NAU - New Areas of Unifying Interest for CKD: A Multidisciplinary Expert Opinion Using the Jandhyala Method

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Abstract

Introduction: The global prevalence of chronic kidney disease (CKD) is rising exponentially. While patient awareness of CKD remains low, we studied the physicians' awareness and how globally it can be improved. We aimed to evaluate the awareness and consensus of physicians on the screening, diagnosis and clinical management of CKD, thus identifying which areas should be the subject of educational or research programs.

Methods: Participants experienced in scientific research and interested in CKD were divided into two groups: primary and secondary care physicians. They underwent the Awareness Round with four open questions, followed by a Consensus Round to rate their level of agreement using a five-point Likert scale- Jandhyala method.

Results: Results showed varying levels of awareness and consensus among primary and secondary care physicians. Both groups identified diabetes and hypertension as major risk factors for CKD development and progression, with high consensus indexes (CI). However, glomerulopathies, polycystic kidney disease, and acute kidney injury had low

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awareness indexes (AI) but high CI, especially in secondary care. Key barriers to CKD diagnosis in primary care included physician inertia (AI 100%) and lack of articulation between specialties (AI 77%). In secondary care, therapeutic inertia (AI 100%) and socioeconomic factors (AI 84%) were significant limitations. Additionally, there was a notable disparity in the management of CKD between primary and secondary care. Primary care showed lower AI for promoting a healthy lifestyle (49%) and avoiding nephrotoxic drugs (25%) compared to secondary care (100% and 79%, respectively).
Conclusion: There is a need for educational programs for physicians exploring topics such as polycystic kidney disease, glomerulopathies and acute kidney disease; as well as the implementation of initiatives focused on CKD referral and management.

Keywords: Awareness; Consensus; Renal Insufficiency, Chronic

INTRODUCTION

About 850 million people worldwide are affected by some form of kidney disease, exceeding other diseases, such as diabetes, osteoarthritis, chronic obstructive pulmonary disease (COPD), asthma, or depressive disorders.[1–4] Chronic kidney disease is currently defined by abnormalities of kidney structure, detected by imagiology or histology, or abnormalities of kidney function for three or more months, assessed by eGFR5 and the presence of one or more markers of kidney damage.

The global prevalence of CKD is rising exponentially,[5–9] and it is estimated to affect around one in 10 individuals[3,10–13] and ~100 million Europeans.[2] In the Portuguese population,[5,14] the prevalence of stage 1 to 5 CKD is 20.9%,[14] and for patients of stage ≥G3a/A1 CKD is estimated to be 9.8%,[5,14] with women more affected. Kidney disease has become the 10th leading global cause of death and is projected to become the fifth leading cause of death and the fifth most common global cause of Years of Life Lost by 2040.[10,15,16]

The most common causes of CKD are hypertension and diabetes, but smoking, obesity, acute kidney injury,[2,11,14,17–22] infectious diseases, heavy metals, industrial and agricultural chemicals, high ambient temperatures, contaminants in food or drinking water, and other ingested substances such as nephrotoxic[23–25] drugs are important risk factors as well.

Nowadays, screening for kidney disease is recommended for high-risk populations including those with diabetes, hypertension, and HIV, and in regions where CKD is highly prevalent due to other causes.[26] Although proteinuria is easy to detect and potentially reduce with appropriate medication,[13,27] its monitoring in real-world practice is low.[27] While CKD is a major burden on health systems,[5,14] accessibility remains a major barrier to its appropriate management.[28,29] Although screening can easily be accomplished by measuring serum creatinine and urinary albumin, less than 10% of patients are aware of their disease.[30–33] It is therefore essential for physicians to be aware of CKD's risk factors, preventive measures, screening and referral criteria.[13,34]

There is an urgent need to develop awareness and education programs in areas of lesser investment, as well as research projects to clarify issues on which there is still no scientific consensus.[33,35,36] In this study we sought to evaluate the level of awareness and consensus of physicians in topics concerning the screening, diagnosis and clinical management of CKD, in order to identify which areas related to CKD should be the subject of educational or research programs.

METHODS

The Jandhyala method is a novel process for assessing proportional group awareness and consensus on responses arising from a list-generating questionnaire[37] on a specific subject between experts.[38] The Jandhyala method enhances the understanding of subject matter awareness across a group of experts and provides standardized categorization of items. This focus allows for a more detailed understanding of what experts know and agree upon, making it particularly useful for identifying educational gaps and areas requiring further research. This method uses an innovative approach that is distinct from other consensus methods and has already[37] been used to develop other instruments.[39,40] It consists of two survey rounds. In the first round, the "Awareness Round", participants provide free-text responses to open-ended questions, which are then thematically coded into mutually exclusive items. These items form the basis of a structured questionnaire used in the second round, the "Consensus Round" where participants rate their agreement using Likert scales. Item awareness, observed agreement, consensus and prompted agreement are then measured.[37]

Participants and Recruitment

A total of 100 physicians from all Portuguese regions, from different clinical settings and with different specialties were recruited using convenience sampling via professional networks and were invited to participate in the study between March and May of 2022. Of these, 98 participated in the Awareness Round (Supplementary Table 1) and 96 participated in the Consensus Round, two weeks later (44 from primary care- Family Medicine; and 52 from secondary care- 23 of Internal Medicine, 18 of Nephrology and 11 of Endocrinology). The results were evaluated in two groups: primary care and secondary care. To be included, participants had to have experience in scientific production and have CKD as an area of interest.

Participants were informed that taking part in the study was voluntary and were given information about how to withdraw. Written informed consent was obtained from all participants after providing information about the study and before the study began. Responses were anonymized and Consensus Round list items were not identifiable to particular participants.

Supplementary Table 1. Participants Characterization (n=98)

	n	%
Region		
North	35	36
Centre	29	30
South	29	30
Islands	5	5
Care		
Primary Care	43	44
Secondary Care	55	56
Speciality		
Family Medicine	43	44
Internal Medicine	24	24
Nephrology	19	19
Endocrinology	12	12
Healthcare service		
Public	94	96
Private	4	4

Awareness Round

During the Awareness Round survey, participants were asked to respond to a series of open short-answer questions, via online, with no limit on the number of answers. In both groups the same questions were applied, except for question number three:

1. What type of patient may be at increased risk of developing chronic kidney disease?
2. What type of patient may be at increased risk of progression of chronic kidney disease?
3. What are the factors that currently limit the ability to diagnose chronic kidney disease? (Primary Care)
4. What are the factors that currently limit the ability to treat chronic kidney disease? (Secondary Care)
5. What changes in clinical management in the patient after a diagnosis of chronic kidney disease?

The responses to the Awareness Round questionnaire were used to assess knowledge awareness by calculating the frequency of each coded item in relation to the overall most frequently occurring coded item - the Awareness Index (AI). The compiled list of items were reviewed and refined by the investigators and included in Consensus Round as structured questionnaires.

Consensus Round

The participants who completed the Awareness Round were asked to participate in the Consensus Round online survey. They were asked to rate their level of agreement with the statements from the Awareness Round survey, using a five--point Likert scale (Strongly agree, Agree, Neither agree nor disagree, Disagree, and Strongly disagree). Responses to the structured questionnaire in Consensus Round were used to determine observed consensus, proportional group awareness and the effect of prompting, i.e. persuasion after reading all items collected in Awareness Round.

The Consensus Index (CI) was calculated as the percentage of participants who agreed or strongly agreed with each statement in the Consensus Round.

