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NEPHROLOGY - ORIGINAL ARTICLE

Prevalence of chronic kidney disease and its association with cardio-metabolic risk factors in the adult Romanian population: the PREDATORR study

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Abstract

Purpose PREDATORR is the first national study analyzing the prevalence of chronic kidney disease and its prognosis and association with socio-demographic, cardio-metabolic and lifestyle risk factors in the adult Romanian population.

Methods Chronic kidney disease was defined according to the KDIGO 2012 criteria as an estimated glomerular filtration rate <60 mL/min/1.73 m^2 and/or urinary albumin-to-creatinine ratio ≥30 mg/g. The socio-demographic, lifestyle and anamnestic data were collected through interviewer-administered questionnaires. Physical examination and biochemical assays were also performed.

Results This cross-sectional study conducted between December 2012 and February 2014 in Romania included 2717 adults. The overall age- and sex-adjusted prevalence of chronic kidney disease was 6.74 % (95 %CI 5.60–7.88 %), of which 3.31 % (2.50–4.13 %) had only reduced kidney function (estimated glomerular filtration rate <60 mL/min/1.73 m^2), 2.98 % (2.21–3.76 %) had only albuminuria, and 0.45 % (0.14–0.74 %) had both. The prevalence of chronic kidney disease increased with age and was similar in women and in men. Age, hyperuricemia, impaired glucose regulation (diabetes/prediabetes), hypertriglyceridemia and a family history of renal disease were

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independent risk factors for the presence of chronic kidney disease.

Conclusions The PREDATORR study showed a high prevalence of chronic kidney disease in the adult Romanian population providing data on its prognosis and association with several cardio-metabolic risk factors.

Keywords Cardio-metabolic risk factors · Chronic kidney disease · Epidemiology · PREDATORR · Romania

Introduction

Chronic kidney disease (CKD) is a group of disorders characterized by structural and functional kidney abnormalities resulting in decreased kidney function [quantified by the estimated glomerular filtration rate (eGFR)] and/or kidney damage (quantified by albuminuria or proteinuria) [1]. Although it has a progressive nature, with first stages lacking clinical manifestations, biomarkers measurable through noninvasive testing are available. These biomarkers allow diagnosis and initiation of therapeutic interventions aiming to reduce the disease progression toward end-stage kidney disease (ESKD) and its associated complications [2–5].

The prevalence of CKD has increased dramatically during the past decades, exceeding 10 % and thus becoming a public health burden due to the high costs of the ESKD and poor outcomes [6, 7]. The increase in CKD prevalence is reflected by the increasing prevalence of ESKD and the increase in the number of patients treated by renal replacement therapy (RRT) [8]. In the USA, the prevalence increased from 10.00 % in the time interval 1988–1994 to 13.07 % for the time period 1999–2004 [9], with similar trends for both men and women. However, the incidence rate of RRT is low, around 100 new patient per million of population [10, 11]. The rising trend of CKD is expected to continue, and this increase may be explained by two main factors: the aging population and the increase in the incidence of type 2 diabetes [12].

Scarce data are available on the CKD prevalence in Romania. They originate from the National Health Evaluation Program performed by the Romanian government in 2007–2008 which included the evaluation of creatinine and urine analysis in persons considered at risk of CKD. Unfortunately, the results on CKD prevalence have been made publicly available only for one county and they showed a prevalence of 6.69 % when the Modification of Diet in Renal Disease (MDRD) Study formula for the eGFR estimation was used and 7.32 % when the CKD–Epidemiology Collaboration (CKD–EPI) equation was used [13]. Also, no information on albuminuria or associated medical history was available.

PREDATORR—PREvalence of DiAbeTes mellitus, prediabetes, overweight, Obesity, dyslipidemia, hyperuricemia and chRonic kidney disease in Romania—is the first national study that evaluates the prevalence of cardio-metabolic diseases (diabetes/prediabetes, obesity/overweight, dyslipidemia, metabolic syndrome, hyperuricemia, arterial hypertension) and CKD in Romanian participants aged 20–79 years [14]. One of the main objectives of the study was to establish the prevalence of CKD in the adult Romanian population, to evaluate the prognosis of CKD by eGFR and albuminuria categories and the interrelation of CKD with various cardio-metabolic, socio-demographic and lifestyle risk factors.

