

Original Paper

Prevalence, Awareness, Treatment and Control of Hypertension in Adults with Chronic Kidney Disease in Turkey: Results from the CREDIT Study

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Key Words

Awareness • Chronic kidney disease • Epidemiology • Hypertension • Prevalence • Turkey

Abstract

Background: In the Chronic Renal Disease In Turkey - CREDIT Study, a large population-based study on 10,748 adults, the prevalence of chronic kidney disease (CKD) and relationship between CKD and other cardiovascular risk factors had been studied. **Methods:** This report presents the results of CREDIT study on the prevalence, awareness, treatment, and control of hypertension among CKD patients. **Results:** The prevalence and awareness of hypertension in CREDIT population was 32.7% and 48.6%, respectively. Of the patients with hypertension, 31.5% were under treatment, and 16.4% had hypertension under control. Prevalence of CKD was 25.3% in patients with hypertension. Among CKD patients (15.7% of the CREDIT study population), 56.3% had hypertension. The prevalence of hypertension was 34.8% at stage 1, 79.8% at stage 3, and 92.3% at stage 5 CKD. Only 13.4% of patients with CKD have optimal blood pressure. Among CKD patients, 61.9% were aware of hypertension, and 44.2% were under treatment. Overall control rate of hypertension in subjects with CKD was 16.3% with the lowest rate at stage 1 (12.3%) and highest rate at stage 4 (40%). The control rate increased to 28.8% for CKD patients under treatment for hypertension. **Conclusion:** As a conclusion, hypertension is highly prevalent in subjects with CKD in Turkey with suboptimal awareness, treatment, and control rates. Appropriate health strategies should be implicated to improve prevention, early diagnosis, and treatment of hypertension, which is one of the leading causes of CKD.

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Introduction

Hypertension is a major cause of end-stage renal disease and a common factor complicating the prognosis of chronic kidney disease (CKD) [1]. Among the Multiple Risk Factor Intervention Trial (MRFIT) population of 332,544 men, the relative risk of end-stage renal disease for subjects with hypertension compared with men with an optimal level of blood pressure was reported as 22.1% during an average of 16 years follow-up [2]. The present evidence suggests that hypertension is both a cause and consequence of CKD [3]. The prevalence of hypertension reaches an estimated 86% in patients with end-stage renal disease [4], and 70–86% of patients with CKD have hypertension [5, 6]. Similar to the increase in the prevalence of hypertension worldwide [7], prevalence of CKD-associated hypertension has been reported to be increasing [8].

Despite the high prevalence; prevention, detection, treatment, and control of hypertension among individuals with CKD is still suboptimal [6, 9]. It was reported that only 37–46% of CKD patients had blood pressure controlled to <130/80 mmHg [6, 10]. The hypertension control rate decreases at stage 5 of CKD [11]. Although hypertension in advanced stages of CKD has been studied, and a stepwise increase in the prevalence and control for hypertension with increase of stage of CKD was reported for stages 3–5 [11, 12]; prevalence and control rates of hypertension in earlier stages of CKD are not very well known.

For the development of national and international health policies for prevention and control of hypertension, reliable information about the epidemiology of hypertension in CKD from different world regions is essential. The prevalence of hypertension shows variability between 25–50% from different countries depending on the race, age, and gender of population [13, 14]. Few studies reported the prevalence of hypertension in Turkey. The PatenT study that was performed in 4,910 participants, showed that the overall age- and sex-adjusted prevalence of hypertension in Turkey was 31.8% in 2003 [15]. The PatenT study also reported the overall awareness, treatment, and control rates of hypertension. The HinT study, an epidemiological cohort conducted in population of PatenT study, reported overall 4-year incidence of hypertension as 21.4% in Turkey [16]. However, the prevalence and control rates of hypertension in patients with CKD in Turkey have not been reported yet.

In the Chronic REnal Disease In Turkey—CREDIT Study, a large population-based study on 10,748 individuals, the prevalence of CKD in Turkey, and the relationship between CKD and other cardiovascular risk factors had been reported [17]. Here, we present the results of the CREDIT study on hypertension to evaluate the prevalence, awareness, treatment, and control of hypertension among CKD patients of all stages in Turkey.

