

**SCREENING FOR CHRONIC KIDNEY DISEASE IN ADULT MALES
IN VOJVODINA: A CROSS-SECTIONAL STUDY**SKRINING HRONIČNIH BUBREŽNIH BOLESTI KOD ODRASLIH MUŠKARACA
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University of Novi Sad, Novi Sad, Serbia**Summary**

Background: Chronic kidney disease (CKD) is one of the most significant global health problems accompanied by numerous complications, with constant increase in the number of affected people. This number is much higher in early phases of disease and patients are mostly asymptomatic, so early detection of CKD is crucial. The aim was examination of the prevalence of CKD in the general population of males in Vojvodina, based on estimated glomerular filtration rate (eGFR) and urine albumin/creatinine ratio (ACR), and exploring the determinants and awareness of CKD.

Methods: This cross-sectional study included 3060 male examinees from the general population, over 18 years of age, whose eGFR and ACR were calculated, first morning urine specimen examined, arterial blood pressure measured and body mass index calculated. Standard biochemistry methods determined creatinine, urea, uric acid and glucose serum concentrations as well as albumin and creatinine urine levels.

Results: Prevalence of CKD in the adult male population is 7.9%, highest in men over 65 years of age (46.7%), while in the other age groups it is 3.6–12.6%. The largest number of examinees with a positive CKD marker suffer from arterial

Kratak sadržaj

Uvod: Hronične bolesti bubrega (HBB) jedan su od najznačajnijih zdravstvenih problema širom sveta, s obzirom na stalan porast broja obolelih, kao i zbog toga što su praćene brojnim komplikacijama. U odnosu na odmakle stadijume, u početnim je broj obolelih višestruko veći a tok je uglavnom asimptomatski, te je od presudnog značaja pravovremeno otkrivanje HBB. Cilj je bio ispitivanje prevalence HBB u opštoj populaciji odraslih muškaraca u Vojvodini, na osnovu procenjene jačine glomerulske filtracije (eJGF) i odnosa albumin/kreatinin u urinu (ACR), kao i ispitivanje determinanti HBB i svesnosti o postojanju HBB.

Metode: U ovu studiju preseka uključeno je 3060 muških ispitanika iz opšte populacije, starijih od 18 godina, kod kojih je vršeno izračunavanje eJGF i ACR, pregled prvog jutarnjeg urina, merenje arterijskog krvnog pritiska, kao i izračunavanje indeksa telesne mase. Standardnim biohemijskim metodama određivane su serumske koncentracije kreatinina, uree, mokraćne kiseline i glukoze, kao i nivo albumina i kreatinina u urinu.

Rezultati: U populaciji odraslih muškaraca zastupljenost HBB iznosi 7,9% i najviša je kod starijih od 65 godina (46,7%), dok u ostalim starosnim grupama iznosi

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List of abbreviations: CKD – chronic kidney disease; ACR – albumin/creatinine ratio in urine; eGFR – estimated glomerular filtration rate; CVD – cardiovascular disease; ESRD – end stage renal disease; DM – diabetes mellitus; HTA – arterial hypertension; BMI – body mass index; FBG – fasting blood glucose; SBP – systolic blood pressure; DBP – diastolic blood pressure.

hypertension (HTA) and diabetes mellitus (DM). Only 1.3% of examinees with $eGFR < 60 \text{ ml/min/1.73 m}^2$ and/or $ACR \geq 3 \text{ mg/mmol}$ had been aware of positive CKD biomarkers.

Conclusions: Obtained results show the prevalence of CKD in adult males is 7.9%, HTA and DM are the most important CKD risk factors and the level of CKD awareness is extremely low (1.3%) indicating the necessity for introduction of early stage disease recognition measures, including raising CKD awareness.

Keywords: chronic kidney disease, prevalence, risk factors, screening

Introduction

Chronic kidney disease (CKD) is defined as abnormality of kidney structure or function, present for ≥ 3 months with implications for health (1). Abnormalities of kidney structure or function include: pathological findings in urine sediment (erythrocyturia, leukocyturia, cylindruria), pathological albuminuria ($\geq 30 \text{ mg/24 h}$ or urinary albumin-creatinine ratio (ACR) $\geq 3 \text{ mg/mmol}$), electrolytic disbalance and other abnormalities caused by tubular defects, histopathological damages, structural damages detected by visual inspection, history of kidney transplantation and/or glomerulus filtration rate (GFR) $< 60 \text{ mL/min/1.73 m}^2$. Chronic kidney disease is divided into 5 stages based on the GFR level and albuminuria or ACR (1).

Number of CKD patients is constantly increasing and epidemiologic data is mostly related to late stages of the disease (2). Although the number of patients treated by the renal replacement modality exceeds 2 million, it is thought that the number of patients in the early CKD stages (first three stages) is more than ten times larger (3, 4). One of the main problems in the detection of these patients is the lack of symptoms (5). Aside from its high prevalence and long asymptomatic course, CKD is relevant since it is accompanied by very high cardiovascular comorbidity and mortality (6). More than 50% of CKD patients die from cardiovascular diseases (CVD) before the beginning of treatment with one of the methods for renal function replacement, that is, the risk of CVD in these patients is higher than the risk of progression to end-stage renal disease (ESRD) (7).