Materials and methods

Study design and participants

PREDATORR was a national epidemiological study with a stratified, cross-sectional, two-cluster random sampling design, conducted between December 2012 and February 2014 according to the World Medical Association Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Participants (Seoul, Korea, October 2008) and the applicable International Conference on Harmonization—Good Clinical Practice Guidelines standards. The study was approved by the Romanian National Ethics Committee. The study design has been previously described [14]. In essence, participants were enrolled from the databases of 101 general practitioners (GPs) affiliated with the National Health Insurance House through an automated random computer decision. Participants were enrolled using automated random computer selection from the GPs'.

Databases. In all, 2728 participants aged 20–79 years were enrolled based on the 2002 Romanian Census in order to have representativeness of the sample for the adult Romanian population. The eligibility was established based on the following inclusion criteria: age between 20 and 79 years, included on the list of a GP, born in Romania and living for the past 10 years mainly in Romania, no pregnancy or lactation. All participants had to provide written informed consent before any study procedure.

Study methodology and reporting of results on the prevalence of CKD were designed according to the recommendations of the European CKD Burden Consortium [15].

Chronic kidney disease

CKD was defined according to the KDIGO 2012 criteria as eGFR <60 mL/min per 1.73 m^2 and/or the presence of albuminuria [16].

The eGFR was calculated using the CKD-EPI equation and the MDRD Study equation [16]. Albuminuria was defined as urinary albumin-to-creatinine ratio (ACR) ≥30 mg/g. Urinary creatinine and urinary albumin were determined using a spot urine sample.

Socio-demographic, lifestyle and clinical data

Interviewer-administered questionnaires were completed to assess the socio-demographic (gender, age, education level, marital status), lifestyle characteristics (physical activity, alcohol drinking, smoking status), personal medical history of diabetes, hypertension, current antihypertensive, antidiabetic or hypolipemiant therapy, and family history of kidney diseases in first and/or second degree relatives. Height, weight, waist circumference, and systolic and diastolic blood pressure were measured and recorded.

The education level was categorized as low (primary/secondary school) or high (university, high school, college). Participants who declared no alcohol consumption during the past month were considered non-drinkers. Sedentariness was considered when participants underwent physical activity <4 days per week.

Body mass index (BMI) was calculated, and participants with a BMI ≥ 25 kg/m^2 were considered as being overweight/obese. Abdominal obesity was defined as a waist circumference ≥94 cm in men and ≥80 cm in women [17]. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or personal history of hypertension, and/or taking antihypertensive therapy.

Biochemical measurements

Fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL)-cholesterol, urinary creatinine and uric acid were determined by enzymatic methods and albuminuria and HbA_{1c} by immunoturbidimetric methods. Fasting plasma creatinine was determined by kinetic (enzymatic colorimetric) Jaffé assay, standardized against the IDMS method. Serum insulin was assessed with a chemiluminescent immunoassay. The low-density lipoprotein (LDL)-cholesterol levels were calculated using the Friedewald formula if total TG levels were <400 mg/dL. All biochemical analyses were performed at the Synevo Romania SRL laboratories according to standardized procedures. Insulin resistance was estimated using the Homeostasis Model Assessment for insulin resistance (HOMA-IR) equation [18]: HOMA-IR = fasting insulinemia (μUI/mL) × fasting glycemia (mg/dL)/405.

Impaired glucose regulation (diabetes/prediabetes) was defined according to the 2012 American Diabetes Association guidelines [19], based on FPG, HbA_{1c} and 2-h plasma glucose during a standard oral glucose tolerance test or self-reported diagnosis. Hypertriglyceridemia was considered when TG levels were ≥150 mg/dL or drug treatment for hypertriglyceridemia while hypercholesterolemia was considered when TC ≥200 mg/dL and/or statin therapy was used. Hypo-HDL cholesterolemia was considered when HDL levels were <40 mg/dL in men or <50 mg/dL in women or taking drug treatment for low HDL levels; hyper-LDL cholesterolaemia was considered when LDL ≥100 mg/dL and/or statin therapy was used. Hyperuricemia was considered when uric acid levels were ≥7 mg/dL in men or ≥6 mg/dL in women.

Statistical analysis

The global prevalence of CKD was adjusted for the age and sex structure of the adult Romanian population according to 2011 Romanian Census. A full analysis method was used in the case of missing data (i.e., absence of laboratory results, incomplete questionnaires). CKD-EPI equation was used for the calculation of eGFR in order to estimate the overall prevalence of CKD and for all the other data analysis, while MDRD equation was used for the calculation of eGFR only for the estimation of the overall prevalence of CKD.