Subjects and Methods

Study design and population

The CREDIT study was a population-based, national survey in Turkey on 10,748 individuals aged over 18 years (mean age, 40.5±16.3 years; 55.7% females) to define the prevalence of CKD. A total of 10,872 participants through the country were included in the CREDIT study. Data of 124 pregnant women were excluded from the study; thus the analysis was performed on 10,748 subjects. Subjects with cognitive dysfunction that interfered with understanding and answering the study questionnaire were excluded from the study. All subjects included in this survey gave informed consent. The study was approved by the Ethics Committee of the Akdeniz University Faculty of Medicine and the Turkish Ministry of Health.

The cluster sampling technique was used to select the study participants. A sampling frame was defined as the 7 official geographical regions of Turkey that included 81 cities. The study sample comprised 23 cities such that a minimum 50% of the total population in each geographical region formed a sampling outline by including both the city with the highest population and a randomly selected city with a low population in each geographical area. The list of districts involved in the postal area codes of the selected cities was used to determine the cluster sampling outline for urban areas. The sample size of the study included ~10 500 participants, and the prevalence of CKD was estimated with a 95% confidence interval. The sampling method of the study was described before in detail by Suleymanlar et al. [17].

Field study and laboratory assessment

Field study included one home visit and interview of potential participants by specially-trained field study teams. The following data were collected during interviews with a standardized questionnaire: subject demographics, socioeconomic status, diet, life-style, current diseases and drugs, family history, and other relevant medical history. In addition, height, weight, waist circumference, and blood pressure were measured. Blood pressure was measured two times at 2 min intervals from both arms and the average of the two measurements were recorded.

Laboratory assessment was performed for the subjects who gave written consent for the laboratory evaluation during interviews. These subjects were visited in the next day for collecting 12-hour fasting blood sample. For laboratory assessment, 12-hour fasting blood samples and morning spot urine samples were obtained from the participants. Additionally, spot urine analysis (by dipsticks) was performed. In the samples; urine albumin and creatinine, serum creatinine, blood glucose, total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol and uric acid concentrations were determined. Albuminuria measurements were excluded in pregnant or menstruating women and in all patients suffering from febrile illness [18].

Data on hypertension

The prevalence of hypertension, awareness of subjects on hypertension, frequency of antihypertensive usage, and hypertension control rate were analyzed in the CREDIT study population with respect to CKD. Awareness represented the subjects with known arterial hypertension or being under antihypertensive treatment. Hypertension was accepted to be under control for blood pressure below 140/90 mmHg. Laboratory findings of subjects with and without hypertension were also summarized.

Definitions

For the purpose of this study, "hypertension" was defined as diagnosis of hypertension, systolic blood pressure ≥ 140 mmHg, and/or diastolic blood pressure ≥ 90 mmHg. Blood pressure was classified into 6 category based on 2007 ESH-ESC Guidelines [19]. Blood pressure categories were optimal (systolic blood pressure/diastolic blood pressure $< 120/80$ mmHg), normal (120-129/80-84 mmHg), high normal or borderline (130-139/85-89 mmHg), and stage 1 (140-159/90-99 mmHg), stage 2 (160-179/100-109 mmHg) and stage 3 ($\geq 180/110$ mmHg) hypertension.

Serum creatinine levels, estimated GFR, and spot urine microalbuminuria were studied as markers for kidney function. CKD was defined as kidney damage with or without a decrease in GFR, which was calculated using a simplified version of the Modification of Diet in Renal Disease (MDRD) formula [20]. CKD was categorized into five stages based on the classification system established by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) [21]. Albuminuria is defined as an albumin-to-creatinine ratio of 30 mg/g or higher, with microalbuminuria defined as an albumin-to-creatinine ratio of 30 mg/g to 299 mg/g, and proteinuria defined as an albumin-to-creatinine ratio of 300 mg/g or higher [22].

"Diabetes mellitus" was defined as diagnosis of diabetes mellitus or fasting blood glucose ≥ 126 mg/dL. The term "dyslipidemia" indicated patients having antilipid treatment or dyslipidemia shown in the lipid profile [total cholesterol > 240 mg/dL (> 6.21 mmol/L) or LDL-cholesterol > 130 mg/dL (> 3.37 mmol/L) or HDL-cholesterol < 40 mg/dL (< 1.03 mmol/L) for men, < 46 mg/dL (< 1.19 mmol/L) for women, or serum triglyceride > 150 mg/dL (> 1.7 mmol/L)].

