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ORIGINAL ARTICLE

Prevalence rates of chronic kidney disease and its association with cardiometabolic factors and cardiovascular diseases. SIMETAP-CKD study

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KEYWORDS
Chronic kidney disease;
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Abstract
Introduction: Chronic kidney disease (CKD) is a major health problem that contributes to the development of cardiovascular disorders such as heart failure and arteriosclerotic cardiovascular disease (ACVD). The aims of this study were to determine the prevalence of CKD and to assess its association with ACVD and cardiometabolic risk factors.
Methods: Cross-sectional observational study conducted in primary care setting. Population-based random sample: 6588 people between 18 and 102 years old (response rate: 66%). Crude and sex- and age-adjusted prevalence rates of CKD according to KDIGO were determined by assessing albuminuria and estimated glomerular filtration rate (eGFR) according to CKD-EPI, and their associations with cardiometabolic factors and ACVD were determined.
Results: The crude prevalence of CKD was 11.48% (95%CI: 10.72–12.27%), without significant difference between men (11.64% [95%CI: 10.49–12.86%]) and women (11.35% [95%CI: 10.34–12.41%]). The age- and sex-adjusted prevalence rate of CKD was 9.16% (men: 8.61%; women: 9.69%). The prevalence of low eGFR (<60 mL/min/1.73 m^2) and albuminuria (≥30 mg/g) were 7.95% (95%CI: 7.30–8.61) and 5.98% (95%CI: 5.41–6.55), respectively.Hypertension, diabetes, prediabetes, increased waist-to-height ratio, heart failure, atrial fibrillation, and ACVD were independently associated with CKD ($p < 0.001$). Very high cardiovascular risk (CVR) according to SCORE was found in 77.51% (95%CI 74.54–80.49) of the population with CKD.
Conclusions: The adjusted prevalence of CKD was 9.2% (low eGFR: 8.0%; albuminuria: 6.0%). Most of the patients with CKD had very high CVR. Hypertension, diabetes, prediabetes, increased waist-to-height ratio and ACVD were independently associated with CKD.

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PALABRAS CLAVE
Enfermedad renal crónica;
Factores de riesgo;
Prevalencia

Tasas de prevalencia de enfermedad renal crónica y su asociación con factores cardiometabólicos y enfermedades cardiovasculares. Estudio SIMETAP-ERC

Resumen
Introducción: La enfermedad renal crónica (ERC) constituye un importante problema de salud que contribuye al desarrollo de alteraciones cardiovasculares como la insuficiencia cardíaca y la enfermedad cardiovascular arteriosclerótica (ECVA). Los objetivos de este estudio fueron determinar la prevalencia de ERC y evaluar su asociación con factores de riesgo cardiometabólicos y la ECVA.
Métodos: Estudio observacional transversal realizado en el ámbito de atención primaria. Muestra aleatoria de base poblacional: 6.588 personas entre 18 y 102 años (tasa de respuesta: 66%). Se determinaron las tasas de prevalencia brutas y ajustadas por sexo y edad de ERC según KDIGO valorando albuminuria y filtrado glomerular estimado (FGe) según CKD-EPI, y sus asociaciones con factores cardiometabólicos y ECVA.
Resultados: La prevalencia cruda de ERC fue 11,48% (IC95%: 10,72–12,27%), sin diferencia significativa entre hombres (11,64% [IC95%: 10,49–12,86%]) y mujeres (11,35% [IC95%: 10,34–12,41%]). La tasa de prevalencia ajustada por edad y sexo de ERC fue 9,16% (hombres: 8,61%; mujeres: 9,69%). La prevalencia del FGe reducido (<60 mL/min/1,73 m^2) y de albuminuria (≥30 mg/g) fueron 7,95% (IC95%: 7,30–8,61) y 5,98% (IC95% 5,41–6,55), respectivamente. Hipertensión, diabetes, prediabetes, índice cintura-talla aumentado, insuficiencia cardíaca, fibrilación auricular y ECVA se asociaban independientemente con ERC ($p < 0,001$). El 77,51% (IC95%: 74,54–80,49) de la población con ERC tenía un riesgo cardiovascular (RCV) muy alto según SCORE.
Conclusiones: La prevalencia ajustada de ERC era del 9,2% (FGe reducido: 8,0%; albuminuria: 6,0%). La mayoría de los pacientes con ERC tenía RCV muy alto. Hipertensión, diabetes, prediabetes, índice cintura-talla aumentado y ECVA se asociaban independientemente con la ERC.

Introduction

Chronic kidney disease (CKD) is characterised by a gradual deterioration of the body's filtering function, removal of toxins, and volume control, which can lead to the development of cardiovascular problems such as heart failure and arteriosclerotic cardiovascular disease (ACVD)[1].

CKD is a major public health problem with an increasing global burden of disease and is linked to serious health outcomes, poor quality of life, and high healthcare costs, most notably those derived from the renal replacement therapy that individuals with end-stage renal disease (ESRD) require. Therefore, there is a need to redirect the strategy toward early detection and early treatment so as to improve health outcomes and reduce the need for renal replacement therapy[1–3].