Univariate and multivariate analyses by multiple logistic regressions were performed in order to identify predictors associated with the presence of CKD. Odds ratios with 95 % CIs are provided. Two-tailed p values <0.05 were considered significant. Analyses were performed using the SPSS software v19.0 (IBM Corp., Armonk, NY, USA).

Results

Of the 2728 participants enrolled in the PREDATORR study, 2717 participants had complete data, the participation rate being 99.6 %. The mean age of the participants was 47.7 ± 15.1 years, and 47.90 % were men.

The age- and gender-adjusted overall prevalence of CKD, defined using CKD-EPI equation, in Romanian adult population was 6.74 % (95 % confidence interval [CI] 5.60–7.88), with the highest percentage in the 60–79 age group (Table 1). The unadjusted prevalence of CKD, defined using CKD-EPI equation, was 9.08 % (95 % CI 8.00–10.16). The overall prevalence of CKD in men and women was similar: 6.73 % (95 % CI 5.60–7.87) and 6.75 % (95 % CI 5.61–7.89), respectively (Table 1).

The overall adjusted prevalence of CKD, defined using MDRD equation, in adult Romanian population was 7.66 % (95 % CI 6.45–8.87). The overall adjusted prevalence of reduced kidney function (eGFR < 60 mL/min/1.73 m^2) associated with ACR <30 mg/g was

Table 1 Prevalence of CKD, reduced kidney function and albuminuria in the Romanian population aged 20–79 years

	Age (years)			Overall
	20–39	40–59	60–79	
Total population				
CKD present (%)	3.69 (2.32–5.05)	4.76 (3.18–6.34)	14.35 (11.14–17.56)	6.74 (5.60–7.88)
eGFR < 60 mL/min/1.73 m^2 and ACR < 30 mg/g (%)	0.78 (0.00–1.70)	1.58 (0.75–2.43)	9.76 (7.28–12.24)	3.31 (2.50–4.13)
eGFR ≥ 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g (%)	2.91 (1.88–3.94)	2.78 (1.42–4.13)	3.40 (1.48–5.32)	2.98 (2.21–3.76)
eGFR < 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g (%)	0.00	0.40 (0.40–0.41)	1.19 (0.00–2.41)	0.45 (0.14–0.74)
Men				
CKD present (%)	3.58 (1.62–5.54)	4.71 (2.39–7.03)	14.60 (9.94–19.25)	6.73 (5.60–7.87)
eGFR < 60 mL/min/1.73 m^2 and ACR < 30 mg/g (%)	1.59 (0.27–2.91)	1.28 (0.05–2.52)	8.07 (4.48–11.67)	3.10 (2.31–3.88)
eGFR ≥ 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g (%)	1.99 (0.52–3.46)	3.43 (1.43–5.42)	4.66 (1.88–7.44)	3.17 (2.38–3.97)
eGFR < 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g (%)	0.00	0.00	1.87 (0.08–3.65)	0.46 (0.16–0.77)
Women				
CKD present (%)	3.79 (1.82–5.75)	4.81 (2.63–6.98)	14.12 (9.74–18.50)	6.75 (5.61–7.89)
eGFR < 60 mL/min/1.73 m^2 and ACR < 30 mg/g (%)	0.00	1.85 (0.48–3.22)	11.30 (7.32–15.28)	3.51 (2.68–4.35)
eGFR ≥ 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g (%)	3.79 (1.82–5.75)	2.22 (0.72–3.72)	2.26 (0.39–4.13)	2.81 (2.06–3.56)
eGFR < 60 mL/min/1.73 m^2 and ACR ≥ 30 mg/g	0.00	0.74 (0.00–1.61)	0.56 (0.00–1.51)	0.43 (0.13–0.72)

Data show adjusted percentages, with 95 % confidence intervals in parentheses. CKD was defined as eGFR < 60 mL/min/1.73 m^2 and/or ACR ≥ 30 mg/g; reduced kidney function as eGFR < 60 mL/min/1.73 m^2 and ACR < 30 mg/g and albuminuria as ACR ≥ 30 mg/g and eGFR ≥ 60 mL/min/1.73 m^2

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate, *ACR* albumin-to-creatinine ratio