Index Score (Jandhyala Score)

The Index Score was used to measure prompting during the Consensus Round. The concept of prompting was pre-specified to have occurred if the absolute difference between the AI and the CI was 0.05 (or 5%). Unprompted consensus was defined when a majority of participants suggested an item during the Awareness Round, and a majority of participants subsequently agreed or strongly agreed that the item was important in the Consensus Round. Any item that during the Awareness Round was suggested by only a few participants, but was deemed to be important in the Consensus Round was considered as completely prompted.

Items with a CI >50% indicate that some education may be required in order to increase awareness about that item. Items with a CI <50% may indicate an opportunity to redefine these norms. The index score identifies items or areas either where more education is required (in the case of items not listed by the participants, or listed by very few of them in the Awareness Round) or where more research is required (in the case of no observed agreement consensus for a statement in the Consensus Round).

The purpose of this methodology is not to force a consensus, but to evaluate the current knowledge and opinions of the selected experts. In order to have an opinion from which to form a consensus, a group of experts must first be aware of the key aspects of the subject of interest – without one there cannot be the other. The expert responses to the structured questionnaire allow the investigators to observe any consensus that arises, and determine whether it is prompted or unprompted. The advantage of the anonymity of the participating experts mitigates the effect of dominant individuals, manipulation or compulsion to confer to certain viewpoints and preserves the independence in item generation during the Awareness Round.

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RESULTS

After the two rounds, it was found that several items not mentioned by the participants in the Awareness Round (Table 1) obtained a high consensus index. In questions 1 and 2, there was agreement between the results obtained in the two groups - primary and secondary care. On the other hand, questions 3 and 4 generated more disagreement (Figs. 1-8 and Supplementary Tables 2-5).

Supplementary Table 2. Awareness Index (AI), Consensus Index (CI) and Jandhyala Score (JI) of Question 1 for Secondary care (SC) and Primary care (PC).

SC 1: What type of patient may be at increased risk of developing chronic kidney disease?				PC 1: What type of patient may be at increased risk of developing chronic kidney disease?			
Item	AI	CI	JI	Item	AI	CI	JI
Diabetes	100%	100%	0%	Diabetes	100%	97%	-3%
Hypertension	83%	100%	17%	Hypertension	86%	100%	14%
Glomerulopathies	28%	98%	70%	Glomerulopathies	53%	94%	41%
Polycystic kidney disease	9%	98%	89%	Polycystic kidney disease	8%	86%	78%
Frequent use of nephrotoxic drugs	38%	90%	52%	Frequent use of nephrotoxic drugs	51%	91%	40%
Other CV risk factors or CV diseases	74%	90%	16%	Other CV risk factors or CV diseases	63%	91%	28%
Obstructive urologic disease or malformation	36%	88%	52%	Obstructive urologic disease or malformation	67%	86%	19%
Elderly	36%	81%	45%	Elderly	49%	94%	45%
Obesity and a non-healthy lifestyle	45%	71%	26%	Obesity and a non-healthy lifestyle	45%	74%	29%
Acute kidney Injury	11%	74%	63%	Acute kidney Injury	6%	63%	57%
Family history of CKD	23%	50%	27%	Family history of CKD	18%	66%	48%

Supplementary Table 3. Awareness Index (AI), Consensus Index (CI) and Jandhyala Score (JI) of Question 2 for Secondary care (SC) and Primary care (PC).

SC 2: What type of patient may be at increased risk of progression of Chronic Kidney Disease?				PC 2: What type of patient may be at increased risk of progression of Chronic Kidney Disease?			
Item	AI	CI	JI	Item	AI	CI	JI
Diabetes	100%	98%	-2%	Diabetes	100%	100%	0%
Hypertension	93%	100%	7%	Hypertension	71%	100%	29%
Glomerulopathies	26%	100%	74%	Glomerulopathies	29%	97%	68%
Polycystic kidney disease	9%	100%	91%	Polycystic kidney disease	21%	86%	65%
Frequent use of nephrotoxic drugs	37%	93%	56%	Frequent use of nephrotoxic drugs	44%	89%	45%
Other CV risk factors or CV diseases	20%	95%	75%	Other CV risk factors or CV diseases	74%	91%	17%
Obstructive urologic disease or malformation	28%	76%	48%	Obstructive urologic disease or malformation	32%	80%	48%
Elderly	26%	78%	52%	Elderly	44%	83%	39%
Obesity and a non-healthy lifestyle	83%	74%	-9%	Obesity and a non-healthy lifestyle	74%	83%	9%
Acute kidney Injury	13%	62%	49%				
Family history of CKD	11%	54%	43%	Family history of CKD	15%	63%	48%
Proteinuria	28%	100%	72%	Proteinuria	35%	100%	65%

Supplementary Table 4. Awareness Index (AI), Consensus Index (CI) and Jandhyala Score (JI) of Question 3 for Secondary care (SC) and Primary care (PC).

SC 3: What are the factors that currently limit the ability to treat Chronic Kidney Disease?				PC 3: What are the factors that currently limit the ability to diagnose Chronic Kidney Disease?			
Item	AI	CI	JI	Item	AI	CI	JI
Illiteracy, adherence, socioeconomic factors	84%	93%	9%	Illiteracy, adherence, socioeconomic factors	44%	94%	50%
Awareness and therapeutic inertia	100%	90%	-10%	Awareness and therapeutic inertia	100%	91%	-9%
Articulation among specialties	51%	74%	23%	Articulation among specialties	77%	74%	-3%
Therapeutic strategies	22%	71%	49%	Therapeutic strategies	10%	38%	28%
Accessibility	78%	52%	-26%	Accessibility	71%	66%	-5%

Supplementary Table 5. Awareness Index (AI), Consensus Index (CI) and Jandhyala Score (JI) of Question 4 for Secondary care (SC) and Primary care (PC).

SC 4: What changes in clinical management in the patient after a diagnosis of Chronic Kidney Disease?				PC 4: What changes in clinical management in the patient after a diagnosis of Chronic Kidney Disease?			
Item	AI	CI	JI	Item	AI	CI	JI
Prescribing nephroprotective therapies	58%	100%	42%	Prescribing nephroprotective therapies	38%	100%	62%
Change surveillance frequency	88%	98%	10%	Change surveillance frequency	100%	97%	-3%
Promote a healthy lifestyle	100%	98%	-2%	Promote a healthy lifestyle	49%	94%	45%
Pharmacological adjustment	65%	100%	35%	Pharmacological adjustment	56%	97%	41%
Avoid nephrotoxic drugs	79%	100%	21%	Avoid nephrotoxic drugs	25%	97%	72%
Referral	49%	69%	20%	Referral	15%	66%	51%

Awareness Round

The most frequently mentioned items in questions 1 and 2 were diabetes and hypertension (Figs. 1 to 4).

Regarding question 1 - What type of patient may be at increased risk of developing chronic kidney disease - diabetes was the most frequently mentioned, with an AI of 100% (Figs. 1 and 2). Family doctors referred to glomerulopathies more often than the colleagues from the hospital (53% *vs* 28%). Polycystic kidney disease had a very low AI in both groups of physicians (9% and 8%).

Glomerulopathies and polycystic kidney disease are considered to be chronic kidney diseases themselves and many participants did not refer to them in the Awareness Round because they considered them part of CKD, leading to a false low AI. In the first question, the items mentioned should include risk factors and not different etiologies of CKD. For this reason, these two items were not included in the Consensus Round.

Acute kidney injury also had a very low AI in primary and secondary care (6% and 11%).