In and of itself, CKD constitutes a cardiovascular risk factor (CVRF)[4]. Whether or not patients with CKD have other associated CVRFs, they are more likely to suffer from cardiovascular and all-cause mortality[1]. Death rates increase exponentially as kidney function worsens, mainly due to cardiovascular causes[1]. There is a strong correlation between clinical prognosis, albuminuria, and reduced estimated glomerular filtration rate (eGFR) (<60 mL/min/1.73 m^2)[2,5]. Meta-analyses conducted by the Chronic Kidney Disease (CKD) Prognosis Consortium[6,7] have documented the association of decreased eGFR and the presence of albuminuria with an increased risk of overall mortality, cardiovascular mortality, renal failure, acute renal failure, and progression of CKD in both the general population and in populations at high cardiovascular risk (CVR), irrespective of other CVRFs. People with CKD are 5–10 times more likely to die prematurely than to progress to ESRD.

Between 8–16% of the world's population has CKD, albeit data differ significantly across countries and regions in the world[3,8–10]. During recent decades, the prevalence of CKD has risen in response to the growing prevalence of hypertension (HTA), obesity and diabetes (DM), as well as the increasing longevity of the population[9,10]. DM and HTA are the leading causes of CKD in countries with high sociodemographic indices and in most countries with low indices[1]. Despite the fact that it has been well established that proper management and treatment of DM, HTA, and dyslipidaemia are effective in slowing the progression of CKD[11–13], the incidence of major adverse cardiovascular and renal events remains high among CKD patients.

The KDIGO (Kidney Disease: Improving Global Outcomes) conference, entitled *Early Identification and Intervention in CKD*[14], identified strategies for early and optimal detection, screening, risk stratification, and treatment of CKD, such as encouraging healthy lifestyles and managing key CVRFs, so as to slow or delay the progression, lessen complications,

and lighten the burden of disease. Participants agreed that these measures should be implemented immediately for those individuals at high risk and that, ideally, this should occur in the primary care setting.

The objectives of the SIMETAP-ERC study were to determine crude and age- and sex-adjusted prevalence rates of CKD in the adult population in accordance with KDIGO[5], by quantifying albuminuria and eGFR on the basis of the Chronic Kidney Disease EPIdemiology collaboration equation (CKD-EPI)[15] and to examine the associations between CKD and cardiometabolic factors and cardiovascular disease.

Material and methods

SIMETAP-ERC is a cross-sectional, observational study, authorised by the Health Service of the Community of Madrid (SERMAS), in which 121 competitively-selected family doctors participated until the required sample size was reached; these physicians belonged to 64 primary care centres (25% of the SERMAS health centres). A simple random sampling of 5.45% of the entire target population aged 18 years or older (194,073 adults) assigned to the SERMAS primary care physicians participating in the study was conducted using random number tables extracted using the Excel RANDOM.BETWEEN(lower, upper) function. Information concerning the material and methods of the SIMETAP study has been reported in detail in an earlier publication[16]. As per protocol, we excluded terminally ill, institutionalised, cognitively impaired, and pregnant subject, or those for whom information on biochemical variables was not available. Informed consent was obtained from all study participants, with a response rate of 65.8% and enrolment of 6588 study subjects with sufficient clinical and laboratory data to be evaluated.

The following variables were taken into account: body mass index (BMI): weight/height^2 (kg/m^2); overweight: BMI 25–29.9 kg/m^2; obese: BMI $\geq$ 30 kg/m^2; adiposity or body fat index CUN-BAE (Clínica Universitaria de Navarra-Body Adiposity Estimator)[17] $(-44.988 + [0.503 \times \text{age}] + [10.689 \times \text{sex}] + [3.172 \times \text{BMI}] - [0,026 \times \text{BMI2}] + [0.181 \times \text{BMI} \times \text{sex}] - [0.2 \times \text{BMI} \times \text{age}] - [0.05 \times \text{BMI2} \times \text{sex}] + [0.0021 \times \text{BMI2} \times \text{age}])$ sex (male = 0, female = 1); CUN-BAE-obesity (>25% [male]; >35% [female]); abdominal obesity: increased abdominal circumference ($\geq$102 cm [men]; $\geq$88 cm [women]); waist-to-height ratio (WHI): abdominal circumference/height; increased WHI: WHI $\geq$ 0.55; HTA: systolic blood pressure (SBP) $\geq$ 140 mmHg and/ or diastolic blood pressure (DBP) $\geq$ 90 mmHg, or being on antihypertensive treatment; hypercholesterolaemia: total cholesterol $\geq$ 200 mg/dL; hypertriglyceridemia: triglycerides $\geq$ 150 mg/dL; cholesterol bound to high-density lipoprotein (c-HDL); low c-HDL: c-HDL < 40 mg/dL (males), < 50 mg/dL (females); cholesterol not bound to HDL (c-non-HDL); cholesterol bound to low-density lipoproteins (c-LDL); cholesterol bound to very low-density lipoproteins and remnants (c-VLDL); plasma atherogenic index: log (TG/c-HDL). Triglyceride-glucose index (TyG): Ln [TGxGPA/2]; atherogenic dyslipidaemia: HTG and low c-HDL; DM in accordance with the criteria of the American Diabetes Association (ADA)18: fasting plasma glucose (FPG) $\geq$ 126 mg/dL or glycated haemoglobin A1c (HbA1c) $\geq$ 6.5% as ascertained by standardised methods (ADA), 5% as measured by standardised methods (National Glycohemoglobin Standardization Program) according to the DCCT (Diabetes Control and Complications Trial) or determination of plasma glucose $\geq$ 200 mg/dL at any time or by means of an oral glucose tolerance test; prediabetes in individuals without DM based on ADA[18] (GPA between 100 and 125 mg/dL or HbA1c between 5.7 and 6.4%) and according to the Spanish Diabetes Society (SED)[19] (GPA between 110 and 125 mg/dL or HbA1c between 6 and 6.4%); metabolic syndrome: according to harmonised IDF/NHLBI/AHA/WHF/IAS/IASO consensus[20]; CVD: coronary heart disease (CHD), cerebrovascular disease (stroke), peripheral arterial disease (PAD); CHD: ischaemic heart disease, acute myocardial infarction, acute coronary syndrome, coronary revascularisation; stroke: cerebral ischaemia, intracranial haemorrhage, transient ischaemic attack; PAD: intermittent claudication, ankle-brachial index $\leq$0.9; CVR categories (low, moderate, high, and very high) according to SCORE21 and SCORE-OP[22] for low-risk countries; eGFR according to the CKD-EPI equation[15]; eGFR categories as per KDIGO:[5] G1 ($\geq$90 mL/min/1.73 m^2), G2 (60–89 mL/min/1.73 m^2), G3a (45–59 mL/min/1.73 m^2), G3b (30–44 mL/min/1.73 m^2), G4 (15–29 mL/min/1.7 m^2), and G5 (<15 mL/min/1.73 m^2); reduced eGFR: GFR < 60 mL/min/1.73 m^2; urine albumin-to-creatinine ratio (ACR) categories according to KDIGO[5]: A1 (<30 mg/g); A2 (30–300 mg/g); A3 (>300 mg/g); albuminuria: ACR $\geq$ 30 mg/g. CKD[5]: reduced eGFR and/ or albuminuria.

