Complementary Therapies in Medicine 47 (2019) 102215

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Use of medicinal plants in patients with chronic kidney disease from Peru

Percy Herrera-Añazco[a,*], Alvaro Taype-Rondan[a], Pedro J. Ortiz[b], Germán Málaga[c], Agueda Muñoz del Carpio-Toia[d], M.G. Alvarez-Valdivia[d], C. Juárez- Huanca[d], L. Ciudad- Fernandez[b,e], R. Bruner- Meléndez[e], W. Samaniego- Mojica[f], E. Perez- Rafael[f]

[a] Universidad San Ignacio de Loyola, Unidad de Investigación para la Generación y Síntesis de Evidencias en Salud, Lima, Peru
[b] Instituto de Gerontología, Facultad de Medicina -Universidad Peruana Cayetano Heredia, Lima, Peru
[c] Conevid, Escuela de Medicina, Universidad Peruana Cayetano Heredia, Lima, Peru
[d] Universidad Católica de Santa María, Escuela de Medicina Humana, Vicerrectorado de Investigación, Arequipa, Peru
[e] Facultad de Medicina – Universidad Nacional de Ucayali, Ucayali, Peru
[f] Universidad Peruana Cayetano Heredia, Lima, Peru

ARTICLE INFO

Keywords:
Medicinal plants
Chronic kidney disease
Healthcare centers
Medical care
Peru

ABSTRACT

Objective: To describe the use of medicinal plants in patients with chronic kidney disease (CKD) in public healthcare centers in Peru.
Methods: A cross-sectional study was conducted in patients with CKD in healthcare centers of three Peruvian regions: Lima, Arequipa, and Ucayali. A structured questionnaire which included socio-demographic data, medical antecedents and characteristics of the use of medicinal plants was used. Prevalence ratios (PR) and 95 % confidence intervals (95% CI) were calculated using crude Poisson regressions with robust variances.
Results: A total of 599 patients with CKD were evaluated, of which 300 (50.1%) reported the use of medicinal plants (160 [30.3%] used these plants for CKD), 379 reported that medicinal plants were not harmful, while 166 (27.8%) stopped using allopathic medicine to use medicinal plants only. In the adjusted analysis, the frequency of the use of medicinal plants for CKD was similar between Lima and Arequipa but was lower in Ucayali than in Lima (PR: 0.32, 95% CI: 0.14 – 0.76). In addition, a higher frequency of the use of medicinal plants for CKD was observed in patients with more advanced stages of CKD (PR: 1.55, 95% CI: 1.06–2.26) and in patients who were aware they had CKD (PR: 2.79 95% CI: 1.39–5.63).
Conclusions: Half of the patients used medicinal plants and about one-third used it for CKD. This use was lower in Ucayali and higher in both the patients who knew they had CKD and those with more advanced stages of the disease. Given these results, physicians should ask and inform regarding medicinal plants consumption to their CKD patients.

1. Introduction

Chronic Kidney Disease (CKD) is a health problem worldwide.[1] Its prevalence in Peru has been evaluated between 16 and 18 % above the world average.[2,3] This prevalence is a challenge for a country that has problems with the care of patients with chronic diseases.[4,5]

Peru is a country with a millenary culture that included the use of medicinal plants (MP) for the management of several diseases, from pre-Columbian times to the present. [6–10] In addition, Peru is one of the twelve megadiverse countries on the planet, which has about 10 % of species of the world´s flora (25 000 species), and towards 2008 it occupied the top position in the number of plant species with supposed medicinal properties used by the population.[11]

The use of MP to alleviate urogenital problems is not infrequent in Peru. Up to 86 species of MP used for kidney problems have been identified [7] and the 'Catalogue of the Flowering Plants and Gymnosperms of Peru', published by the Ministry of Health of Peru (MINSA) shows the use of several MP for "kidney diseases".[10] A study demonstrated that about 40 % of patients admitted to hospitals in Cusco used MP for "urinary problems" and 4 out of 10 had taken them with medical prescription.[9]

It has been described that patients in Peru consider that MP do not have adverse effects.[9,12] However, the Kidney Disease Improving Global Outcomes (KDIGO) advises against the use of MP in patients with CKD since some of these medicines have demonstrated to be nephrotoxic.[13] In fact, some MP of common use in Peru such as Cat's claw ("uncaria

* Correspondent author at: Olavegoya 1879. Jesus Maria. Lima, Peru.
E-mail address: pherrera@usil.edu.pe (P. Herrera-Añazco).

https://doi.org/10.1016/j.ctim.2019.102215
Received 26 July 2019; Received in revised form 21 September 2019; Accepted 10 October 2019
Available online 19 October 2019
0965-2299/

Table 1
Characteristics of the patients studied, stratified by site (n = 599).