Statistical analysis

SPSS 15.0 (SPSS for Windows, 2007, Chicago, USA) was used for statistical analysis. Data were summarized using descriptive statistics (mean \pm standard deviation for continuous variables, number and percentages for qualitative variables). Odds ratios with 95% confidence interval (CI) were calculated for the prevalence of hypertension in overall and each stage of CKD. The number of subjects varies for different analyses because of missing data for some variables. The analysis was performed on the number of subjects weighted according to age groups, gender, geographical area, and settlement.

Table 1. Prevalence of hypertension with the regard to presence and stages of chronic kidney disease (CKD) in the CREDIT study population

Stage of CKD	n	Hypertension [n (% of subjects in each stage)]	p value*	Odds ratio	95%CI
No CKD	7,200	2,233 (31.0%)			
CKD of any stage	1,344	756 (56.3%)	<0.001	2.86	2.54–3.22
Stage 1	468	163 (34.8%)			
Stage 2	441	243 (55.1%)	<0.001	2.30	1.76–3.00
Stage 3	400	319 (79.8%)	<0.001	3.21	2.36–4.36
Stage 4	23	19 (82.6%)	0.74	1.21	0.40–3.64
Stage 5	13	12 (92.3%)	0.42	2.53	0.25–25.38

NKF K/DOQI Classification: Stage 1, signs of kidney damage as evidenced by microalbuminuria or macroalbuminuria and normal GFR (≥ 90 mL/min/1.73 m²); Stage 2, microalbuminuria or macroalbuminuria and with mild decrease in GFR (60–89 mL/min/1.73 m²); Stage 3, moderate decrease in GFR (30–59 mL/min/1.73 m²); Stage 4, severe decrease in GFR (15–29 mL/min/1.73 m²); and Stage 5, GFR <15 mL/min/1.73 m² or dialysis. *p values are for comparison to previous stage.

Results

CREDIT study population

Hypertension was detected in 3,413 (32.7%) individuals of the CREDIT study population. The prevalence of hypertension was significantly higher in women than men [(35.9% vs. 29.4%, $p < 0.001$, odds ratio: 0.74 (95% Confidence interval: 0.68–0.81)] and increased with age (10.9% in subjects aged <35 years, 44.7% in subjects aged 35–65 years, 79.7% in subjects aged over 65). The awareness rate was 48.6% in CREDIT study population being higher among women (56.8%) than men (38.4%). The awareness also increased with age—from 14.1% in subjects aged 18–29 years to 76.0% in subjects aged 80 year or over. Antihypertensive treatment rate was 31.5% among patients with hypertension (23.2% for men and 38.2% for women). Hypertension was under control in 16.4% of patients. The control rate was 36.8% for the patients under antihypertensive treatment. Among untreated and treated hypertensives; 64.0% vs. 33.7% had stage 1, 21.6% vs. 18.9% had stage 2, 7.2% vs. 10.6% had stage 3 hypertension, respectively. Among patients who were under treatment; 57.5 %, 33.1%, and 9.4 % were receiving one drug, two drugs, and three or more antihypertensive drugs respectively.

Hypertension in chronic kidney disease

Of the CREDIT study population, 1,344 (15.7%) had stage 1–5 CKD. The prevalence of hypertension among subjects with CKD was 56.3%. CKD was significantly more common among women than men [18.4% vs. 12.8%, $p < 0.001$, odds ratio 1.54 (95% CI: 1.37–1.74)]. Hypertension was significantly more prevalent in subjects with CKD than subjects without CKD [(56.3% vs. 31.0%, $p < 0.001$, odds ratio: 2.86 (95%CI: 2.54–3.22)] (Table 1). The prevalence of hypertension in CKD group was similar in women than men [(57.0% vs. 55.1%,)] and increased with age (18.5% in subjects aged <35 years, 58.4% in subjects aged between 35–65 and 86.2% in subjects aged over 65). Hypertension prevalence increased with increase in stage of CKD (34.8% in stage 1, 92.3% in stage 5 CKD) (Table 1). Only 13.4% of patients with CKD have optimal blood pressure. Subjects with CKD had higher rate of both high normal and stage 1–3 hypertension than subjects without CKD ($p < 0.001$) (Fig. 1).