Statistical analysis was performed with the Statistical Package for the Social Sciences. Qualitative variables were analysed using percentages, chi-square test, and odds ratios (OR) with 95% confidence interval (95% CI). Continuous variables were assessed using mean with standard deviation ($\pm$SD) and Student's *t*-test or analysis of variance. Medians and interquartile ranges (IQR) were determined for age and renal parameters. Crude and age- and sex-adjusted prevalence rates were determined by direct method, using standardised ten-year age groups of the Spanish population in January 2015 reported by the National Institute of Statistics[23].

To assess the individual effect of comorbidities and CVRFs on the dependent variable CKD, a multivariate logistic regression analysis was carried out using the backward stepwise method, initially introducing all the variables that showed an association in the univariate analysis up to a value of $p < 0.10$ into the model, except for the CUN-BAE variables obesity[17] and metabolic syndrome[20], as these are complex variables whose defining criteria were already included in the analysis, and erectile dysfunction, as it only affects men. Subsequently, the variable that contributed least to the fit of the analysis was eliminated at each step. All tests were regarded as statistically significant if the 2-tailed p-value was less than 0.5. A bibliographic search was performed in PubMed, Medline, Embase, Google Scholar, and Web of Science to compare the CKD prevalence rates of the present study with other similar studies published since 2001.

Results

Study population

The study population comprised 6588 adults between the ages of 18 and 102.8 years, with a mean (±SD) age of 55.1 (±17.5) years and a median (IQR) age of 54.69 (41.68–68.09) years. The percentage difference between men (44.1% [95%CI: 42.9–45.3 %]) and women (55.9% [95%CI: 54.7–57.1 %]) was significant ($p < 0.01$). The median (IQR) ages of the male and female populations were 55.0 (42.4–67.5) years and 54.5 (41.0–68.8) years, respectively, with the difference in mean [±SD] ages between men (55.3 [±16.9] years) and women (55.0 [±18.0] years) being non-significant ($p = 0.634$).

Chronic kidney disease prevalence rates

The crude prevalence rate of CKD was 11.48% (95% CI: 10.72–12.27%); the difference was not significant ($p = 0.711$) among males (11.64% [95% CI: 10.49–12.86%]) and females (11.35% [95% CI: 10.34–12.41%]). When adjusted for age and sex, the prevalence rate of CKD was 9.16% (8.61% among men; 9.69% among women).

The distribution of decadal age-group-specific rates of CKD prevalence increased precisely with age ($R^2 = 0.999$) according to the polynomial function and $= 0.044x^3 - 0.319x^2 + 0.761x - 0.313$, with no significant differences detected between sexes (Fig. 1). The age- and sex-adjusted prevalence of CKD in the ≥60-year-old population was 23.75% (23.49% in men; 24% in women), with no significant difference ($p = 0.923$) between the crude prevalence rates of CKD in males (23.39% [95% CI: 20.99–25.93 %]) and females (23.23% [95% CI: 21.11–25.45 %]). In the ≥70-year-old population, the age- and sex-adjusted prevalence rate of CKD was 33.56% (34.09% for men; 33.27% for women), with no significant difference ($p = 0.470$) between the crude prevalence rates of CKD among males (34.33% [95% CI: 30.54–38.29%]) and females (32.52% [95% CI: 29.40–35.76%]).

The prevalence rates of the different types of CKD depending on eGFR and albuminuria categories according to KDIGO5 were as follows: G1 and G2 with albuminuria (ACR ≥ 30 mg/g): 3.54% (95% CI: 3.09–3.98); G3a with/without albuminuria: 5.48% (95% CI: 4.93–6.03); G3b with/ without albuminuria: 1.82% (95% CI: 1.50–2.14); G4 with/ without albuminuria: 0.49% (95% CI: 0.32—0.65); G5 with/without albuminuria: 0.15% (95% CI: 0.6—0.25) (Table 1). There were no significant differences between sexes in the CKD categories according to eGFR, except in the G2 category, which was significantly higher ($p = 0.12$) in men (39.36% [95% CI: 37.58–41.16]) than in women (36.35% [95% CI: 34.79–37.92]). The percentage of study subjects with a lower eGFR (<60 mL/min/1.73 m^2) was 7.95% (95% CI: 7.30–8.61), with no significant difference ($p = 0.169$) between men (7.44% [95% CI: 6.48–8.39]) and women (8.36% [95% CI: 7.47–9.25]) (Table 2).