Regarding question 2 - What type of patient may be at increased risk of progression of chronic kidney disease - diabetes and hypertension were the most frequently mentioned items by both groups, although in the group of primary care, hypertension only reached an AI of 71% (Figs. 3 and 4). Urologic disease had an AI of 28% by the secondary care specialties but reached 50% by family doctors. Proteinuria reached an AI of 28% in the secondary care specialties and 35% in primary care. Glomerulopathies also had low AI of 26% and 29%. Acute kidney injury had an AI of 35% in the secondary care group, but no awareness from primary care. Polycystic kidney disease also had very low AI among secondary care specialties (9%), but a higher one among family doctors (21%).

Regarding question 3 for primary care - What are the factors that currently limit the ability to diagnose chronic kidney disease - the most common item was considered to be the physician's inertia (AI 100%) and the second one was the lack of coordination between the various departments and primary and secondary care (AI 77%) (Fig. 5). In secondary care, (What are the factors that currently limit the ability to treat chronic kidney disease?), therapeutic inertia was also the item with the highest AI and the second one with an AI of 84% was illiteracy, adherence, socioeconomic factors (Fig. 6).

Regarding question 4 - What changes in clinical management in the patient after a diagnosis of chronic kidney disease - promoting a healthy lifestyle had an AI of 100% by secondary care specialties, but only 49% AI in primary care. The avoidance of nephrotoxic drugs had an AI of 79% in secondary care, but only 25% in primary care (Figs. 7 and 8).

Table 1. Statements from Awareness Round and included terms. Statements refer to KDIGO guidelines.

Statements	Included Terms
Question 1 - Primary Care	
The person with diabetes has an increased risk of developing CKD	Diabetes with hypertension, diabetes without therapeutic reconciliation
The person with hypertension has an increased risk of developing CKD	Hypertension, long-standing hypertension, undiagnosed hypertension, uncontrolled hypertension
The person with glomerulopathy has an increased risk of developing CKD (Removed)	Glomerulonephritis, glomerulopathy, nephropathy, autoimmune disease, kidney disease
The person with polycystic kidney disease has an increased risk of developing CKD (Removed)	Polycystic kidney
The person with obstructive urological pathology or malformation has an increased risk of developing CKD	Prostatic hypertrophy, hydronephrosis, recurrent complicated urinary infection, recurrent renal lithiasis, malformation, renal lithiasis, recurrent pyelonephritis, obstructive urological disease, nephrectomy, sequelae of structural damage, renal lithiasis, nephrectomy, non-arterosclerotic renal artery stenosis
The person with acute kidney injury has an increased risk of developing CKD	Renal hypoperfusion, acute kidney disease
A person who frequently takes nephrotoxic drugs has an increased risk of developing CKD	Nephrotoxins, chronic pain, NSAIDs
The person with CV risk factors or CV pathology has an increased risk of developing CKD	Stroke, peripheral arterial disease, ischemic heart disease, heart failure, high cv risk, very high cv risk, multiple cv risk factors, arteriosclerotic cv disease, cardiovascular disease, established metabolic disease, uncontrolled cardiovascular risk factors
The elderly person has an increased risk of developing CKD	The older person is at increased risk of developing CKD
The person with obesity or who does not practice a healthy lifestyle has an increased risk of developing CKD	Obesity, overweight, alcohol, drug and tobacco consumption, sedentary lifestyle, protein intake
A person with a family history of CKD is at increased risk of developing CKD	Background, family kidney disease, family kidney disease
Question 2 - Primary Care	
CKD has an increased risk of progression in the person with diabetes	Diabetes, diabetes with target organ damage, long-term diabetes, uncontrolled diabetes
CKD has an increased risk of progression in the person with hypertension	Hypertension, uncontrolled hypertension, undiagnosed hypertension
CKD has an increased risk of progression in the person with glomerulopathy	Autoimmune disease, vasculitis associated nephropathy, glomerular disease, genetic disease, glomerulopathy, primary nephropathy, hereditary nephropathy, tubulointerstitial nephropathy
CKD has an increased risk of progression in the person with polycystic kidney disease	Polycystic kidney disease
CKD has an increased risk of progression in the person with obstructive urological pathology or malformation	Obstructive urological disease, recurrent urinary infection, renal lithiasis, genitourinary malformation, renal disease, pyelonephritis, renal transplantation
CKD has an increased risk of progression in people taking nephrotoxic drugs	Chronic pain, nephrotoxins, NSAIDs
CKD has an increased risk of progression in the person with CV risk factors or CV pathology	Dyslipidemia, cardiovascular disease, atherosclerotic cardiovascular disease, hyperuricemia, heart failure, cardiorenal syndrome, cardiovascular risk factors, uncontrolled cardiovascular risk factors
CKD has an increased risk of progression in the elderly	Elderly, advanced age, polymedicated user
CKD has an increased risk of progression in the person with obesity or who does not practise a healthy lifestyle	Obesity, alcohol consumption, drugs, proteins, sedentary lifestyle, smoking, poor adherence to therapy, no restriction of salt intake, no adequate therapy
CKD has an increased risk of progression in the person or with a family history of CKD	History, family kidney disease
CKD has an increased risk of progression in the person with proteinuria	Albuminuria, proteinuria
Question 3 - Primary Care	
Access to the health system currently limits the ability to diagnose CKD, given the difficulty in accessing consultations and exams	Access to health care, access to microalbuminuria, access to cystatin c, access to renal ultrasound, access to albumin creatinine ratio, access to glomerular filtration rate
The articulation of care in the health system currently limits the ability to diagnose CKD, due to the difficulty of referral between levels of care, insufficient consultation time and the lack of elements in the information system such as indicators, alerts, calculators and specific ICPC-2 coding for CKD	Insufficient consultation time, lack of automatic alerts, lack of calculators, lack of ICPC-2 coding, lack of indicators, lack of protocols