According to the 2016 European Guidelines on CVD prevention, individuals with moderate CKD (GFR 30–59 mL/min/1.73 m^2) and severe CKD (GFR $< 30 \text{ mL/min/1.73 m}^2$) are high-risk and very high-risk categories, respectively (8). Individuals at highest risk gain most from preventive efforts. Consequently, it is clear that early CKD detection is of utmost importance and one of the ways to achieve it is by using suitable laboratory tests.

Among the most common causes of CKD and progression to ESRD are diabetes mellitus (DM) (33% of adult CKD cases) and arterial hypertension (HTA)

3,6–12,6%. Najveći broj ispitanika sa pozitivnim markerima HBB boluje od hipertenzije i dijabetes melitusa. Samo je 1,3% ispitanika sa $eJGF < 60 \text{ ml/mi/1,73 m}^2$ i/ili $ACR \geq 3 \text{ mg/mmol}$ znalo da ima pozitivne biomarkere HBB.

Zaključak: Dobijeni rezultati ukazuju da prevalenca HBB kod odraslih muškaraca u Vojvodini iznosi 7,9%, da su HTA i DM najznačajniji faktori rizika za HBB, te da je izrazito niska svest o postojanju HBB (1,3%), što ukazuje na neophodnost preduzimanja mera za prepoznavanje bolesti u ranom stadijumu, uključujući i podizanje svesti o HBB.

Ključne reči: hronična bolest bubrega, prevalenca, faktor rizika, skrining

(21% of adult CKD cases) (9, 10). The reason is a constant rise in the number of these patients which is »a medical catastrophe of world-wide dimensions« (11).

Prevalence of CKD in Europe is from 3.3% in Norway up to 17.3% in North Germany, 8.9% in Brazil, 12.9% in Japan, 13.1% in North America, 16% in Australia and 17.2% in India (12–17). For the population on the territory of Serbia data is scarce and mostly related to reports on the number of patients treated by one of the renal replacement modalities. The only published study on CKD screening was done in 2012 on HTA and DM patients, as well as patients over 60 years of age (18). However, as far as we know, studies on the prevalence of CKD in the general population on the territory of Serbia have never been published. The aim of this study is to examine the prevalence of CKD in the general population of adult males in Vojvodina–Northern Serbia, based on $eGFR$ (mL/min/1.73 m^2) and ACR (mg/mmol), and to explore the determinants and awareness of CKD.

Material and Methods

Study group

This cross-sectional study included 3060 male examinees from the general population, over 18 years of age, from the Vojvodina–Northern Serbia region, who undertook a physical examination at The Workers Health Care Center in Novi Sad in the period from January to June 2015. The study was conducted according to the principles of the Helsinki Declaration and approved by the Ethics Committee of The Workers Health Care Center. Informed consent for participating in the study was obtained from all participants prior to inclusion in the study.

All the examinees filled in a questionnaire consisting of personal and family health history (kidney diseases, HTA, DM, CVD (myocardial infarction, stroke)), and lifestyle (smoking). All the examinees were examined by a doctor, specialist in occupational medicine, and their medical records were used as required by the study. Furthermore, as required by the study, only current smokers were defined as smokers

and everyone else was defined as non-smokers. Additionally, for the calculation of body mass index (BMI (kg/m^2)) the examinees' height and mass were measured. Depending on their BMI, the examinees were put into three categories: normal-weight ($\text{BMI} < 25 \text{ kg}/\text{m}^2$), overweight ($25 \leq \text{BMI} < 30 \text{ kg}/\text{m}^2$) and obese ($\text{BMI} > 30 \text{ kg}/\text{m}^2$). All the examinees had their blood pressure measured with the Riva Rocci method, three times on the left arm in a sitting position, and the measure of central tendency of the last two measurements was used for defining the final value of systolic and diastolic blood pressure (SBP and DBP) (19).

Hypertension was defined based on prior diagnosis, that is, the use of antihypertensive therapy, and the examinees with $\text{SBP} \geq 140 \text{ mmHg}$ and/or $\text{DBP} \geq 90 \text{ mmHg}$ were assigned to survey high blood pressure category. The examinees with prior diagnosis of DM, that is, the examinees using hypoglycemic therapy were assigned to diabetes patients category and the examinees with fasting blood glucose (FBG) $\geq 7 \text{ mmol}/\text{L}$ to survey DM category. The examinees with acute inflammation diseases or malignity were not included in the study.

Laboratory parameters

All the examinees had their urine and blood analyzed. Blood and urine samples were analyzed on the same day, immediately after sampling. First voided urine testing was performed by one experienced laboratory technician. The chemical analysis (proteinuria, glycosuria, hematuria) with Acon commercial test strips (Acon Laboratories Inc., USA) was performed, as well as microscopic examination of urine sediment (leukocyturia, erythrocyturia, cylindruria). Proteinuria, hematuria, and glycosuria were defined when dipstick analysis quantified them as 1+ or more, leukocyturia when 8+ or more leukocytes were present per high-power field, erythrocyturia when 3+ or more erythrocytes were present per high-power field and cylindruria when there was a presence of casts in urine sediment. The same urine sample was used for determining albumin level (immunoturbidimetric method on a biochemistry analyzer ADVIA 1800 commercial systems Siemens Healthcare Diagnostics Inc., Germany) and creatinine (Jaffe's kinetic method). ACR (mg/mmol) was calculated from the received values. The examinees with ACR greater than $3 \text{ mg}/\text{mmol}$ were defined as having albuminuria (1), and those with the value of ACR greater than $30 \text{ mg}/\text{mmol}$ were defined as having severe albuminuria. The same biochemistry analyzer was used to determine serum creatinine level with the same method as for urine creatinine, as well as serum glucose concentration with the enzymatic hexokinase method. Estimated glomerular filtration rate (eGFR) ($\text{ml}/\text{min}/1.73 \text{ m}^2$) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-

