

High Prevalence of Early Chronic Kidney Disease in High Risk Outpatients

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is a significant public health problem. The aim of this study was to determine the presence of early stages of renal disease in hypertensive and diabetic outpatients without previously diagnosed renal damages. **Methods:** In this cross-sectional study we studied a random sample of outpatients with essential hypertension and/or diabetes mellitus type 2 in the general practice ambulance of city Sarajevo. Renal function was evaluated by using MDRD (Modification of Diet in Renal Disease) equation and with measurement of renal biomarkers. K/DOQI classification was used to define the stages of CKD. **Results:** The study included 200 patients, of whom 75 (37.5%) were females, mean age of 54.81 ± 6.1 years, and 125 (62.5%) male, mean age 52.46 ± 8.2 years. More than half of respondents (54.0%) were hypertensive during the follow up period. Early CKD was detected in 52% respondents. Higher prevalence of early CKD was verified in the group of patients who had hypertension associated with diabetes mellitus type 2 (59.6% vs. 47.2% in hypertension group vs. 54.0% in diabetic group, $p < 0.05$). Significant negative correlation was found between estimated glomerular filtration rate and presence of albuminuria ($p < 0.001$), duration of hypertension ($p = 0.003$), duration of type 2 diabetes mellitus ($p = 0.021$), stages of hypertension ($p = 0.012$), female gender ($p < 0.001$) and older age of subjects ($p = 0.040$). **Conclusion:** Our results confirmed high prevalence of CKD and the importance of early detection of CKD in high risk groups of patients in order to prevent the progression of the same. Prevention of chronic kidney disease in our country is still not carried out satisfactorily. Required is a much greater collaboration between primary care health givers and nephrologists.

Key words: early chronic kidney disease, diabetes mellitus type 2, hypertension.

1. INTRODUCTION

Chronic kidney disease (CKD) is defined as either low glomerular filtration rate (GFR; < 60 ml/min/1.73 m²) and/or kidney damage defined by urine, imaging and histological abnormalities for more than 3 months (1) and ranked in five stages according to the value of GFR.

Chronic kidney disease is a significant global, public health problem (2, 3). The number of patients with end-stage of renal disease (ESRD) is increasing worldwide at an estimated annual rate of 7% (4). The most common causes of CKD in developed countries are diabetes type 2 and hypertension (5, 6, 7). In the world, 972 million people with hypertension (HTN) were registered in 2000. It is anticipated that this number will increase at about 1.56 million patients by 2025 (8). The risk of ESRD due to hypertensive nephropathy is 1.6 times higher for men than for women. The world prevalence of type 2 diabetes mellitus (DM) is significantly increasing as a result of aging of population, urbanization and the consequences that incurred in connection with lifestyle changes. In 2010, 285 million people had DM in the world (9). Diabetes mellitus and arterial

hypertension are major and growing problems of all age groups in Bosnia and Herzegovina, but there are no epidemiological data of the number of patients with CKD, except the number of patients on renal replacement therapy (RRT). According to the data of Institute for Public Health of the Canton Sarajevo for 2013, the overall prevalence of hypertension was 17.8% and of diabetes 6.5% in population of this Canton. Most patients with early stages of chronic kidney disease are asymptomatic (10). The rising prevalence of ESRD represents an increase of requirements for kidney health services and burden on the economy for the health system of each community.

The aim of this study was to determine the presence of early renal disease in patients with hypertension and/or type 2 diabetes mellitus in primary care, and to identify factors that contribute to the appearance of early renal damage in these categories of patients.

2. METHODS

This cross-sectional and observational pilot study was conducted over a period of one year at the primary care ambulance