The prevalence of albuminuria (ACR ≥ 30 mg/g) in men (7.37% [95% CI: 6.42–8.32]) was significantly higher ($p < 0.01$) than in women (4.89% [95% CI: 4.19–5.58]). The percentage of stage A1 albuminuria was significantly higher (p < 0.01) in females than in males. The percentages of stages A2 and A3 albuminuria were significantly higher ($p < 0.01$) in men than in women (Table 2).

Analyses of the populations with and without CKD

The median (IQR) ages of the populations with and without CKD were 77.33 (65.22–83.38) years and 52.42 (40.33–65.18) years, respectively, with the difference in mean ages being significant ($p < 0.01$) (Table 3). There was no significant difference ($p = 0.711$) in the percentage of males and females between the two populations (Table 4). All quantitative clinical variables were significantly higher in the CKD population than in the non-CKD population, except TC, c-HDL, c-LDL, c-No-HDL, alanine aminotransferase, and eGFR concentrations, which were higher in the non-CKD population, and DBP, aspartate aminotransferase concentrations, and total cholesterol/c-HDL and c-No-HDL/c-HDL indices, the differences of which were not significant (Table 3). The median (IQR) creatinine, eGFR, and ACC of the CKD population were 1.09 (0.91–1.30) mg/dL, 55.6 (46.5–73.3) mL/min/1.73 m^2, and 36.1 (5.1–100.9) mg/g, respectively. The median (IQR) creatinine, eGFR, and ACC for the population without CKD were 0.80 (0.68—0.90) mg/dL, 94.2 (82.7–106.0) mL/min/1.73 m^2, and 5.3 (3.0–8.7) mg/g, respectively.

All ORs for CVRFs and comorbidities between the populations with and without CKD displayed correlations with CKD, except for current smoking status, which revealed an association with subjects without CKD, and being overweight, for which the OR was not significant (Table 4).

According to CVR assessment by SCORE[21] and SCORE-OP[22] for low-risk countries, 22.49% (95% CI: 19.56–25.63) of the CKD population had a high level of CVR and 77.51% (95% CI: 74.54–80.49) had a very high level of CVR. The comparison between study groups of subjects with and without CKD, the OR for high CVR was 1.7 (95% CI 1.4–2.0) and the OR for very high CVR was 10.4 (95% CI 8.7–12.4).

Multivariate analysis revealed that the CVRFs and comorbidities that were independently associated with CKD were AHT, DM, pre-diabetes according to ADA criteria, increased WHtR, heart failure, atrial fibrillation, PAD, CHD, and stroke (Table 5).

Discussion

The surveys conducted in high-income countries have indicated similar CKD prevalence rates (11.3% in the USA[24], 12.5% in Canada[25], and 11.1% in Norway[26]). According to the 2019 GKHA (Global Kidney Health Atlas)[3] report by the International Society of Nephrology (ISN), which is based on two surveys carried out in 2017 and 2019, the average prevalence rate of CKD in 21 Western European countries was 10.1%, and in Spain, it was 9.6%. The ISN-KDDC[27] study, conducted in 12 developing countries with non-random convenience sampling, whose selection bias may have overestimated prevalence, yielded a CKD prevalence rate of 14.3%, with considerable variability and even significant differences in comparison with other studies undertaken in their respective countries. While the ISN-KDDC study[27] demonstrated prevalence rates in India and China of 16.8%

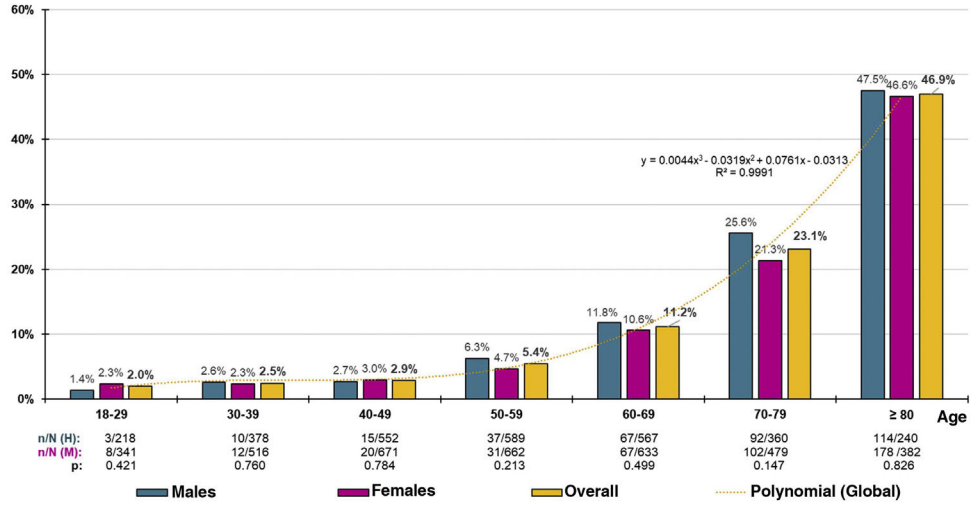

Figure 1 CKD prevalence rates by age and sex. CKD: chronic kidney disease; M: male; F: female; n: number of cases; N: sample size; p: p-value of the difference (M−F).

