Archives of Current Medical Research
Arch Curr Med Res 2023;4(1):31-39

Received: 09 July 2022
Revised: 10 November 2022
Acccepted: 08 December 2022
DOI: 10.47482/acmr.1142775

ORIGINAL ARTICLE

Chronic kidney disease observational cohort study and assessment of baseline characteristics and their relationship with diabetes status and kidney function

Sümeyra Koyuncu[1] **Koray Uludağ**[1] **Tamer Arıkan**[1] **Ali İhsan Günal**[1]

1 Kayseri City Training and Research Hospital, Department of Internal Medicine, Division of Nephrology, Kayseri, Turkey

Abstract

Background: Chronic kidney disease (CKD) may result in end-stage renal disease (ESRD) and undesirable outcomes such as death and dialysis. We carried out an observational cohort study to ascertain risk factors for renal outcomes and all-cause mortality in patients with CKD.

We aimed to conduct a historical cohort study to determine the risk factors affecting renal outcomes, all-cause mortality, and comorbid burden in patients with CKD living in the Central Anatolian region of Turkey.

Methods: A single-center, retrospective, observational cohort study was conducted at the outpatient Nephrology Clinic of Health Sciences University, Kayseri Medical Faculty, from January 1, 2010, to December 31, 2020. We designed the study in patients with stage 3-4 renal failure. Age 18 to 70 years and eGFR 15 to 59 mL/min/1.73 m2 were inclusion criteria. Baseline demographic and laboratory data were documented.

Results: One thousand seventy-three patients with CKD were enrolled in the study. Mean (SD) age was 55.87 (8.83) years, and 53.2% were men. %45.9 and %84.4 had diabetes mellitus and hypertension, respectively. The mean body mass index was 26.73 (3.95) kg/m2. Mean eGFR was 34.14 (10.45) mL/min/1.73 m2 using chronic kidney disease epidemiology collaboration. Median (p25-p75) urinary protein-creatinine ratio was 48.80 [22.40, 89.00] mg/mmol. Older patients had a lower eGFR, and the male gender was more common in stage 3 patients. Stage 4 patients had lower hemoglobin and serum calcium levels. Also, low eGFR was associated with high uric acid levels.

Conclusions: This study, along with future analysis may elucidate the natural history and clinical consequences of CKD. Controllable factors could be understood, and CKD progression and adverse outcomes may be prevented in this way.

Keywords: Chronic Kidney Disease, Diabetes, Hypertension.

Cite this article as: *Koyuncu S, Uludağ K, Arıkan T, Günal Aİ. Chronic kidney disease observational cohort study and assessment of baseline characteristics and their relationship with diabetes status and kidney function. Arch Curr Med Res. 2023;4(1):31-39*

Corresponding Author:
Sumeyra Koyuncu, Kayseri City Training and Research Hospital, Department of Internal Medicine, Division of Nephrology, Kayseri, Turkey
E-Mail: sumeyraozberk@hotmail.com

INTRODUCTION

The incidence of end-stage renal disease (ESRD) has increased worldwide during the past three decades (1). Subjects with ESRD have substantial risks of various complications, such as cardiovascular disease (CVD), bone mineral disorders, infectious diseases, and malignancies (2). On the other hand, the prevalence of chronic kidney disease (CKD) is approximately 10–15% in the adult population living in countries that come from diverse traditions and different backgrounds. CKD may progress to ESRD requiring renal replacement therapy, have a negative impact on quality of life, and have important cost implications for the healthcare system (3). Also, progression rates vary widely in patient subgroups, some progressing rapidly, while others may be relatively stable in kidney function over time (4). Because CKD can be progressive and is associated with adverse consequences, prevention of progression may necessitate early intervention in the clinical ground. Although a decrease in renal function and the presence of proteinuria would have invaluable prognostic significance, the current knowledge, individually from Turkey, regarding the predictors of the progress of CKD is scarce in the literature (5). Especially appropriate care and surveillance in a nephrology clinic could help in minimizing complications and optimizing prognosis in CKD patients (6).

