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Diabetes and Chronic Kidney Disease in Turkey (DIAKIT): A Cross-Sectional Cohort Study

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Abstract

Background: Chronic kidney disease (CKD) is a global public health problem with increasing disease burden affecting nearly 10% of adult population worldwide. We aimed to detect the prevalence of CKD, patients' distribution among CKD stages, and factors associated with having CKD in diabetic patients in Turkey.

Methods: This cross-sectional study, conducted in 2022, included 1591 patients with diabetes (mean age, 63±10 years; female: 65.5%) from the Cappadocia Cohort study. CKD was diagnosed by an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 or

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urinary albumin-to-creatinine ratio (UACR) ≥30 mg/g, which was measured in spot urine samples collected in the morning for three consecutive days.

Results: In this cohort of adult diabetic patients, the prevalence of CKD was 25.1%. More than half of the diabetic patients with CKD (53.8%) had albuminuria without a decrease in eGFR, 28.1% had decreased eGFR without albuminuria, and 18.2% had both albuminuria and decreased eGFR. While the percentage of CKD patients who are female vs. male was 60% vs 40%, CKD prevalence was higher in males (29.2%) than in females (22.9%) (*P=0.007*). Among patients with CKD, only 9.4% were aware that they had CKD. Age, male sex, HbA1c, triglyceride, uric acid, C-reactive protein, and hypertension Grade 1, 2 and 3 were associated with the presence of CKD, with uric acid showing the strongest association.

Conclusions: More than half of our patients with CKD would not have been diagnosed if urinary albumin excretion was not measured. Early detection of CKD by regular screening of diabetic patients using both UACR and eGFR measurements is essential for early diagnosis and prompt treatment to slow down disease progression.

Keywords: Albuminuria, chronic kidney disease, diabetes mellitus, glomerular filtration rate, urinary albumin-to-creatinine ratio

Background

Chronic kidney disease (CKD) is a global public health problem with increasing disease burden affecting nearly 10% of adult population

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worldwide[1], and is estimated to rank fifth among the causes of death in 2040.[2] In general, the prevalence of CKD is higher in low- and middle-income countries.[3] A large population-based national survey on adults (age >18 years) which investigated the CKD prevalence and its relationship with cardiovascular risk factors (The CREDIT study) demonstrated that CKD is also an important public health problem in Turkey with a prevalence rate of 15.7%.[4]

CKD is one of the most common complications of diabetes mellitus (DM) and nearly half of patients with type 2 DM develop CKD in their lifetime with a prevalence ranging from 27% to 84% across countries.[5] Many factors including diet, age, lifestyle, obesity and inflammation or oxidative-stress contribute to the development of CKD.[6] DM is among the leading causes of CKD and end-stage kidney disease (ESKD) worldwide.[7,8] CKD in patients with type 2 DM is associated with increased morbidity and mortality accounting for 10% of deaths in in this patient population.[9]

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Diabetes mellitus is one of the most common preventable diseases in Turkey with a prevalence rate increasing rapidly. The results of the Turkish Diabetes Epidemiology Study-II (TURDEP-II)[10] revealed that the crude prevalence of DM was 16.5% (95% CI: 16.1-17.0) and increased by 90% in 2010 as compared to 1998. According to the International Diabetes Federation Report for Turkey, the age-adjusted prevalence rate of DM was 14.5% in 2021 and has been estimated to increase to 17% in 2045.[11] Given that diabetes is one of the leading causes of CKD, the prevalence of CKD is estimated to increase in line

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with increasing prevalence of DM. In the CREDIT study, the prevalence of DM was 12.7% in the overall study population and higher in patients with CKD vs. non-CKD (26.6% vs. 10.1%).[4] According to the data from the Turkish Society of Nephrology National Registry System, DM ranks first in the etiology of ESKD.[12]

Despite the well-documented role of diabetes in ESKD, to the best of our knowledge, there is no data about the prevalence and distribution of CKD stages along with the risk factors associated with having CKD specifically among diabetic patients in Turkey.

We hypothesized that the prevalence of CKD among patients with type 2 diabetes in Turkey is higher than previously reported and associated with modifiable risk factors. Therefore, the present study aimed to detect the prevalence of CKD, distribution of patients among CKD stages, and factors associated with having CKD in a cohort of diabetic patients retrieved from a cohort of patients with chronic diseases followed for a long time in Turkey.

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Methods

Study population

This cross-sectional cohort study, performed in 2022, comprised a subgroup of diabetic patients from the Cappadocia Cohort study, which is an observational study initiated in 2012 evaluating the prevalence, incidence and risk factors of common chronic diseases including DM in Avanos and Gülşehir towns in Turkey.[13] The rationale for using Cappadocia cohort is the long-term stability and uniqueness of this cohort, which includes dedicated people regularly followed-up. The

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present study did not use old, archived data but current demographic information, patient characteristics, new clinical and laboratory data were obtained from diabetic patients among the cohort. The present study was approved by the Clinical Researches Ethics Committee of Ankara University Faculty of Medicine (dated: 06 June 2022, approval no: 12.540.22) and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consents for their participation in the study and agreed to provide their contact information and to be called at certain times.

