The interactions of several factors like the lack of population's knowledge about brain death and the low number of nephrologists could explain the low prevalence of living and decease donor transplantation in Bolivia

of Transplantation (STALYC). However, Bolivia is the fourth country with the largest number of living donor renal transplant activity (7.4 pmp) as compared with the rest of the Latin American region that has 7.1 transplants pmp. If we consider both types of transplant donors, we have a total of 9 transplants pmp, with Uruguay, Brazil, and Argentina being the countries with most renal transplantation activity (27–28 pmp). This shows that attitudes toward living donation among the Bolivian population needs to be improved, and we must approach to the attitudes of Bolivians residing in Spain which is favorable and represents a group that may be encouraged to become donors, with only 10% of the population against living donation [29].

To improve CKD prevention and treatment policies, various cooperation agreements were signed among some Latin American countries and STALYC [28, 30]. One of the most important agreements entails the developing and/or improvement of the deceased donor transplantation program. Even though a culture of venerating people who have passed away still exists in our country, a larger number of people are willing to donate organs: 49% are in favor, 21% are against, and 30% are undecided according the study of Rios et al. [31]. Policies on education and information about concepts and definitions of transplantation, xenotransplantation, deceased donation, or brain death are some of the factors that influence donation, as shown by Rios et al. in a survey of Bolivians living in Spain where 73% of the participants were unaware

of the different definitions [32]. While lack of knowledge was not statistically significant associated to the decision-making process at the time of organ donation, there are other social, personal, familiar, and educational factors involved and that need to be addressed in our country couple with better health policies in order to improve deceased organ donation [33].

All patients in the dialysis program have the option to get a living or deceased donor kidney transplant. Patients who lack a living donor can access the waiting list for deceased donor transplantation, which is organized and supervised by the Ministry of Health through the National Renal Health Program. Organ allocation is based on standard criteria (UNOS, United Network for Organ Sharing), in addition to the Ministry of Health's Transplantation Manual [1].

The main immunosuppression scheme used in Bolivia is the use of basiliximab 20 mg IV x2 for acute kidney rejection prophylaxis and the use of prednisone, cyclosporine or tacrolimus, and mycophenolate as maintenance immunosuppressive regimen. Since 2014, the cost of immunosuppressant medications for patients without medical insurance is covered by the local governments.

Table 9.1 Evolution of regulatory acts and laws regulating transplant activity and organ trafficking in Bolivia

Enactment dates	*Transplant Law in Bolivia and the evolution of regulatory acts*
November 5, 1996	First law on transplantation and donation of organs, cells, and tissues (Law no.1716)
June 21, 1997	Act no. 24671 that regulates Law no. 1716, for public and private healthcare and health insurance facilities nationwide
December 2011	Act no. 1115 that repeals Act no. 24671. These are the new regulations for Law no. 1716, which set the scope of application, implementing categories of donors, recipients, and the responsibilities and duties of healthcare facilities and professionals that participate in the donation and transplantation of organs, cells, and tissues
January 23, 2014	Act no.1870 amends and complement Act no. 1115, on paragraph "b," on the definition of brain death. It incorporates that the recipients of organs, cells, and tissues must be Bolivian citizens, with the exception of foreign nationals and their living donors who are in transit. It also provides public support for kidney transplants to patients lacking health insurance
Enactment dates	*Laws regulating organ trafficking*
July 1978	Article 90 of the health code, sanctioned by Law no. 15629
November 5, 1996	Articles 17, 18, 19 of Law no. 1716
July 31, 2012	Article 281 b of the criminal code, amended by Article 34 of Law no. 263

Organ Procurement and Transplantation Network Policies

The Political Constitution of the Plurinational State of Bolivia recognizes that the state shall protect the right to health, promoting public policies that seek to improve the quality of life, collective well-being, and people free access to health services. In addition, it points out that specific laws will regulate the donation and transplantation of cells, tissues, and organs under the principles of humanity, solidarity, opportunity, gratuity, and efficiency. In spite of good intentions and regulations, there is not an organized system to allow a deceased donor procurement activity, representing a limited number of transplants, keeping a long waiting list, and maintaining HD centers overfilled with patients.

The first procurement and cornea transplant was reported in Bolivia in 1948, and the first kidney transplant was performed in 1979, as previously described. Over two decades, the law did not regulate kidney transplants, and only in November 1996, the transplant Law no. 1716 was enacted [34], 17 years after the first kidney transplant [35]. Since then, several amendments have been done by the promulgation of several acts that regulate the transplantation activity in the country (Table 9.1).

In Bolivia information and promotion of organ donation has not had an important impact in the population due to some country's idiosyncratic and religion factors. The programs have not been able to reach the whole territory of the country nor the various social groups; it has not been made any plans for the near future in order to increase the awareness of organ donation in schools, in universities, or to the general population. Another barrier is the lack of a national procurement center and the lack of improvement of current procurement policies. These are major weaknesses of this model, which has failed to increase the number of donors over the years.