EPI) equation (20). CKD is defined according to the guideline (1), when there is $\text{eGFR} < 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ or when there is $\text{eGFR} > 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ and there is a presence of albuminuria $> 30 \text{ mg}/24\text{h}$ or $\text{ACR} > 3 \text{ mg}/\text{mmol}$.

Statistical analysis

Data was statistically analyzed using statistical software STATISTICA 14 (StatSoft Inc., Tulsa, OK, USA) and is presented graphically and in tabular presentation. Descriptive statistics, including median, arithmetic mean, and standard deviation (SD) were used to describe the studied parameters. Differences in distributions of individual parameters between study groups were analyzed using the parametric Student's t-test, or the nonparametric Mann-Whitney test in case a distribution showed a significant deviation, while Chi-square test was used for categorical data. Value of $p < 0.05$ was considered statistically significant. Multiple regression analysis was used to form a model for predicting disease indicators.

Results

Table 1 shows some basic characteristics of the examinees. Prevalence of CKD in the adult male population is 7.9%. The percentage of the examinees with CKD increases with older age and it is highest in the examinees over 65 years of age (46.7%), while in other age groups it is between 3.6% and 12.6%. Only 1.3% of the examinees with $\text{eGFR} < 60 \text{ ml}/\text{min}/1.73 \text{ m}^2$ and/or $\text{ACR} \geq 3 \text{ mg}/\text{mmol}$ were aware of having positive CKD biomarkers.

The prevalence of the examinees with diagnosed HTA is 22.4% and as many as 31.5% of the examinees, who had not been diagnosed with HTA, had elevated SBP and/or DBP during the examination. Sixteen point two percent of the examinees with diagnosed HTA had positive CKD markers ($\text{eGFR} < 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ and/or $\text{ACR} \geq 3 \text{ mg}/\text{mmol}$) as well as 6.5% with survey high blood pressure. The prevalence of the examinees with diagnosed DM is 4.1% and there was 5.1% of the examinees with survey $\text{FBG} \geq 7 \text{ mmol}/\text{L}$ without previous DM diagnosis. Positive CKD markers were present in 22.4% of the examinees with DM and 19.1% of the examinees with survey $\text{FBG} \geq 7 \text{ mmol}/\text{L}$. Sixty one percent of the examinees with DM also has HTA.

Approximately one-fifth of the examinees (21.4%) are obese and 44% is overweight. Positive CKD markers are present in 9.6% of the examinees with normal weight, 5% of overweight examinees and 9.6% of obese examinees ($p > 0.05$). Percentage of adult males who currently smoke was 40.6%. There was no significant difference in CKD prevalence between smoking and non-smoking (6.7% vs. 8.4%, $p > 0.05$). The examinees with positive CVD history

Table I Characteristics of participants.

