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A population-based survey of Chronic REnal Disease In Turkey—the CREDIT study

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Abstract

Background. Chronic kidney disease (CKD) is a growing health problem worldwide that leads to end-stage kidney failure and cardiovascular complications. We aimed to determine the prevalence of CKD in Turkey, and to evaluate relationships between CKD and cardiovascular risk factors in a population-based survey.

Methods. Medical data were collected through home visits and interviews. Serum creatinine, blood glucose, total cholesterol, triglycerides, HDL, LDL and uric acid were determined from 12-h fasting blood samples, and spot urine tests were performed for subjects who gave consent to laboratory evaluation.

Results. A total of 10 872 participants were included in the study. The final analysis was performed on 10 748 subjects (mean age 40.5 ± 16.3 years; 55.7% women) and excluded 124 pregnant women. A low glomerular filtration rate (GFR) (<60 mL/min/1.73 m^2) was present in 5.2% of the subjects who were evaluated for GFR, while microalbuminuria and macroalbuminuria were observed in 10.2% and 2% of the subjects, respectively. The presence of CKD was assessed in subjects who gave consent for urinary albumin excretion measurement (n = 8765). The overall prevalence of CKD was 15.7%; it was higher in women than men (18.4% vs. 12.8%, $P < 0.001$) and increased with increasing age of the subjects. The prevalence of hypertension (32.7% in the general population), diabetes (12.7%), dyslipidaemia (76.3%), obesity (20.1%) and metabolic syndrome (31.3%) was significantly higher in subjects with CKD than subjects without CKD ($P < 0.001$ for all).

Conclusions. The prevalence of CKD in Turkey is 15.7%. Cardiovascular risk factors were significantly more prevalent in CKD patients.

Keywords: chronic kidney disease; epidemiology and outcomes; risk factors

Introduction

Chronic kidney disease (CKD) is a growing health problem worldwide that leads to end-stage kidney failure and cardiovascular complications [1]. CKD is defined as kidney damage and/or decreased kidney function expressed as glomerular filtration rate (GFR) for at least 3 months, regardless of the cause [2,3].

CKD is classified into five stages based on the severity of the disease [2,3]. Annual reports from the United States Renal Data System (USRDS) and the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA) have shown that incidence and prevalence rates of stage 5 CKD, also known as end-stage renal disease (ESRD), are on the rise [4,5]. International comparisons published in the 2009 USRDS atlas indicated that Taiwan [(415 per million people (pmp)], Jalisco-Mexico (372 pmp) and the USA (361 pmp) are the countries having the highest incidences of ESRD. In terms of prevalence, Taiwan (2288 pmp), Japan (2060 pmp) and the USA (1698 pmp) had the highest rates [5]. The data from the Turkish Society of Nephrology (TSN) 2008 annual registry indicated that the incidence of ESRD in Turkey

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has increased nearly 4-fold since 2000, while the prevalence of ESRD has doubled (incidence, 52 vs. 188 pmp; prevalence, 358 vs. 756 pmp, respectively) [6,7].

In the USA, the prevalence of stage 1–4 CKD was 13.1% according to results from the National Health and Nutrition Examination Survey (NHANES) 1999–2004 data [8]. In a systematic review of population-based studies, the median CKD (defined as <60 mL/min/1.73 m^2) was 7.2% for persons aged 30 years or older but varied from 23.4% to 35.8% in the elderly population [9].

CKD patients at high risk for developing ESRD need to be identified and monitored for timely transition to renal replacement therapy. Moreover, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) appear to have renoprotective effects and may be used in early-stage CKD to prevent progression of the disease [10–13].

In this large population-based study, we aimed to determine the prevalence of CKD in Turkey, and to assess the relationship between CKD and other cardiovascular risk factors such as diabetes, hypertension, dyslipidaemia, obesity and metabolic syndrome.

Materials and methods

Study design

We performed a population-based, national survey in Turkey on populations aged over 18 years. All subjects included in this survey gave informed consent to participate in the field study. Subjects with cognitive dysfunction that interfered with understanding and answering the study questionnaire were excluded from the study.

The study was approved by the Ethics Committee of the Akdeniz University Faculty of Medicine and the Turkish Ministry of Health.

Sampling method

A cluster sampling technique was used to select the study participants. A sampling frame was defined as the seven official geographical regions of Turkey, which 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 list of residences within 80 km of the centre of the selected cities, which are defined as rural areas according to the Turkish Statistical Institute [14] classification, was used to determine the cluster sampling outline for rural areas.

The sample size of the study included ~10 500 participants, and the prevalence of CKD was estimated with a 95% confidence interval according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiatives (NKF KDOQI) practice guidelines and the NHANES-III [2,15]. The number of subjects in each study subgroup was calculated on the basis of age distribution of women and men in each geographical area (since the sampling method was cluster sampling, the effect size was set at 1.2).

Field study

The data were collected through home visit and interviews of potential participants by specially trained field study teams. During interviews, the study questionnaire was given which included questions on subject demographics, socioeconomic status, diet, lifestyle, 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 was recorded.

Laboratory assessment

Laboratory assessment was performed for subjects who gave written consent for the laboratory evaluation during interviews. These subjects were visited the next day to collect 12-h fasting blood samples. At the same time, morning spot urine samples were obtained from the participants. Additionally, spot urine analysis (by dipsticks) was performed during home visits, and results were recorded on the study questionnaire. Albuminuria measurements were excluded in pregnant or menstruating women and in all patients suffering from febrile illness [16].