in Institute for Occupational Medicine of Canton Sarajevo. A total of 247 patients known to have DM and/or arterial hypertension were included in the study, but finally the study population consisted of 200 adult patients of both genders, aged between 18 and 60 years. Twenty two patients were excluded because they did not want to collect urine for laboratory analysis, fifteen patients had already a history of renal disease and ten patients had fever or urinary tract infection. Respondents stopped taking antihypertensive therapy 48 hours before collecting research material. Hypertension was defined as systolic pressure ≥ 140 mmHg and diastolic pressure ≥ 90 mmHg. Diabetes mellitus type 2 is a type of diabetes that is characterized by hyperglycemia, insulin resistance and obesity. Acute kidney injury, earlier diagnosed chronic renal insufficiency and renal disease of other etiology were excluding criteria for this study. None of the patients involved in the study has been previously tested for early renal damage. The study was conducted with the approval of ethics committee of Medical faculty University of Sarajevo. All patients gave their informative consent for the participation in the study. Measurement of blood pressure and body mass index (BMI) has been done to each patient on a routine medical examination, as well as a determination of the hypertension duration and duration of DM type 2 after examining the medical records. Staging of hypertension has been done by using the classification of the World Health Organization (11). Concentration of the serum creatinine was measured with spectrophotometry using the kinetic Jaffe reaction (continuous method with alkaline picrate) on Dimension RxL Max system, Siemens. Micro albuminuria, defined as an excretion >30 mg of albumin in 24 hours urine, was measured by using nephelometric method at the Institute of Clinical Chemistry and Biochemistry of the University Clinical Center in Sarajevo. Kidney function was assessed by using estimated glomerular filtration rate (eGFR) with MDRD equation (Modification of Diet in Renal Disease) (12). K/DOQI CKD Guidelines (The National Kidney Foundation's classification) was used for staging of eGFR and classification of CKD (1). The stage 1 and stage 2 of CKD were considered as early CKD or kidney damage. The difference between mean values of more than two investigated groups was determined using ANOVA method, while the difference between mean values of variables of two groups was tested by paired t-test or Mann-Whitney test. The correlation coefficient was determined by Spearman's method. P values less than 0.05 were considered as significant.

3. RESULTS

The study included 200 patients, of whom 75 (37.5%) were females, mean age of 54.81 ± 6.1 years, and 125 (62.5%) male, mean age 52.46 ± 8.2 years. The largest number of respondents was older than 50 years (79.5%). More than half of respondents (54.0%) were hypertensive during the follow up period. Hypertension with DM type 2 was confirmed in 33.5% of followed patients, while those who suffered from type 2 DM isolated were present in 12.5% cases. In the majority of diabetic patients (81.5%), duration of diabetic disease was less than 10 years (4.8 ± 3.0 years). Most of patients with HTN had high blood pressure less than 10 years (73.1%), with an average disease duration of 5.9 ± 2.8 years.

Proteinuria and micro albuminuria are most commonly found in patients who had hypertension associated with diabetic disease (32.8% and 22.4%; $p < 0.05$).

As expected the increase of CKD stages is followed by decreasing of the average values of eGFR. In the group of HTN patients, mean average of eGFR was significantly higher in the first stage of CKD then in the second (103.50 (95.00-114.00) vs. 77.00 (68.00-82.00) mL/min/1.73m², $p < 0.05$) and in the third stage of CKD (46.50 (42.00-52.00) mL/min/1.73m², $p < 0.01$). In diabetic patients, the mean average of eGFR was also significantly higher in the first stage of CKD then in the second (111.00 (101.00-118.00) vs. 81.00 (76.00-85.00) mL/min/1.73m², $p < 0.05$), as well as in the third stage of CKD (48.00 (39.00-50.50) mL/min/1.73m², $p < 0.01$). A similar relationship was found in the group of patients who had HTN associated with type 2 DM. Significant inter groups difference in the value of glomerular filtration rate was only found between DM type 2 and HTN/DM type 2 group of patients in the second stage of CKD ($p < 0.05$) (Figure 1).

Proteinuria levels are significantly higher in patients with HTN/DM type 2 associated in the first stage of CKD than in those who suffer only from HTN or only from DM type 2 and

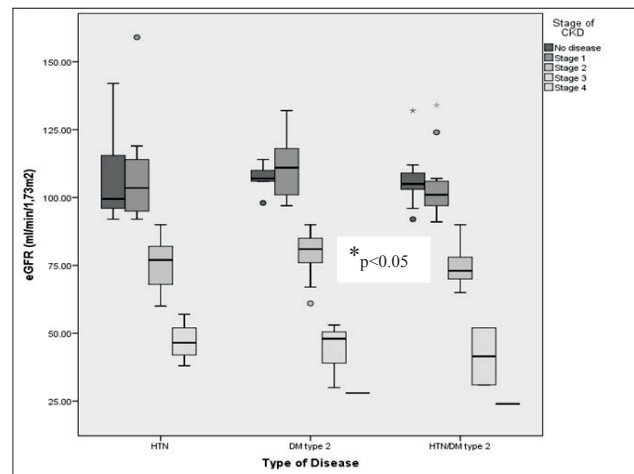


Figure 1. Estimated glomerular filtration rate according to the type of basic disease and stages of chronic kidney disease Notes: Data are presented as median and interquartile range; HTN-hypertension; DM-diabetes mellitus. *significant difference in GFR between DM type 2 and HTN/DM type 2 group of patients in the second stage of CKD ($p < 0.05$).