The subjects from the Cappadocia cohort (aged ≥18 years) who had documented DM and/or receiving any glucose lowering agent for at least one year were included. Pregnant women and subjects with active infection or malignant disease were excluded.

Study Procedures

All participants were visited at home. A detailed questionnaire form [see Additional file 1 for more details], which was specifically developed for the present study, was used to inquire patients' data. Participants' height and body weight were measured using a body composition analyser (Tanita InnerScan BC-601 Body Analyzer with Stand, Tanita Corp., Tokyo, Japan). Body mass index (BMI; body weight in kilograms divided by square of height in meters [kg/m^2]) was calculated for each participant. Patients with a BMI value of ≥30 kg/m^2 were defined as obese. Patient awareness of their diagnosis of CKD was assessed via direct questioning. Blood pressure was measured in both arms using an automated blood pressure measurement device

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(Omron M3 Automatic Blood Pressure Monitor, Omron Healthcare Co., Ltd. Kyoto, Japan) and repeated for at least three times; the measurements and their arithmetic mean were recorded. A systolic/diastolic blood pressure value of ≥140/90 mmHg and/or previously diagnosed hypertension (HT) and/or using anti-hypertensive medication were considered as presence of HT. Each participant was asked to collect the first urine sample in the morning on three consecutive days and store them at 2-8°C. After three days, the blood of each participant was collected; both blood and urine samples were transferred for laboratory analyses (including complete blood count, biochemical analysis) and stored at 2-8ºC until the time of analysis. Laboratory testing was centralized, HelixLab Sağlık Hizmetleri Araştırma Geliştirme A.Ş. in Ankara, Türkiye was the central laboratory.

The diagnosis of CKD was established based on estimated glomerular filtration rate (eGFR) or urinary albumin-to-creatinine ratio (UACR) (e-GFR <60 mL/min/1.73 m^2 and/or UACR ≥30 mg/g).[14] eGFR was calculated using the 2009 CKD-EPI formula.[15] For UACR, three urine samples obtained in the morning, as was recommended by KDIGO guideline[14], on three consecutive days were used and their arithmetic mean was recorded. Patients were considered to have albuminuria if UACR was between 30 to 300 mg/g in two of the three measurements or >300 mg/g even in a single measurement. Only 3% patients did not collect three urine samples. We did not confirm chronicity (≥3 months), hence prevalence may be overestimated due to incorrect

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inclusion of patients with acute kidney injury or transient proteinuria. However, in such a population study, acute kidney injury is not expected to be high enough to significantly affect the prevalence rate.

Statistical analysis

The statistical analyses were performed using the PASW Statistics for Windows, Version 18.0 (SPSS Inc. Chicago, IL, USA). Descriptive statistics were expressed as number and percentages for categorical variables and as mean, standard deviation, median, minimum and maximum for numerical variables. Parametric and non-parametric statistical analysis methods were used for comparison between two and multiple groups. Risk factors associated with having CKD were identified using logistic regression analysis method. In determining the factors affecting to have DM plus CKD, variables with *P* values <0.200 and/or clinically appropriate variables were selected in univariate analysis. In logistic regression analysis, Backward LR method was used. Hosmer-Lemeshow test was used for testing the goodness-of-fit. Missing data rates varied among variables; however, they were at acceptable levels [see Additional file 2 (Table S1 and S2) for more details]. The maximum missing data rate was 4%-8%. As it was thought that missing data would not significantly affect the analyses, no imputation method was applied. Therefore, each analysis was conducted using the available data for the relevant variable (complete case analysis). The level of statistical significance was set at a *P* value of <0.05.

Results

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The present study included a total of 1591 eligible diabetic patients from the Cappadocia cohort: 1033 patients who were already in the Cappadocia cohort, and 558 patients who were recruited and were added to the Cappadocia cohort by the permission of the local health authorities of Gülşehir & Avanos (Figure 1). The mean age of the patients was 63±10 years, 65.5% were female, 60.9% were obese, 68.9% were hypertensive, and 13.6% were current smokers. The mean BMI was 32.0±5.6 kg/m^2, and the mean duration of DM was 11.0±7.5 years. The mean HbA1c level of the study population was 8.6±2.0%, with 34.1% of the patients having an HbA1c level of >9%. The general and clinical characteristics of the study population are summarized in Table 1.

[Insert Figure 1 here]

[Insert Table 1 here]

Of the patients, 47 used SGLT2 inhibitors, 527 used biguanids, 128 used DPP4 inhibitors and 227 used insulin. Overall, 11.4% of the patients had an eGFR value of <60 mL/min/1.73 m^2, and the UACR was ≥30 mg/g in 18.2%. The distribution of the patients according to eGFR and UACR is summarized in Table 2. Additionally, we classified patients by eGFR and albuminuria categories according to KDIGO 2024 guidelines. A KDIGO heatmap is presented in Figure 2.[14,16] Sensitivity analysis-GFR stages by age and sex is also presented in Additional file 3 (Table S3-S5).

[Insert Table 2 here]

[Insert Figure 2 here]

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CKD was present in 385 (25.1%) of diabetic patients based on eGFR and/or UACR values. The majority of patients had early-stage CKD (Stage 1, 28.1%; Stage 2, 25.7%, and Stage 3A, 32.5%). The distribution of diabetic patients according to the presence and stages of CKD is given in Table 3.