Urine albumin (immunoturbidimetric method) and creatinine (alkaline picrate method), serum creatinine (alkaline picrate method), blood glucose (hexokinase method), total cholesterol (cholesterol oxidase method), triglycerides (glycerol phosphate oxidase method), HDL cholesterol (accelerator selective detergent method), LDL cholesterol, and uric acid (uricase method) concentrations were determined.

Definitions

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 [$186 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times (0.742$ if woman) $\times (1.212$ if African American)] [17]. Since there were no African American subjects in our study population, the last variable of the formula was not used.

CKD was categorized into five stages based on the classification system established by the NKF KDOQI [2]: stage 1, signs of kidney damage as evidenced by microalbuminuria or macroalbuminuria and normal GFR (≥90 mL/min/1.73 m^2); stage 2, microalbuminuria or macroalbuminuria and with mild decrease in GFR (60–89 mL/min/1.73 m^2); stage 3, moderate decrease in GFR (30–59 mL/min/1.73 m^2); stage 4, severe decrease in GFR (15–29 mL/min/1.73 m^2); and stage 5, GFR <15 mL/min/1.73 m^2 or dialysis.

The urinary albumin-to-creatinine ratio was determined as milligrams per gram. 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 30–299 mg/g, and macroalbuminuria defined as an albumin-to-creatinine ratio of 300 mg/g or higher [18].

For the purpose of this study, 'hypertension' was assumed to be present if there was a recorded diagnosis of hypertension, systolic blood pressure >140 mmHg and/or diastolic blood pressure ≥90 mmHg. 'Diabetes mellitus' was defined as diagnosis of diabetes mellitus or fasting blood glucose ≥126 mg/dL. The term 'dyslipidaemia' indicated patients having anti-lipid treatment or dyslipidaemia shown in the lipid profile (total cholesterol >240 mg/dL or LDL cholesterol >130 mg/dL or HDL cholesterol <40 mg/dL for men, <46 mg/dL for women, or serum triglyceride >150 mg/dL). The term 'obesity' indicated a body mass index ≥30 kg/m^2. The American Heart Association (AHA) criteria were used for the diagnosis of metabolic syndrome, which included the presence of three or more of the following components: elevated waist circumference (for men ≥102 cm and for women ≥88 cm), elevated triglycerides (≥150 mg/dL), reduced HDL (for men <40 mg/dL and for women <50 mg/dL), elevated blood pressure (≥130/85 mmHg) or elevated fasting glucose (≥100 mg/dL) [19].

Statistical analysis

Analyses were performed on populations weighted according to age groups, gender, geographical area and residence. Student's *t*-tests and Mann–Whitney *U*-tests were used for comparisons of continuous variables, which showed normal and non-normal distribution, respectively. Chi-square tests were used to compare proportions between groups. The Mantel–Haenszel test for linear association was used to test the significance of linear relationships between ordinal variables. The relative risk of risk factors for CKD prevalence was expressed as odds ratios with 95% confidence intervals (CI). Statistical significance was defined as $P < 0.05$.

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Results

Study population

A total of 10 872 participants from throughout the country were included in the study. The data from 124 pregnant women were excluded, giving a final total of 10 748 subjects. The majority of the study population (71.6%) came from urban areas, while the remainder lived in rural areas. The distribution of subjects according to the geographical regions of Turkey was parallel to the population density of the regions, which is highest in the Marmara, Central Anatolia and the Aegean Regions. The mean age of subjects was 40.5 ± 16.3 years. The distribution of subject age groups showed that the majority of subjects (>70%) were aged below 50 years. Of all the subjects, 55.7% were women (Table 1).

Kidney function

Creatinine levels and GFR were determined in 10 056 subjects, and microalbuminuria as well as urinalysis was performed in 9064 subjects.

Serum creatinine. Overall, the mean creatinine level of the subjects was 0.90 ± 0.28 mg/dL. The creatinine level was significantly higher in men than women (1.00 ± 0.29 mg/dL and 0.80 ± 0.23 mg/dL, respectively, $P < 0.001$). There was a slight increase in creatinine level with increasing age (Table 2).

Glomerular filtration rate. The estimated mean GFR was 91.8 ± 20.9 mL/min/1.73 m^2, and it was significantly higher in men and in younger groups of subjects ($P < 0.001$, for both analyses) (Table 2).

Table 1. Characteristics of the study population (n = 10 748)

		n (%) or mean ± SD
Gender	Female	5983 (55.7%)
	Male	4765 (44.3%)
Mean age (years)	Total	40.54 ± 16.30
	Female	41.16 ± 16.71
	Male	39.91 ± 15.86
Age groups	<30 years	1902 (17.7%)
	30–39 years	2540 (23.6%)
	40–49 years	2196 (20.4%)
	50–59 years	1816 (16.9%)
	60–69 years	1594 (14.8%)
	70–79 years	573 (5.3%)
	≥80 years	127 (1.2%)
Residence	Urban	7697 (71.6%)
	Rural	3051 (28.4%)
Geographical region	Central Anatolia	2073 (19.3%)
	Mediterranean	975 (9.1%)
	Marmara	4502 (41.9%)
	Aegean	910 (8.5%)
	East Anatolia	646 (6%)
	Southeastern Anatolia	676 (6.3%)
	Black Sea	966 (9%)

The number of subjects is crude (unadjusted) figures.