The hypertension awareness rate was 61.9% among subjects with CKD. Awareness rate increased with increase in stage of CKD (40.9% in stage 1 CKD, 83.3% in stage 5 CKD) (Fig. 2). The awareness rate was being higher among women (66.2%) than men (55.2%). The awareness also increased with age—from 13.5% in subjects aged 18–29 years to 82.1% in subjects aged 80 year or over.

Fig. 1. Distribution of subjects to 2007 ESH-ESC blood pressure categories with respect to chronic kidney disease (CKD).

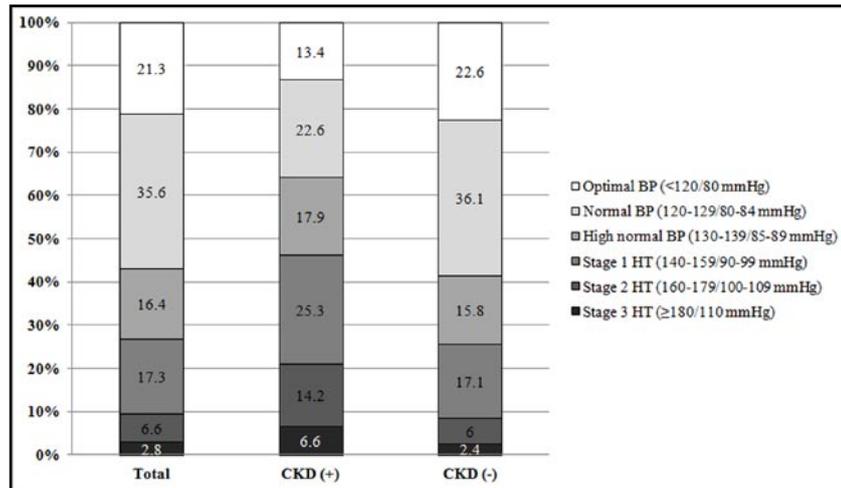
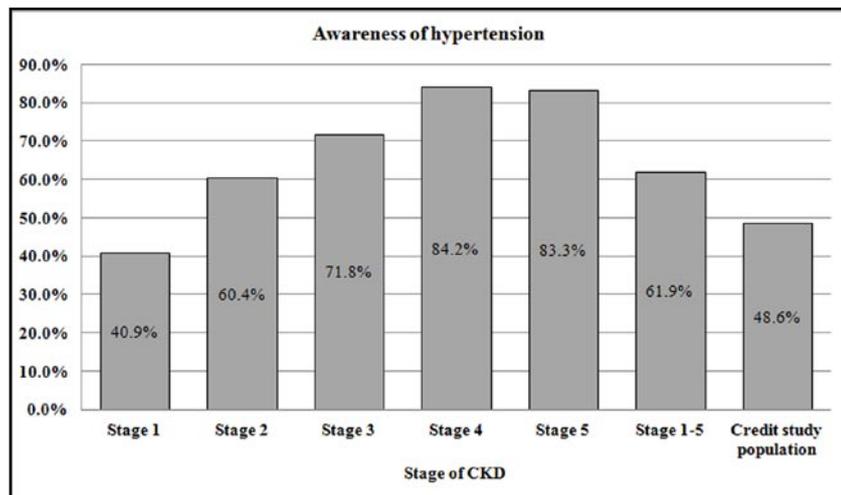


Fig. 2. The rates of awareness of hypertension with respect to stages of chronic kidney disease (CKD) and hypertension.



Antihypertensive treatment rate was 44.2% for patients with CKD and hypertension (37.1% for men and 48.6% for women), increasing with stage of CKD (24.4% in stage 1 CKD, 70.0% in stage 5 CKD) (Table 2). Hypertension was under control in 16.3% of patients with CKD and hypertension (17.3% for men and 15.8% for women). The control rate was 28.8% under antihypertensive treatment for these patients (Fig. 3). The hypertension control rate was higher in patients with stage 3–4 CKD (Table 2). Rate of stage 1 hypertension decreased with antihypertensive treatment for both patients with hypertension and patients with CKD and hypertension (Fig. 4). Of the untreated and treated hypertensives in CKD group; 46.1% vs. 30.1% had stage 1, 25.9% vs. 26.7% had stage 2, 11.7% vs. 14.5% had stage 3 hypertension respectively. The rate of patients having blood pressure less than 130/85 mmHg was just 9.8% in treated hypertensive CKD patients. Among patients who were under treatment; 51.9%, 34.1%, and 14% were receiving one drug, two drugs, and three or more antihypertensive drugs respectively.