CKD is associated with hypertension, diabetes, proteinuria, obesity, and cardiovascular events, which increase as GFR declines. Also, some studies reported that patients with CKD had a higher death risk than those with ESRD (7,8). Besides traditional risk factors, proteinuria and anemia might play a role in developing CVD in CKD (9,10). In population studies, CVD significantly jeopardizes patients with CKD, increasing their risk with decreasing renal function.[11] However, the number of cohorts is not enough to estimate prognostic consequences precisely in the CKD population. The prevalence of CVD in CKD ranges from 26.8% to 39.1% in various studies (10-12). High cardiovascular mortality results from arteriosclerosis with increased arterial stiffness in CKD patients (13). Patients should be recognized, traced congruously, and treated suitably to overcome challenges for healthcare systems globally. Although significant results were obtained in identifying individuals with CKD from community studies, relatively little has been documented about the features of CKD patients receiving nephrological management.

We conducted a historical cohort study aiming to identify risk factors affecting renal outcomes, all-cause mortality, and comorbid burden in patients with CKD who live in the central Anatolian region of Turkey. We define the baseline demographic and laboratory features of patients forming the cohort, stratified by initial GFR levels and diabetes status in this paper.

MATERIALS AND METHODS

The study design was a single-center, retrospective, observational cohort of individuals observed until death, loss to follow-up, or ESRD. They consisted of recently referred or prevalent patients. It was carried out at the outpatient Nephrology Clinic of Health Sciences University, Kayseri Medical Faculty, from January 1, 2010, to December 31, 2020. Approval was obtained from the Kayseri City Hospital Ethics Committee (Date 09.09.2021, Decision Number 473). The research has attempted to evaluate particularly individuals receiving nephrology care to overcome heterogeneity in management and identify unique risks.

Consecutive patients were included throughout the enrollment period between January 2010 and December 2018. Laboratory databases and medical records were implemented for the enrollment of patients. The inclusion criteria were: 1) age 18–70 years and 2) eGFR 10–59 mL/min/1.73 m^2. Exclusion criteria were: 1) polycystic kidney disease, 2) liver cirrhosis, 3) existing malignancy or chemotherapy over the previous two years, 4) prior organ transplantation or treatment with chronic dialysis, 5) pregnancy, 6) heart failure (New York Heart Association [NYHA] class 3-4), 7) solitary kidney, 8) immunosuppressive treatment, 9) active infection/inflammatory disorders. A total of 14347 patients were screened for eligibility. The number of excluded patients was thirteen thousand and two hundred seventy-four, arising from lack of information regarding their previous medical records (n=5481), eGFR > 59 mL/min/1.73 m^2 (n=4238), age > 70 years (n =3316), or the existence of exclusion criteria (n = 239), resulting in a final cohort of 1073 subjects.

The endpoints were CKD progression as measured with a decline in eGFR and all-cause death. The MDRD and CKD-EPI creatinine equation were used to calculate the eGFR regularly. A composite renal event was attributed to a reduction in eGFR of more than 50% from baseline, a doubling of serum creatinine, or the onset of ESRD. Registrations about events were screened throughout the study period from medical records. Information on the time of death and the precise reasons for dying were gathered.

Baseline assessment includes demographic data, family and medical history, pre-existing comorbidities, medications, blood pressure, and body mass index (BMI). Laboratory data were documented and maintained regularly for assessment of serum creatinine, whole blood count, and other biochemical parameters such as lipid profile, uric acid, HbA1c, high-sensitivity C-reactive protein (CRP), calcium, phosphorus, intact parathyroid hormone (PTH), serum albumin, urine protein, and urine creatinine. After a 5-minute waiting, the arterial tension is checked using a sphygmomanometer in the outpatient department. If there were systolic blood pressure (BP) > 140 mmHg or diastolic BP > 90 mmHg, or drug use, it was accepted as a hypertension diagnosis. Diabetes was described as fasting glucose >126 mg/dl, random glucose > 200 mg/dl, or antidiabetic use. Dyslipidemia was defined as total serum cholesterol > 200 mg/dL, or triglycerides > 150 mg/dL, or high-density lipoprotein (HDL) cholesterol < 40 mg/dL in men or < 48 mg/dL in females, or low-density lipoprotein (LDL) cholesterol > 100 mg/dL, or lipid-lowering drug use.

Baseline values were reported as means (SD) or medians (p25-p75) for continuous variables, whereas categorical variables were represented as numbers and percentages. Baseline characteristics were compared across groups using t-tests or chi-square testing, as appropriate. If the continuous variable's distribution did not correspond to the normal distribution, the Kruskal-Wallis rank-sum test was employed. The percentages of missing values for variables were as follows: BMI (2.9), CRP (2.3), HA1c (5.1), and BP (17.8). Other variables having less than 2% missingness were albumin, phosphorus, uric acid, urine protein-creatinine ratio (UPCR), and PTH. The chained equations method using the MICE package in R was applied for imputing missing data values. A two-sided P value less than 0.05 was considered significant.