Decreased kidney function, defined as a moderate or severe decrease in GFR, was detected in 4.4% of the subjects who were evaluated for GFR. A moderate decrease (GFR, 30–59 mL/min/1.73 m^2) was observed in 4.1%, while a GFR of 15–29 mL/min/1.73 m^2 was noted in 0.24%, and a GFR <15 mL/min/1.73 m^2 GFR in 0.13%. Increasing subject age produced a consistent increase in the prevalence of mild and moderate decreases in GFR ($P < 0.001$) (Figure 1).

Microalbuminuria. Of all the subjects, 10.2% had microalbuminuria, and 2% had macroalbuminuria. Both of these, particularly microalbuminuria, were higher in females and in older age groups (Figure 2). Spot urine tests revealed that the median (IQR) albuminuria level was 6.59 (10.05) mg/g creatinine. The median albuminuria was significantly higher for women than men (7.55 vs. 5.71 mg/g creatinine, respectively, $P < 0.001$). It was also significantly higher for patients aged over 50 years (Table 2).

Prevalence of CKD

The presence of CKD was assessed in all subjects who volunteered for urinary albumin excretion measurements. The prevalence of CKD was 15.7% (n = 1373) among 8765 subjects evaluated. 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)] (Table 3). The prevalence of CKD also increased with increasing age of the subjects. The odds ratios of CKD ranged from 1.45 (95% CI: 1.14–1.84) to 2.18 (95% CI: 1.76–2.70) for every 10-year increase in age for subjects over 30 years (Table 3). The prevalence of CKD was found to be 11.5% in the population aged <60 years, while it was as high as 38.3% in subjects aged 60 years or over [$P < 0.001$, odds ratio 1.43 (95% CI: 1.37–1.49)]. Stage 3 CKD was especially more common among subjects aged over 60 years (1.6% vs. 21.5%). CKD prevalence was slightly higher among subjects living in rural areas than in those living in urban areas (16.8% vs. 15.2%, $P = 0.049$). CKD prevalence was highest among subjects from the Marmara region (19.7%) followed by Southeastern Anatolia (18.6%), the Black Sea (16.1%), East Anatolia (14.2%), the Aegean (13.8%), Central Anatolia (12.6%) and the Mediterranean (11.7%) regions.

The majority of subjects with CKD were in stage 1–3. The prevalence rates for CKD stage 1, 2, 3, 4 and 5 were 5.4%, 5.2%, 4.7%, 0.3% and 0.2%, respectively. The percentage of subjects in stage 2 and 3 increased and those with stage 1 decreased with increasing age (Figure 3).

Concomitant cardiovascular risk factors

In the general population, the prevalence rates for hypertension, diabetes, dyslipidaemia, obesity and metabolic syndrome were 32.7%, 12.7%, 76.3%, 20.1% and 31.3%, respectively. The prevalence of hypertension was higher in subjects with CKD than in those without CKD (56.3% and 31%, $P < 0.001$). Similarly, the prevalence rates of diabetes (26.6% vs. 10.1%), dyslipidaemia (83.4% vs. 75.8%), obesity (29.2% vs. 20%) and metabolic syndrome (46% vs. 29.8%) were significantly higher in subjects with

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Table 2. Mean serum creatinine, glomerular filtration rate and microalbuminuria with respect to gender and age groups of the study population

	Serum creatinine (mg/dL)			GFR (mL/min/1.73 m^2)			Albuminuria (mg/g creatinine)		
	n	Mean ± SD	P-value	*n*	Mean ± SD	P-value	*n*	Mean ± SD (median; IQR)	P-value
Gender									
Female	5110	0.80 ± 0.23	<0.001	5110	89.6 ± 19.9	<0.001	4615	35.1 ± 165.6 (7.55; 10.95)	<0.001
Male	4947	1.00 ± 0.29		4947	94.2 ± 21.6		4449	28.9 ± 145.2 (5.71; 8.75)	
Age groups[a]									
<30	3137	0.86 ± 0.19		3137	105.6 ± 20.4		2696	24.4 ± 91.5 (6.18; 8.36)	
30–39	2241	0.88 ± 0.25	0.064	2241	94.4 ± 16.8	<0.001	2030	21.4 ± 100.4 (5.76; 7.63)	0.021
40–49	1860	0.90 ± 0.22	0.43	1860	87.8 ± 15.4	<0.001	1700	33.3 ± 228.6 (5.90; 8.75)	0.68
50–59	1333	0.95 ± 0.48	<0.001	1333	81 ± 15.8	<0.001	1259	43.9 ± 189 (7.27; 13.21)	<0.001
60–69	790	0.95 ± 0.33	0.99	790	77 ± 16	<0.001	728	53.5 ± 201.3 (8.76; 18.95)	0.051
70–79	543	0.99 ± 0.27	0.12	543	71 ± 17.4	<0.001	502	46 ± 153.3 (11.65; 21.34)	0.001
≥80	153	0.99 ± 0.22	0.99	153	67.6 ± 14.6	0.32	150	50.3 ± 99.2 (14.93; 29.96)	0.006
Total	10 056	0.90 ± 0.28		10 056	91.8 ± 20.9		9064	32.1 ± 156 (6.59; 10.05)	

The numbers of subjects are adjusted (to age, gender, geographic region and residence) figures.
GFR, glomerular filtration rate; SD, standard deviation; IQR, interquartile range.
[a]P-values correspond to the comparisons with previous age group.

CKD compared with subjects without CKD ($P < 0.001$ for all analyses). Furthermore, the prevalence of these cardiovascular risk factors gradually increased in subjects having advanced stages of the disease. Thus, CKD was found to be strongly associated with these cardiovascular risk factors (Table 4).