CKD and renal function in hypertension

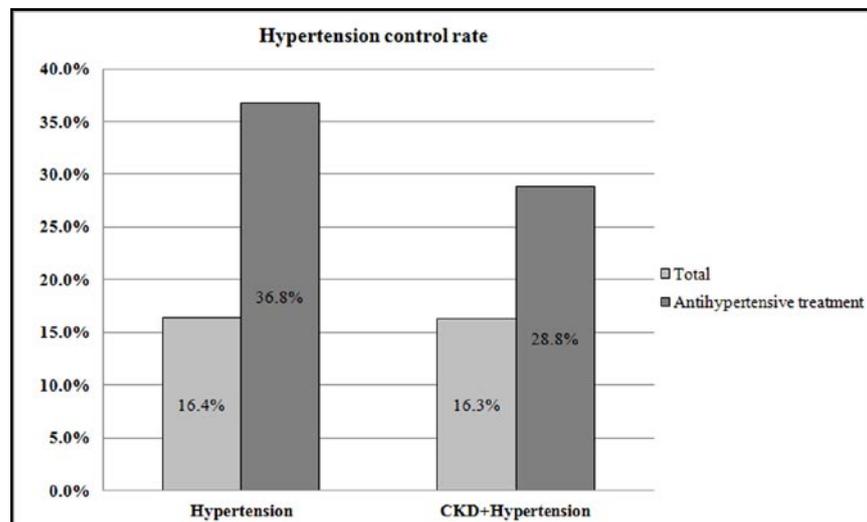
Prevalence of CKD was 25.3% among patients with hypertension (5.5% had stage 1, 8.1% had stage 2, 10.7% had stage 3, 0.6% had stage 4, and 0.4% had stage 5 CKD).

Serum creatinine and albuminuria levels were significantly higher in subjects with hypertension than subjects without hypertension ($p < 0.001$ for both variable). Glomerular filtration rate (GFR) was significantly lower in subjects with hypertension ($p < 0.001$). The rates of high serum creatinine, low GFR, microalbuminuria, and proteinuria were also

Table 2. Antihypertensive treatment and hypertension control rates in patients with hypertension, chronic kidney disease (CKD) in the CREDIT study population

	Antihypertensive treatment	Hypertension control rate
CREDIT study population	9.6%	
Patients with hypertension	31.5%	16.4%
Patients with CKD + hypertension	44.2%	16.3%
Stage 1	24.4%	12.3%
Stage 2	37.3%	13.3%
Stage 3	58.1%	19.6%
Stage 4	66.7%	40.0%
Stage 5	70.0%	9.1%

Fig. 3. The hypertension control rate in patients with hypertension, CKD+ hypertension, in those who were under antihypertensive treatment.



remarkably higher in subjects with hypertension. These findings indicated impaired renal function in hypertension (Table 3).

The frequency of microalbuminuria, proteinuria, and low GFR increased with the increase in stage of hypertension from optimal blood pressure to stage 3 hypertension (Fig. 5).

Furthermore, fasting blood glucose level, diabetes prevalence, and rates of high LDL-cholesterol, low HDL-cholesterol, high triglyceride, and dyslipidemia were all higher in subjects with hypertension (Table 3).

Discussion

The prevalence of hypertension and CKD continues to rise worldwide. It is known that the epidemiology of hypertension vary between different countries, thus national data for hypertension, particularly in subjects with CKD, are crucial to develop local strategies for early diagnosis and appropriate treatment approaches and to increase awareness [8, 23, 24]. The present population-based study is the first to report the prevalence and control rates of hypertension in patients with CKD in Turkey. This study showed that hypertension is highly prevalent among subjects with CKD in Turkey, and awareness, treatment and control rates for hypertension are still suboptimal.