RESULTS

Baseline demographic and clinical characteristics were evaluated in one thousand seventy-three patients with CKD. Mean (standard deviation [SD]) age was 55.87 (8.83) years, and 53.2% were men. The proportion of diabetes mellitus (DM) was %45.9, and %84.4 of subjects had a diagnosis of hypertension. Mean systolic and diastolic BPs were measured as 135.09 (24.50) and 81.18 (12.61) mmHg, respectively. The BMI was calculated to be 26.73 (3.95) kg/m^2. 18.9% of the total cohort had a history of coronary artery disease (CAD). Congestive heart failure (CHF) was noted in ninety-seven patients. 5.1% and 6.7% of the subjects had peripheral vascular disease (PAD) and cerebrovascular disease (CeVD), respectively. Mean eGFRs were 32.99 (10.03) and 34.14 (10.45) mL/min/1.73 m^2 using MDRD formula and chronic kidney disease epidemiology collaboration (CKD-EPI) creatinine equation, respectively. Mean hemoglobin and median [25%-75% percentiles] CRP levels were 12.41 (2.02) g/dl and 3.20 [1.50, 6.40] mg/L, respectively. The mean calcium, phosphorus, and the median intact PTH level were 9.31 (0.64), 4.46 (0.95) mg/dl, and 129.30 [72.00, 214.20] μg/L. Serum albumin level was 4.09 (0.50) g/dL, and serum uric acid level was 7.39 (1.65) mg/dl. Median UPCR was 48.80 [22.40, 89.00] mg/mmol. Plasma lipid levels were given entirely in Table 1. The proportion of patients taking an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker was 57.5%. The percentage of patients on vitamin D supplementation and phosphate binders were 24.6% and 16.5%, respectively. 62.8%, 45.7%, and 38% of subjects were using diuretics, Ca channel blockers, and B-Blockers, respectively. 32.6% of patients were under dyslipidemia treatment with lipid-lowering drugs (Table 1).

Table 1. Baseline characteristics of the cohort by CKD stage

	Overall	Stage 3	Stage 4	p-value
n	1073	688	385	
Age, years	55.87 (8.83)	54.87 (8.86)	57.65 (8.50)	<0.001
Male, n (%)	571 (53.2)	441 (64.1)	130 (33.8)	<0.001
BMI, kg/m^2	26.73 (3.95)	26.91 (4.04)	26.43 (3.77)	0.055
Diabetes mellitus, n (%)	492 (45.9)	311 (45.2)	181 (47.0)	0.612
Hypertension, n (%)	906 (84.4)	588 (85.5)	318 (82.6)	0.248
Systolic blood pressure, mmHg	135.09 (24.50)	134.11 (24.10)	136.85 (25.13)	0.079
Diastolic blood pressure, mmHg	81.18 (12.61)	80.75 (12.59)	81.96 (12.63)	0.133
Coronary artery disease, n (%)	203 (18.9)	132 (19.2)	71 (18.4)	0.828
Congestive heart failure, n (%)	97 (9.0)	63 (9.2)	34 (8.8)	0.946
Cerebrovascular disease, n (%)	72 (6.7)	41 (6.0)	31 (8.1)	0.235
Peripheral vascular disease, n (%)	55 (5.1)	40 (5.8)	15 (3.9)	0.222
Serum creatinine, mg/dl	2.01 (0.49)	1.75 (0.29)	2.47 (0.42)	<0.001
eGFR (MDRD), ml/min/1.73 m^2	32.99 (10.03)	38.14 (7.60)	23.79 (6.70)	<0.001
eGFR (CKD-EPI), ml/min/1.73 m^2	34.14 (10.45)	40.11 (7.93)	23.47 (3.83)	<0.001
White blood cell, X10^3/μL	8.24 (1.84)	8.24 (1.84)	8.25 (1.84)	0.928
Hemoglobin, g/dl	12.41 (2.02)	12.63 (1.97)	12.01 (2.03)	<0.001
CRP, mg/L	3.20 [1.50, 6.40]	3.35 [1.50, 6.40]	3.00 [1.50, 6.30]	0.530
Calcium, mg/dl	9.31 (0.64)	9.34 (0.63)	9.25 (0.66)	0.026
Phosphorus, mg/dL	4.46 (0.95)	4.42 (0.95)	4.52 (0.95)	0.081
PTH, μg/L	129.30 [72.00, 214.20]	123.55 [70.50, 213.85]	140.60 [73.10, 215.10]	0.137
Serum albumin, g/dl	4.09 (0.50)	4.09 (0.50)	4.09 (0.51)	0.988
UPCR, mg/mmol	48.80 [22.40, 89.00]	46.45 [21.48, 88.32]	54.20 [24.50, 93.70]	0.223
Uric acid, mg/dl	7.39 (1.65)	7.28 (1.61)	7.58 (1.69)	0.004
Total cholesterol, mg/dl	209.79 (34.21)	207.38 (34.25)	214.09 (33.76)	0.002
LDL, mg/dl	117.87 (30.47)	116.57 (30.73)	120.18 (29.91)	0.063
HDL, mg/dl	49.08 (10.53)	49.62 (10.63)	48.12 (10.29)	0.025
Triglyceride, mg/dl	194.86 [132.22, 273.95]	187.92 [124.98, 263.79]	206.87 [144.64, 285.88]	0.002
HbA1c, %	6.91 (1.74)	6.92 (1.77)	6.88 (1.68)	0.734
ACEI/ARB, n (%)	617 (57.5)	375 (54.5)	242 (62.9)	0.010
Diuretic use	674 (62.8)	426 (61.9)	248 (64.4)	0.456
CCB, n (%)	490 (45.7)	312 (45.3)	178 (46.2)	0.830
Beta blocker, n (%)	408 (38.0)	264 (38.4)	144 (37.4)	0.804
Lipid-lowering drug, n (%)	350 (32.6)	238 (34.6)	112 (29.1)	0.076
Antiplatelet agent, n (%)	380 (35.4)	241 (35.0)	139 (36.1)	0.774
Phosphorus-lowering drug, n (%)	177 (16.5)	106 (15.4)	71 (18.4)	0.231
Uric acid-lowering drug, n (%)	562 (52.4)	340 (49.4)	222 (57.7)	0.011
Vitamin D use, n (%)	264 (24.6)	166 (24.1)	98 (25.5)	0.682