Characteristics	Total (599 patients) n (%)	Lima (274 patients) n (%)	Arequipa (203 patients) n (%)	Ucayali (122 patients) n (%)	p (chi-2)
Age (year-specific) *	64 (53 - 74)	60.5 (49 - 70)	62 (52 - 72)	74.5 (68 - 81)	<0.001 **
Male sex	298 (49.7)	146 (53.3)	124 (61.1)	28 (23.0)	<0.001
Level of education					<0.001
Illiterate or elementary school	290 (48.8)	106 (39.0)	99 (49.3)	85 (70.2)	
Secondary School	226 (38.0)	134 (49.3)	62 (30.8)	30 (24.8)	
Higher Education	78 (13.1)	32 (11.8)	40 (19.9)	6 (5.0)	
Average monthly income in dollar's	180 (60 - 271)	181 (30 - 301)	158 (0 - 301)	150 (90 - 181)	0.0577 **
Urban residence (during the last 5 years)	474 (79.1)	222 (81.0)	142 (70.0)	110 (90.2)	<0.001
Medical antecedents					
Arterial Hypertension	326 (54.4)	162 (59.1)	112 (55.2)	52 (42.6)	0.009
Diabetes Mellitus	224 (37.4)	121 (44.2)	60 (29.6)	43 (35.2)	0.004
Cardiovascular Disease	79 (13.2)	21 (7.7)	39 (19.2)	19 (15.7)	0.001
Dyslipidemia	82 (13.7)	15 (5.5)	30 (14.8)	37 (30.3)	<0.001
Others	10 (1.7)	10 (3.6)	0 (0.0)	0 (0.0)	0.002 ***
Stage of Chronic Kidney Disease					<0.001
Stage 3 CKD	219 (36.7)	45 (16.5)	64 (31.7)	110 (90.2)	
Stage 4 CKD	72 (12.1)	32 (11.7)	29 (14.4)	11 (9.0)	
Stage 5 CKD	306 (51.3)	196 (71.8)	109 (54.0)	1 (0.8)	
How long they knew they had CKD					<0.001
Patients who were not aware they had CKD	174 (29.0)	75 (27.4)	8 (3.9)	91 (74.6)	
Knew it less than a year ago	153 (25.5)	89 (32.5)	53 (26.1)	11 (9.0)	
Knew it since 1 or 3 years ago	152 (25.4)	70 (25.5)	66 (32.5)	16 (13.1)	
Knew it since more than 3 years ago	120 (20.0)	40 (14.6)	76 (37.4)	4 (3.3)	

tomentosa") has evidenced nephrotoxicity[15,16] and others lack studies about their adverse effects on the kidney.[14]

Previous studies conducted in patients with CKD in Tanzania and Egypt have found frequent use of MP [17,18]; however, the characteristics of their use could be different in the Peruvian population due to cultural differences among our countries. To our knowledge, there are no studies about this topic in our country.

The proper knowledge of the frequency and characteristics of the use of MP in patients with CKD will allow us to study this problem in depth to design better strategies focused on reducing the potential dangers of their use. This study was aimed at describing the use of MP in patients with CKD, treated in healthcare centers in three regions in Peru.

2. Material and methods

2.1. Study design and setting

This cross-sectional study was conducted in patients with the diagnosis of CKD who were treated in three public hospitals in the city of Lima; two public hospitals of Arequipa; and a healthcare center in Ucayali.

These three cities were selected to explore our research question in different natural regions of Peru that could have a different exposure to MP.[8–10] The city of Lima (capital of Peru) is located on the coast, the city of Arequipa is located on the mountain range, and the city of Ucayali is located in the forest.

Patients older than 18 years with the diagnosis of CKD stages 3, 4, and 5 were chosen. We defined stage3 CKD if the glomerular filtration rate (GFR) was between 30–59 ml /min/1.73 m^2. Stage 4 CKD if the GFR was between 15–29 ml/min/1.73 m^2, and stage 5 CKD if the GFR was less than 15 ml / min/1.73 m^2.[13]

The patients were treated for different medical conditions. in the healthcare centers studied. Patients that could not answer the questionnaire because of their conditions were excluded (critically ill patients and others having pre-existing neuro-psychiatric conditions).