Mean values of kidney function and/or damage indicators, such as serum creatinine, GFR and microalbuminuria, in subjects with and without hypertension, diabetes, dyslipidaemia, obesity and metabolic syndrome also demonstrated that renal function in subjects with cardiovascular risk factors was significantly impaired compared with healthy individuals (Table 5). The prevalence of decreased GFR and microalbuminuria was higher in subjects having these risk factors, particularly in those having hypertension and diabetes (Figure 4). The prevalence of CKD among subjects with and without hypertension was 25.3% and 10.6%, respectively [$P < 0.001$, odds ratio 1.58 (95% CI: 1.48–1.68)]. Similarly, CKD was significantly more common in subjects with diabetes than in subjects without dia-

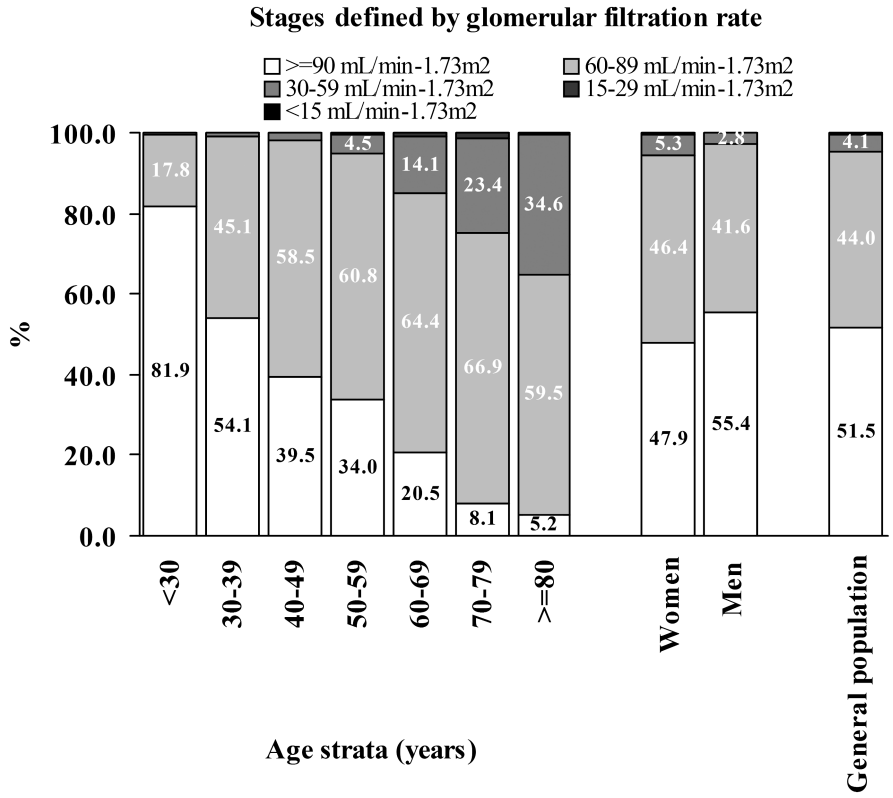

Fig. 1. Percentage of subjects according to glomerular filtration rate with respect to gender and age groups. There was a significant relation between the stage of glomerular filtration rate and age group ($P < 0.001$).

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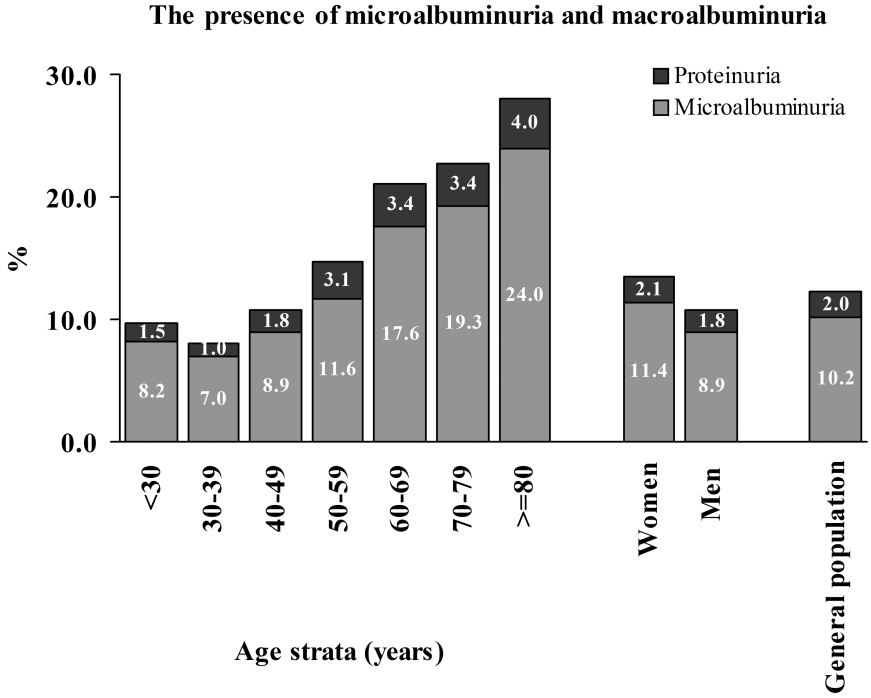

Fig. 2. Percentage of subjects with microalbuminuria (30–299 mg/g creatinine) or macroalbuminuria (>300 mg/g creatinine) with respect to gender and age group.

betes [32.4% vs. 13%; P < 0.001, odds ratio 1.22 (95% CI: 1.18–1.27)].