[Insert Table 3 here]

Of the diabetic patients with CKD, 53.8% had albuminuria without a decrease in eGFR, 28.1% had decreased eGFR without albuminuria, and 18.2% had both albuminuria and decreased eGFR (Figure 3).

[Insert Figure 3 here]

The demographic, clinical and laboratory characteristics of diabetic patients in the CKD and non-CKD groups were presented in Table 4. The groups were different in terms of sex, mean age, and age groups, but comparable in terms of mean BMI. Patients in the CKD group were significantly older. Mean HbA1c, glucose, and triglyceride values were significantly higher but HDL-C value was significantly lower in the CKD group.

CKD was more prevalent in the age-group of 60-69 years followed by 70-79 years. While the percentage of CKD patients who are female vs male was 60% vs 40%, CKD prevalence was higher in males (29.2%) than in females (22.9%) ($P = 0.007$). Of the patients with CKD, only 36 (9.4%) were aware that they had CKD.

[Insert Table 4 here]

In order to identify the factors associated with having CKD among diabetic patients, a logistic regression model was established using

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age, sex, duration of DM, obesity, presence of grade 1, 2, 3 HT, use of anti-hypertensive medications, and serum levels of glucose (<100 and ≥100 mg/dL), Hb1Ac (>9.00% and ≤9%), LDL-C (<100 and ≥100 mg/dL), HDL-C (>55 and ≤55 mg/dL for females and >45 and ≤45 mg/dL for males), triglyceride (≥150 and <150 mg/dL), uric acid (>7.3 and ≤7.3 mg for females and >8.5 and ≤8.5 mg/dL for males), and CRP (>5 and ≤5 mg/dL). In this model, the likelihood of having CKD was increased by 1.048 fold with one unit increase in age (95% CI, 1.025-1.071, $P < 0.001$), by 1.99 fold with male sex (95% CI, 1.350-2.924, $P = 0.001$), by 2.04 fold with an HbA1c >9.0% (95% CI, 1.418-2.923; $P < 0.001$), by 1.45 fold with a CRP level >5 mg/L (95% CI, 1.139-2.301; $P = 0.041$), by 1.63 fold with a triglyceride level ≥150 mg/L (95% CI, 1.154-2.285; $P = 0.005$), by 3.49 fold with a uric acid level higher than the upper limit of the normal (ULN) (95% CI, 2.030-5.991; $P < 0.001$), and by 1.47 fold with presence of Grade 1, 2 or 3 HT (95% CI: 1.053-2.049; $P = 0.024$) (Table 5).

[Insert Table 5 here]

Discussion

In this cohort of adult diabetic patients, the prevalence of CKD was 25.1% based on the measurement of urinary albumin excretion on three consecutive days in combination with eGFR. Diabetic patients with CKD were significantly older and had significantly higher mean HbA1c level. Age, HbA1c, triglyceride, uric acid, and CRP levels, and presence of hypertension were significantly associated with the presence of CKD.

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The association between diabetes and having CKD is well-documented with higher prevalence rates of CKD detected in diabetic vs. non-diabetic patients.[4] In a meta-analysis of 19 general population-based studies from 13 European countries, the CKD prevalence among diabetic patients by countries ranged from 15.4% (95% CI, 12.9-17.8) in Netherlands to 41.5% (95% CI, 36.2-46.7) in Germany showing higher but varying prevalence of CKD among diabetic patients in different countries.[18] There are local and national studies on CKD prevalence in Turkey and there are diabetic patients among the patients included in these studies.[19-21] However, this is the first study evaluating the prevalence of CKD, patients' distribution among CKD stages, and factors associated with having CKD specifically among diabetic patients in Turkey, by testing urinary albumin levels on three consecutive days. In the present study, one in four diabetic patients had CKD, which was similar to that reported from Ireland (24.6%), Spain (23.9%) and slightly lower than Norway (28.4%) but significantly lower than Germany (41.5%) and higher than Netherlands (15.4%).[18] However, two other studies from different regions of Spain, in which eGFR in type 2 diabetic patients was estimated by the Modification of Diet in Renal Disease study-(MDRD) equation, reported higher prevalence rates (34.1% and 34.6%, respectively) than that found in the present study and that reported in the above-mentioned meta-analysis from Spain.[22,23] These results have suggested that the prevalence of CKD shows variation among countries and even between

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the studies from the same country probably due to the differences in study population and the methods used to identify CKD.