The studies from different world regions reported the prevalence of hypertension in general population as 45-63%, awareness rate as 40-88% treatment rate as 25-84%, and control rate as 20-65% [25, 26]. In the PatenT study from Turkey, which reported the prevalence of hypertension as 31.8%, the awareness rate was 40.7% among 1,804 subjects

Table 3. Renal function, diabetes mellitus status, and lipid profile of subjects with or without hypertension in the CREDIT study population

		Hypertension (+) (n=3,413)	Hypertension (-) (n=7,031)	p
Serum creatinine (mean±SD)				
	mg/dL	0.94±0.42	0.88±0.18	<0.001
	μmol/L	71.7±32.0	67.1±13.7	
High serum creatinine (>1.3 mg/dL for men, >1.2 mg/dL for women)		6.8%	2.5%	<0.001
GFR (mL/min/1.73 m ²) (mean±SD)		82.6±19.2	96.5±20.3	<0.05
Low GFR (<60 mL/min/1.73 m ²)		10.8%	1.3%	<0.001
Albuminuria (mg/kg creatinine) [median (IQR)]		8.1 (14.8)	6.0 (8.2)	<0.001
Microalbuminuria (30-299 mg/g)		14.5%	7.9%	<0.001
Proteinuria (>300 mg/g)		3.0%	1.5%	
Uric acid (mean±SD)				
	mg/dL	4.7±1.5	4.3±1.3	<0.001
	μmol/L	279.6±89.2	255.8±77.3	
High uric acid (>7 mg/dL)		6.2%	2.8%	<0.001
Fasting blood glucose (mean±SD)				
	mg/dL	105.4±56.7	87.6±31.1	<0.001
	mmol/L	5.8±3.1	4.8±1.7	
Diabetes mellitus or fasting blood glucose ≥126 mg/dL (≥6.9 mmol/L)		25.5%	6.2%	<0.001
LDL-cholesterol (mean±SD)				
	mg/dL	121.9±36.0	105.9±33.9	0.001
	mmol/L	3.1±0.9	2.7±0.8	
High LDL-cholesterol (>130 mg/dL or >3.37 mmol/L)		37.8%	21.7%	<0.001
HDL-cholesterol (mean±SD)				
	mg/dL	44.5±12.6	46.0±13.0	>0.05
	mmol/L	1.1±0.3	1.1±0.3	
Low HDL-cholesterol (<40 mg/dL or <1.03 mmol/L for men, <46 mg/dL or <1.19 mmol/L for women)		48.4%	41.7%	<0.001
Triglyceride (mean±SD)				
	mg/dL	192.3±128.8	149.9±104.5	<0.001
	mmol/L	2.1±1.4	1.6±1.1	
High triglyceride (>150 mg/dL or >1.7 mmol/L)		54.7%	37.5%	<0.001
Dyslipidemia		86.6%	70.7%	<0.001
Body mass index (kg/m ²) (mean±SD)		28.5±4.9	25.1±4.2	<0.001
Body mass index	<25 kg/m ²	22.4%	51.3%	
	25-30 kg/m ²	42.8%	35.7%	
	≥30 kg/m ²	34.8%	13.0%	

SD: standard deviation, IQR: Interquartile range.

with hypertension, and 31.1% were receiving treatment, and only 8.1% had their blood under control [15]. In the CREDIT study population presented here, the prevalence and awareness rates for hypertension were 32.7% and 48.6 %, respectively. Among patients with hypertension, antihypertensive treatment rate was 31.5 % and control rate was 16.4%. The results of the CREDIT study population were very similar to those of PatenT study expect hypertension control rate, which was higher in the CREDIT study population. Higher hypertension control rate in the CREDIT study population may be due to improvement in diagnosis and treatment of hypertension since the PatenT study which was conducted in 2003.