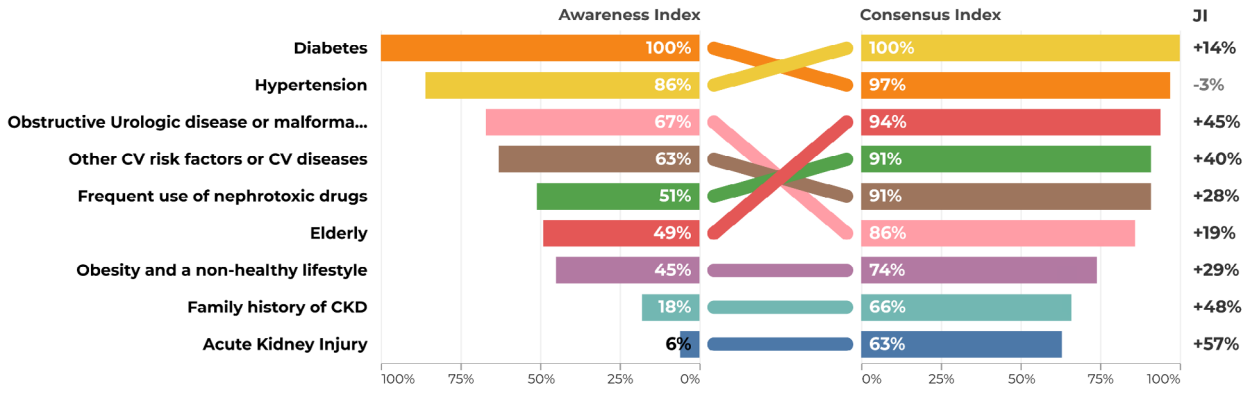
Statements	Included Terms
Illiteracy about CKD, limited adherence to therapeutic attitudes, and the user's devaluation of CKD limit the ability to treat CKD	Devaluation of the disease, lack of literacy, patient inertia
Limited awareness of CKD, lack of knowledge, absence of clinical suspicion and therapeutic inertia limit a physician's ability to treat CKD	Lack of awareness, lack of knowledge, lack of clinical suspicion, medical inertia, complex disease
Current therapeutic strategies limit the ability to treat CKD, given the lack of specific treatments for CKD causes	Lack of specific treatment
Question 4 - Primary Care	
After diagnosis of CKD it is essential to review the need for pharmacological adjustment of previously prescribed drugs	Adjust medication, intensify medication, adjust dosage
After diagnosis of CKD it is essential to prescribe nephroprotective therapies, if they have not yet been instituted	Add nephroprotectant, add prognostic modifier drug, add SGLT2 inhibitor
After diagnosis of CKD it is essential to avoid the use of nephrotoxic drugs	Suspend NSAIDs, suspend nephrotoxic drugs, avoid drug interactions, avoid diuretics
After diagnosis of CKD it is essential to promote a healthy lifestyle	Lifestyles, diet, review salt, protein and water intake, smoking cessation, exercise, increase user literacy
After diagnosis of CKD it is essential to review the frequency of patient surveillance and make it more frequent if necessary	Improve control of CV risk factors, analytical monitoring, more regular monitoring
After diagnosis of CKD, it is essential to consider referral to specialized healthcare services	Referral, referral to nephrology, specific clinical assessment
Question 1 - Secondary Care	
The person with diabetes has an increased risk of developing CKD	Type 1 diabetes mellitus, type 2 diabetes mellitus, long-standing diabetes, poorly controlled diabetes
The person with hypertension has an increased risk of developing CKD	Hypertension, uncontrolled hypertension, hypertension with microalbuminuria, long-term hypertension
The person with glomerulopathy has an increased risk of developing CKD	Autoimmune disease, systemic lupus erythematosus, vasculitis, glomerulonephritis, IgA nephropathy
The person with polycystic kidney disease has an increased risk of developing CKD	Polycystic kidney disease
The person with obstructive urological pathology or malformation has an increased risk of developing CKD	Urological malformation, obstructive urological disease, renal lithiasis, pyelonephritis, urinary infection
The person with acute kidney injury has an increased risk of developing CKD	Acute kidney injury
A person who frequently takes nephrotoxic drugs has an increased risk of developing CKD	Nephrotoxic drugs, NSAIDs, chronic pain, chemotherapy, aminoglycosides, iodinated contrast agents
The person with CV risk factors or CV pathology has an increased risk of developing CKD	Dyslipidemia, cardiovascular disease, atherosclerotic cardiovascular disease, heart failure, cardiovascular risk factor, metabolic syndrome
The elderly person is at increased risk of developing CKD	Elderly, polymedicated user, frail patient
The person with obesity or who does not practise a healthy lifestyle has an increased risk of developing CKD	Obesity, smoker
The person with a family history of CKD has an increased risk of developing CKD	History of CKD
Question 2 - Secondary Care	
CKD has an increased risk of progression in the person with diabetes	Diabetes, diabetes with CV risk factors, diabetes with target organ damage, poorly controlled diabetes, diabetes with heart failure
CKD has an increased risk of progression in the person with hypertension	Hypertension, long-term hypertension
CKD has an increased risk of progression in the person with glomerulopathy	Autoimmune disease, monoclonal gammopathy, glomerular disease, glomerulonephritis, interstitial nephritis
CKD has an increased risk of progression in the person with polycystic kidney disease	Polycystic kidney disease
CKD has an increased risk of progression in the person with obstructive urological pathology or malformation	Obstructive urological disease, complicated urinary infection, genitourinary malformation, recurrent pyelonephritis
CKD has an increased risk of progression in the person with acute kidney injury	Obstructive urological disease, complicated urinary tract infection, acute kidney injury, genitourinary malformation, recurrent pyelonephritis
CKD has an increased risk of progression in people who frequently take nephrotoxic drugs	Nephrotoxic drugs, NSAIDs, diuretics, polymedicated user
CKD has an increased risk of progression in the person with CV risk factors or CV pathology	Dyslipidemia, cardiovascular disease, atherosclerotic cardiovascular disease, heart failure, cardiorenal syndrome, long-term or uncontrolled cardiovascular risk factors
CKD has an increased risk of progression in the elderly	Elderly, multimorbidity, frailty

Statements	Included Terms
CKD has an increased risk of progression in the person with obesity or who does not practise a healthy lifestyle	Obesity, diet, protein intake, sedentary lifestyle, smoking
CKD has an increased risk of progression in the person or with a family history of CKD	History of CKD
CKD has an increased risk of progression in the person with proteinuria	Albuminuria, proteinuria
Question 3 - Secondary Care	
Access to the health system currently limits the capacity to treat CKD, given the low importance attributed to the pathology and difficulty in accessing exams	Access to health care, access to microalbuminuria, lack of adequate follow-up, timely diagnosis
Care articulation in the health system currently limits CKD treatment capacity, due to difficult referral between specialities, implementation of multidisciplinary care protocols and insufficient consultation time	Articulation of care, lack of indicators, difficulties in referral, insufficient consultation time
Illiteracy about CKD, limited adherence to therapeutic attitudes as well as other user-related socio-economic factors limit the ability to treat CKD	Devaluation of the disease, lack of knowledge, lack of literacy, adherence to therapy, change in lifestyles
Limited awareness of CKD and therapeutic inertia limit the physician's ability to treat CKD	Lack of medical awareness, lack of scientific evidence, lack of clinical suspicion, fear of decompensation, fear of nephrotoxicity, control of CV risk factors
Current therapeutic strategies limit the ability to treat CKD, due to the limited number of nephroprotective drugs and the difficulty of timely implementation of recent evidence	Therapeutic conciliation, effective treatment, specific treatment, cost of specific treatment
Question 4 - Secondary Care	
After diagnosis of CKD it is essential to review the need for pharmacological adjustment of previously prescribed drugs	Medication adjustment, intensify medication, review interactions, optimize medication, adjust dosage
After diagnosis of CKD it is essential to prescribe nephroprotective therapies, if they have not yet been instituted	Add nephroprotectant, add prognostic modifier drug, add SGLT-2 inhibitor
After diagnosis of CKD it is essential to avoid the use of nephrotoxic drugs	Review polymedication, suspend NSAIDs, suspend nephrotoxic drugs
After diagnosis of CKD it is essential to promote a healthy lifestyle	Lifestyles, diet, review salt, protein and water intake, smoking cessation, exercise, reduce alcohol consumption, increase user literacy
After diagnosis of CKD it is essential to review the frequency of patient surveillance and make it more frequent if necessary	Improve control of CV risk factors, analytical monitoring, more regular monitoring
After diagnosis of CKD it is essential to consider referral to nephrology	Referral to nephrology, treatment of the cause of CKD