Discussion

This was the first epidemiological study to assess the prevalence of CKD in Turkey. Using the criteria of CKD established by the KDOQI guidelines, the overall prevalence of CKD in Turkey was 15.7%. By employing similar KDOQI criteria, the prevalence of CKD was 13.1% in the USA based on the NHANES-III (1999–2004) data [8] and 10.2% in Norway based on the HUNT-II (1995–97) data [20]. Although the US and Norwegian studies showed the highest prevalence for stage 3 CKD (7.7% in the USA and 4.2% in Norway), our Turkish stage 1–3 cohort were more evenly distributed, and each comprised nearly one-third of the CKD population. This suggests that Turkey shows a higher proportion of albuminuria in the absence of kidney dysfunction.

A number of studies have focused on the prevalence of stage 3–5 CKD based on GFR <60 mL/min/1.73 m^2 and calculated GFRs using the MDRD equation. The prevalence of low estimated GFR in Turkey (5.2%) is lower compared with Italy (6.4%) [21], Switzerland (8.1%) [22] and Iceland (7.2%) [23], but is higher than India (4.2%) [24] and China (2.5%) [25].

The MDRD equation has mostly been replaced with the Cockcroft–Gault equation since the latter gives a more accurate estimate of GFR in CKD patients [17]. In epidemiological studies that reported CKD rates using both equations, the Cockcroft–Gault-calculated rate was always higher than the MDRD-calculated rate. As an example, the NHANES-III 1988–94 survey showed that the US prevalence of low GFR was 4.5% by the MDRD and 7% by the Cockcroft–Gault equation [15].

An earlier diagnosis of stage 4 CKD patients would allow for future planning, such as early access (peritoneal dialysis catheter or arteriovenous fistula) for dialysis or transplantation from a donor in the family [26,27]. Furthermore, knowledge on the prospective incidence of ESRD from a well-established population-based cohort will help in identifying those patients at the highest risk for developing this condition.

Table 3. The prevalence of chronic renal disease with respect to gender and age groups

	Total number of subjects	Subjects with CKD, *n* (%)	P-value	Odds ratio (95% CI)
Gender				
Female	4490	827 (18.4%)	<0.001	1.54 (1.37–1.74)
Male	4273	546 (12.8%)		
Age groups[a]				
<30	2595	259 (10%)		
30–39	1947	165 (8.5%)	0.084	0.84 (0.68–1.02)
40–49	1645	207 (12.6%)	<0.001	1.56 (1.25–1.93)
50–59	1218	222 (18.2%)	<0.001	1.55 (1.26–1.90)
60–69	719	235 (32.7%)	<0.001	2.18 (1.76–2.70)
70–79	491	203 (41.3%)	0.002	1.45 (1.14–1.84)
≥80	150	82 (54.7%)	0.004	1.71 (1.18–2.47)
Total	8765	1373 (15.7%)		

The numbers of subjects are adjusted (to age, gender, geographic region and residence) figures.
CKD, chronic renal disease; CI, confidence interval.
[a]P-values correspond to the comparisons with previous age group.

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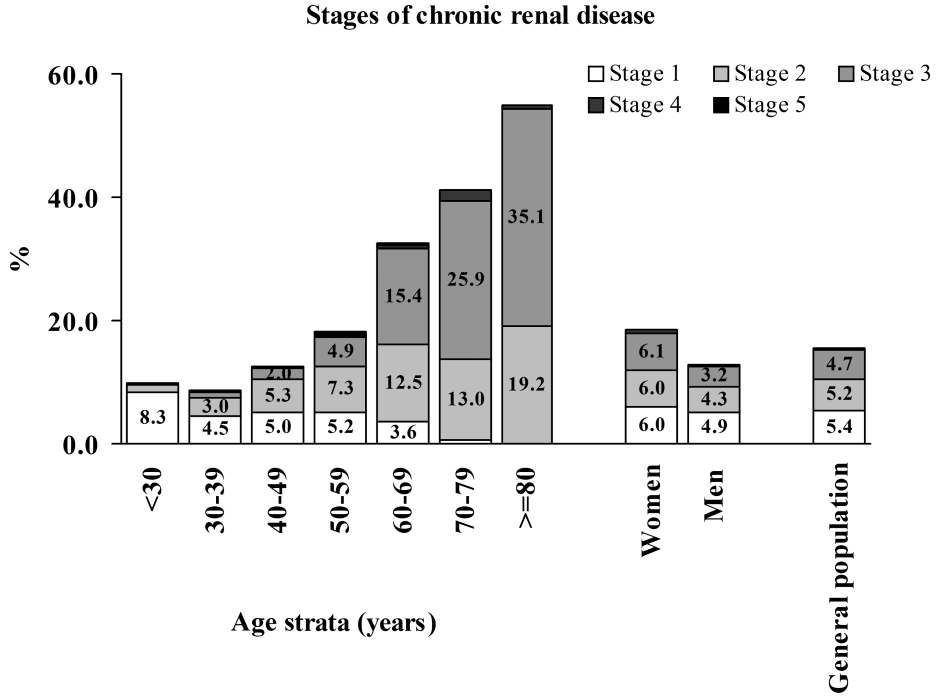

Fig. 3. Percentage of subjects with chronic renal disease according to the stages of the disease with respect to gender and age group.