Urinary albumin excretion is of critical importance to diagnose CKD in diabetic patients as it usually elevates before a decline in eGFR[24], suggesting that albuminuria testing in combination with eGFR measurement is critical in early diagnosis and should be considered while screening diabetic patients for CKD. Moreover, baseline albuminuria as well as increased urinary albumin excretion from baseline has been demonstrated to be associated with progression to ESKD.[25] Although KDIGO recommended the use of both UACR and eGFR in diagnosing CKD, eGFR is more frequently used in the patients[14,16], and urinary albumin measurement remains underutilized.[26,27] In a national cohort study of US adults who were at high-risk for CKD, researchers investigated the extent of albuminuria under-detection from lack of testing and evaluate its association with CKD treatment among patients with diabetics or hypertension.[26] The estimated prevalence of albuminuria in the overall study population was 17.1%, but only 35.2% of cases were detected by UACR testing. Among patients with diabetes and hypertension, the detection rate was higher at 62.1% among diabetic and hypertensive patients. They also reported higher rate of UACR measurement among patients with diabetes compared with those with.[26] Underutilization of albuminuria may be resulting from the fact that blood sample is routinely taken during health examination from almost all patients, which makes the measurement of eGFR easier; however, patients may be usually

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reluctant to collect urine sample, leading to underutilization of albuminuria testing. There may be some other reasons for underutilization of albuminuria which needs to be critically analysed. In the present study, we measured albuminuria in three consecutive spot urine samples to avoid under or over-diagnosis with only one sample. We considered albuminuria if UACR was 30-300 mg/g in at least two of the three measurements, and if UACR was >300 mg/g even in a single measurement. The frequency of CKD based on eGFR alone and albuminuria alone was 11.4% and 18.2%, respectively, whereas it was 25.1% when both eGFR and urinary albumin excretion were considered. Our findings showed that more than half of the patients with CKD (n=207; 53.8%) would not have been diagnosed if urinary albumin excretion was not measured, which emphasizes the importance of detection of albuminuria in diagnosing CKD, particularly in early diagnosis in diabetic patients. Encouraging, even mandating, spot urine albumin-creatinine measurements at least annually (which is the case in diabetes and kidney disease guidelines) and integrating them into national healthcare system monitoring programs would allow the data from this study to be applied to real-world settings. This would allow for much earlier diagnosis of CKD in diabetic patients, who constitute a significant portion of the CKD burden, and the initiation of treatments to slow disease progression at earlier stages. On the other hand, a study from Spain conducted in 2642 diabetic patients from primary care centres found similar prevalence rates of CKD in diabetic patients with albuminuria without low eGFR and in those with reduced

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eGFR without albuminuria (13.5% and 14.7%, respectively).[22] The CaReMe CKD study of 2.4 million possible CKD patients (those who had a CKD diagnosis or one pathological UACR or eGFR value) from 11 countries reported that the rate of UACR measurement shows variation among countries; highest in Israel and lowest in Belgium.[28] These outcomes from various studies support the recommendation that both eGFR and urinary albumin measurement should be considered while diagnosing CKD as their combination provides more accurate diagnosis and higher prediction for progression to ESKD.[14] Furthermore, screening for CKD was found to be especially cost-effective in patients with diabetes and high-risk ethnic groups, but not in populations without diabetes and hypertension in a systematic review that evaluated 21 studies and was published in 2023.[29]

Despite the high prevalence of CKD in our study, the patients' awareness of CKD was very low as 9.4%. In general, patients usually do not know about their disease if they have not been diagnosed yet or informed about their disease after being diagnosed. The fact that additional albuminuria testing in the present study identified new patients with CKD, who have not been diagnosed previously and thus have not been informed, can explain both low awareness and high prevalence rates. Earlier studies have reported a positive correlation between awareness and CKD stages indicating high awareness in patients with advanced-stage CKD.[30,31] In the present study, more than half of the patients with CKD (53.8%) were in stage 1 or 2, which may explain, in part, the low awareness among our study population.

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It is important to identify the factors associated with having CKD to take early measures to prevent onset and/or progression of the disease. In the present study, regression analysis revealed that older age, HbA1c, uric acid, triglyceride, and CRP levels and presence of HT (Grade 1, 2 or 3) were the factors positively associated with presence of CKD ($p<0.05$ for each). A uric acid level of >ULN was strongly associated with presence of CKD (OR=3.487, 95% CI, 2.030-5.991, $P < 0.001$). This finding supports the result of a dose-response meta-analysis of eight cohort studies investigating the association of serum uric acid with CKD, in which linear dose-response analysis demonstrated that each 1 mg/dL increase in serum uric acid concentration increases the risk of CKD by 24% in type 2 diabetic patients with preserved kidney function at baseline.[32] Despite studies reporting higher CKD prevalence among females[33,34], we found that CKD prevalence was higher among male diabetic patients similar to that reported by Sweileh et al.[35] The differences are probably due to the variations between study populations and the methods used, particularly the methods used to identify albuminuria (measurements in one vs. three urine samples in consecutive three days).

The present study has several strengths and limitations/weaknesses. While the large patient population and the use of three albuminuria measurements are among its strengths, several limitations should be acknowledged. The facts that it is a survey study with cross-sectional design yielding no causality and that awareness was self-reported can be considered as limitations. Another limitation was that CKD

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chronicity was not confirmed as the eGFR value was measured only once, although CKD is defined as the presence of a persistent reduction in eGFR for >3 months[14]; therefore, CKD prevalence may have been overestimated due to the potential inclusion of patients with acute kidney injury or transient proteinuria. Thus, the findings should be interpreted cautiously. Furthermore, the generalizability of these findings may be limited, and cannot be generalized to whole Turkish population as the study was a cohort study conducted in a single region of Turkey. In addition, as this study was designed as an observational prevalence study, medication use was not systematically assessed leading to missing data/no data on drug use, preventing its inclusion in the analysis.