2.2. Survey

A structured questionnaire based on previous studies related to the topic [9,17,18] was developed. It was composed of 17 items aimed at collecting sociodemographic data, information about medical antecedents, and characteristics of the use of MP.

The validity of the content of the questionnaire was evaluated by experts' opinions with the participation of specialists in traditional medicine (01), internal medicine (02), and nephrology (01). Likewise, the viability of the application of the instrument was evaluated by means of a pilot study applied to 20 patients with CKD.

2.3. Procedures

Coordination was made with researchers who were working as specialists in each of the healthcare centers selected for the study. These specialists carried out the survey after the outpatient consultation or during hospitalization between March 2018 and March 2019. It was not a random sample and the collection of data was made after selecting 100 patients in each center or while waiting for the deadline of the survey (whichever occurred first).

Patients that fulfilled the inclusion criteria were chosen. Some aspects were taking into account to determine if the patient was diagnosed with CKD stages 3,4, and 5. These aspects included the diagnosis made and registered in the clinical histories or the estimation of glomerular filtration rate with the use of CKD – EPI equation [13] with the last value of creatinine.

The researcher asked patients for oral informed consent and the questionnaire was applied to those who agreed on participating, clarifying all their doubts. Enough time was given to answer each question. The answers were recorded in a data collection card, and they were later digitized into a database using Microsoft Excel.

2.4. Statistical analysis

Absolute and relative frequencies and measures of central tendency and dispersion were used for the descriptive presentation of the results.

Factors associated with the consumption of MP for CKD were evaluated. Prevalence ratios and confidence intervals by using crude Poisson regressions with adjustment for robust variances were calculated in 95 % (CI95%). Adjusted regression included all the variables that have obtained a p-value < 0.20 in the crude analysis. All the analyses were carried out using Stata Statistical Software v14.

Table 2
Characteristics of the use of medicinal plants (N = 599).

Characteristics	N (%)
Use or used medicinal plants some time in their lives for a chronic disease	300 (50.1)
Diseases- Chronic diseases for which medicinal plants were used *	
CKD	160 (30.3)
Diabetes Mellitus	51 (9.7)
Arterial Hypertension	32 (6.1)
Others	193 (32.2)
Number of different medicinal plants used for a chronic disease in the last 12 months	
0	314 (59.4)
1	79 (14.9)
2	73 (13.8)
3 to 20	63 (11.9)
Times when medicinal plants were used for a chronic disease in the last 12 months	
0	301 (57.0)
1 to 4	98 (18.6)
5 to 60	129 (24.4)
Form in which medicinal plants were used *	
Natural form	170 (32.1)
As extract	32 (6.1)
In the form of capsules	16 (3.0)
Others	148 (28.8)
Reasons for which these medicinal plants were used *	
Relative or friend advice	221 (41.7)
Reliance on traditional medicine	111 (20.9)
To prevent diseases	45 (8.5)
By publicity/reading of journals/TV/Internet	24 (4.5)
As supplement to other medications /drugs	10 (1.9)
Treatment of no serious diseases	10 (1.9)
Medical advice	18 (3.4)
Herbalist advice, herbs seller	57 (10.8)
Mistrust in hospital medicine	5 (0.9)
No access to another treatment	4 (0.8)
Pharmacist´s advice	2 (0.4)
How harmful medicinal plants are considered **	
0	379 (63.4)
1	72 (12.0)
2	52 (8.7)
3	65 (10.9)
4	15 (2.5)
5	15 (2.5)
Have stopped using biomedicine to use medicinal plants	166 (27.8)

* In these questions, the participant could select more than one option.
** Visual analogue scale scores that vary from 0 to 5, where 0 corresponds to "nothing harmful " and 5 to "very harmful".

2.5. Ethical aspects

The participation in the study was absolutely voluntary and no data that identified the participants were recorded in the data collection cards. The protocol of this study was approved by the Institutional Ethics Committee at Universidad Peruana Cayetano Heredia in Lima, Peru (approval code number: 180-05-19)

3. Results

Data from 599 patients with CKD which included 274 patients from Lima, 203 from Arequipa, and 122 from Ucayali were analyzed. The median age was 64 years (RCI: 53 to 74 years), 298 (49.7%) patients were male, 326 (54.4%) patients suffered from arterial hypertension, diabetes mellitus was present in 224 (37.4%) of them, and 51.3% presented with stage 5 CKD. Of all the patients with CKD, 174 (29.0%) ones were not conscious of suffering from CKD (the characteristics of the patients studied are shown in Table 1).