Table 1 Percentages of the categories of CKD, as per KDIGO[5].

			Albuminuria categories			
			A1 Normal or slight increase	A2 Moderate increase	A3 Severe increase	
	eGFR categories	(mL/min/1.73 m²)	< 30 mg/g	30 – 300 mg/g	> 300 mg/g	Σ (G)
G1	Normal or high	≥90	52.78	1.52	0.09	54.39
G2	Slightly decreased	60–89	35.75	1.70	0.23	37.67
G3a	Mild - moderate decrease	45–59	4.22	1.12	0.14	5.48
G3b	Moderately - severely decreased	30–44	1.05	0.71	0.06	1.82
G4	Severe decrease	15–29	0.18	0.21	0.09	0.49
G5	ESRD or renal failure	<15	0.05	0.06	0.05	0.15
		Σ (A)	94.02	5.33	0.65	100.0

CKD: chronic kidney disease; ESRD: end-stage renal disease; eGF: estimated glomerular filtration rates according to CDK-EPI[15]; KDIGO[5]: Kidney Disease: Improving Global Outcomes; Σ (A): sum of percentages of categories of albuminuria; Σ (G): sum of percentages of categories of eGF.
KDIGO[5] risk scales: green (low risk); yellow (moderately increased risk); orange (high risk); red (very high risk).

Table 2 Percentages of the categories of eGF and albuminuria among males and females.

Males	A1	A2	A3	Σ (G)	Females	A1	A2	A3	Σ (G)	Dif. Σ (G)	*p*
G1	51.48	1.65	0.10	53.24	G1	53.80	1.41	0.8	55.29	−2.06	0.97
G2	36.88	2.10	0.38	39.36	G2	34.85	1.38	0.11	36.35	3.01	0.12
G3a	3.20	1.52	0.24	4.96	G3a	5.02	0.81	0.5	5.89	−0.93	0.100
G3b	0.83	0.83	0.7	1.72	G3b	1.22	0.62	0.5	1.90	−0.18	0.587
G4	0.21	0.21	0.17	0.59	G4	0.16	0.22	0.3	0.41	0.18	0.299
G5	0.3	0.0	0.10	0.14	G5	0.5	0.11	0.0	0.16	−0.3	0.836
Σ (A)	92.63	6.30	1.07	10.	Σ (A)	95.11	4.56	0.33	10.		
Dif. Σ (A)	−2.48	1.74	0.74								
p	<0.01	0.02	<0.01								

A1: urine albumin to creatinine ratio (UACR) < 30 mg/g; A2: UACR between 30 and 300 mg/g; A3: UACR > 300 mg/g; eGF: estimated glomerular filtration rates according to CKD-EPI[15]; G: categories of eGF according to KDIGO[5]; Σ (A): sum of percentages of albuminuria categories; Σ (G): sum of percentages of eGF; Dif. Σ (A): difference of Σ (A) between males and females; Dif. Σ (G): difference of Σ (G) between males and females; p: p-value of the difference in means.

and 29.9%, respectively, other studies[28,29] performed with random sampling in these same countries have reported much lower prevalence rates (7.5% and 16.8%, respectively). This bias was also evidenced in the USA between the KEEP programme[30] with actively referred study subjects and the National Health and Nutrition Examination Survey (NHANES), with different CKD prevalence rates (28.7% and 13.1%, respectively). The adjusted prevalence of the

Table 3 Clinical characteristics of the populations with and without CKD.

	With CKD		Without CKD		Difference in means	*p*
	N	Mean (±SD)	N	Mean (±SD)		
Age (years)	756	72.69 (14.97)	5.832	52.87 (16.52)	19.82	<0.01
BMI (kg/m^2)	756	29.28 (5.17)	5.832	27.28 (5.10)	2.00	<0.01
Abdominal circumference (cm)	756	99.49 (13.69)	5.832	92.56 (13.95)	6.93	<0.01
Waist-to-height index	756	0.62 (.9)	5.832	0.56 (.9)	0.6	<0.01
Adiposity (%)	756	38.79 (7.97)	5.832	34.22 (8.62)	4.57	<0.01
SBP (mmHg)	756	128.35 (15.61)	5.832	121.09 (15.23)	7.26	<0.01
DBP (mmHg)	756	73.75 (9.72)	5.832	73.28 (9.77)	0.47	0.211
GPA (mg/dL)[a]	756	109.20 (37.04)	5.832	94.31 (23.61)	14.89	<0.01
HbA1c (%)[b]	687	6.17 (1.22)	4.546	5.56 (0.81)	0.62	<0.01
TyG Index	756	8.74 (0.62)	5.832	8.46 (0.60)	0.28	<0.01
Total cholesterol (mg/dL)[c]	756	184.47 (40.95)	5.832	193.85 (39.00)	−9.38	<0.01
c-HDL (mg/dL)[c]	756	52.62 (15.19)	5.832	55.12 (14.60)	−2.50	<0.01
c-LDL (mg/dL)[c]	750	105.09 (35.45)	5.776	115.34 (34.21)	−10.25	<0.01
c-VLDL (mg/dL)[c]	750	26.14 (13.14)	5.776	22.52 (12.16)	3.62	<0.01
c-non-HDL (mg/dL)[c]	756	131.86 (38.37)	5.832	138.72 (38.36)	−6.86	<0.01
Triglycerides (mg/dL)[d]	756	134.69 (73.43)	5.832	118.68 (84.20)	16.01	<0.01
CT/non-HDL	756	3.71 (1.09)	5.832	3.72 (1.14)	−0.1	0.797
c-non-HDL /c-HDL	756	2.71 (1.09)	5.832	2.72 (1.14)	−0.1	0.797
TG/c-HDL	756	2.94 (2.27)	5.832	2.48 (2.58)	0.46	<0.01
c-LDL/c-HDL	750	2.12 (0.85)	5.776	2.23 (0.89)	−0.11	0.02
AIP	756	.1 (0.28)	5.832	−.8 (0.29)	0.9	<0.01
Uric acid (mg/dL)	740	5.80 (1.65)	5.428	4.85 (1.42)	0.96	<0.01
AST (U/L)	571	25.35 (84.02)	4.241	22.76 (34.14)	2.59	0.180
ALT (U/L)	737	23.20 (14.20)	5.676	25.09 (17.25)	−1.89	0.04
GGT (U/L)	713	41.00 (55.53)	5.362	32.34 (50.10)	8.66	<0.01
UACR (mg/g)	756	91.39 (159.07)	5.832	6.70 (5.14)	84.69	<0.01
eGF (mL/min/1.73 m^2)	756	60.30 (23.03)	5.832	94.47 (16.54)	−34.17	<0.01
Creatinine (mg/dL)	756	1.19 (0.62)	5.832	0.80 (0.17)	0.39	<0.01