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index eGFR, estimated GFR; PTH, intact parathyroid hormone; CRP, C-reactive protein; LDL, low-density lipoprotein; HDL high-density lipoprotein; MDRD, Modification of Diet in Renal Disease; CKD-EPI, chronic kidney disease epidemiology collaboration; CKD, chronic kidney disease; UPCR, urinary protein-creatinine ratio; CCB, calcium channel blocker.

The proportions of subjects with stage 3-4 CKD were 64% and 36%, respectively. The baseline features were summarized by CKD stages in Table 1. Patients with a lower eGFR were older than those with a higher eGFR, and the male gender predominated among stage 3 patients. Stage 3 patients were more likely to have a higher BMI, but the difference was marginal for statistical significance. Prevalence of DM and hypertension were not significantly different between CKD Stage 3 and 4 patients. Also, stage 3 and 4 CKD patients had no noteworthy diversities in the frequency of cardiovascular diseases such as CAD, CHF, CeVD, and PAD.

The hemoglobin levels were lower in stage 4 patients compared to stage 3 patients. Serum calcium decreased, and serum phosphate and PTH increased with decreasing eGFR, although the last two did not reach statistical significance. Uric acid levels increased in proportion to eGFR decline. High-density lipoprotein (HDL) cholesterol levels were higher in stage 3 patients, while higher total cholesterol and triglycerides were seen in stage 4 patients. More patients were taking RAS inhibitors and uric acid-lowering drugs in stage 4 CKD. The percentage of patients using other agents was similar in terms of statistical significance between the two groups.

There were also some disparities between individuals with and without diabetes (Table 2). Diabetic patients were more likely to be male, hypertensive, tended to have a higher BMI, systolic BP, and diastolic BP than non-diabetics. Patients with diabetes were slightly older than those without diabetes, but the trend did not achieve statistical significance. CAD, CHF, CeVD, and PAD were more common in diabetic patients. They also had high serum albumin, uric acid, and UPCR levels as compared with non-diabetic patients. While HDL levels were lower in patients with diabetes, LDL levels were higher than in those without diabetes. ACEI/ARB, diuretic, and other anti-hypertensive agent use were frequent in diabetic patients. This patient group was using anti-hyperlipidemic, uric acid-lowering drugs, and antiplatelet agents more commonly than those without diabetes.