A total of 300 (50.1%) participants included in the study used MP some time in their lives for chronic disease, and 160 (30.3%) used MP for CKD. In the last 12 months, 136 (25.7%) patients used two or more MP. Some of the reasons for the use of MP were: 221 (41.7%) patients used them after a relative or a friend´s advice and 111 (20.9%) did so because they trust traditional medicine. When they were asked to mention how harmful they consider medicinal plants were, 379 (63.4%) of them expressed that these plants were not harmful, and 166 (27.8%) reported they had stopped using allopathic medicine to use only MP. The characteristics of the use of MP are shown in Table 2 and the names of the most used MP for CKD are shown in Table 4.

The adjusted analysis found that the frequency of the use of MP for CKD was lower in Ucayali than in Lima (PR: 0.32, 95% CI: 0.14 – 0.76), higher in patients with more advanced stages of CKD (PR: 1.55, 95% CI: 1.06–2.26), and higher in patients who were aware they had CKD (PR: 2.79, 95% CI: 1.39–5.63), as it is shown in Table 3.

4. Discussion

Our results demonstrate that half of the patients used MP for some chronic disease and 1 in every 3 patients used them for CKD. The frequency of the use of MP for CKD was higher when the patient had known for a longer time that he/she was suffering from CKD and in patients with advanced stages of the disease. However, such frequency was lower in Ucayali than in Lima. More than half of the participants consider that the use of MP is not harmful, and slightly more than a quarter of patients stopped the treatment with allopathic medicine to take MP.

The frequency of the use of MP in our population is similar to what has been reported in other Latin American countries, where it is estimated that from 40 to 70 % of the population use medicinal plants regularly.[19] Nevertheless, this frequency varies according to the region of the country studied. A study carried out in two hospitals in Cusco (Peru) identified that more than 70 % of the surveyed people used MP some time in their lives, [9] which could be explained because Cusco is the cradle of Inca culture with a millenary tradition of use of medicinal plants. In Tanzania, the prevalence was 70.3% [18] while in Egypt it was 52% [17]; however, this prevalence in Egypt was framed to the use of traditional and complementary medicine that was not only limited to MP [17] and in the case of Tanzania it was not specified, [18] so this percentage is likely to be lower. In England, where there is a totally different social and cultural environment, 80 % of people use MP and although only 51 % believe that they are harmless, 55 % consider that the harmful effects are lower than those of allopathic medicine.[12] The use of MP is generalized even in high-risk populations, as in the case of pregnant women; so, in Mexico, up to 30 % of women take MP during the first trimester of pregnancy.[20]

Nearly one-third of participants used MP for CKD some time in their lives. The frequency of this use differed according to the city (6 % in Ucayali, 28 % in Lima, and 36 % in Arequipa). The more likely explanation for this difference is the poor frequency of self-knowledge of CKD (being aware of having CKD) among the patients of Ucayali (25 % versus around 50 % and 70 % in Arequipa and Lima). Thus, the self-knowledge of the disease may “activate” the patient, who starts seeking treatments, including the use of MP.

The poor self-knowledge of CKD is not infrequent in other countries (21.22); however, in our population, it is higher than the one found in the North American population (9 %), probably because our study was carried out in patients treated in healthcare centers and the North American study was conducted in the general population.[22]

Although the variation of self-knowledge among patients in different cities is a complex phenomenon that results from several social and cultural differences, [21] part of the problem related to the disproportion of nephrologists across Peruvian regions, with a higher rate in Lima than in Arequipa/Ucayali.[5] This lack of assistance given by a specialist (or general practitioners with an adequate training of CKD management) could also explain that the longer time a patient knows about the diagnosis and the more advanced the disease, the more likely these patients are to use MP for CKD, even when the KDIGO clinical practice guideline suggests to avoid their use in these patients.[13]

Table 3
Factors associated with the use of medicinal plants for CKD (N = 529).