Consensus Round

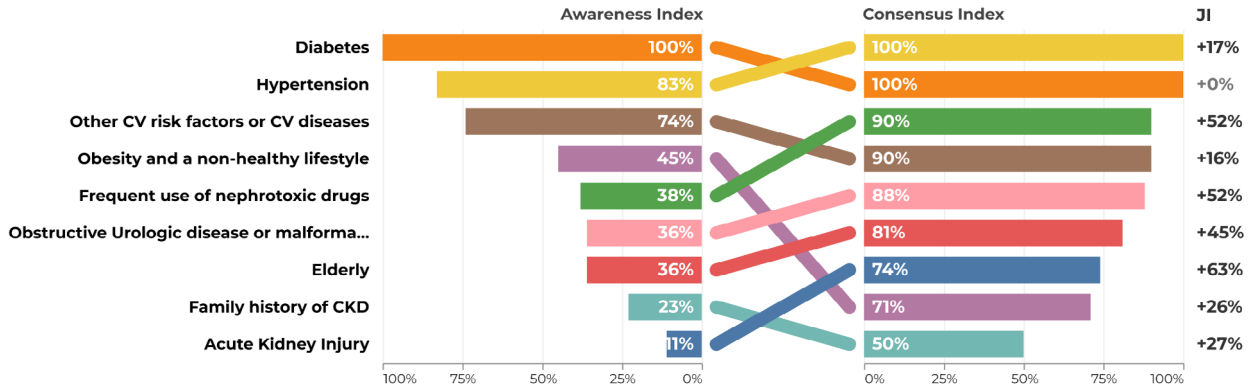
All items generated from the Awareness Round were retained in the final measure, except Glomerulopathies and polycystic kidney disease in the first question. Most of the participants agreed or strongly agreed with the statements generated during the Awareness Round (Table 1). The AI, the CI and the Index Score or Jandhyala Score can be seen in Figs. 1 to 8.

Regarding question 1 - What type of patient may be at increased risk of developing chronic kidney disease - diabetes had a CI of 100% in secondary care specialties and 97% in primary care, although Hypertension had a CI of 100% in both groups (Figs. 1 and 2). Some items showed a low AI, but a high CI, with a consequent high Index score, such as glomerulopathies, polycystic kidney disease and acute kidney injury.



JI- Jandhyala Index

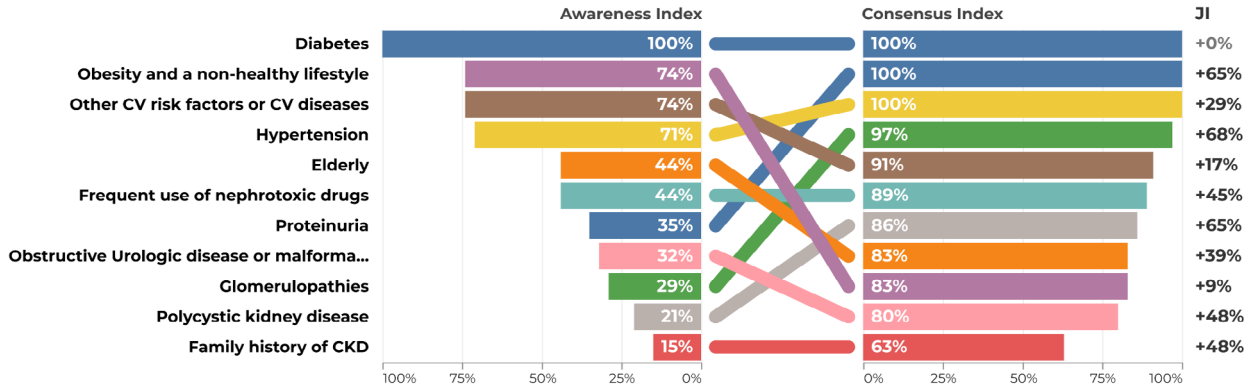
Figure 1. Awareness Index, Consensus Index and Jandhyala Score of Question 1 for Primary care.



JI- Jandhyala Index

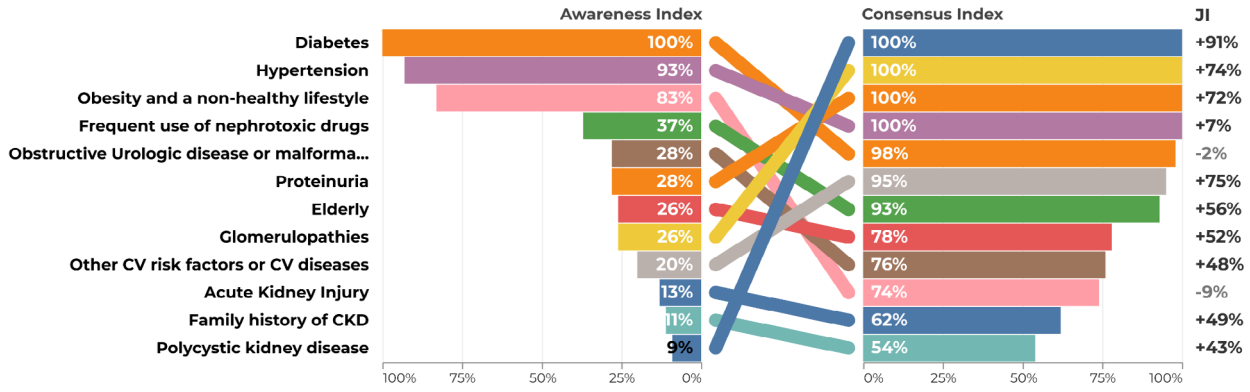
Figure 2. Awareness Index, Consensus Index and Jandhyala Score of Question 1 for Secondary care.

Regarding question 2 - What type of patient may be at increased risk of progression of chronic kidney disease - glomerulopathies, polycystic kidney disease, nephrotoxic drugs, obstructive urologic pathology or malformation, acute kidney injury, elderly people, obesity and a non--healthy lifestyle and proteinuria showed a low AI but a high CI and consequent high Index score (Figs. 3 and 4).



JI- Jandhyala Index

Figure 3. Awareness Index, Consensus Index and Jandhyala Score of Question 2 for Primary care.

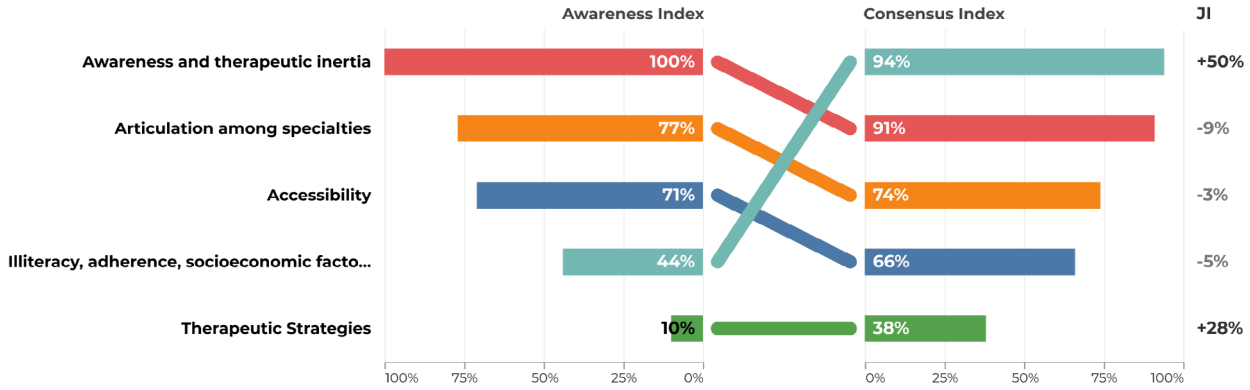


JI- Jandhyala Index

Figure 4. Awareness Index, Consensus Index and Jandhyala Score of Question 2 for Secondary care.