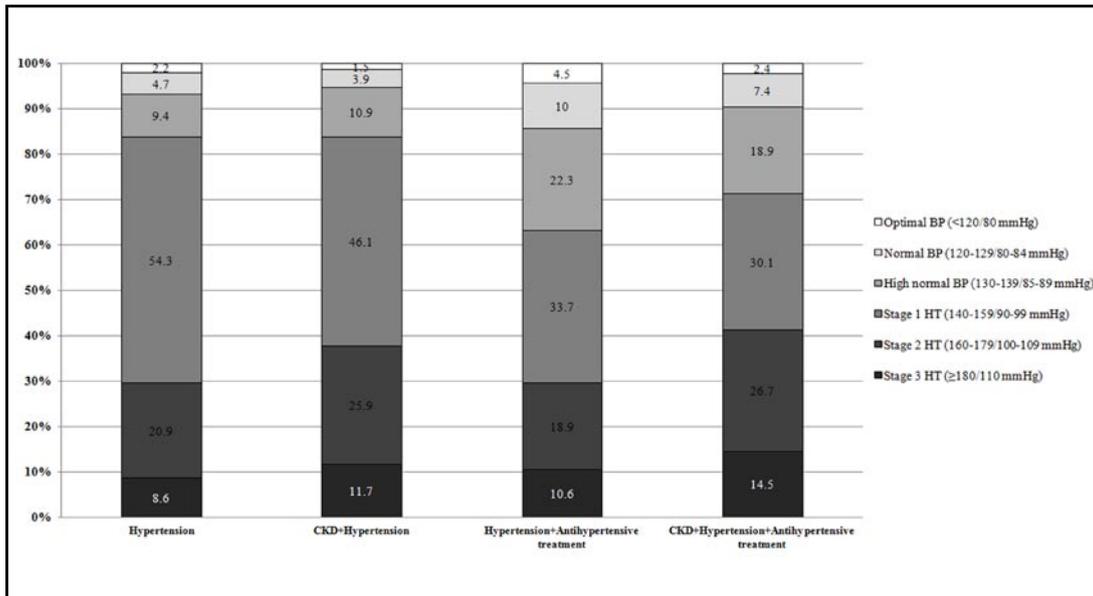


Fig. 4. Distribution of subjects to 2007 ESH-ESC blood pressure categories with respect to hypertension, chronic kidney disease (CKD), and antihypertensive treatment.

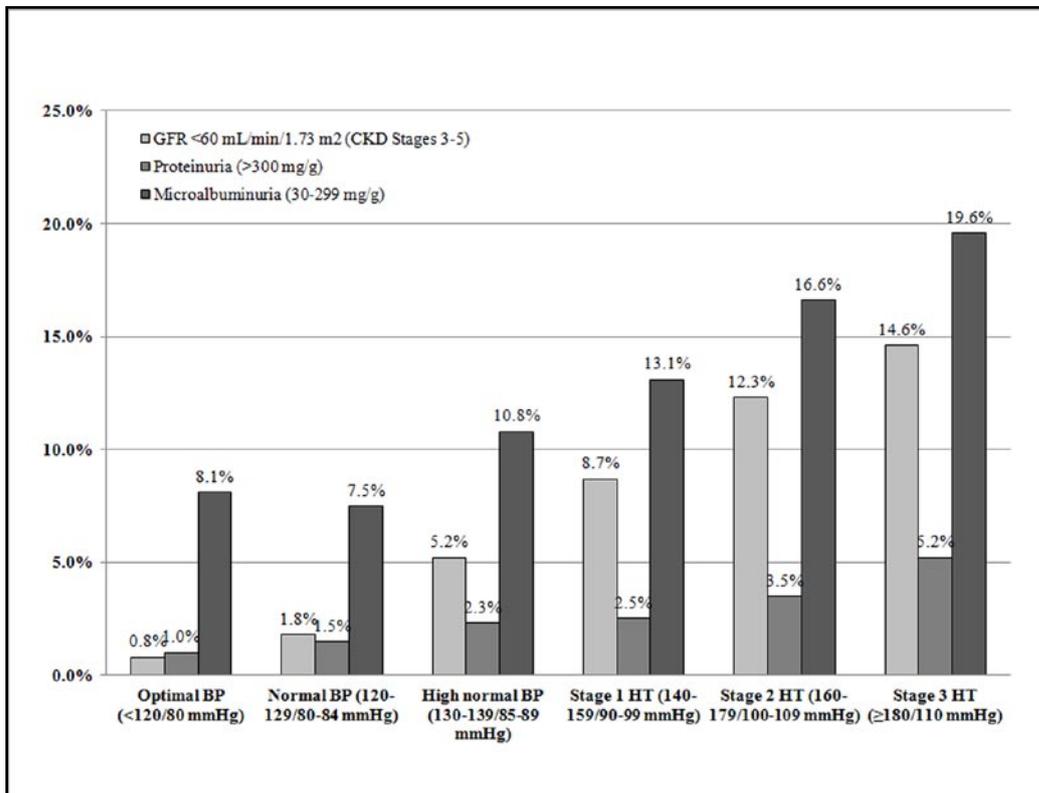


Fig. 5. Renal function parameters (GFR, proteinuria, microalbuminuria) of patients with hypertension (HT) according to 2007 ESH-ESC blood pressure categories.