Variables	Use or used medicinal plants some time in their lives for CKD			
	No	Yes	crude PR (CI 95%)	adjusted PR (CI 95%)
Place where the survey was carried out:				
Lima	125 (61.3)	79 (38.7)	Ref	Ref
Arequipa	129 (63.5)	74 (36.5)	0.94 (0.73 - 1.21)	0.85 (0.65 - 1.11)
Ucayali	115 (94.3)	7 (5.7)	**0.15 (0.07 - 0.31)**	**0.32 (0.14 - 0.76)**
Age in years				
16 to 57	119 (66.5)	60 (33.5)	Ref	
58 to 71	120 (68.2)	56 (31.8)	0.95 (0.70 - 1.28)	
72 to 95	130 (74.7)	44 (25.3)	0.75 (0.54 - 1.05)	
Sex				
Female	188 (72.6)	71 (27.4)	Ref	Ref
Male	181 (67.0)	89 (33.0)	1.20 (0.93 - 1.56)	0.94 (0.74 - 1.21)
Level of instruction:				
Illiterate or Elementary School	184 (71.3)	74 (28.7)	Ref	
Secondary Education	129 (66.5)	65 (33.5)	1.17 (0.89 - 1.54)	
Higher Education	52 (72.2)	20 (27.8)	0.97 (0.64 - 1.47)	
Average monthly income in soles				
<350	131 (69.3)	58 (30.7)	Ref	
350 to 800	134 (69.4)	59 (30.6)	1.00 (0.74 - 1.35)	
>800	102 (70.8)	42 (29.2)	0.95 (0.68 - 1.33)	
Residence in the last 5 years				
Rural	69 (65.7)	36 (34.3)	Ref	
Urban	300 (70.8)	124 (29.2)	0.85 (0.63 - 1.16)	
Medical antecedents				
No	83 (69.7)	36 (30.3)	Ref	
Yes	286 (69.8)	124 (30.2)	1.00 (0.73 - 1.36)	
Stage of Chronic Kidney Disease				
Stage 3 CKD	184 (86.0)	30 (14.0)	Ref	Ref
Stage 4 CKD	45 (69.2)	20 (30.8)	**2.19 (1.34 - 3.60)**	1.38 (0.86 - 2.22)
Stage 5 CKD	140 (56.5)	108 (43.5)	**3.11 (2.16 - 4.46)**	**1.55 (1.06 - 2.26)**
How long they knew they had a CKD				
Did not know	138 (92.0)	12 (8.0)	Ref	Ref
Knew it less than a year ago	85 (64.4)	47 (35.6)	**4.45 (2.47 - 8.03)**	**2.51 (1.28 - 4.93)**
Knew it since 1 or 3 years ago	79 (59.4)	54 (40.6)	**5.08 (2.84 - 9.07)**	**2.90 (1.49 - 5.62)**
Knew it more than 3 years ago	67 (58.8)	47 (41.2)	**5.15 (2.87 - 9.26)**	**2.79 (1.39 - 5.63)**

Table 4
Medicinal plants used for the management of chronic kidney disease (N = 160).

Plant	N (%)
Number of plants: median (IQR)	2 (1 - 4)
Horsetail (*Equisetum arvense*)	60 (37.5)
Chancapiedra (*Phyllanthus niruri*)	33 (20.6)
Barley (*Hordeum vulgare*)	22 (13.8)
Linseed (*Linum usitatissimum*)	21 (13.1)
Sávila (*Aloe vera*)	16 (10.0)
Llantén (*Plantago major*)	16 (10.0)
Chamomile (*Chamaemelum nobile*)	13 (8.1)
Pineapple plants (*Ananas comosus*)	12 (7.5)
Cat's claw (*Uncaria tomentosa*)	11 (6.9)
Tuna (*Opuntia ficus-indica*)	8 (5.0)
"Espina de perro" (*Xanthium Spinosum*)	7 (4.4)
Mint leaves (*Mentha spicata*)	7 (4.4)
Emollient (drink usually prepared with roasted grains of barley, herbs, sugar and lemon juice)	6 (3.8)
Others	82 (51.3)

IQR: interquartile range.