Adiposity: body fat index CUN-BAE CUN-BAE;[17] AIP: atherogenic index of plasma; ALT: alanine-aminotransferase; AST: aspartate-aminotransferase; BMI: body mass index; c-HDL: cholesterol bound to high-density lipoprotein; c-LDL: cholesterol bound to low-density lipoprotein; c-VLDL: cholesterol bound to very low-density lipoproteins and remnants; c-non-HDL: cholesterol not bound to HDL (c-non-HDL); CKD: chronic kidney disease; DBP: diastolic blood pressure; eGF: estimated glomerular filtration rate, as per CKD-EPI[15]; GGT: gamma-glutamyl transferase; N: sample size; p: p-value of the difference in means; SBP: systolic blood pressure; SD: standard deviation; TyG Index: Triglyceride-glucose index; UACR: urine albumen/ creatinine.

[a] To convert mg/dL to mmol/L, multiply by 0.5556.

[b] To convert from % according to the Diabetes Control and Complications Trial (DCCT) to mmol/mol according to the International Federation of Clinical Chemistry (IFCC), multiply by 0.9148 and add 2.152.

[c] To convert from mg/dL to mmol/L, multiply by 0.2586.

[d] To convert from mg/dL to mmol/L, multiply by 0.1129.

present SIMETAP-ERC study (9.2%) was somewhat lower than that of the Hill et al.[9] meta-analysis (13.4%), and very much in line with that of the GBD-CKD Collaboration[10] meta-analysis (9.1%); both meta-analyses exhibited substantial heterogeneity among the studies analysed. The prevalence of ESRD in the SIMETAP-ERC study (0.15%) was comparable to that of the ISN GKHA report[3], which ranged from 0.1% in upper middle-income countries to 0.2% in high-income countries.

In Spain, the ENRICA study[31] yielded a crude prevalence of CKD of 15.1%, similar to the 14.4% in the IBERICAN study's primary care population cohort.[32] These results differ from the EPIRCE[33] study, which, adopting the Modification of Diet in Renal Diseases (MDRD)[34] method to assess eGFR, yielded a CKD prevalence of 9.2%, the same as in the present study using the CKD-EPI equation[15]. The SIMETAP-ERC study confirmed that the prevalence of CKD increased with age, doubling for every decade after the age of 40 years (Fig. 1). Other studies performed in Spain that used the MDRD[34] method to calculate the prevalence of reduced eGFR have reached disparate results, such as the EPIRCE[33] study (21.4%) in the ≥ 65-year-old population and the PREVICTUS[35] study (25.9%), as well as the study by Salvador González et al.[36] (15.1%) in populations aged 60 years or older. These studies[33,35,36] have demonstrated lower figures than others that have determined eGFR using the CKD-EPI equation[15], such as the ENRICA study[31], in which the crude prevalence of CKD was 37.3% in the population aged ≥65 years, or the present study, in which the age-adjusted prevalence rates of CKD in the ≥60 years and ≥70

Table 4 CVRF and comorbidities in the populations with and without CKD.