| Participants | N (%) | Mean \pm SD | CKD participants | | | |
|-----------------------------|---------------|-----------------|--|---|---------------|----------------|
| | | | ACR \geq 3 mg/mmol alone N (%) | eGFR<60 mL/min/1.73 m ² alone N (%) | Both N (%) | Total N (%) |
| Total | 3060 (100) | – | 180 (5.9) | 42 (1.4) | 17 (0.6) | 239 (7.9) |
| Age (years) | | 40.8 \pm 11.8 | | | | |
| 18–25 | 298 (9.8) | 22.4 \pm 2.0 | 17 (5.7) | 0 | 1 (0.3) | 18 (6) |
| 26–35 | 795 (25.9) | 30.6 \pm 2.8 | 26 (3.5) | 0 | 1 (0.1) | 27 (3.6) |
| 36–45 | 772 (25.2) | 40.4 \pm 2.8 | 34 (4.4) | 1 (0.1) | 1 (0.1) | 36 (0.2) |
| 46–55 | 716 (23.4) | 50.4 \pm 2.8 | 52 (7.3) | 4 (0.6) | 4 (0.6) | 60 (8.5) |
| 56–65 | 370 (12.1) | 59.9 \pm 3.2 | 32 (8.6) | 11 (2.9) | 4 (1.1) | 47 (12.6) |
| >65 | 109 (3.4) | 73.0 \pm 5.4 | 19 (17.4) | 26 (23.8) | 6 (5.5) | 51 (47.7) |
| Hypertension* | | | | | | |
| Yes, diagnosed | 669 (22.4) | – | 73 (10.9) | 24 (3.6) | 11 (1.7) | 108 (16.2) |
| Survey high SBP or DBP | 940 (31.5) | – | 47 (5.0) | 12 (1.3) | 2 (0.2) | 61 (6.5) |
| No | 1375 (46.1) | – | 35 (2.5) | 4 (0.3) | 3 (0.2) | 42 (3) |
| DM | | | | | | |
| Yes, diagnosed | 125 (4.1) | – | 25 (20) | 2 (1.6) | 1 (0.8) | 28 (31.4) |
| With hypertension | 75 (60) | – | 15 (20) | 1 (1.3) | 1 (1.3) | 16 (21.6) |
| Without hypertension | 50 (40) | – | 10 (20) | 1 (2) | 0 | 11 (22) |
| Survey FBG \geq 7 mmol/L | 157 (5.1) | – | 14 (8.9) | 13 (8.3) | 3 (1.9) | 30 (19.1) |
| No | 2778 (81.8) | – | 0 | 0 | 0 | 0 |
| BMI (kg/m ²) | | 27.2 \pm 4.0 | | | | |
| <25 | 1059 (34.6) | 22.9 \pm 1.7 | 64 (6.1) | 26 (2.5) | 11 (1.0) | 101 (9.6) |
| 25–29.99 | 1348 (44.0) | 27.2 \pm 1.4 | 57 (4.2) | 11 (0.3) | 6 (0.5) | 74 (5) |
| \geq 30 | 653 (21.4) | 33.5 \pm 2.6 | 59 (9.0) | 5 (0.7) | 0 | 64 (9.7) |
| Current smoking | | | | | | |
| Yes | 1244 (40.6) | – | 68 (5.5) | 5 (0.4) | 10 (0.8) | 83 (6.7) |
| No | 1816 (59.4) | – | 114 (6.3) | 20 (1.1) | 19 (1.0) | 153 (8.4) |
| Cardiovascular disease | | | | | | |
| Yes | 25 (0.8) | – | 6 (24) | 2 (8) | 2 (8) | 10 (40) |
| No | 3035 (99.2) | – | 176 (5.8) | 23 (0.8) | 15 (0.5) | 214 (7.1) |
| Positive family history for | | | | | | |
| Kidney disease | 15 (0.5) | – | 2 (13.4) | 0 (0) | 3 (20) | 5 (30.4) |
| Hypertension | 220 (7.2) | – | 15 (6.8) | 4 (1.8) | 2 (0.9) | 21 (9.5) |
| DM | 278 (9.1) | – | 17 (6.1) | 0 (0) | 1 (0.3) | 18 (6.4) |
| Cardiovascular disease | 251 (8.2) | – | 2 (0.8) | 16 (6.4) | 0 (0) | 18 (7.2) |

Legend: Cardiovascular disease – stroke or ischemic heart disease, DM – diabetes mellitus, ACR – urine albumin/creatinine ratio, BMI – body mass index, FBG – fasting blood glucose, SBP – systolic blood pressure, DBP – diastolic blood pressure, *without diagnosed DM.

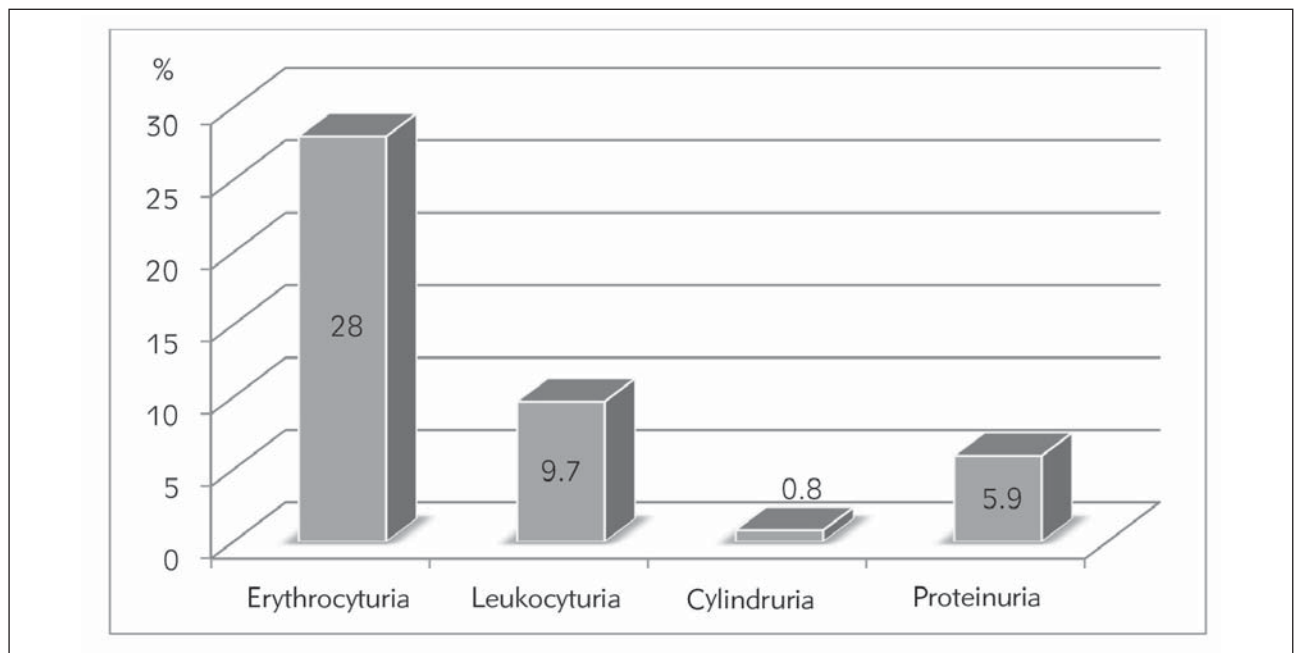


Figure 1 The pathological findings in urine sediment (erythrocyturia, leukocyturia, cylindruria) and chemical examination of urine (proteinuria) in all subjects.