The present study showed that among subjects with CKD in Turkey, the prevalence, awareness and control rates of hypertension were 56.3%, 61.9%, and 16.3%. Only 13.4% of patients with CKD have optimal blood pressure. The Fourth National Health and Nutrition Examination Survey (NHANES IV) data of 3,213 patients with CKD demonstrated that only

37% of patients had optimal blood pressure [10]. The recent report of the Chronic Renal Insufficiency Cohort (CRIC) study in 3,612 adult CKD subjects showed the prevalence of hypertension as 85.7%, awareness rate as 98.9%, and control rate as 67.1% [6]. The Kidney Early Evaluation Program revealed hypertension prevalence, awareness, and control rates among 10,813 adults with kidney disease as 86.2%, 80.2%, and 13.2%, respectively [9]. Although the prevalence and awareness of hypertension in CKD among CREDIT study population was found lower than that of both the CRIC study and the Kidney Early Evaluation Program, control rate was similar to the rate in the Kidney Early Evaluation Program.

An important finding of our study is stepwise increase in the prevalence of hypertension with increase in stage of the CKD, particularly for early stages. The prevalence of hypertension was significantly increased from stage 1 to stage 2 and 3 CKD (34.8%, 55.1%, and 79.8%, respectively), however the change in the prevalence of hypertension from stage 3 to 5 CKD did not show significant difference. Previous studies focused on the prevalence of hypertension in advanced stages of CKD. Cheng et al. studied 324 stage 3–5 CKD patients [11] and found that while there was no significant change in the prevalence of hypertension between CKD stage 3, 4, and 5 (15.0%, 14.9%, and 15.7%, respectively), a stepwise increase in the prevalence of isolated systolic hypertension with stages of CKD (28.1%, 39.4%, and 45.7% in stage 3, 4, and 5, respectively). Lower rates of hypertension reported by Cheng et al. may be explained with the small sample size of the study [11].

Similar to the prevalence of hypertension; awareness, treatment, and control rates increased with the stages of CKD as reported in the literature [9]. However, the control rate decreased at stage 5 CKD (19.6 %, 40.1 %, and 9.1 % in stage 3, 4, and 5, respectively). Cheng et al. also reported that the control rate decreased significantly with the advancement of CKD (51.9%, 40.4% and 38.6% in stage 3, 4 and 5, respectively) [11].

The antihypertensive treatment rate was found to be 31.5 % among patients with hypertension, 44.2 % for patients with CKD. All were lower than treatment rate reported in the CRIC study (98.3%) and the Kidney Early Evaluation Program (70.0%) [6, 9]. In the present study, 51.9 %, 34.1%, and 14 % of the CKD patients who were under antihypertensive treatment were using one, two, and three or more antihypertensive drugs, respectively. These percentages were 15%, 25%, and 26%, in the CRIC study [6]. These findings showed that although it is higher in subjects with CKD, treatment rate is still lower in hypertensive patients in Turkey compared to rates reported from developed countries. Furthermore single-drug regimens are preferred more than combined regimens in Turkey. Although, antihypertensive treatment increased control rate in both in hypertension and CKD (36.8% and 28.8%, respectively), control rates were still suboptimal. Thus, antihypertensive treatment is still inadequate and ineffective in patients with hypertension in Turkey.

As reported before in the literature, the present study showed that renal function deteriorated in subjects with hypertension. It is well known that creatinine level increases [27] and glomerular filtration rate decreases [28] with increase in blood pressure. Hanratty et al. recently reported that glomerular filtration rate declined at 1.5 mL/min/1.73 m² per year among 10,420 patients with hypertension and around 4% develop CKD in 45 months [29]. Segura et al. reported that 14.6% of patients with hypertension developed CKD in average follow-up duration of 13.2 years [30].

The major limitation of the present study was its cross-sectional design based on single study visit. However, this is the first study to report the prevalence, awareness and control of hypertension among CKD subjects in Turkey, which provide basic data for further prospective follow-up studies.

As a conclusion, hypertension is prevalent among subjects with CKD in Turkey. However, awareness, treatment and control rates of hypertension in CKD are suboptimal. To reduce the incidence of hypertensive nephropathy, appropriate health strategies should be implicated to improve prevention, early diagnosis, education and treatment of hypertension, and to increase awareness of the effects of hypertension in CKD.

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