Basic DISEASE									
Number of patients	Total number (200)		HTN (108)		DM type 2 (25)		HTN/DM type 2 (67)		
	N	%	N	%	N	%	N	%	
Without of CKD	84	42.0	54	50.0	9*	36.0	21**†	31.3	
With CKD	Stage I	15	7.5	8	7.4	2	8.0	5	7.4
	Stage II	89	44.5	43	39.8	11*	44.0	35**†	52.2
	Stage III	10	5.0	3	2.7	2*	8.0	5**	7.4
	Stage IV	2	1.0	0	0.0	1	4.0	1	1.4
Early CKD (Stage I,II)	104	52.0	51	47.2	13	54.0	40**†	59.6	

Table 1. Distribution of patients according to the stage of chronic kidney disease and the presence of early renal disease in monitored groups of patients and in relation to total number of respondents. Notes: Data are presented as percentages; HTN-hypertension; DM-diabetes mellitus. CKD-chronic kidney disease; *significant difference in the number of respondents between HTN and DM type 2 group ($p < 0.05$); **significant difference in the number of respondents between HTN and HTN/DM type 2 group ($p < 0.05$); †significant difference in the number of respondents between HTN/DM type 2 and DM type 2 group ($p < 0.05$).

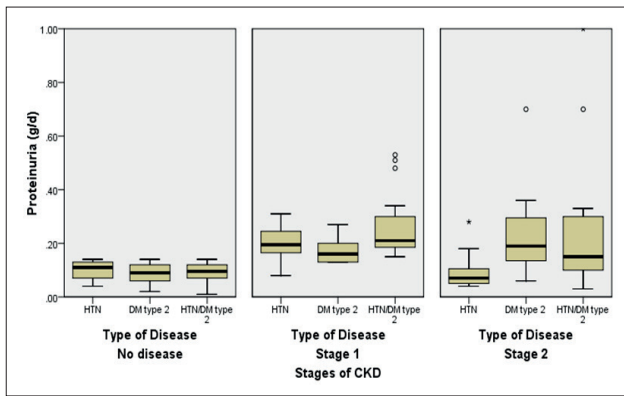


Figure 2. Proteinuria in relation to the basic disease and stages of chronic kidney disease. Notes: Data are presented as median and interquartile range. HTN- Hypertensio arterialis; DM- Diabetes mellitus, CKD- Chronic kidney disease. Stage 1: HTN; 0.195 (0.1625-0.2475), DM type 2; 0.16 (0.13-0.2175), HTN/DM type 2; 0.21 (0.18-0.30). Stage 2: HTN; 0.07 (0.05-0.1075), DM type 2; 0.19 (0.1-0.36), HTN/DM type 2; 0.15 (0.09-0.315).

in patients with DM type 2 and HTN/DM type 2 associated in the second stage of CKD than in those with only hypertension (Figure 2).

Patients with type 2 DM had the first stage of CKD in 8.0%, the second stage in 44.0%, the third stage in 8.0% and the fourth stage in 4.0% patients. The first stage of renal disease was confirmed in 7.4% subjects with HTN associated with type 2 DM, the second stage in 52.2%, the third stage in 7.4% and the fourth stage in 1.4% patients, while patients with only HTN had the first stage of CKD in 7.4%, the second stage in 39.8% and the third stage in 2.7% cases. Early CKD was detected in 52.0% respondents. In relation to the basic disease, early CKD was detected in 47.2% of hypertensive patients and in 54.0% of diabetic patients. Significantly the highest prevalence of early CKD was verified in the group of patients suffering from hypertension and DM type 2 combined (59.6%, $p < 0.05$) (Table 1).

Significant negative correlation was found between eGFR and presence of albuminuria ($r = -0.704$, $p < 0.001$), serum creatinine ($r = -0.703$, $p < 0.001$), duration of HTN ($r = -0.223$, $p = 0.003$), stages of HTN ($r = -0.190$, $p = 0.012$), duration of DM type 2 ($r = -0.241$, $p = 0.021$), female gender ($r = -0.432$, $p < 0.001$) and older age of subjects ($r = -0.145$, $p = 0.040$), (Table 2).