Table 2 Prognosis of CKD, classified by eGFR and albuminuria categories (KDIGO 2012 (15)) in the Romanian population aged 20–79 years

eGFR categories	**Albuminuria categories**		
	A1 (ACR<30mg/g)	**A2** (ACR: 30–300mg/g)	**A3** (ACR>300mg/g)
G1 (eGFR ≥90 mL/min/1.73m^2)	69.91 (67.82 – 71.99)	2.18 (1.52 – 2.85)	0.26 (0.03 – 0.49)
G2 (eGFR: 60–89 mL/min/1.73m^2)	23.18 (21.26 – 25.10)	0.55 (0.22 – 0.89)	0.04 (0.00 – 0.12)
G3a (eGFR : 45–59 mL/min/1.73m^2)	2.33 (1.64 – 3.02)	0.22 (0.01 – 0.44)	0.07 (0.00 – 0.20)
G3b (eGFR : 30–44 mL/min/1.73m^2)	0.63 (0.27 – 0.99)	0.04 (0.00 – 0.12)	0.07 (0.00 – 0.20)
G4 (eGFR : 15–29 mL/min/1.73m^2)	0.15 (0.00 – 0.32)	0.07 (0.00 – 0.20)	0.04 (0.00 – 0.12)
G5 (eGFR <15 mL/min/1.73m^2)	0.26 (0.03 – 0.49)	0.00	0.00

Data show adjusted percentages, with 95 % confidence intervals in parentheses

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate, *ACR* albumin-to-creatinine ratio

Green low risk (if no other markers of kidney disease, no CKD), *yellow* moderately increased risk, *orange* high risk, *red* very high risk

3.31 % (95 % CI 2.50–4.13) and that of albuminuria (ACR ≥ 30 mg/g) associated with normal kidney function (eGFR ≥ 60 mL/min/1.73 m^2) was 2.98 % (95 % CI 2.21–3.76) (Table 1). Only 0.45 % (95 % CI 0.14–0.74) of participants had both albuminuria and reduced kidney function (Table 1).

In the participants aged 20–59 years, the diagnosis of CKD was predominantly established based on albuminuria, while in participants older than 60 years, the CKD diagnosis was mostly based on reduced kidney function (Table 1).

Regarding the prognosis of CKD, classified by eGFR and albuminuria categories, according to KDIGO 2012 guidelines [16], 1.85 % of the participants were categorized as having high and very high risk (Table 2). The A3 albuminuria category was detected in 0.48 % of the participants, and the G4-G5 eGFR categories (eGFR < 29 mL/min/1.73 m^2) were found in 0.52 % of the participants (Table 2).

Table 3 Clinical and biological characteristics by CKD presence and gender

Variable	Male		Female	
	CKD present	CKD absent	CKD present	CKD absent
Age (years) (mean, SD)	58.73 (15.26)***	46.62 (14.81)	57.53 (16.19)***	47.05 (14.79)
Marital status (%)				
Widowed	8.0	2.3	21.6	11.1
Divorced	4.6	4.3	4.1	6.4
Single	5.7	16.6	7.2	12.6
Married	81.6	76.9	67	69.9
High education (%)	16.1**	6.8	22.9**	12.5
Sedentary (%)	70.9*	81.3	72.9	80.2
Alcohol drinking (yes) (%)	69.8	78.1	22.9*	37.0
Body mass index (Kg/m^2) (mean, SD)	29.43 (4.42)**	27.86 (4.86)	30.79 (6.88)***	27.39 (6.16)
Waist circumference (cm) (mean, SD)	104.89 (12.88)**	100.04 (14.52)	98.36 (14.59)***	90.38 (15.82)
Fasting glycaemia (mg/dL) (mean, SD)	111.32 (51.07)***	88.91 (29.22)	100.95 (45.08)**	86.01 (25.47)
HbA_{1c} (%) (mean, SD)	6.45 (1.52)***	5.55 (0.84)	5.96 (1.27)***	5.49 (0.79)
HOMA-IR (mean, SD)	4.16 (3.53)***	2.67 (4.15)	4.69 (10.71)*	2.35 (2.38)
Uric acid (mg/dL) (mean, SD)	6.28 (1.79)**	5.72 (1.36)	5.81 (3.06)***	4.40 (1.51)
Systolic blood pressure (mmHg) (mean, SD)	144.57 (23.75)***	133.66 (17.31)	135.48 (20.15)***	127.39 (21.92)
Diastolic blood pressure (mmHg) (mean, SD)	80.95 (14.78)	79.17 (11.44)	79.27 (11.93)*	76.89 (11.37)
Total cholesterol (mg/dL) (mean, SD)	210.80 (52.62)	202.44 (45.09)	218.29 (64.37)	207.85 (76.07)
Triglycerides (mg/dL) (mean, SD)	217.96 (169.59)**	157.77 (123.99)	155.70 (125.98)**	113.77 (68.79)
HDL cholesterol (mg/dL) (mean, SD)	47.35 (16.25)	48.97 (14.73)	57.79 (15.37)	58.47 (15.05)
LDL cholesterol (mg/dL) (mean, SD)	122.28 (45.75)	123.20 (38.31)	129.12 (56.01)	126.92 (73.01)
eGFR (mL/min/1.73 m^2) (mean, SD)	74.45 (27.74)***	100.22 (16.09)	73.30 (32.09)***	100.54 (16.96)
ACR (mg/g) (mean, SD)	121.29 (95.61)**	5.54 (10.51)	190.45 (136.37)**	4.99 (6.18)