Similarly, a poor Peruvian health system with lacks in the distribution of basic medicines and high rates of out-of-pocket expenses could also motivate the wide use of MP.[23,24]

Many MP are used by our patients for the treatment of CKD, although there could be a misinterpretation of the properties attributed to these types of medicines when dealing with kidney problems. At the north of Peru, in Callejón de Huaylas or the Amazon, medicinal plants used for "urinary problems" are used as diuretics, for "kidney pain", urinary infections, urolithiasis, or "kidney disorders" which are poorly defined because there is not a classification scheme which identifies the specific MP used for each problem.[6,7,8,25] This problem is similar in other regions of the world since the pathogenesis of the kidney disease is not specified when it is said that MP are beneficial.[26] This lack of knowledge of the real properties of MP is based on the millenary character of their use and the belief that they have no adverse effects.[6–10] This indistinct use for chronic kidney diseases or other conditions or urinary symptoms is worrying because, in spite of the beliefs, the use of medicinal plants is really associated with adverse effects such as the nephrotoxic ones and can be a potential cause of the fast progression rate of the disease in low-income and middle-income countries.[27]

MP consumption may lead to nephrotoxicity when patients use an inadequate dosage, when MPs are contaminated with toxic substances such as pesticides, or when they enhance the toxic effects of biomedicines.[27,28] This renal damage can take several forms, including acute kidney injury, tubular function defects, dyselectrolytemias, systemic hypertension, CKD, renal papillary necrosis, urolithiasis and urothelial cancer.[28]

Although the nephrotoxicity of some Chinese MP containing aristocholic acid is known worldwide, other nephrotoxic elements such as Oxalic Acid, Djenkolic Acid, and Arabinogalactans have been identified in MP. However, the presence of these elements has not been identified in many of them, which could cause renal damage, such as the interstitial nephritis associated with the use of "cat´s claw ("uncaria tomentosa"), which is one of the commonly used medicinal plants used by patients in our study, and a widely used MP in our country.[15,16]

Up to 86 species of plants have been associated with beneficial effects to the urinary level in Peru, but their medicinal properties have been studied in less 35 % of them.[7] Although some systematic reviews have suggested beneficial effects of certain MP in patients with CKD

(such as the progression of the disease with the use of traditional Chinese medicine), these reviews recognize the inadequate methodological quality of the studies included.[28,29] Thus, although the use of MP could be promising, [30–32] a fair balance of risks and benefits has not been established yet.[33] This is worrying because, in our population, one of every three patients with CKD discontinue allopathic medicine to use MP. This could not be noticed by practitioners, since patients may not report health professionals about their use, and professionals are not sensitized to go into an in-depth search for information about the MP consumption.[34] The reasons for this substitution of allopathic medicine by MP is not clear and should be deeply studied.

Our study has some limitations: the results cannot generalize to other institutions, other regions of Peru or even to centers located in other places of the same region because of possible social and cultural differences, health literacy, and the number of nephrologists or other health professionals.[5,21] It is probable that the percentage of patients that reported having discontinued allopathic medicine to use MP is underestimated because our questionnaire was headed by health professionals. Lastly, some commonly used MP are not probably recognized as such by patients, so their use is underestimated.

However, this study is a first effort made for determining the frequency of the use of medicinal plants in patients with CKD in a country with a millenary tradition of the use of MP.

In conclusion, half of the patients used MP and about one-third used them for CKD. The frequency of the use was higher in patients who have known for a longer time that they were suffering from the disease and also in patients with more advanced stages of the disease; this frequency was lower in Ucayali. Most of the patients do not consider that MP are harmful and just over a quarter discontinue the use of biomedicine to start using MP.

Doctors and patients, in general, should take into account the results of our study that demonstrates the high frequency of the use of MP among patients with CKD. Proper advice on the adverse effects and the need to request their doctors about the usefulness of using MP instead of asking friends or publicity is of great importance. Finally, clinical studies about the beneficial or harmful effects of Peruvian medicinal plants are needed.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None to declare.