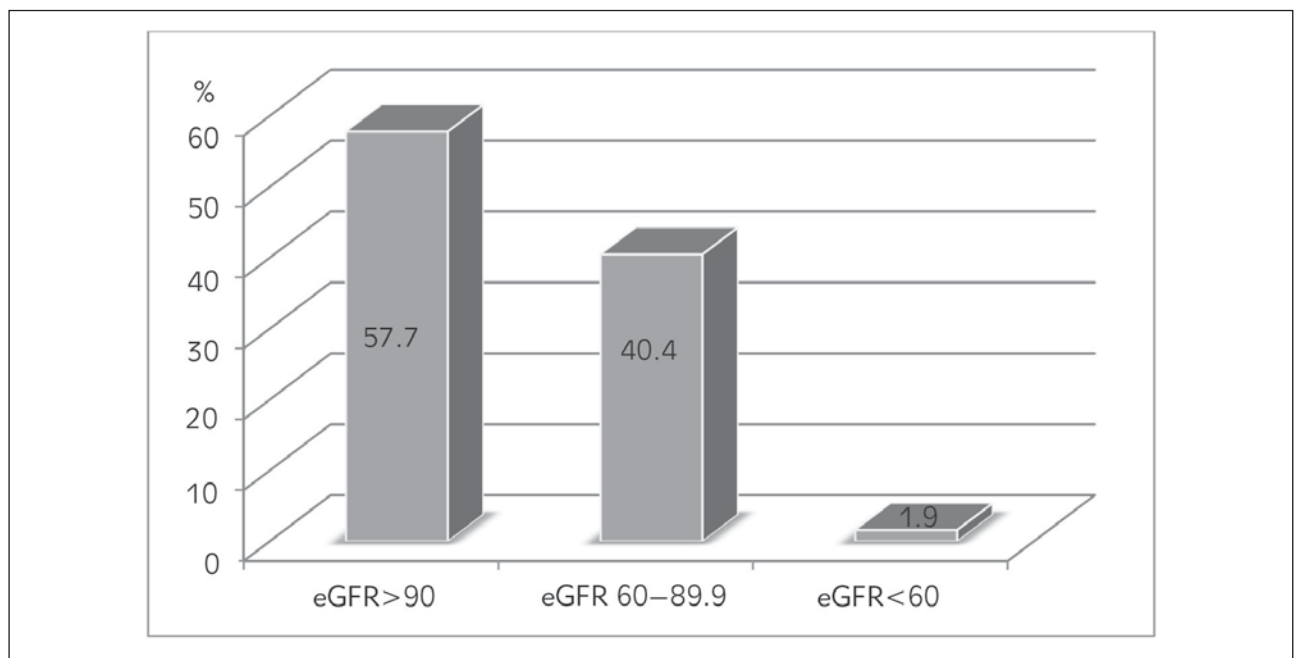


Figure 2 Estimated glomerular filtration rate (eGFR (mL/min/1.73 m²)) distribution in all subjects.

(ischemic heart disease or stroke), 0.8% of the examinees had significantly higher CKD prevalence in comparison with the examinees with negative CVD history (40% vs. 7.3%, $p < 0.01$).

One-third of the examinees with positive family history (PFH) for kidney disease has CKD, that is, 9.5% with PFH for HTA, 6.4% with PFH for DM and 7.2 with PHF for CVD.

In the examinees with eGFR > 90 mL/min/1.73 m² and ACR < 3 mg/mmol, with no abnormalities detected in first morning urine sample, without diagnosed kidney diseases, HTA, DM, CVD, with negative family history of kidney diseases, the ACR level was (median, lower-upper quartile): 0.44 (0.28–0.77) mg/mmol.

Figure 1 shows the prevalence of pathological findings in chemical (proteinuria) and microscopic