	With CKD n.º of cases (%) *N* = 756	Without CKD, n.º of cases (%) *N* = 5.832	OR	P value
Male sex	338 (44.7)	2.566 (44.0)	1.0 (0.9–1.2)	0.711
Smoking	101 (13.4)	1.325 (22.7)	0.5 (0.4–0.7)	<0.01
Lack of physical activity	396 (52.4)	2.683 (46.0)	1.3 (1.1–1.5)	0.01
Overweight	313 (41.4)	2.203 (37.8)	1.2 (1.0–1.4)	0.53
Obesity	304 (40.2)	1.529 (26.2)	1.9 (1.6–2.2)	<0.01
CUN-BAE-obesity	709 (93.8)	4.123 (70.7)	6.3 (4.6–8.5)	<0.01
Abdominal obesity	474 (62.7)	2.448 (42.0)	2.3 (2.0–2.7)	<0.01
Increased WHtR	602 (79.6)	3.094 (53.1)	3.5 (2.9–4.2)	<0.01
Prediabetes (SED)	89 (11.8)	434 (7.4)	1.7 (1.3–2.1)	<0.01
Prediabetes (ADA)	225 (29.8)	1.224 (21.0)	1.6 (1.4–1.9)	<0.01
Diabetes	286 (37.8)	749 (12.8)	4.1 (3.5–4.9)	<0.01
Hypertension	581 (76.9)	1.966 (33.7)	6.5 (5.5–7.8)	<0.01
Hypercholesterolemia	586 (77.5)	3.515 (60.3)	1.9 (1.7–2.2)	<0.01
Low c-HDL	283 (37.4)	1.536 (26.3)	1.7 (1.4–2.0)	<0.01
Hypertriglyceridemia	317 (41.9)	1.630 (27.9)	1.9 (1.6–2.2)	<0.01
Atherogenic dyslipidaemia	173 (22.9)	768 (13.2)	2.0 (1.6–2.4)	<0.01
Metabolic syndrome	560 (74.1)	2.291 (39.3)	4.4 (3.7–5.2)	<0.01
ACVD	196 (25.9)	419 (7.2)	4.5 (3.7–5.5)	<0.01
Coronary heart disease	107 (14.2)	214 (3.7)	4.3 (3.4–5.5)	<0.01
Stroke	82 (10.8)	168 (2.9)	4.1 (3.1–5.4)	<0.01
PAD	61 (8.1)	89 (1.5)	5.7 (4.1–7.9)	<0.01
Erectile dysfunction[a]	157 (46.4)	347 (13.5)	5.6 (4.4–7.1)	<0.01
Heart failure	102 (13.5)	82 (1.4)	10.9 (8.1–14.8)	<0.01
Atrial fibrillation	113 (14.9)	137 (2.3)	7.3 (5.6–9.5)	<0.01

ADA: prediabetes, according to the American Association of Diabetes[18]; Low c-HDL: cholesterol bound to high-density lipoprotein <40 mg/dL (males), <50 mg/dL (females); CUN-BAE-obesity[17]: adiposity or body fat indes (Clínica Universitaria de Navarra–Body Adiposity Estimator) >25% (males), >35% (females); Atherogenic dyslipidaemia: hypertriglyceridemia and low c-HDL; PAD: peripheral arterial disease; ACVD: atherosclerotic cardiovascular disease; CKD: chronic kidney disease; CVRF: cardiovascular risk factors; Hypercholesterolaemia: total cholesterol ≥200 mg/dL; Hypertriglyceridemia: triglycerides ≥150 mg/dL; increased WHtR: waist-to-height ratio ≥0.55; Lack of physical activity: physical activity <150 min/week; N: sample size; Obesity: body mass index ≥30 kg/m^2; Abdominal obesity: abdominal circumference ≥102 cm (males), ≥88 cm (females); OR: odds ratio between both populations (95% confidence interval); SED: prediabetes according to the Spanish Society of Diabetes[19]; Overweight: BMI 25.0–29.9 kg/m^2; Smoking: cigarette or tobacco use in the past year.

[a] N males: 338 with CKD; 2566 without CKD.

Table 5 Multivariate analysis of the effect of comorbidities and CVRF on CKD.

CKD	β[a]	Wald	OR Exp(β)[b]	*p*[c]
Hypertension	1.17 (0.10)	129.53	3.21 (2.63–3.93)	<0.01
Diabetes	0.95 (0.11)	76.57	2.59 (2.09–3.19)	<0.01
Heart failure	1.18 (0.18)	42.67	3.26 (2.29–4.65)	<0.01
Atrial fibrillation	0.95 (0.16)	36.06	2.59 (1.90–3.54)	<0.01
Prediabetes (ADA)	0.56 (0.11)	27.74	1.75 (1.42–2.15)	<0.01
Increased WHtR	0.49 (0.11)	21.57	1.64 (1.33–2.01)	<0.01
PAD	0.66 (0.20)	11.29	1.94 (1.32–2.86)	0.01
Ischaemic cardiopathy	0.37 (0.14)	6.44	1.44 (1.09–1.91)	0.11
Stroke	0.39 (0.17)	5.57	1.47 (1.07–2.04)	0.18

ADA: American Association of Diabetes; CKD: chronic kidney disease; CVRF: cardiovascular risk factors; Increased WHtR: waist-to-height ratio ≥0.55; PAD: peripheral arterial disease.

[a] β coefficient (± deviation).

[b] Odds-ratio Exp (β) (95% confidence interval).

[c] p: p-value of Wald test with one degree of freedom.

years of age populations were 23.8% and 33.6%, respectively. The choice of the CKD-EPI[15] equation rather than the MDRD[34] method is in keeping with the recommendations of the KDIGO5 guidelines and the Spanish consensus for the detection and management of CKD[37], as it is more closely related to reduced eGFR values, is more accurate for values >60 mL/min/1.73 m^2, and has a greater capacity to predict overall mortality, cardiovascular mortality, or the risk of kidney failure[37].

All anthropometric parameters were significantly greater in the CKD population and a correlation existed with obesity, adiposity, abdominal obesity, and increased CTI. Whilst obesity has been associated with an increased risk of CKD[38], only increased CTI has displayed an independent correlation with CKD in the present study, together with other comorbidities such as AHT, DM, pre-diabetes, HF, AF, PAD, CHD, and stroke, which have also been found to be associated in other studies[26,31–33,36].