HOMA-IR homeostasis model assessment for insulin resistance, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *eGFR* estimated glomerular filtration rate, *ACR* albumin-to-creatinine ratio, *CKD* chronic kidney disease, *SD* standard deviation

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Regarding the prevalence of cardio-metabolic diseases, PREDATORR study has revealed that in the adult Romanian population, the age- and sex-adjusted prevalence of diabetes was 11.6 % (95 % CI 9.6–13.6 %) and the overall prevalence of prediabetes was 16.5 % (95 % CI 14.8–18.2 %). The age- and gender-adjusted prevalence of obesity was 31.5 % (95 % CI 29.4–33.6 %), overweight was 34.7 % (95 % CI 32.6–36.8 %), while the prevalence of hypertension was 52.4 % (95 % CI 50.2–54.6 %).

The prevalence of CKD stratified by overweight/obesity, diabetes/prediabetes and hypertension was 9, 13.8 and 6.7 % in women and, respectively, 7.6, 14.5 and 7.7 % in men.

Age and cardio-metabolic characteristics such as BMI, waist circumferences, FPG, HOMA-IR, HbA_{1c}, TG, uric acid and SBP were significantly higher in the CKD group compared to the participants without CKD, for both sexes ($p < 0.01$) (Table 3).

In the univariate analysis, age, diabetes/prediabetes, hyperuricemia, overweight/obesity, abdominal obesity, hypertriglyceridemia, metabolic syndrome and family history of kidney diseases were associated with the presence of CKD ($p < 0.001$) (Table 4).

The multivariate analysis by binominal logistic regression, adjusted for covariates (sex, educational level, marital status, alcohol drinking, sedentariness), showed that age, hyperuricemia, diabetes/prediabetes and hypertriglyceridemia were independent predictors for the presence of CKD (Table 4). Participants with family history of kidney diseases had a 5.37-fold higher risk of having CKD ($p < 0.001$). In both regression analyses, absent CKD was considered as reference category.

Discussion

The analysis of this representative sample of the Romanian population shows that the age- and sex-adjusted prevalence of CKD is high (6.74 %), up to 837,000 persons with low eGFR (<60 mL/min/1.73 m^2). The identified prevalence is

Table 4 Predictive factors of CKD (univariate and multivariate logistic regression)

Variable	CKD absent	CKD present	
		Univariate logistic regression	Multivariate logistic regression
Age			
OR	1	1.05 (1.04–1.07)***	1.05 (1.03–1.06)***
Overweight/obesity			
%	65.06	81.32	
OR	1	2.36 (1.61–3.46)***	0.85 (0.47–1.53)
Abdominal obesity			
%	70.42	86.81	
OR	1	2.71 (1.76–4.19)***	1.15 (0.59–2.22)
Hyperuricemia			
%	14.64	39.01	
OR	1	3.74 (2.72–5.13)***	2.81 (1.87–4.23)***
Hypertension			
%	62.23	65.76	
OR	1	1.17 (0.86–1.61)	1.17 (0.79–1.72)
Diabetes/prediabetes			
%	25.88	59.02	
OR	1	4.07 (2.99–5.53)***	2.46 (1.61–3.74)***
Hypercholesterolemia			
%	59.96	63.74	
OR	1	1.18 (0.86–1.61)	0.90 (0.52–1.56)
Hyper-LDL cholesterolemia			
%	76.50	76.33	
OR	1	0.99 (0.69–1.44)	1.05 (0.57–1.93)
Hypertriglyceridemia			
%	31.18	45.05	
OR	1	1.80 (1.33–2.45)***	1.62 (1.00–2.63)*
Hypo-HDL cholesterolemia			
%	30.45	31.52	
OR	1	1.04 (0.75–1.44)	0.78 (0.48–1.28)
Metabolic syndrome			
%	37.11	57.14	
OR	1	2.27 (1.67–3.08)***	0.67 (0.38–1.18)
Family history of kidney diseases (yes)			
%	5.82	23.27	
OR	1	4.85 (3.21–7.32)***	5.37 (3.34–8.65)***