Parameters	Estimated glomerular filtration rate	
	r	P
Albuminuria (mg/L)	-0.704**	0.000
Proteinuria (g/d)	-0.028	0.694
Glycemia (mmol/l)	0.092	0.193
Triglyceride (mmol/l)	-0.018	0.797
Cholesterol (mmol/l)	0.022	0.760
Creatinine (µmol/l)	-0.703**	0.000
Duration of HTN (years)	-0.223**	0.003
Duration of DM 2 (years)	-0.241*	0.021
Stage of HTN	-0.190*	0.012
Female	-0.432**	0.000
Age (years)	-0.145*	0.040
BMI (kg/m ²)	-0.125	0.079

Table 2. The correlation of estimated glomerular filtration rate with clinical and laboratory parameters. Notes: BMI – body mass index

4. DISCUSSION

In recent decades, the population with CKD is constantly increasing (13). Chronic kidney disease is often asymptomatic and late referral to nephrologists is common. Based on AusDiab study, 1.7 million people in Australia suffer from CKD, and each year an average of 2.300 people ends up on hemodialysis or kidney transplantation (14). In 80-90% cases CKD remains unrecognized (14). Chronic kidney disease often develops in those with conventional risk factors for atherosclerosis, such as hypertension, DM, hyperlipidemia, and a history of cardiovascular disease (CVD). In Japan and the US, the main cause of ESRD is DM, but the second most common cause is glomerulonephritis in Japan and hypertension in the US (15).

According to Renal Registry for Bosnia and Herzegovina, the number of dialysis patients in Bosnia and Herzegovina is constantly increasing. From 2002 to 2012, this number increased to 66.2% (1.531 vs. 2.544 ESRD patients). The most common cause of CKD in Bosnia and Herzegovina is glomerulonephritis. Diabetic disease is in third place and essential hypertension in fifth place. Hypertension is also a common comorbidity in patients with CKD. Diabetes mellitus was present in 18.2% of all ESRD patients in our country in 2012 (16).

Johnson and colleagues report that early identification of patients with CKD and its treatment can reduce to 50% cardiovascular events and halt the progression of the disease to the terminal stage (14). Therefore, the detection of early CKD, especially in high-risk patients is of great importance, and primary care physicians play a crucial role in that program. Early detection of CKD has multiple benefit associated with less progression of kidney disease, lower cost treatment, reducing the need and number of days of hospitalization, reducing the need for hemodialysis and kidney transplantation, and reducing morbidity and mortality. In our study, from total number of 200 patients, in 104 (52.0%) we found the presence of early CKD. In relation to the basic disease, early CKD was mostly recorded in the group of patients with hypertension associated with DM type 2 (59.6%), followed by those with only diabetes (54.0%) and in third place were patients with high blood pressure (47.2%). A significant negative correlation between eGFR and duration of hypertension and duration of type 2 DM, as well as between eGFR and stages of hypertension suggest a close relationship between hypertension, DM type 2 and development of CKD. It was also confirmed that female gender and older age of subjects with hypertension and DM type 2 are in high risk for developing CKD. Our examination also confirmed a significant negative correlation between eGFR and albuminuria. This underlines the importance of CKD classification based on GFR and levels of albuminuria as important prognostic parameters for development of ESRD and mortality in diabetic and hypertensive patients. These results also indicate that the use of GFR and the presence of micro albuminuria improves early identification of CKD in high-risk patients like diabetics and hypertensives as well as that general health care should be more focused on the actions of prevention of CKD.

To our knowledge, serious screening in terms of early detection of CKD in high-risk patients has not be done in Bosnia and Herzegovina. Patients are referred very late to a nephrologist, or even when they already have a serious kidney damage. Alongside all this, the number of patients with ESRD who require some form of renal replacement therapy increases every year.

5. CONCLUSION

The results of this study indicate that there exists a close relationship between hypertension, DM and CKD, and further emphasize the importance of early detection of CKD in high-risk groups of patients in order to prevent the progression of the CKD or even ESRD. In general practice, it is necessary to introduce a screening test for the presence of early CKD in whole country, especially in populations of high-risk patients and close cooperation between primary care physicians and nephrologists in local community.

CONFLICT OF INTEREST: NONE DECLARED.

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