References

1. Coresh J. Update on the burden of CKD. *J Am Soc Nephrol.* 2017;28(4):1020–1022. https://doi.org/10.1681/ASN.2016121374.
2. Francis ER, Kuo CC, Bernabe-Ortiz A, et al. Burden of chronic kidney disease in resource-limited settings from Peru: A population-based study. *BMC Nephrol.* 2015;16:114. https://doi.org/10.1186/s12882-015-0104-7.
3. Herrera-Añazco P, Taype-Rondan A, Lazo-Porras M, Alberto Quintanilla E, Ortiz-Soriano VM, et al. Prevalence of chronic kidney disease in Peruvian primary care setting. *BMC Nephrol.* 2017;18(July (1)):246. https://doi.org/10.1186/s12882-017-0655-x.
4. Herrera-Añazco P, Benites-Zapata VA, León-Yurivilca I, Huarcaya- Cotaquispe R, Silveira-Chau M. Chronic kidney disease in Peru: A challenge for a country with an emerging economy. *J Bras Nefrol.* 2015;37(4):507–508. https://doi.org/10.5935/0101-2800.20150081.
5. Herrera-Añazco P, Atamari-Anahui N, Flores-Benites V. Number of nephrologists, hemodialysis services, and prevalence trend of chronic kidney disease in the ministry of health of Peru. *Rev Peru Med Exp Salud Publica.* 2019;36(January-March (1)):62–67. https://doi.org/10.17843/rpmesp.2019.361.4253.
6. Osman NA, Hassanein SM, Leil MM, NasrAllah MM. Hot and cold: Medicinal plant uses in Quechua speaking communities in the high Andes (Callejón de Huaylas, Ancash, Perú). *J Ren Nutr.* 2015;25(November (6)):466–471. https://doi.org/10.1016/j.jep.2014.06.042.
7. Bussmann R. The globalization of traditional medicine in northern peru: From shamanism to molecules. *Evid Based Complement Alternat Med.* 2013;2013:291903https://doi.org/10.1155/2013/291903.
8. Bussmann RW, Glenn A. Medicinal plants used in Northern Peru for reproductive problems and female health. *J Ethnobiol Ethnomed.* 2010;6(November):30. https://doi.org/10.1186/1746-4269-6-30.
9. Oblitas G, Hernández-Córdova G, Chiclla A, Antich-Barrientos M, Ccorihuamán-Cusitito L, Romaní F. Empleo de plantas medicinales en usuarios de dos hospitales referenciales del Cusco, Perú *Rev Peru Med Exp Salud Pública.* 2013;30(1):64–68.
10. *Catalogue Floristico De Plantas Medicinales Peruanas. Lima: Centro Nacional De Salud Intercultural.* Instituto Nacional De Salud; 2013. [citado 2017 Noviembre 11].Available from:. http://www.bvs.ins.gob.pe/insprint/CENSI/catalogo_floristico_plantas_medicinales.pdf.
11. *Ministerio de Salud. I Foro Investigación y biocomercio en plantas medicinales y alimenticias de uso tradicional en el Perú* Lima: MINSA; 2008. Revisado en julio 2019. Available from: https://repositorio.ins.gob.pe/xmlui/handle/INS/172.
12. Zahn R, Perry N, Perry E, Mukaetova-Ladinska EB. Use of herbal medicines: Pilot survey of UK users' views. *Complement Ther Med.* 2019;44(June):83–90. https://doi.org/10.1016/j.ctim.2019.02.007.
13. Kidney Disease - Improving Global Outcomes (KDIGO). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Supplement.* 2013;3(1):1–150.
14. Pamo-Reyna O. Características de los trabajos publicados sobre las propiedades de las plantas en revistas médicas peruanas. *Rev Peru Med Exp Salud Pública.* 2009;26(3):314–323.
15. Hilepo JN, Bellucci AG, Mossey RT. Acute renal failure caused by 'cat's claw' herbal remedy in a patien twith systemic lupus erythematosus. *Nephron.* 1997;77:361.
16. Valerio Jr LG, Gonzales GF. Toxicological aspects of the South American herbs cat's claw (Uncaria tomentosa) and Maca (Lepidium meyenii): a critical synopsis. *Toxico lRev.* 2005;24:11–35.
17. Osman NA, Hassanein SM, Leil MM, Nasr Allah MM. Complementary and alternative medicine use among patients with chronic kidney disease and kidney transplant recipients. *J Ren Nutr.* 2015;25(November 6):466–471. https://doi.org/10.1053/j.jrn.2015.04.009.
18. Stanifer JW, Lunyera J, Boyd D, Karia F, Maro V, et al. Traditional medicine practices among community members with chronic kidney disease in northern Tanzania: An ethnomedical survey. *BMC Nephrol.* 2015;23(October 16):170. https://doi.org/10.1186/s12882-015-0161-y.