Predictors of ESRD have been studied in long-term prospective studies such as the Okinawa screen, the Multiple Risk Factor Intervention Trial (MRFIT) and the Norwegian HUNT study. In a 10-year follow-up of the Okinawa population, proteinuria, haematuria and hypertension were identified as predictors of ESRD [28]. In contrast, proteinuria and estimated GFR were ESRD predictors in the MRFIT study having a 25-year follow-up [29]. However, their predictive value was limited since the combined GFR and proteinuria could detect only 27% of the eventual ESRD cases [29,30]. A 10-year follow-up of HUNT-II showed that the combination of the albumin/creatinine ratio (not just proteinuria) and estimated GFR narrowed the population at risk for developing ESRD to 1.4% and correctly predicted 66% of the patients eventually progressing to ESRD [31].

The Kidney Early Evaluation Program (KEEP) study conducted by the National Kidney Foundation revealed an independent relationship between CVD and several measures of CKD, such as estimated GFR, microalbuminuria and anaemia [32]. The early detection and management of cardiovascular risk factors will be important for Turkey since the mortality pattern is very similar to that of developed nations even though industrialization is ongoing, the population is young, and overall cholesterol levels are comparatively low [33]. Turkey was one of the 22 European countries participating in the EUROASPIRE III

Table 4. The frequency of concomitant hypertension, diabetes mellitus, dyslipidaemia, obesity or metabolic syndrome in the study population with respect to presence and stage of chronic renal disease

Chronic renal disease status	Hypertension		Diabetes mellitus		Dyslipidaemia		Obesity		Metabolic syndrome	
	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
General population	32.7		12.7		76.3		20.1		31.3	
No CKD	31	reference	10.1	reference	75.8	reference	20	reference	29.8	reference
CKD (any stage)[a]	56.3	*2.86 (2.54–3.22)*	26.6	*3.22 (2.77–3.74)*	83.4	*1.60 (1.37–1.86)*	29.2	*1.65 (1.45–1.88)*	46	*2.01 (1.77–2.27)*
Stage 1 CKD[b]	34.8	1.19 (0.98–1.45)	16.4	*1.73 (1.33–2.26)*	74.3	0.92 (0.74–1.14)	23.7	*1.25 (1–1.55)*	31.1	1.06 (0.86–1.31)
Stage 2 CKD[c]	55.1	*2.30 (1.76–3)*	32.1	*2.41 (1.74–3.35)*	84.2	*1.85 (1.33–2.57)*	29.7	*1.36 (1.01–1.82)*	51.4	*2.34 (1.77–3.11)*
Stage 3 CKD[c]	79.8	*3.21 (2.36–4.36)*	32.3	1.01 (0.74–1.38)	92.6	*2.36 (1.50–3.70)*	34.7	1.26 (0.95–1.68)	57	1.26 (0.94–1.68)
Stage 4 CKD[c]	82.6	1.21 (0.40–3.64)	40.9	1.45 (0.60–3.49)	87.5	0.56 (0.16–1.97)	29.2	0.82 (0.33–2.04)	68.2	1.62 (0.64–4.06)
Stage 5 CKD[c]	92.3	2.53 (0.25–25.38)	45.5	1.20 (0.28–5.18)	91.7	1 57 (0.15–16.94)	33.3	1.14 (0.26–5.09)	66.7	0.93 (0.21–4.18)

Significant ORs are denoted in italic font type.
Hypertension (HT), diagnosis of HT or blood pressure ≥140/90 mmHg; diabetes mellitus (DM), diagnosis of DM or fasting blood glucose ≥126 mg/dL; dyslipidaemia, anti-lipid use or dyslipidaemia in lipid profile; obesity, body mass index ≥30 kg/m^2; metabolic syndrome, as defined according to the AHA criteria; OR, odds ratio.
[a]CKD of any stage vs. no CKD.
[b]Stage 1 vs. no CKD.
[c]Versus previous stage.

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Table 5. Mean serum creatinine, glomerular filtration rate and microalbuminuria in subjects with and without concomitant hypertension, diabetes mellitus, dyslipidaemia, obesity or metabolic syndrome

		Serum creatinine (mg/dL)		GFR (mL/min/1.73 m^2)		Microalbuminuria (mg/g creatinine)	
		Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD (median; IQR)	P-value
Hypertension	No	0.88 ± 0.18	<0.001	96.5 ± 20.3	<0.001	25.9 ± 146.7 (5.98; 8.15)	<0.001
	Yes	0.94 ± 0.42		82.6 ± 19.2		45 ± 176.6 (8.10; 14.77)	
Diabetes mellitus	No	0.88 ± 0.26	<0.001	94 ± 20.8	<0.001	27.1 ± 144.5 (6.23; 8.83)	<0.001
	Yes	0.94 ± 0.44		82 ± 19.4		74.1 ± 260.5 (10.76; 25.22)	
Dyslipidaemia	No	0.85 ± 0.20	<0.001	100.5 ± 21.8	<0.001	32.1 ± 211.5 (6.31; 8.74)	0.006
	Yes	0.91 ± 0.30		89.2 ± 19.9		31.8 ± 137.3 (6.65; 10.45)	
Obesity	No	0.90 ± 0.28	0.17	93.7 ± 21.1	<0.001	29.7 ± 143.7 (6.42; 9.33)	<0.001
	Yes	0.90 ± 0.30		84.7 ± 18.5		41.3 ± 196.2 (7.42; 12.35)	
Metabolic syndrome	No	0.88 ± 0.25	<0.001	95.9 ± 21	<0.001	27.9 ± 156 (6.18; 8.73)	<0.001
	Yes	0.92 ± 0.35		83.9 ± 18.4		42.7 ± 178.5 (7.57; 13.42)	