Conclusions

The present study demonstrated that one in four diabetic patients had CKD. Since the disease is asymptomatic at early stages, most patients remain undiagnosed and are usually not aware of their disease until advanced stages. These findings highlight a high burden of CKD in Turkish diabetic patients and underscore the importance of early detection and comprehensive management strategies. Measurement of urinary albumin excretion can identify CKD at early stages when the patients have normal eGFR level and accordingly they can be aware of their disease at early stages, which in turn may support timely initiation of kidney protective therapies to prevent them progressing to ESKD. Therefore, both albuminuria and eGFR should be considered while screening diabetic patients for CKD, which would ensure early

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detection of CKD for both planning protective therapies and increasing patients' awareness.

Supplementary information

Additional file 1. Data Report Form

Additional file 2. Missing Data-Imputational analysis

Additional file 3. Sensitivity Analysis-GFR stages by age and sex

Abbreviations

BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
CKD	Chronic Kidney Disease
CRP	C-Reactive Protein
DM	Diabetes Mellitus
DIAKIT	Diabetes and Chronic Kidney Disease in Turkey
eGFR	Estimated Glomerular Filtration Rate
ESKD	End-Stage Kidney Disease
HbA1c	Hemoglobin A1c
HDL-C	High-Density Lipoprotein Cholesterol
HT	Hypertension
IDF	International Diabetes Federation
LDL-C	Low-Density Lipoprotein Cholesterol
MDRD	Modification of Diet in Renal Disease
OR	Odds Ratio

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PASW	Predictive Analytics Software (SPSS)
P	P-value (Statistical Significance)
SPSS	Statistical Package for the Social Sciences
TURDEP-II	Turkish Diabetes Epidemiology Study-II
UACR	Urinary Albumin-to-Creatinine Ratio
ULN	Upper Limit of Normal
VLDL-C	Very Low-Density Lipoprotein Cholesterol

Declarations

Ethics approval and consent to participate

All participants provided written informed consents for their participation in the study and agreed to provide their contact information and to be called at certain times. The study was approved by the Clinical Researches Ethics Committee of Ankara University Faculty of Medicine (dated: 06 June 2022, approval no: 12.540.22) and was conducted in accordance with the Declaration of Helsinki.

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Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

MA, KA, BT, SS, EAB, MSU, OG, SK, and BA have received funding support for the present manuscript from Turkish Society of Nephrology

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Authors' Contributions

The corresponding author (MA) conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results, drafted and revised the manuscript, and approved the final version and has had full access to the data in the study and final responsibility for the decision to submit for publication. Each author has contributed sufficiently to the intellectual content of the submission and has final approval of the version to be published and agreement to be accountable for all aspects of the work

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in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Clinical Trial Number

Not applicable.

Prior Publication

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Figure Legends

Figure 1. Patient flow chart.

Figure 2. KDIGO heatmap. Prognosis of patients by GFR and albuminuria categories according to KDIGO 2024 guidelines. Green cells indicate low risk of disease progression; yellow cells indicate moderately increased risk of disease progression; orange cells indicate; high risk of disease progression; red cells indicate very high risk of disease progression. CKD, chronic kidney disease; GFR, glomerular filtration rate; ACR, albumin-to-creatinine ratio.

Figure 3. Distribution of CKD patients according to eGFR and UACR values. CKD, chronic kidney disease; eGFR; estimated glomerular filtration rate, UACR; urinary albumin/creatinine ratio.

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Table 1. General and clinical characteristics of the study population

	N†	
Sex	1591	
Male		549 (34.5)
Female		1042 (65.5)
Age, years	1591	63±10
Age groups	1591	
18-39 years		21 (1.3)

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40-49 years		113 (7.1)
50-59 years		420 (26.4)
60-69 years		647 (40.7)
70-79 years		336 (21.1)
≥80 years		54 (3.4)
Duration of diabetes, years	1567	11.0±7.5
BMI classification	1521	
Underweight (BMI <18.4 kg/m^2)		1 (0.1)
Normal weight (BMI 18.5-24.9 kg/m^2)		123 (8.1)
Overweight (BMI 25.0-29.9 kg/m^2)		471 (31.0)
Obese		926 (60.9)
Obesity Class I (BMI 30.0-34.9 kg/m^2)		523 (34.4)
Obesity Class II (BMI 35.0-39.9 kg/m^2)		264 (17.4)
Obesity Class III (BMI ≥40.0 kg/m^2)		139 (9.1)
BP classification[17]	1570	
Optimal (<120/<80 mmHg)		191 (12.2)
Normal (120-129/80-84 mmHg)		310 (19.7)
High Normal (130-139/85-89 mmHg)		403 (25.7)

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Grade 1 HT (140-159/90-99 mmHg)		451 (28.7)
Grade 2 HT (160-179/100-109 mmHg)		146 (9.3)
Grade 3 HT (≥180/≥110 mmHg)		69 (4.4)
Hypertension	1574	
Absent		490 (31.1)
Present		1084 (68.9)
Smoking	1567	
Current smoker		213 (13.6)
Former smoker		296 (18.9)
Never smoker		1058 (67.5)
HbA1c, %	1563	
<7.00		428 (27.4)
7.00-8.00		325 (20.8)
8.01-9.00		277 (17.7)
>9.00		533 (34.1)

BMI, body mass index; BP, blood pressure; HT, hypertension.