CKD absent was considered the reference category. The analysis was adjusted for covariates (sex, educational level, marital status, alcohol drinking, sedentariness). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The 95 % confidence intervals are given in parentheses

OR odds ratio, *CI* confidence interval, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *CKD* chronic kidney disease

consistent with the one previously reported by Cepoi et al. [13] in a large sample originating from only one region of Romania. Researchers analyzed data from 60,000 participants included in the National Health Evaluation Program and estimated that the CKD prevalence in this population was 7.32 %. Compared to other European and non-European countries, we have found a lower prevalence of CKD in Romania. The most comprehensive evaluation of the CKD in the USA came from the Third National Health and Nutrition Examination Survey (NHANES III). In this survey, data were collected from 18,723 participants of different age, sex and ethnic groups, and it was estimated that CKD prevalence was 11 % [20]. An expected finding in our study was that the prevalence of CKD increased with age from 3.69 % in the 20–39-year age group to 14.35 % in the 60–79-year age group. As previously mentioned, increasing

age represents a risk factor for the development of the CKD. It has been shown that aging is associated with structural and functional renal changes that affect both the renal cortical and the medullar tissue [21]. Although it has been suggested that eGFR is decreasing more rapidly with age in women than in men, statement supported by a higher prevalence of CKD in women in other studies [22], in our study the CKD prevalence was similar in both men and women in the 60–79-year age group (14.60 vs. 14.12 %).

Compared to those without CKD, both men and women with CKD included in our study had higher values for the components of the metabolic syndrome. It has been shown that patients with metabolic syndrome have higher risk of developing CKD [23], and it is not clear whether the presence of the metabolic syndrome per se is associated with renal damages or these are due to individual risk factors [24]. In our study, the factors associated with CKD presence in the multivariate analysis were diabetes, hyperuricemia and the presence of hypertriglyceridemia. Therefore we can hypothesize that in our population the association between the metabolic syndrome and CKD as well as between obesity and hypertension and CKD may be dependent on the interplay between glycaemia/diabetes, serum uric acid and TG concentration.

A potential explanation for the lack of the association hypertension-CKD would be that controlled hypertension has prevailed, SBP and DBP values being nearly in normal range in analyzed subjects (Table 3). Mainly uncontrolled hypertension is a risk factor for developing CKD and is associated with a more rapid progression of CKD [25]. However, another reason might be the existence of transitory high blood pressure values as a consequence of "white coat effect."

Recently uric acid has been recognized as a potential risk factor for CKD [26]. In humans, data supporting the uric acid involvement in the CKD development come from a meta-analysis published by Wang et al. [27]. The authors included 11 studies enrolling a total of 753 participants and showed that lowering the uric acid levels was followed by an increase in the eGFR [27]. Two other subsequent meta-analyses including a lower number of studies confirmed the association [28, 29]. Evidence is accumulating on the link between high TG levels and the risk of CKD. In a cohort of 10,685 healthy men, Ryu et al. [30] showed that increased TG levels were associated with an increased risk of incident CKD, independent of the presence of hypertension and diabetes. The main strengths of the PREDATORR study are the representativeness of the sample for the adult Romanian population. This study used a multistage stratified cluster sampling procedure to obtain a representative sample of the primary care population in Romania. In addition, the socio-demographic, lifestyle and anamnestic parameters were registered using an interviewer-administered questionnaire and all laboratory measurements were performed in the same certified laboratory. Concerning limitations, our study has a cross-sectional design that makes causal inferences impossible. Additionally, the CKD prevalence might be overestimated as eGFR and albuminuria was only measured at one occasion. Another limitation would be the fact that the participants were proportionally enrolled based on the 2002 Romanian Census as the new 2011 Census data became available after the study started. However, to overcome this limitation, data were adjusted according to the results of the 2011 Romanian Census.

In conclusion, the PREDATORR study, by showing a high prevalence of CKD in the adult Romanian population, suggests that CKD is an important public health problem and calls for immediate action to initiate prevention programs that may reduce the economic burden of CKD in Romania. It provides evidence that the cardio-metabolic diseases may increase the risk of CKD in Romanian adult population.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest that could have direct or potential influence or impart bias on the work.

Informed consent Informed consent was obtained from all individual participants included in the study.

Research involving Human Participants and/or Animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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