In the case of deceased donors, the Regional Transplant Coordinator, working under the Regional Health Service (SEDES), will register the deceased donor in the national waiting list, managed by the Ministry of Health, for the allocation of organs, cells, and tissues among registered recipient patients, using criteria set in standard applicable manuals and protocols [1]. Deceased donation process will be managed by the Regional Transplant Coordinator and overseen by the Regional Transplant Commission, operating under SEDES. Healthcare workers are required to give notice immediately to the Regional Transplant Coordinator of the existence of patients with brain death directly or through the local hospital coordinator (Fig. 9.6).

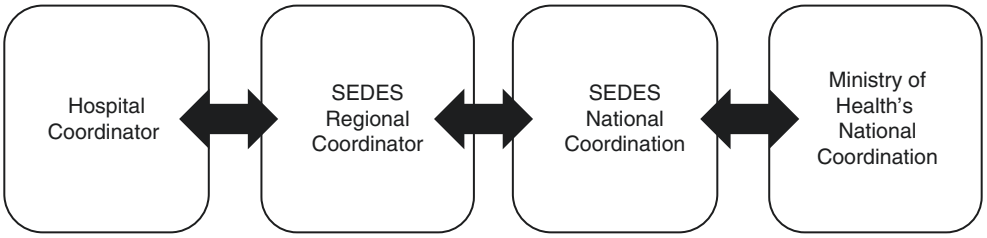

Fig. 9.6 Deceased donation process of notification. The entire process is overseen by the Regional Transplant Coordinator and overseen by the Regional Transplant Commission, operating under the regional health service (SEDES). Healthcare workers are required to give notice immediately to the Regional Transplant Coordinator of the existence of patients with brain death directly or through the local hospital coordinator

Nephrology Practice and Job Market

Throughout history, in Bolivia, specialists who have not been incorporated into a hospital which supports and encourages them and offers appropriate, reliable, and high-quality laboratory and imaging technologies, and specialists who have not had a group of colleagues, residents, interns, or students to work with, have tempted to migrate to other countries. However, in recent years more specialist have returned to Bolivia after finishing their training abroad, and they usually are characterized for having devotion to teach, interest in basic or epidemiological clinical research, passion for clinical nephrology, and interest in dialysis in its various forms or toward various aspects of renal transplantation. These specialists have an open and fertile field to develop fully as an outstanding professional in the field of nephrology.

Nephrologists can work in some of the private or public schools of medicine spread over the various regions of Bolivia; they can participate in the training of specialists in one of the five existing fellowship programs in the country; they can contribute to the training of nurses in public or private nursing schools. Finally, they have much to teach to the community in general, about the role of the kidney in health and disease and, above all, about the prevention of CKD and its progression.

Nephrologists with a passion for basic research still have no institution to work, as we lack as a country specialized laboratories. Nevertheless, if they have a passion for clinical and epidemiological research, there is much for them to do. They can organize or participate in courses on research methodology, data analysis, and biostatistics, bibliography search, and writing of medical papers, sponsored by the Scientific Societies of Medical Students of the various schools of medicine, the Bolivian Medical Association, the Bolivian Society of Nephrology, or other scientific societies.

If nephrologists are interested in clinical practice, they can focus on an in-depth study of the main nephropathies, including community- and hospital-acquired AKI, glomerulopathies, tubulointerstitial diseases, hypertension, diabetic nephropathy, renal complications during pregnancy and the various aspects of CKD. Moreover, they can devote themselves to an in-depth analysis and description of infrequent clinical cases and, finally, if they are trained, to the various aspects of interventional nephrology.

If the specialists are interested in RRT, they can actively engage in the startup and development of CAPD and APD units, intermittent HD, and in CRRT.

Finally, if nephrologists are interested in transplantation, they can actively participate in the organization, implementation, and development of the coordination and procurement of organs and in the dissemination of the advantages of renal transplantation and the concept of cerebral death and the importance of organ donation to the community. Furthermore, they can be actively involved in the clinical aspects of transplantation and, above all, in the assessment of recipients and potential donors and in the diagnosis and treatment of the various complications throughout the renal transplantation period.

In conclusion, Bolivia offers the specialist in nephrology great possibilities to work in the different areas of nephrology. However, it must be highlighted that to do so, great motivation and passion for work are required above all, given that contrary to other countries in Latin America, North America, and Europe, the economic incentives are negligible, for example, the average salary for a nephrology in public hospital (run by the Minister of Health) or in hospitals run by the short-term insurances (i.e., Caja Nacional de Salud) ranges from US$ 800 to US$ 1200 per month.

Conclusion

In Bolivia, CKD prevalence and incidence rates have been growing steadily, probably as a result of the increase in life expectancy, aging of the population, a growing epidemic of type 2 diabetes, and a fast epidemiological transition across the country. Chronic noncommunicable diseases like CKD impose an enormous cost, barely supported at present and unlikely afforded by the government in the future. There is ongoing national CKD detection program in Bolivia, but it needs to be improved. Data about CKD and AKI are scarce,

and public health awareness is low. High-risk patients must be studied, using simple determinations such as creatinine and proteinuria. For these programs to succeed, lifestyle changes must be encouraged, and public awareness must be increased through teaching and media-oriented activities. In concert, continuous activities in the area of education, research, and advocacy will be crucial in addressing the challenges of practicing nephrology in Bolivia and will enable the design of effective policies to prevent and control kidney disease in the future.

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