Despite the decline in the risk of major adverse cardiovascular events over the last few decades as a result of better control of DM, HTA, and dyslipidaemia, the prevalence of individuals with DM2 and CKD among the adult population remains very high and the trend continues to be on the rise[39], which is probably due to this better control contributing to increased longevity, and thus, more time to for CKD to develop[40]. The SIMETAP-DM study[41] found that 27.6% of the adult population with DM had CKD, a lower prevalence than the NHANES[42] survey in the USA (43.5%) and similar to that of other Spanish studies, such as the one by Fernández-Fernández et al.[43] (25.3%) and PERCEDIME2[44] (27.9%). In the present study, 37.8% of the population with CKD had DM; 29.8% had pre-diabetes, based on ADA 28 criteria and 11.8% as per SED criteria[19]. Despite the fact the ORs between populations with and without CKD according to ADA[18] and SED[19] prediabetes were similar (1.6 and 1.7, respectively), only ADA[18] prediabetes was independently associated with CKD, the same as DM, which substantiates the close relationship between alterations in glycaemic metabolism and CKD[9,11].

In the present study, SBP was significantly higher (7.3 mmHg) in the CKD population than in the non-CKD cohort, and 79.6% of the CKD population had HTA; this last factor was the one that was most strongly independently associated with CKD.

The fact that all the parameters included in the CUN-BAE variables, obesity[17] and metabolic syndrome[20] were associated with CKD accounts for the fact that both variables demonstrated a very strong association with CKD (OR 6.3 and 4.4, respectively).

On the other hand, the SIMETAP-ERC study found that 25.9% of the CKD population had CVD (CHD: 14.2%; stroke: 10.8%; PAD: 8.1%) and that both CVD taken as a whole, and CHD, stroke, or PAD taken individually, exhibited an independent association with CKD. Approximately 55% of patients with HF and 50% of individuals with AF have some degree of renal failure and some 20% of subjects with CKD have AF[45,46]. In the present study, 13.5% and 14.9% of the participants with CKD had HF and AF, respectively, and both conditions were identified as independent factors closely linked to CKD. More than 77% of the CKD population had a very high CVR according to SCORE[21,22], which included patients with severe CKD (eGFR« 30 ml/min/1.73 m^2), with DM and target organ damage or major CVRF (smoking, HTA, or pronounced hypercholesterolaemia), with clinical or imaging-documented ARVD, and subjects with a score $\geq$10. This high percentage is explained by the fact that the median age of the population is 77 years with a high frequency of CVAD (26%) and cardiometabolic factors (DM 38%; obesity: 40%; metabolic syndrome 74%; HTA 77%; hypercholesterolaemia 78%).

Limitations of the present study include the fact that it did not assess the presence of renal damage directly (renal biopsy) or indirectly through imaging tests, the inability to determine causality, the possible variability between interviewers, calibration, or the possible heterogeneity of the measurement and laboratory equipment, in addition to the fact that it did not include pregnant women, terminally ill or institutionalised patients, or those with cognitive impairment. Moreover, the cross-sectional design of the present study did not allow us to assess the persistence of albuminuria or reduced eGFR, to estimate incidence rates, or to infer causal relationships between risk factors and CKD.

The varying sampling methodologies and eGFR determinations and the different median ages of the comparison study populations might account for the different CKD prevalence rates. One strength of the present study was the large, random sampling on a populational basis that included all age groups. The SIMETAP-ERC study reveals that CKD is strongly influenced by age; therefore, age-adjusted rates are necessary to be able to compare rates with other populations. Other strengths of the present study were that it evaluated the association of CKD with numerous cardiometabolic variables, in addition to eGFR measurements according to CKD-EPI[15] and UACR in the entire population.

Late referral to nephrology of ESRD patients with DM or HTA is common in Spain[47]. The most efficient strategy to lessen the burden of CKD and limit its progression is early detection by screening for reduced eGFR and albuminuria in individuals with DM, HTA, obesity, and ASVCD, thereby facilitating diagnosis and treatment in the early stages of CKD[48–50].

The SIMETAP-ERC study indicates a progressive prevalence of CKD, especially after the age of 50, the health burden of which increases the risk of ESRD, overall mortality, and cardiovascular mortality. Evaluating the epidemiological situation of CKD is extremely important to optimise available health resources, plan interventions aimed at preventing this health problem, and reduce the burden of the disease by implementing early detection and prevention strategies that are easy to apply in the primary care setting, such as lifestyle changes and adequate control of the main risk factors associated with CKD.

Conclusions

The age- and sex-adjusted prevalence of CKD in the adult population was 9.2% (reduced eGFR: 8%; albuminuria: 6%). The 10-year age-specific CKD prevalence rates increased with age without significant differences between men and women, doubling for every 10-year age group after the age of 40 with a prevalence rate of 24% in people aged 60 years and older and 34% after the age of 70 years.

The most frequent comorbidities associated with CKD were HTN (77%), hypercholesterolaemia (77%), metabolic syndrome (74%), abdominal obesity (63%), hypertriglyceridemia (42%), obesity (40%), DM (38%), low HDL-C (37%), pre-diabetes (30%), and CVD (26%). Variables independently associated with CKD were HTN, DM, pre-diabetes, increased CTI, heart failure, atrial fibrillation, and AVCD. The high cardiovascular burden of CKD (77% with very high CVR) in an elderly population justifies the need to implement population-based measures for early detection and optimal control of associated cardiometabolic factors.

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Research ethics committee

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Conflict of interests

The authors have no conflict of interests to declare.

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