Hypertension (HT), diagnosis of HT or blood pressure ≥140/90 mmHg; diabetes mellitus (DM), diagnosis of DM or fasting blood glucose ≥126 mg/dL; dyslipidaemia, anti-lipid use or dyslipidaemia in lipid profile; obesity, body mass index ≥30 kg/m^2; metabolic syndrome, as defined according to the AHA criteria; GFR, glomerular filtration rate; SD, standard deviation; IQR, interquartile range.

study, which aimed to describe lifestyles, risk factors and therapeutic management of coronary heart disease patients. In this study, 20% of the Turkish patients hospitalized for coronary heart disease were under 50 years of age, constituting the youngest patients in all of Europe [34,35]. Moreover, the prospective Turkish Adult Risk Factors study, a large population-based survey that accumulated data on coronary heart disease and related risk factors since 1990, has shown that coronary mortality is highest in Turkey among 30 European countries at 7.6 per 1000 person-years for men and 3.84 for women in the age group of 45–74 years [36].

In the present cohort, we found that the overall prevalence of diabetes was 12.7%. In contrast, the TURDEP study in 2002 had predicted a prevalence of 7.2% in the overall Turkish population [37]. This increased prevalence may be related to increased life expectancy as well as lifestyle changes in the Turkish population, such as changes in dietary habits, more sedentary lifestyle and increased urbanization. In a more recent study in an older population cohort, the prevalence of diabetes was 11% of individuals aged over 35 years [38]. The prevalence of diabetes was more than doubled in subjects diagnosed with CKD (26.6%). Diabetes was clearly associated with CKD progression since the prevalence of diabetic patients increased with advanced stages of kidney disease. Kidney damage is very common in diabetes. For example, the NHANES-III showed that close to one-third of the diabetic population (28.8%) in the USA had microalbuminuria [39].

Hypertension is the second major cause of ESRD, and is also very common in Turkey. The prevalence, awareness, treatment and control of hypertension in Turkey (PatenT) study reported that the age- and sex-adjusted rate of hypertension was 31.8% in a population of ~15 million people [40]. A 4-year follow-up of this study showed that the incidence rate of hypertension in Turkey was 21.4%, and this reached as high as 43.4% for individuals aged over 65 years [41]. Our current study showed that the percentage of patients with hypertension increased steadily with progressing CKD, such that nearly all patients with ESRD (92.3%) had elevated blood pressure.

Obesity and metabolic syndrome are also risk factors for CKD. In a Swedish study, obesity (in men) and morbid obesity (in women) at anytime during the lifespan were associated with a 3–4-fold increase in the risk of CKD [42]. In a prospective 9-year study, the odds ratio of incident CKD was 1.24 among subjects with metabolic syndrome after adjustments for diabetes and hypertension [43]. Obesity and metabolic syndrome were highly prevalent in this cohort, and the prevalence of both risk factors was significantly greater in subjects with CKD. Even higher rates of obesity (one-third of the adult population) have been reported in some Turkish studies, while metabolic syndrome ranged from 18% to 41% depending on the definition [44,45].

The major limitation of this study was the use of single measurements to detect serum creatinine and albuminuria. Many of those screened may have had transient albuminuria or a transient decline in GFR. Ideally, a repeat test should be performed after a few months to eliminate cases with transient kidney injury, which is relevant at the individual level. Nevertheless, it is difficult to perform more than single testing in large-scale cross-sectional surveys at the population level [24,46]. Another limitation was the difficulty of diagnosing elderly subjects having reduced GFR with CKD. The prevalence of CKD, particularly stage 3 CKD, was found to be significantly higher in subjects aged 60 years and older. However, it is very likely that most of the elderly participants had age-related renal impairments rather than CKD [47], making it necessary to evaluate age-related renal functional changes during evaluation of high-prevalence CKD among subjects aged over 60 years. In addition, the MDRD equation has not been validated for the Turkish population, and its accuracy in predicting actual GFR in Turkish men and women is not known. A validation study for the MDRD equation in the Turkish population is currently being conducted by the Turkish Society of Nephrology.

In conclusion, similar to many other countries, CKD is a major health problem in Turkey. Associations between CKD and several cardiovascular risk factors emphasize that this is a major public health problem and a major predictor of over-