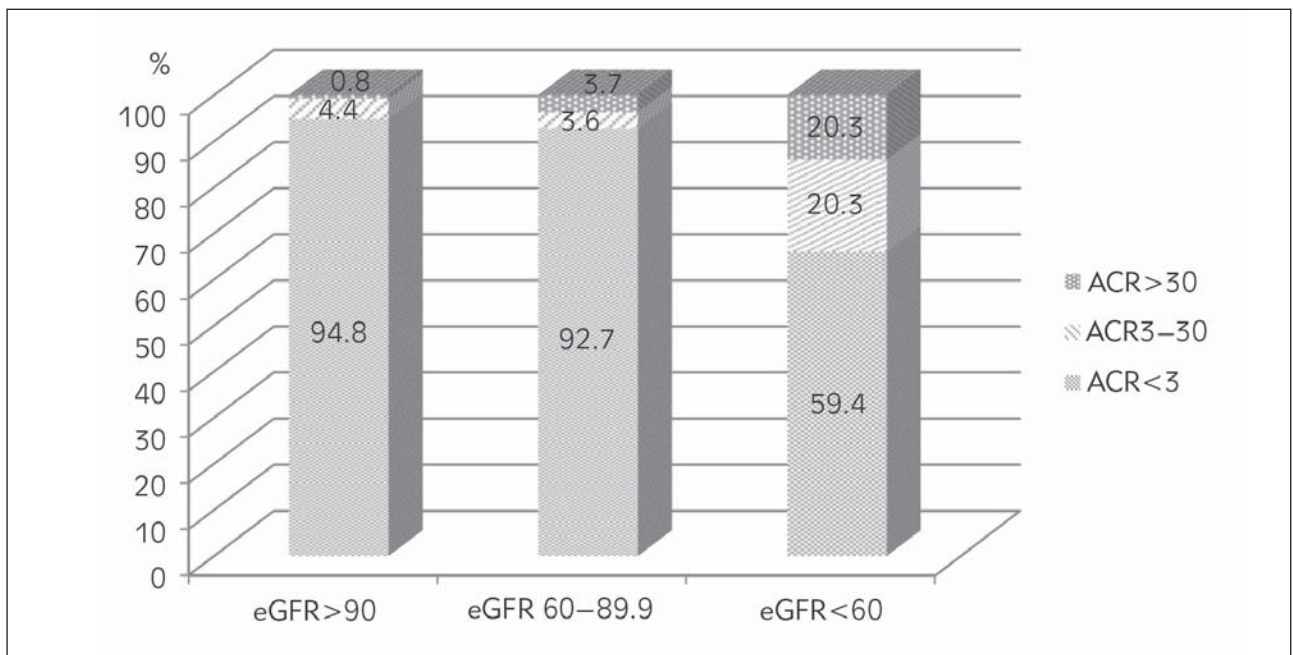


Figure 3 Urine albumin/creatinine ratio (ACR (mg/mmol)) distribution according to estimated glomerular filtration rate (eGFR (mL/min/1.73 m²)) values in all subjects.

Table II Characteristics of subjects with diabetes mellitus, hypertension, and survey fasting blood glucose level ≥ 7 mmol/L and high systolic (≥ 140 mmHg) and/or diastolic (≥ 90 mmHg) blood pressure.

| Subjects | Diagnosed DM* | Survey FBG ≥ 7 mmol/L | Diagnosed HTA | Survey high SBP and/or DBP |
|---|------------------|----------------------------|------------------|----------------------------|
| Total number (%) | 125 (4.1) | 157 (5.1) | 669 (21.9) | 940 (30.7) |
| Age (mean \pm SD, years) | 54.6 \pm 10.1 | 54.1 \pm 12.3 | 51.2 \pm 11.1 | 41.3 \pm 12.5 |
| FBG (mean \pm SD, mmol/L) | 9.7 \pm 3.3 | 8.3 \pm 1.7 | 5.9 \pm 1.2 | 5.5 \pm 0.9 |
| BMI (mean \pm SD, kg/m ²) | 27.8 \pm 4.7 | 27.3 \pm 4.5 | 28.4 \pm 4.5 | 27.3 \pm 3.9 |
| BMI (kg/m ²) | | | | |
| <25 (N, %) | 45 (36.0) | 58 (37.1) | 165 (24.6) | 268 (28.5) |
| 25-29.99 (N, %) | 38 (30.4) | 53 (33.7) | 276 (41.1) | 458 (48.7) |
| ≥ 30 (N, %) | 42 (33.6) | 46 (29.2) | 228 (34.3) | 214 (22.8) |
| BP (mean \pm SD, mmHg) | | | | |
| Systolic | 151.6 \pm 21.7 | 150.6 \pm 21.5 | 156.6 \pm 20.1 | 143.3 \pm 11.2 |
| Diastolic | 92.2 \pm 11.5 | 92.8 \pm 11.6 | 98.4 \pm 11.6 | 90.7 \pm 7.3 |
| Subjects treated with ACEi (N,%) | 34.4 (43) | – | 31.4 (210) | – |
| Subjects treated with AT1 receptor antagonist (N,%) | 10.4 (13) | – | 11.5 (77) | – |
| Current smokers (N, %) | 45 (36) | 50 (31.8) | 226 (33.9) | 389 (41.4) |
| eGFR (mL/min/1.73 m ²) (N,%): | | | | |
| >90 | 52 (41.6) | 43 (27.4) | 254 (38.1) | 556 (59.1) |
| 60-89 | 70 (56.0) | 98 (62.4) | 380 (56.8) | 370 (39.4) |
| <60 | 3 (2.4) | 16 (10.2) | 34 (5.1) | 14 (1.5) |
| Subjects with (N,%): | | | | |
| ACR ≥ 3 mg/mmol | 26 (20.8) | 17 (10.8) | 84 (12.6) | 49 (5.2) |
| Proteinuria | 15 (12.0) | 16 (11.2) | 53 (7.9) | 48 (5.1) |
| Glycosuria | 31 (24.8) | 18 (11.5) | 6 (0.9) | 10 (1.1) |
| Erythrocyturia | 27 (21.6) | 35 (22.3) | 159 (23.9) | 176 (18.7) |

Legend: *with and without HTA, FBG – fasting blood glucose, BP – blood pressure, BMI – body mass index, ACEi – angiotensin convertase inhibitors, AT1 – angiotensin receptors type 1, ACR – albumin/creatinine ratio, eGFR – estimated glomerular filtration rate.