DISCUSSION

The study was conducted in the CKD population at stages 3-4 living in the central Anatolian region. It may give critical health data regarding initial comorbid conditions, CKD course, varied sequelae, including bone-mineral problems, anemia, and cardiovascular issues. Different laboratory and clinical indicators would also be obtained concerning potential risks for negative consequences through this study. The nephrologists were treating subjects, thereby providing better patient care. Furthermore, the study's longitudinal design could give data-driven models capable of identifying patients at high risk for CKD progression and clarifying numerous associations for clinical practice and cardiovascular disease consequences. In this paper, we provide the beginning features of the cohort and highlight the main disparities comparing stage 3 and 4 CKD patients. We also analyzed differences between patients with and without diabetes. The goal of our study was to create a similar cohort for the other studies carried out in the past, most of which looked at risk variables for CKD progression and the development of cardiovascular illnesses. The data retrieved from the study could supplement and expand the information obtained from prior research (14-18).

When the baseline characteristics of the patients were compared to those of the CRIC study, our patients were younger and had higher creatinine levels. The proportion of male patients in our study was similar to that of the CRIC research, but it was less than in Asian cohort studies (2,19). Diabetes was found in 45.9 percent of our subjects, comparable to that of CRIC participants. On the other hand, the CKD-JAC study had superior glycemic control in diabetics than the CRIC study, while the mean A1C was 8.5%, relatively poorer in our cohort. We can attribute this situation to the diet incompatibility of our patients to a large extent. In addition, non-compliance with treatment may be another factor. The vast majority of the individuals (84.4%) had hypertension diagnoses in our study. Data from the National Health and Nutrition Examination Survey indicated that the hypertension prevalence was 29.0% during 2015–2016 in the US (20). 34.2 million people have diabetes (10.5% of the US population) according

Table 2. Baseline demographic and clinical characteristics of the cohort according to diabetes status

	No	Yes	p-value
n	581	492	
Age, years	55.43 (8.78)	56.38 (8.87)	0.077
Male, n (%)	280 (48.2)	291 (59.1)	<0.001
BMI, kg/m^2	26.38 (3.85)	27.16 (4.02)	0.001
Hypertension, n (%)	478 (82.3)	428 (87.0)	0.041
Systolic blood pressure, mmHg	127.84 (22.20)	143.66 (24.35)	<0.001
Diastolic blood pressure, mmHg	76.19 (10.96)	87.08 (11.88)	<0.001
Coronary artery disease, n (%)	93 (16.0)	110 (22.4)	0.010
Congestive heart failure, n (%)	33 (5.7)	64 (13.0)	<0.001
Cerebrovascular disease, n (%)	26 (4.5)	46 (9.3)	0.002
Peripheral vascular disease, n (%)	22 (3.8)	33 (6.7)	0.043
Serum creatinine, mg/dl	1.98 (0.48)	2.04 (0.50)	0.074
eGFR (MDRD), ml/min/1.73 m^2	33.10 (10.08)	32.86 (9.98)	0.693
eGFR (CKD-EPI), ml/min/1.73 m^2	34.18 (10.44)	34.08 (10.48)	0.873
White blood cell, X10^3/μL	8.17 (1.83)	8.32 (1.85)	0.170
Hemoglobin, g/dl	12.42 (2.09)	12.40 (1.93)	0.896
CRP, mg/L	3.00 [1.30, 6.30]	3.55 [1.60, 6.50]	0.073
Calcium, mg/dl	9.29 (0.63)	9.33 (0.65)	0.241
Phosphorus, mg/dL	4.45 (0.96)	4.46 (0.95)	0.863
PTH, μg/L	134.60 [75.00, 210.70]	123.20 [68.15, 216.95]	0.423
Serum albumin, g/dl	4.06 (0.50)	4.13 (0.51)	0.012
UPCR, mg/mmol	44.60 [18.30, 83.00]	54.85 [26.92, 99.00]	<0.001
Uric acid, mg/dl	7.23 (1.61)	7.58 (1.67)	<0.001
Total cholesterol, mg/dl	206.67 (33.10)	213.47 (35.15)	0.001
LDL, mg/dl	114.95 (30.00)	121.31 (30.70)	0.001
HDL, mg/dl	50.00 (10.52)	48.00 (10.46)	0.002
Triglyceride, mg/dl	194.17 [130.14, 270.83]	198.04 [134.00, 276.33]	0.233
HbA1c, %	5.52 (0.38)	8.54 (1.23)	<0.001
ACEI/ARB, n (%)	297 (51.1)	320 (65.0)	<0.001
Diuretic use	341 (58.7)	333 (67.7)	0.003
CCB, n (%)	225 (38.7)	265 (53.9)	<0.001
Beta blocker, n (%)	199 (34.3)	209 (42.5)	0.007
Lipid-lowering drug, n (%)	169 (29.1)	181 (36.8)	0.009
Antiplatelet agent, n (%)	174 (29.9)	206 (41.9)	<0.001
Phosphorus-lowering drug, n (%)	87 (15.0)	90 (18.3)	0.169
Uric acid-lowering drug, n (%)	277 (47.7)	285 (57.9)	0.001
Vitamin D use, n (%)	140 (24.1)	124 (25.2)	0.728