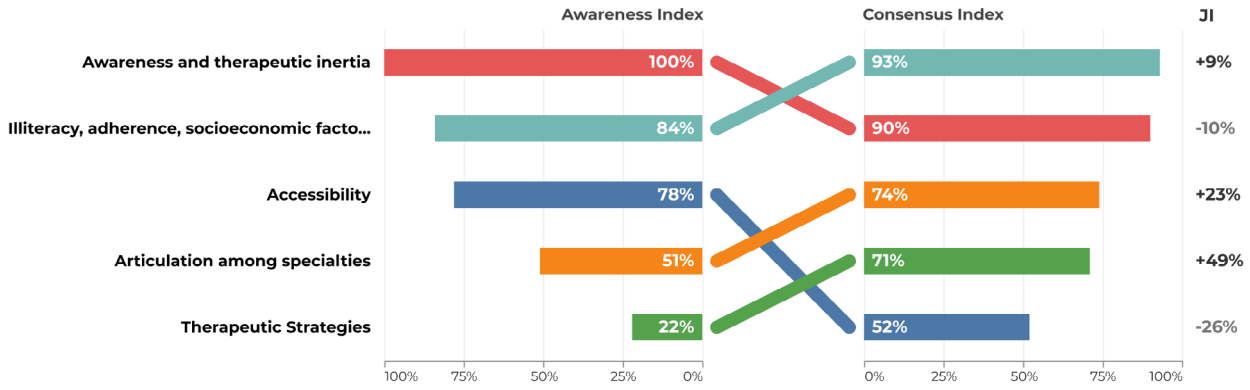
Regarding question 3 for primary care - What are the factors that currently limit the ability to diagnose chronic kidney disease - illiteracy, adherence, socioeconomic factors was the item with the highest index score of 50% (Fig.

5). In the secondary care group, in question 3 (What are the factors that currently limit the ability to treat chronic kidney disease?), the item with a higher Index score was therapeutic strategies (49% (Fig. 6)).



JI- Jandhyala Index

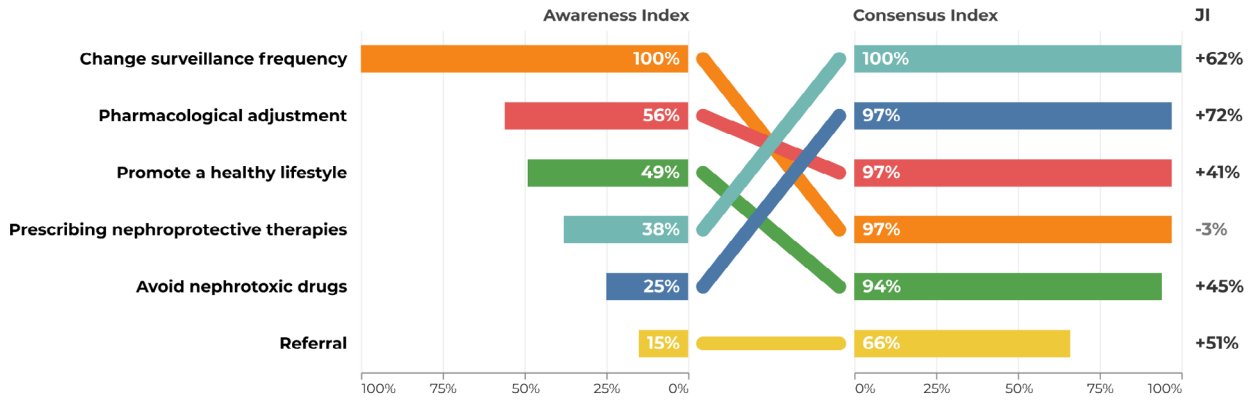
Figure 5. Awareness Index, Consensus Index and Jandhyala Score of Question 3 for Primary care.



JI- Jandhyala Index

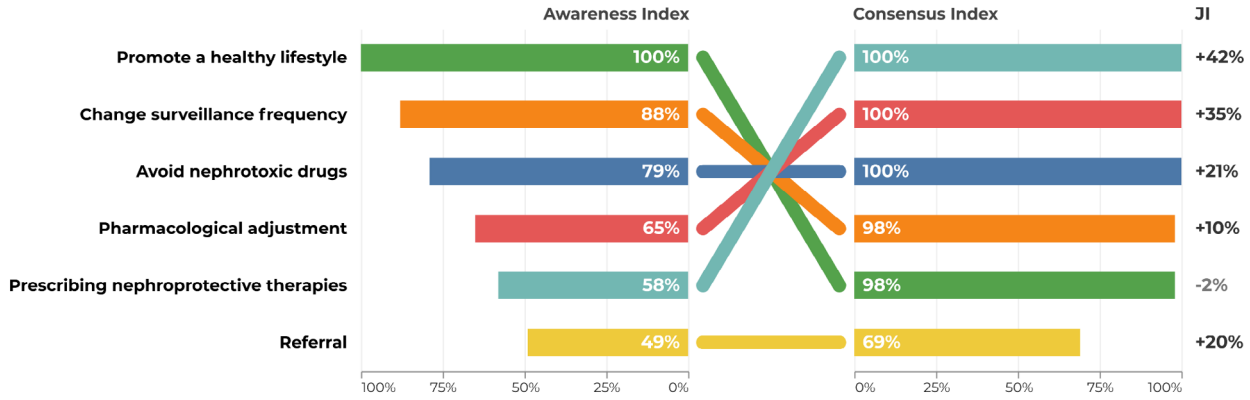
Figure 6. Awareness Index, Consensus Index and Jandhyala Score of Question 3 for Secondary care.

Regarding question 4 - What changes in clinical management in the patient after a diagnosis of chronic kidney disease? - in primary care, prescribing nephroprotective drugs, avoiding nephrotoxic drugs and referral had a low AI and a higher CI and Index Score, while in secondary care, the index scores were much lower (Figs. 7 and 8).



JI- Jandhyala Index

Figure 7. Awareness Index, Consensus Index and Jandhyala Score of Question 4 for Primary care.



JI- Jandhyala Index

Figure 8. Awareness Index, Consensus Index and Jandhyala Score of Question 4 for Secondary care.

DISCUSSION

Disease Illiteracy

In general, the results showed a low awareness of some diseases, such as polycystic kidney disease, although it is responsible for 10% of end-stage renal disease (ESRD).[41] We consider that its low frequency, hereditary nature, and high family clustering may lead to early referral to nephrology appointment, so non-nephrologist colleagues may follow a reduced number of patients with this disease. The same circumstance may happen with some glomerulopathies, which are important causes of ESRD, but had a low AI in questions 1 and 2. Another explanation is the fact that these entities are considered to be chronic kidney diseases themselves and many participants did not refer to them in the Awareness Round, because they considered them part of CKD, leading to a false low AI. Development and progress may be misleading terms and there were different interpretations of the first question. Therefore, the items of polycystic kidney disease and glomerulopathies were removed from the Consensus Round in the first question.

A low AI of AKI as a risk factor for development and progression to CKD proved its under-recognition as a cause of CKD, although patients with AKI have a 9-fold higher risk of CKD and 3-fold higher risk of ESRD.[42] The diagnosis of AKI occurs frequently in the nephrology/internal medicine setting, which leads to low exposure of non-nephrologist colleagues to the common and validated phenomenon of the AKI-CKD transition.

A low AI of proteinuria and glomerulopathies as contributors to CKD progression confirmed its low recognition. They are both relevant factors for progression, although proteinuria is common in several kidney disease mechanisms, including not only glomerulopathies but also other diseases. Thus, there is an opportunity to emphasize its role as a marker for diagnosis, progression and therapeutic target for CKD (anti-proteinuria therapies), with an impact on the reduction of renal outcomes. The presence of proteinuria is associated with 10-fold higher risk of CKD progression and 5-fold higher risk of ESRD.[43] A focus on expanding screening and longitudinal monitoring of proteinuria in primary care is essential and there should be protocols that would allow both greater adherence and better management of kidney disease by clinicians. In the case of glomerulopathies, the eminently nephrological nature and their relatively low prevalence partially explains these results.