Data are presented as n (%) or mean±SD, where appropriate.

†N indicates the total number of patients included in the analysis.

Table 2. Distribution of patients according to estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (UACR)

	N†	**n (%)**

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eGFR, mL/min/1.73 m²	1574	
<60		180 (11.4)
≥60		1394 (88.6)
UACR, mg/g	1544	
<30		1263 (81.8)
30-300		213 (13.8)
>300		68 (4.4)

†N indicates the total number of patients included in the analysis. eGFR; estimated glomerular filtration rate; UACR; urinary albumin/creatinine ratio.

Table 3. Distribution of diabetic patients according to the presence and stages of chronic kidney disease (CKD)

	N†	**n (%)**
All patients	1535	
Non-CKD		1150 (74.9)
DM+CKD		385 (25.1)
CKD stages in patients with DM+CKD	385	
Stage 1 (eGFR ≥90.0, UACR ≥30)		108 (28.1)
Stage 2 (eGFR 60.0-89.9, UACR ≥30.0)		99 (25.7)
Stage 3A (eGFR 45.0-59.9)		125 (32.5)
Stage 3B (eGFR 30.0-44.9)		43 (11.2)
Stage 4 (eGFR 15.0-29.9)		5 (1.3)
Stage 5 (eGFR <15.0)		5 (1.3)

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CKD, chronic kidney disease; DM, diabetes mellitus. eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2); UACR, urinary albumin/creatinine ratio (mg/g)

†N indicates the total number of patients included in the analysis.

Table 4. Demographic, clinical and laboratory characteristics of diabetic patients according to the chronic kidney disease (CKD) groups (non-CKD and CKD)

Characteristics	**N†**	**Non-CKD**	**N†**	**CKD**	***P***
Sex‡	1150		385		
Male		373 (32.4)		154 (40.0)	**0.007**
Female		777 (67.6)		231 (60.0)	
Age, years	1150	62±9	385	66±10	**<0.001**
Age groups	1150		385		
18-39 years		16 (1.4)		1 (0.3)	
40-49 years		90 (7.8)		16 (4.2)	
50-59 years		333 (29)		78 (20.3)	**<0.001**
60-69 years		485 (42.2)		146 (37.9)	
70-79 years		201 (17.5)		118 (30.6)	
≥80 years		25 (2.2)		26 (6.8)	
Duration of DM, years	1115	10.4±7.2	363	12.9±8.1	**<0.001**
BMI, kg/m²	1115	31.8±5.6	363	32.5±5.9	0.129

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BMI classification			
Underweight	1 (0.1)	0 (0.0)	
Normal	96 (8.6)	23 (6.3)	
Overweight	337 (30.2)	121 (33.3)	
Obese	681 (61.1)	219 (60.3)	
Obesity Class I	405 (36.3)	106 (29.2)	‡
Obesity Class II	186 (16.7)	68 (18.7)	
Obesity Class III	90 (8.1)	45 (12.4)	
BP	1145	382	
Systolic	136.70±18.74	143.42±21.00	**<0.001**
Diastolic	76.36±10.24	77.27±11.75	0.143
BP classification (S/D)	1145	382	
Optimal (<120/<80 mmHg)	155 (13.5)	31 (8.1)	
Normal (120-129/80-84 mmHg)	236 (20.6)	64 (16.8)	**<0.001**
High Normal (130-139/85-89 mmHg)	317 (27.7)	79 (20.7)	

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Grade 1 HT (140-159/90-99 mmHg)		304 (26.6)		133 (34.8)	
Grade 2 HT (160-179/100-109 mmHg)		97 (8.5)		45 (11.8)	
Grade 3 HT (≥180/≥110 mmHg)		36 (3.1)		30 (7.9)	
Glucose, mg/dL	1150	154.9±63.0	385	174.9±76.7	**<0.001**
HbA1c, %	1142	8.40±2.05	382	8.99±2.26	**<0.001**
Sodium, mEq/L	1145	136.7±4.9	385	136.2±4.6	**0.024**
Chloride, mEq/L	1146	99.5±3.8	384	99.7±5.09	0.887
Phosphorus, mg/dL	1150	3.80±0.56	385	3.80±0.58	0.979
Calcium, mg/dL	1142	9.39±0.53	384	9.36±0.70	0.991
Creatinine, mg/dL	1150	0.73±0.16	385	1.06±0.59	**<0.001**
Uric acid, mg/dL	1150	4.99±1.38	385	5.87±1.62	**<0.001**
Total Cholesterol, mg/dL	1150	191.7±41.5	385	195.2±48.0	0.267
LDL-C, mg/dL	1150	111.2±34.7	384	113.8±40.1	0.302
HDL-C, mg/dL	1150	45.32±11.45	385	43.40±11.08	**0.004**

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VLDL-C, mg/dL	1150	35.17±19.33	385	38.37±21.86	**0.001**
Triglyceride, mg/dL	1150	175.7±94.8	385	190.6±100.1	**0.001**
C-reactive protein, mg/L	1149	4.60±5.55	385	6.55±9.78	**0.002**

CKD, chronic kidney disease; DM, diabetes mellitus; BMI, body mass index; BP, blood pressure; S/D, systolic/diastolic; HT, hypertension; LDL-C, low density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.