(erythrocyturia, leukocyturia, cylindruria) examination of first morning urine sample. Erythrocyturia is present in 28% of the examinees, leukocyturia in 9.7%, cylindruria in 0.8% and protenuria in 5.9%. In the examinees with $ACR > 3$ mg/mmol, pathological findings of first morning urine sample examination were present in 59.9%.

Figures 2 and 3 show the distribution of the examinees according to the eGFR values, as well as distribution of ACR values according to the eGFR values in all the examinees. Estimated GFR < 60 mL/min/1.73 m² is present in 1.9% of the examinees. $ACR \geq 3$ mg/mmol is present in 12.5% of the examinees with eGFR ≥ 60 mL/min/1.73 m². $ACR \geq 3$ mg/mmol is present in 40.6% of the examinees with eGFR < 60 mL/min/1.73 m², where half of the examinees have $ACR > 30$ mg/mmol.

The examinees with positive CKD biomarkers when compared to other examinees had significantly higher serum creatinine concentration (99.0 ± 28.9 mmol/L vs. 89.1 ± 9.1 , $p < 0.01$), urea (6.6 ± 4.95 vs. 5.6 ± 2.2 mmol/L, $p < 0.01$) and uric acid (290.5 ± 74.7 vs. 268.0 ± 62.2 mmol/L, $p < 0.05$).

Table II shows the characteristics of subjects with DM, HTA, and survey FBG ≥ 7 mmol/L and high SBP (≥ 140 mmHg) and/or DBP (≥ 90 mmHg). CKD prevalence in the examinees with diagnosed DM is 22.4%, in examinees with survey FBG ≥ 7 mmol/L it is 19.1%, in the examinees with diagnosed HTA 16.7% and in survey high SBP and/or DBP 6.5%. Multiple regression analysis identified age ($b = -0.551$, $p < 0.001$) and smoking ($b = 0.270$, $p < 0.001$) as the most significant predictors of eGFR.

Discussion

This cross-sectional study of CKD prevalence in the male adult population on the territory of Northern Serbia found CKD presence in 7.9% of the examinees. Only 1.9% of men have eGFR < 60 mL/min/1.73 m², but when $ACR \geq 3$ mg/mmol is introduced as a diagnostic criterion, the prevalence increases to 7.9%. Out of the examinees with $ACR \geq 3$ mg/mmol, $ACR > 30$ mg/mmol was present in 20% of the examinees with eGFR < 60 mL/min/1.73 m², in 3.7% of the examinees with eGFR 60–89.9 mL/min/1.73 m² and in 0.8% of the examinees with eGFR ≥ 90 mL/min/1.73 m².

CKD prevalence significantly varies in European countries, from 3.3 to 17.7% and it is higher in the southern than in the northern parts of Europe (14, 19). These variations result from not only increase in the number of DM, HTA and obesity patients, but also from other factors such as nutrition, public health service organization, genetic factors, heterogeneity of laboratory methods, study population heterogeneity, etc. (14). Furthermore, nutrition differences can have

a different impact on CKD prevalence, due to its influence on blood creatinine level (protein rich diet), as well as the renal protective or renal damaging effect of certain micros and macronutrients (21, 22). Well-organized public health service can have an important influence on decreased CKD prevalence (23). In applied methodology, there are still inter-laboratory variations, although in most studies the methodology of determining serum creatinine and albumin levels is similar (24).

CKD prevalence varies by gender, where CKD prevalence is higher in women, which could, along with different smoking prevalence, alcohol use, cardiovascular diseases and different hormone metabolism, glomerular hemodynamics, probably be explained by insufficient validity of the estimated GFR formula in the female population (17, 19, 25–28). Furthermore, CKD prevalence significantly increases with age, and in this study it is significantly higher ($p < 0.001$) in the over 65 age group (46.7%) in comparison to other groups: it was 3.6–8.5% in 18–55 age group and 12.6% in 56–65 age group. In this and other studies age is a prominent independent risk factor for CKD, in men and women, where people over 65 years of age have significantly higher risk of CKD development compared to those below 65 years of age (19, 25). Specifically, the risk of CKD and albuminuria increases 1.5 times with every 10 years of life, and thus a decrease in GFR with aging cannot be considered as completely normal physiology (18, 29).

There was 21.4% of obese examinees in the general population in this study and 44% of overweight ones. In the European and USA studies the results show similar prevalence of obese (22.3–26.1%) and overweight examinees (33.1–39.4%), while in India the prevalence of obese (11.7%) and overweight (26.4%) examinees is significantly lower in comparison to other countries (13, 15, 25, 27, 29). Although studies state obesity as a CKD risk factor in the general population, specifically in the male population, this study has not shown significant CKD prevalence (9.6 vs. 5 vs. 9.7%, respectively, $p > 0.05$) between groups of examinees with BMI < 25 , 25–29.9, and ≥ 30 kg/m² (19, 25, 30). The results of other studies state higher CKD prevalence among obese (16.6–31.7%) and overweight (31.6–40.0%) examinees in comparison to healthy weight subjects (15, 26, 29). However, for all the stated facts, the study shows that in patients with advanced CKD, higher BMI is combined with small risk of all-cause mortality, which could indicate domination of protective nutrition effect relative to adverse metabolic effects of obesity (30).