In the future, awareness campaigns on risk factors for CKD should be conducted. We propose developing focused training programs on critical areas of CKD management, conducted through online modules, short workshops, or integrated into continuing medical education (CME) programs. Also, awareness-raising activities in schools, workplaces, and community centers, supported by local health organizations, and comprehensive public awareness campaigns using various media channels can further increase understanding of CKD and early detection.

Referral/Networking

Access to health care had a medium AI and a lower CI, probably due to different points of view, depending on the department. It may be due to some difficulty in accessing nephrology appointments in some hospitals and also the low access in primary care, leading to a low diagnosis rate. Referral is the item where there is a lower CI, especially in primary care. This result may reflect different interpretations from different departments. Referral depends on the stage of CKD, its risk of progression, and access to a medical specialist. Aging is a significant risk factor for CKD, particularly in societies with a growing elderly population. Despite its importance, the role of aging in CKD is often underrecognized. Addressing this gap, it is crucial to implement targeted interventions for the elderly, including regular screening, early detection, and management of CKD, to improve outcomes in this vulnerable population.

Chronic kidney disease stages and their adjustment for age should be discussed as well as the criteria for referral of CKD to nephrology. There is a need to review the inter-specialty referral criteria and a practical guide on CKD diagnosis and its different etiologies should be promoted.

Disease Management and Treatment

In question 3, awareness and therapeutic inertia had a high AI and CI, which represents a recognition of sometimes inadequate perception of the problem by colleagues and failure to apply appropriate diagnostic measures. Moreover, the intrinsic limitation of creatinine and GFR formulas to detect incipient forms of CKD (particularly in elderly, highly comorbid and malnourished patients) and low adherence to serial assessment of proteinuria are aspects to be taken into account. Therapeutic strategies had a low AI in both groups, but especially in the primary care. While both primary and secondary care physicians are involved in both diagnosis and treatment processes, their day-to-day activities differ. Primary care focuses on early detection, ongoing monitoring, and initial management of CKD to ensure timely and accurate diagnoses. In this sense, therapeutic strategies play a minor role in the diagnostic capacity of CKD. In contrast, secondary care, concentrates on advanced treatment adjustments and managing complications. Understanding these distinct but complementary roles is crucial for optimizing CKD management across the healthcare continuum. Therefore, there is a need to strengthen communication between these two players. Promoting internships and training programs in Nephrology departments and in Primary care facilities for medical students and overall healthcare professionals, along with continuous education opportunities, can enhance practical knowledge and skills in CKD diagnosis and management. Additionally, mobile health applications can help patients monitor their health, receive medication reminders, and access educational content, supporting self-management and treatment adherence. Utilizing electronic alerts to signal the achievement of a certain GFR threshold and easier and quicker referrals to nephrology is also a strategy to be considered.

In question 4, the use of nephroprotective drugs has a high CI, but a low AI. Training courses and interdisciplinary meetings in which the different specialties involved in the diagnosis and treatment of CKD can discuss strategies and create therapeutic algorithms adapted to the characteristics of subgroups of patients should be promoted. For example, it would be important to have pain management protocols for patients with chronic pain. In these protocols, nephrotoxic drugs with analgesic effects, such as NSAIDs, would be avoided and in patients with regular and high consumption of NSAIDs, regular CKD screening should be considered.

The promotion of a healthy lifestyle is one of the fundamental pillars of the work of primary health care professionals. Due to its transversality, it may not have been initially associated with the specific area of CKD, justifying the lower AI obtained.

Therapeutic adjustment, with the avoidance of nephrotoxic drugs and the implementation of nephroprotective measures, is essential in the management of CKD. A proposal for the future is to conduct a systematic review based on international guidelines to create an algorithm for the management of CKD at the primary care system and across different specialties.

Strengths and Limitations

The main strengths of this study were the inclusion of a high number of experts, from all over the country and from various specialties with different views of CKD. Since the topic presented several interpretations, starting from an open questionnaire allowed us to see the main areas of interest of the expert panel. The main limitation was the difficulty of categorizing the items from Awareness to Consensus Round. In the Awareness Round, participants answered open-ended questions, leading to many different answers that were difficult to integrate into categories. Additionally, the Jandhyala method allows a maximum of two rounds and no face-to-face meetings, denying the opportunity to discuss pertinent topics.[38]

CONCLUSION

Based on our results, there are some measures, such as educational programs, that can be taken in order to increase awareness of some items, specifically polycystic kidney disease, glomerulopathies and acute kidney disease. There was a recognition of sometimes inadequate perception of the problem by colleagues and failure to apply appropriate diagnostic measures and also a need to review the inter-specialty referral criteria. These results seem to call for the implementation of initiatives focused on CKD referral and management.

There is also a need to train physicians to potentiate action for CKD in areas of high consensus and identify areas of disagreement.

The results also stress the need to advocate for equitable and affordable access to the entire spectrum of kidney care everywhere. Based on our study, we believe there is a high likelihood of success in implementing outreach projects or initiatives focused on CKD literacy, referral and disease management.

LEARNING POINTS/TAKE HOME MESSAGES

We detected a low awareness of polycystic kidney disease, glomerulopathies and acute kidney disease in healthcare professionals;

There was a recognition of sometimes inadequate perception of the problem by colleagues and failure to apply

appropriate diagnostic measures and also a need to review the inter-specialty referral criteria;
Based on our results, we consider there is a high likelihood of success in implementing outreach projects or initiatives focused on CKD literacy, referral and disease management.

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Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).
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Contributorship Statement

LLD and TTG: Bibliographical search, study design, data collection, analysis and interpretation of results, drafting of the article, critical reviewing of the content of the article.
JC and HM: Study design, critical reviewing of the content of the article.
JM, FA, AN, CA, IA, JPN, JSN, JD, MBV, ML, NC and SH: Critical reviewing of the content of the article.
All authors approved the final version to be published.

REFERENCES

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; 392: 1789–58. doi: 10.1016/S0140-6736(18)32279-7.
2. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2020;395:709-33. doi: 10.1016/S0140-6736(20)30045-3.
3. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Kidney Int. 2019;96:1048-50. doi: 10.1016/j.kint.2019.07.012.
4. Bello AK, Johnson DW, Feehally J, Harris D, Jindal K, Lunney M, et al. Global Kidney Health Atlas (GKHA): design and methods. Kidney Int Suppl. 2017;7:145-53. doi: 10.1016/j.kisu.2017.08.001.
5. Santos-Araújo C, Mendonça L, Carvalho DS, Bernardo F, Pardal M, Couceiro J, et al. Twenty years of real-world data to estimate chronic kidney disease prevalence and staging in an unselected population. Clin Kidney J. 2022;16:111-24. doi: 10.1093/ckj/sfac206.
6. Ng JK, Li PK. Chronic kidney disease epidemic: How do we deal with it? Nephrology. 2018;23 Suppl 4:116-20. doi: 10.1111/nep.13464.
7. Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J Kidney Dis. 2003;42:677-84. doi: 10.1016/s0272-6386(03)00916-8.
8. Raymond NT, Zehnder D, Smith SC, Stinson JA, Lehnert H, Higgins RM. Elevated relative mortality risk with mild-to-moderate chronic kidney disease decreases with age. Nephrol Dial Transplant. 2007;22:3214--20. doi: 10.1093/ndt/gfm396.
9. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease- A Systematic Review and Meta-Analysis. PLoS One. 2016;11:e0158765. doi: 10.1371/journal.pone.0158765.
10. World Health Organization. The top 10 causes of death [accessed 26 October 2022] Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
11. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int. 2011;80:1258-70. doi: 10.1038/ki.2011.368.