Data are presented as n (%) or mean±SD, where appropriate.

†N indicates the total number of patients included in the analysis. ‡ *P* value is not available due to small number of patients.

‡ percentage of CKD cases by sex; please note; prevalence by sex: in males, 154/(154+373) = 29.2%; in females, 231/(231+777) = 22.9%, (*P = 0.007*).

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Table 5. Factors associated with having CKD in diabetic patients

Factors	***P***	**OR**	**95% CI**
Age, (1-year)	<0.001	1.048	1.025-1.071
Male sex	0.001	1.986	1.350-2.924
Diabetes duration	0.080	1.019	0.998-1.041
Hypertension (grade 1, 2 or 3)	0.024	1.469	1.053-2.049
Hb1Ac >9.00%	0.007	1.619	1.139-2.301

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Triglyceride ≥150 mg/dL	0.005	1.624	1.154-2.285
Uric acid >ULN	<0.001	3.487	2.030-5.991
CRP >5 mg/L	0.007	1.617	1.141-2.291

721 OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; ULN,
722 Upper Limit of the Normal (>7.3 mg/dL for females and >8.5 mg/dL for
723 males.

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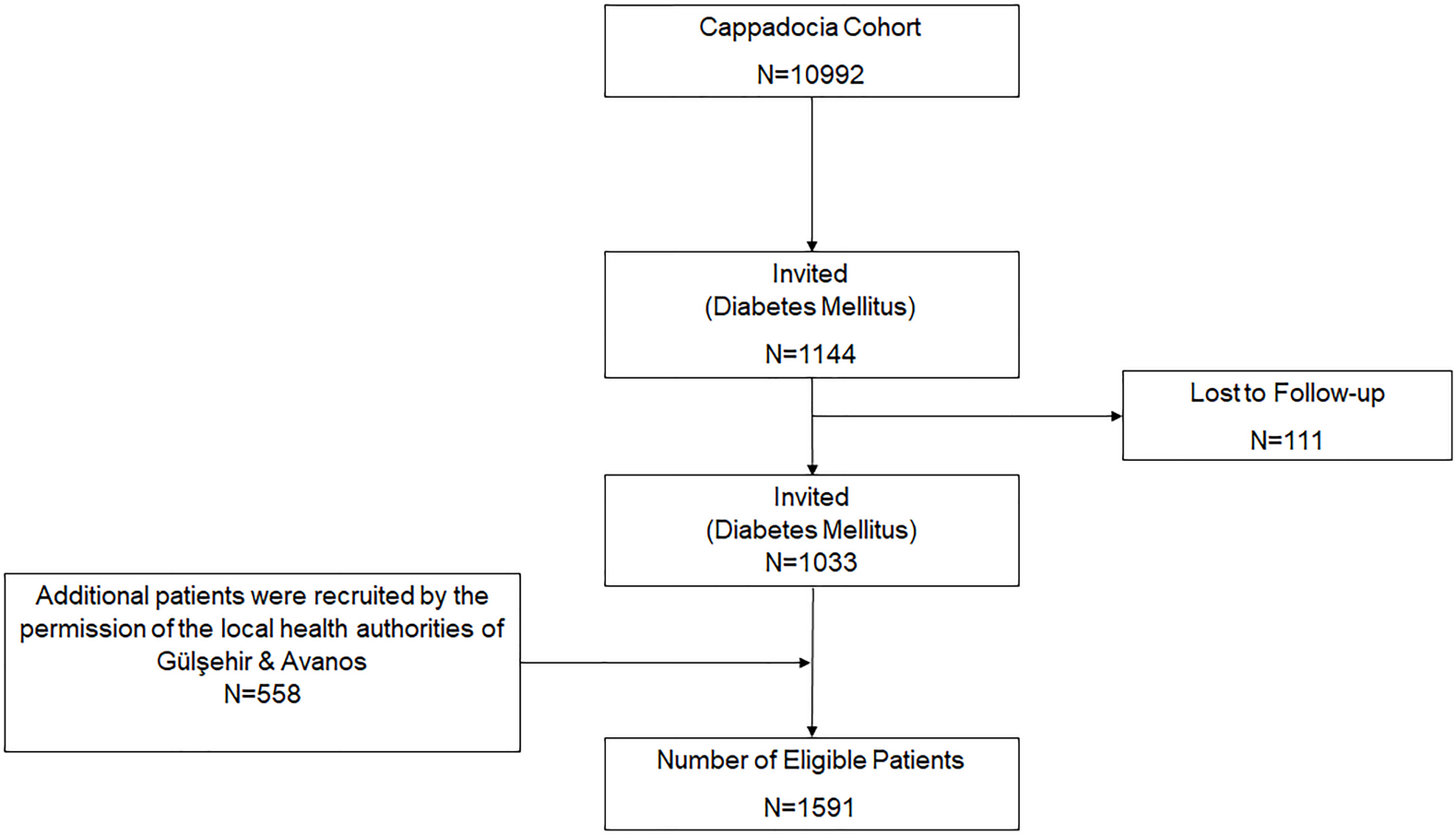
Cappadocia Cohort
N=10992
Invited
(Diabetes Mellitus)
N=1144
Lost to Follow-up
N=111
Invited
(Diabetes Mellitus)
N=1033
Additional patients were recruited by the permission of the local health authorities of Gülşehir & Avanos
N=558
Number of Eligible Patients
N=1591