19. Stanifer JW, Kilonzo K, Wang D, Su G, Mao W, et al. Traditional medicines and kidney disease in low- and middle-income countries: Opportunities and challenges. *Semin Nephrol.* 2017;37(May 3):245–259. https://doi.org/10.1016/j.semnephrol.2017.02.005.
20. Macías-Peacok B, Pérez-Jackson L, Suárez-Crespo MF, Fong-Domínguez CO, Pupo-Perera E. Consumo de plantas medicinales por mujeres embarazadas. *Rev Med Inst Mex Seguro Soc.* 2009;47(3).
21. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, et al. Chronic kidney disease: Global dimension and perspectives. *Lancet.* 2013;382(July (9888)):260–272. https://doi.org/10.1016/S0140-6736(13)60687-X.
22. Dharmarajan SH, Bragg-Gresham JL, Morgenstern H, Gillespie BW, Li Y, et al. State-level awareness of chronic kidney disease in the U.S. *Am J Prev Med.* 2017;53(September (3)):300–307. https://doi.org/10.1016/j.amepre.2017.02.015.
23. Bellido-Zapata A, Ruiz-Muggi JE, Neira-Sánchez ER, Málaga G. Implementación y aplicación de la "Guía de práctica clínica para el diagnóstico, tratamiento y control de la diabetes mellitus tipo 2 en el primer nivel de atención" en una red de establecimientos de salud públicos de Lima. *Acta Med Peru.* 2018;35(1):14–19.
24. Hernández-Vásquez A, Rojas-Roque C, Santero M, Prado-Galbarro FJ, Rosselli D. Health-related out-of-pocket expenses in older peruvian adults: Analysis of the national household survey on living conditions and poverty 2017. *Rev Peru Med Exp Salud Publica.* 2018;35(July-September (3)):390–399. https://doi.org/10.17843/rpmesp.2018.353.3815.
25. Sanz-Biset J, Campos-de-la-Cruz J, Epiquién-Rivera MA, Cañigueral S. A first survey on the medicinal plants of the Chazuta valley (Peruvian Amazon). *J Ethnopharmacol.* 2009;122(March (2)):333–362. https://doi.org/10.1016/j.jep.2008.12.009.
26. Mahesh Chand G, Chand T. A Critical review on commonly used herbal drugs in CKD. *J Med Plants Stud.* 2015;3(4):44–47.
27. Jha V. Herbal medicines and chronic kidney disease. *Nephrology (Carlton).* 2010;15(June Suppl 2):10–17. https://doi.org/10.1111/j.1440-1797.2010.01305.x.
28. Zhang HW, Lin ZX, Tung YS, Kwan TH, Mok CK, et al. Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease. *Cochrane Database Syst Rev.* 2014(December (12)):CD008353https://doi.org/10.1002/14651858.CD008353.pub2.
29. Zhang HW, Lin ZX, Xu C, Leung C, Chan LS. Astragalus (a traditional Chinese medicine) for treating chronic kidney disease. *Cochrane Database Syst Rev.* 2014(October (10)):CD008369https://doi.org/10.1002/14651858.CD008369.pub2.
30. Hsieh CF, Huang SL, Chen CL, Chen WT, Chang HC, et al. Non-aristolochic acid prescribed Chinese herbal medicines and the risk of mortality in patients with chronic kidney disease: Results from a population-based follow-up study. *BMJ Open.* 2014;4(February (2)):e004033https://doi.org/10.1136/bmjopen-2013-004033.
31. Hsieh CF, Chang HC, Huang SL, Chen CL, Chen WT, et al. Prescribed renoprotective Chinese herbal medicines were associated with a lower risk of all-cause and disease-specific mortality among patients with chronic kidney disease: A population-based follow-up study in Taiwan. *Evid Based Complement Alternat Med.* 2017;2017:5632195https://doi.org/10.1155/2017/5632195.
32. Chen HY, Pan HC, Chen YC, Chen YC, Lin YH. Traditional Chinese medicine use is associated with lower end-stage renal disease and mortality rates among patients with diabetic nephropathy: A population-based cohort study. *BMC Complement Altern Med.* 2019;19(April (1)):81. https://doi.org/10.1186/s12906-019-2491-y.
33. Yang B, Xie Y, Guo M, Rosner MH, Yang H, et al. Nephrotoxicity and Chinese herbal medicine. *Clin J Am Soc Nephrol.* 2018;13(October (10)):1605–1611. https://doi.org/10.2215/CJN.11571017.
34. Carvalho- Mastroianni P, Rossi Varallo P, Amaral Costa M, Da Silva Sacramento L. Development of instrument to report and assess causality of adverse events related to herbal medicines. *Vitae.* 2017;24(1):13–22. https://doi.org/10.17533/udea.vitae.v24n1a02.