12. Coresh J, Hu JR, Bello AK, Feldman HI, Fogo AB, Ganji MR, et al. Action plan for determining and monitoring the prevalence of chronic kidney disease. Kidney Int Suppl. 2017;7:63-70. doi: 10.1016/j.kisu.2017.07.002.
13. Vanholder R, Annemans L, Brown E, Gansevoort R, Gout-Zwart JJ, Lameire N, et al. Reducing the costs of chronic kidney disease while delivering quality health care: a call to action. Nat Rev Nephrol. 2017;13:393-409. doi: 10.1038/nrneph.2017.63.
14. Vinhas J, Aires I, Batista C, Branco P, Brandão J, Nogueira R, et al. RENA Study: Cross-Sectional Study to Evaluate CKD Prevalence in Portugal. Nephron. 2020;144:479-87. doi: 10.1159/000508678.
15. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. Lancet. 2018;392:2052-90. doi: 10.1016/S0140-6736(18)31694-5.
16. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1736–88. doi: 10.1016/S0140-6736(18)32203-7.
17. Dunkler D, Kohl M, Heinze G, Teo KK, Rosengren A, Pogue J, et al. Modifiable lifestyle and social factors affect chronic kidney disease in high-risk individuals with type 2 diabetes mellitus. Kidney Int. 2015;87:784-91. doi: 10.1038/ki.2014.370.
18. Fraser SD, Roderick PJ, May CR, McIntyre N, McIntyre C, Fluck RJ, et al. The burden of comorbidity in people with chronic kidney disease stage 3: a cohort study. BMC Nephrol. 2015;16:193. doi: 10.1186/s12882-015-0189-z. Erratum in: BMC Nephrol. 2020;21:543. doi: 10.1186/s12882-020-02205-w.
19. Mok Y, Ballew SH, Matsushita K. Prognostic Value of Chronic Kidney Disease Measures in Patients With Cardiac Disease. Circ J. 2017;81:1075–84.
20. Valmadrid CT, Klein R, Moss SE, Klein BE. The risk of cardiovascular disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus. Arch Intern Med. 2000;160:1093-100. doi: 10.1001/archinte.160.8.1093.
21. Yacoub R, Habib H, Lahdo A, Al Ali R, Varjabedian L, Atalla G, et al. Association between smoking and chronic kidney disease: a case control study. BMC Public Health. 2010;10:731. doi: 10.1186/1471-2458-10-731.
22. Lu JL, Molnar MZ, Naseer A, Mikkelsen MK, Kalantar-Zadeh K, Kovesdy CP. Association of age and BMI with kidney function and mortality: a cohort study. Lancet Diabetes Endocrinol. 2015;3:704-14. doi: 10.1016/S2213-8587(15)00128-X.
23. Soderland P, Lovekar S, Weiner DE, Brooks DR, Kaufman JS. Chronic kidney disease associated with environmental toxins and exposures. Adv Chronic Kidney Dis. 2010;17:254-64. doi: 10.1053/j.ackd.2010.03.011.
24. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382:260-72. doi: 10.1016/S0140-6736(13)60687-X. Erratum in: Lancet. 2013;382:208.
25. Ekrikpo UE, Kengne AP, Bello AK, Effa EE, Noubiap JJ, Salako BL, et al. Chronic kidney disease in the global adult HIV-infected population: A systematic review and meta-analysis. PLoS One. 2018;13:e0195443. doi: 10.1371/journal.pone.0195443.
26. Luyckx VA, Cherney DZ, Bello AK. Preventing CKD in Developed Countries. Kidney Int Rep. 2020;5:263–77. doi: 10.1016/j.ekir.2019.12.003.
27. Bello AK, Ronksley PE, Tangri N, Kurzawa J, Osman MA, Singer A, et al. Quality of Chronic Kidney Disease Management in Canadian Primary Care. JAMA Netw Open. 2019;2:e1910704. doi: 10.1001/jamanetworkopen.2019.10704.
28. Chow CK, Nguyen TN, Marschner S, Diaz R, Rahman O, Avezum A, et al. Availability and affordability of medicines and cardiovascular outcomes in 21 high-income, middle-income and low-income countries. BMJ Glob Health. 2020;5:e002640. doi: 10.1136/bmjgh-2020-002640.
29. Khatib R, McKee M, Shannon H, Chow C, Rangarajan S, Teo K, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. Lancet. 2016;387:61--9. doi: 10.1016/S0140-6736(15)00469-9.
30. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bull World Health Organ. 2018;96:414–22D.
31. Ene-Iordache B, Perico N, Bikbov B, Carminati S, Remuzzi A, Perna A, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health. 2016;4:e307-19. doi: 10.1016/S2214-109X(16)00071-1.
32. Whaley-Connell A, Shlipak MG, Inker LA, Kurella Tamura M, Bomback AS, Saab G, et al. Awareness of kidney disease and relationship to end-stage renal disease and mortality. Am J Med. 2012;125:661-9. doi: 10.1016/j.amjmed.2011.11.026.
33. Vanholder R, Annemans L, Bello AK, Bikbov B, Gallego D, Gansevoort RT, et al. Fighting the unbearable lightness of neglecting kidney health: the decade of the kidney. Clin Kidney J. 2021;14:1719-30. doi: 10.1093/ckj/sfab070.
34. Bello AK, Levin A, Manns BJ, Feehally J, Drueke T, Faruque L, et al. Effective CKD care in European countries: challenges and opportunities for health policy. Am J Kidney Dis. 2015;65:15-25. doi: 10.1053/j.ajkd.2014.07.033.
35. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Köttgen A, Levey AS, et al. Evolving importance of kidney disease: from subspecialty to global health burden. Lancet. 2013;382:158-69. doi: 10.1016/S0140-6736(13)60439-0.
36. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388:1545–602. doi: 10.1016/S0140-6736(16)31678-6.
37. Jandhyala R. A novel method for observing proportional group awareness and consensus of items arising from list-generating questioning. Curr Med Res Opin. 2020;36:883–93. doi: 10.1080/03007995.2020.1734920.
38. Jandhyala R. Delphi, non-RAND modified Delphi, RAND/UCLA appropriateness method and a novel group awareness and consensus methodology for consensus measurement: a systematic literature review. Curr Med Res Opin. 2020;36:1873–87. doi: 10.1080/03007995.2020.1816946.
39. Jandhyala R. Development and Validation of the Medical Affairs Pharmaceutical Physician Value (MAPPval) Instrument. Pharmaceut Med. 2022; 36: 47–57. doi: 10.1007/s40290-021-00413-9.
40. Jandhyala R. Design, validation and implementation of the post-acute (long) COVID-19 quality of life (PAC-19QoL) instrument. Health Qual Life Outcomes. 2021;19:229. doi: 10.1186/s12955-021-01862-1.
41. Perrone RD, Ruthazer R, Terrin NC. Survival after end-stage renal disease in autosomal dominant polycystic kidney disease: contribution of extrarenal complications to mortality. Am J Kidney Dis. 2001;38:777–84.
42. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int. 2012;81:442–8.
43. Cravedi P, Remuzzi G. Pathophysiology of proteinuria and its value as an outcome measure in chronic kidney disease. Br J Clin Pharmacol. 2013;76:516–23.