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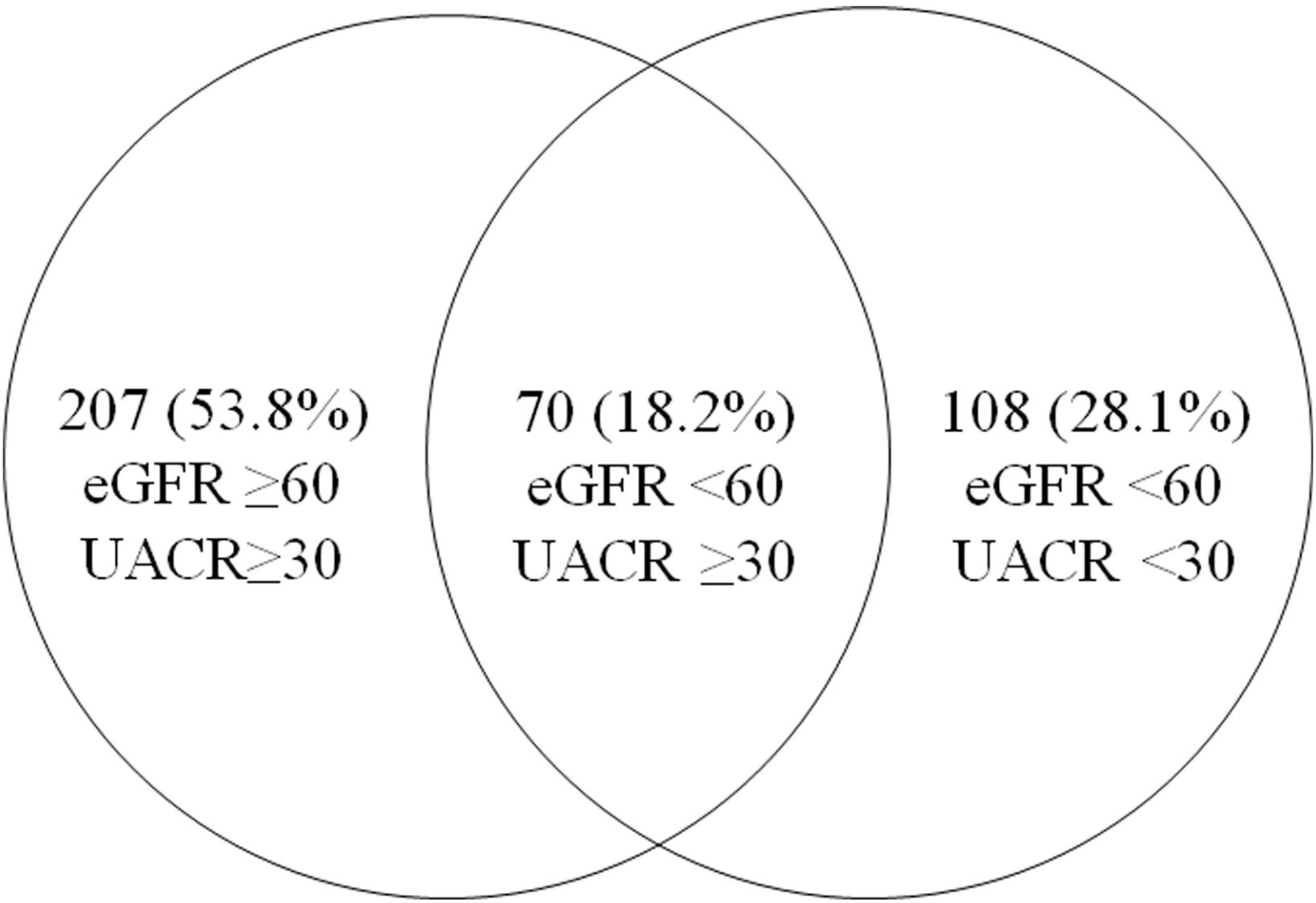
GFR categories (mL/min per 1.73 m ^{2})				Albuminuria (ACR) categories (mg/g)		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30	30-300	>300
	G1	Normal or high	≥90	45.7%	6.1%	1.0%
	G2	Mildly decreased	60-89	29.2%	4.8%	1.6%
	G3a	Mildly to moderately decreased	45-59	5.5%	1.8%	0.8%
	G3b	Moderately to severely decreased	30-44	1.5%	1.0%	0.3%
	G4	Severly decreased	15-29	0.0%	0.1%	0.3%
	G5	Kidney failure	<15	0.0%	0.1%	0.3%


207 (53.8%)
eGFR ≥60
UACR≥30
70 (18.2%)
eGFR <60
UACR ≥30
108 (28.1%)
eGFR <60
UACR <30