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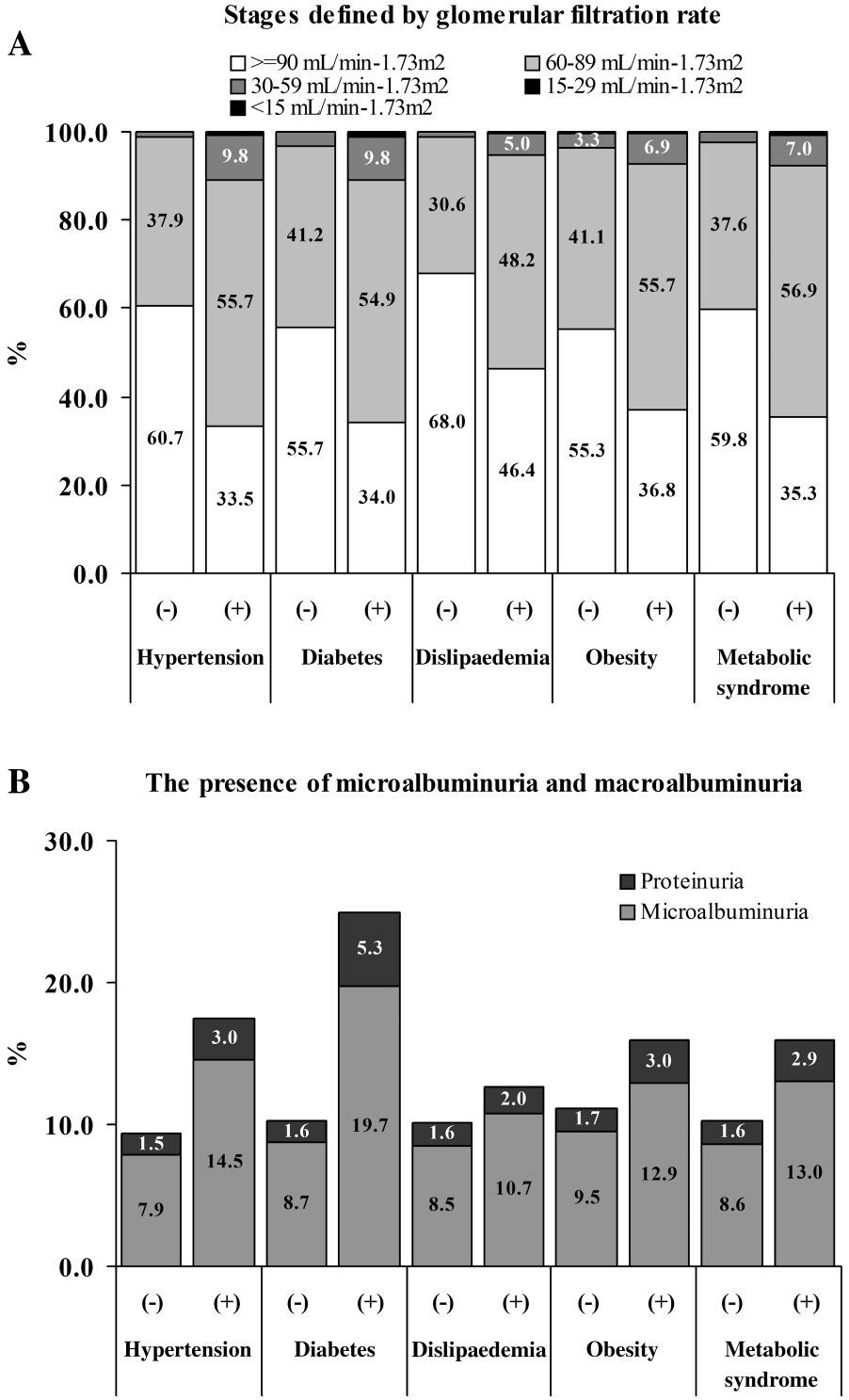

Fig. 4. Glomerular filtration rate (**A**), and microalbuminuria [as microalbuminuria (30–299 mg/g creatinine) or macroalbuminuria (>300 mg/g creatinine)] (**B**) in subjects with and without concomitant hypertension, diabetes mellitus, dyslipidaemia, obesity or metabolic syndrome.

all morbidity and mortality. Longitudinal studies will be needed to establish relationships between GFR, microalbuminuria, cardiovascular outcomes and the risk for ESRD development. The population examined in the present study is currently being followed up as a longitudinal study, and results will be evaluated at the fifth year.

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Conflict of interest statement. None declared.

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ADAMTS13—marker of contractile phenotype of arterial smooth muscle cells lost in benign nephrosclerosis

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Abstract

Background. Hypertensive nephrosclerosis alone and in combination with other renal diseases is a leading cause of terminal renal insufficiency. Histologic lesions manifest as benign nephrosclerosis (bN) with arteriolar hyalinosis and later fibrosis. Procoagulant micromilieus have been implicated in fibrosis. Hyalinosis is considered to consist of plasma insudation possibly containing procoagulant factors like von Willebrand factor (VWF). Therefore, it is hypothesized that VWF cleaving protease ADAMTS13 (a disintegrin-like and metalloprotease with thrombospondin type-1 motif, 13) is normally expressed by arteriolar vascular smooth muscle cells (VSMCs) and diminished in bN and that this reduction contributes to fibrosis in bN.

Methods. ADAMTS13 expression was examined by immunohistochemistry and quantitative real-time polymerase chain reaction in VSMCs of various human organs. Fifty-four specimens with and seven without bN were immunostained for ADAMTS13, VWF, CD61 and VSMC differentiation markers in arteriolar walls.

Results. Expression of ADAMTS13 is confirmed in VSMCs. In bN, ADAMTS13 immunostaining of arterial VSMCs correlated inversely with fibrotic but not hyalinotic lesions. Smooth muscle myosin heavy chain showed an inverse correlation with hyalinotic, as opposed to fibrotic lesions of bN. Smoothelin showed an inverse correlation with both hyalinotic and fibrotic lesions of bN. VWF was absent in normal controls and hyalinotic lesions, but present exclusively in fibrotic lesions in 7/54 (13%) bN cases. CD61 was absent in all arteriolar walls.

Conclusions. The present results establish ADAMTS13 as a novel marker of contractile VSMCs that is retained in early hyalinotic bN but partially lost later in fibrotic bN. Loss of ADAMTS13 and accumulation of VWF in fibrotic

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