Some studies indicate that smoking is associated with development of albuminuria and consequent progression of kidney disease, while other studies did not find association between smoking and decreased GFR or appearance of albuminuria (19, 31, 32). We found that 40.1% of the male population are smok-

ers, which is a significantly higher prevalence than in other studies where it is 13.1–29.1%, and it is higher in the male population than in the female one (19.26–28.32). Although this study indicated smoking as an independent indicator of decreased eGFR, there were no significant differences in CKD prevalence between smokers and nonsmokers (6.7 vs. 8.4%, $p > 0.05$).

Diabetes mellitus and HTA are the most important risk factors for CKD (13, 15, 19, 32). In this study, 21.9% of the examinees had previously diagnosed HTA and another 30.7% survey high SBP or/and DBP, while 4.1% had previously diagnosed DM and another 5.1% survey $\text{FBG} \geq 7$ mmol/L. CKD prevalence in the examinees with diagnosed DM was 22.4%, in survey $\text{FBG} \geq 7$ mmol/L examinees 19.1%. In the examinees with diagnosed HTA, CKD prevalence was 16.2%, and in survey high SBP and/or DBP it was 6.5%. This difference in CKD prevalence in the examinees with diagnosed HTA and survey high blood pressure examinees could be explained by the fact that their blood pressure was measured only once, during the examination, which is not enough to make an HTA diagnosis.

Diabetes mellitus and HTA prevalence vary around the world. Diabetes mellitus prevalence in the general population is 6.7–7.4% in Poland, England and the USA, up to 10.8% in Spain and 18.8% in India, and HTA prevalence is 27.1–34.1% in the USA, Poland and England and up to 42.4–43.1% in Spain and India (13, 15, 27, 29). In Serbia, the study by Marinkovic et al. (33) indicated HTA prevalence of 53%, where 20.1% of the examinees had previously diagnosed HTA and another 32.4% of the examinees had survey high SBP and/or DBP. Somewhat higher HTA prevalence was found in female examinees.

In the only published study in Serbia for early detection of CKD in patients with HTA and DM, over 60 years of age, $\text{eGFR} < 60$ mL/min/1.73 m² was present in 15–23% of the examinees and microalbuminuria was present in 17–41% of the examinees, depending on the group (18). Another study, in which DM and HTA were independently associated with increased risk of CKD, suggested that CKD prevalence in DM patients is 7.1–41.5% (14, 17, 25, 26, 34, 35), and in HTA patients 12.6–34.5% (13, 14, 17, 19, 26, 29, 34, 36). We found that out of the examinees with CKD, 55% have HTA (43.3%) and DM (11.7%). Studies indicate different HTA and DM prevalence in CKD patients, from surprisingly low 27.7% in Canada, to extremely high 86.3% in Poland (67.8% HTA and 18.5% DM), and 96.1% in India (64.5% HTA and 31.6% DM) and England (74.2% HTA and 21.9% DM) (15, 26, 27, 29).

Zero point eight percent of the examinees in this study had a history of CVD, which is surprisingly low taking into consideration the life habits and type of nutrition in this region and is also lower than indicated in other studies (2.6–6.8%) (17, 25, 34). However,

we found that this group of examinees had significantly higher CKD prevalence compared to the group with negative history of CVD (40 vs. 6.9 %, $p < 0.001$), which is somewhat higher prevalence than in other studies (21.5–23.9%) (17, 34).

The CKD awareness is one of the significant factors for individual prevention of kidney disease progression and reduction of damaging effects of CKD (37). In this study, only 1.3% of the examinees, with $\text{eGFR} < 60$ mL/min/1.73 m² and/or $\text{ACR} \geq 3$ mg/mmol, had CKD awareness. It is the lowest value in comparison to other studies which state that this percentage is 1.9–22.8% (13, 15, 26, 34). The results of the studies indicate that low level of general education, low income, as well as age, are independently associated with low CKD awareness (38). Considering low CKD awareness level of the examinees in this study, as well as in most other studies, in order to timely recognize and diagnose CKD, it is important not only to raise the awareness level in the general population, but also to educate medical staff at the primary healthcare protection level.

This study had some limitations. Firstly, since this is a cross-sectional study, CKD markers were assessed only once which could have overestimated CKD prevalence in the population of the examinees. Furthermore, the prediction equation formula to estimate GFR calculated from serum creatinine was used. Secondly, the study included only male examinees. Primarily, it had been planned to include all patients who undertook a physical examination at The Workers Health Care Center in the period from January to June 2015. However, most of the patients were men (88.5%) and due to this gender discrepancy, the results of female population are not presented in this study.

Conclusion

The present paper presents the results of screening for CKD in adult men carried out in Northern Serbia. CKD prevalence is 7.9%, and the awareness of 1.3% is the lowest ever reported. The most important CKD contributing factors in this population are HTA and DM. Considering the obtained results, it can be concluded that it is necessary to introduce measures to raise the awareness level of CKD, particularly among health workers, in order to recognize early stage kidney function impairment which can result in ESRD.

Contribution statement

CV conceived the idea for the study. DjM, CV and IB contributed to the design of the research. All authors were involved in data collection. VP analyzed the data. CV coordinated funding for the project. All authors edited and approved the final version of the manuscript.

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Conflict of interest statement

The authors stated that they have no conflicts of interest regarding the publication of this article.

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