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index eGFR, estimated GFR; PTH, intact parathyroid hormone; CRP, C-reactive protein; LDL, low-density lipoprotein; HDL high-density lipoprotein; MDRD, Modification of Diet in Renal Disease; CKD-EPI, chronic kidney disease epidemiology collaboration; CKD, chronic kidney disease; UPCR, urinary protein-creatinine ratio; CCB, calcium channel blocker

to the National Diabetes Statistics Report (21). As one would expect, these two diagnoses were more common in CKD patients than described in the reports.

Obesity is widely established to be one of the predictors for CKD progression (22). The CRIC research participants seem to be more overweight than our participants. The mean BMI was 32.1 kg/m^2 in the CRIC and 23.5 kg/m^2 in the CKD-JAC study. In comparison, it was 26.7 kg/m^2 in our cohort. In addition, we found a significant difference in overweight between diabetic and non-diabetic subjects. Ethnicity is one of the differences in baseline variables between our study and other cohort studies. Our cohort consists of Turkish individuals, whereas the CRIC cohort consisted of 45 percent white, 46 percent black, and 5 percent Hispanic people. There is little understanding of the relationship between ethnicity and CKD. More investigation is thus needed to elucidate this relationship.

CKD patients have an increased rate of developing cardiovascular disease (23). It is envisaged that our cohort study may provide explanations for this kind of issue. Diabetic patients had a higher CVD prevalence than those without diabetes in our cohort, as in the CRIC cohort. These outcomes support clinical study observations signifying the CVD load commences early in the ESRD population having diabetes in the duration of CKD (24). The total frequency of CVD (32%) seems to be higher in our cohort than in Mediterranean cohort of patients followed by nephrologists (29.7 percent).[25] In contrast to prior findings (25), our study revealed that a decreased GFR was not associated with a significant incidence of cardiovascular illness. The risk of developing CVD in patients with CKD exceeds the hazard of reaching end-stage renal disease(26). In other words, it can be interpreted as if the CVD frequency is relatively decreasing or there is no difference due to the increased mortality risk as the CKD progresses.

Mean blood pressure levels were higher than the prescribed limit(27). Similarly, other CKD cohorts previously documented unsatisfactory BP levels (28), and thus the results in our cohort underline the importance of good BP treatment in CKD as a primary intervention. CKD stage 3 and 4 patients did not have considerable variability in BP levels. While there is much disagreement, most specialists do not believe that a blood pressure target of 130/80 mmHg is a life-saving or kidney preventive measure in patients with CKD (29).

Anemia was more common and severe in CKD stage 4 individuals than in CKD stage 3 patients. As predicted, the hemoglobin levels decreased as the eGFR increased. Phosphate-lowering drug use was low in the total study population, and there was no difference between the two-stage. Therefore, it may be expected that serum phosphorus increases with decreasing eGFR. Vitamin D and the use of its analogs were also at low levels, suggesting that they should be used more commonly in treating hyperparathyroidism.

The proteinuria in our study was higher than in the CRIC study, perhaps due to the strict control of BP in the CRIC study. It was also verified in a study that rigorous blood pressure control was associated with better control of proteinuria (30). The amount of proteinuria was more prominent in stage 4 CKD than in stage 3 CKD, but it did not reach statistical significance. As expected, patients with diabetes were more likely to have higher proteinuria.

Possible biases or residual confounding might have restricted inferences about causation because of the retrospective observational design. Second, the number of young diabetics was not sufficient in this study, similar to CRIC. Third, some forms of renal diseases were underrepresented in the cohort, like glomerulonephritis. Fourth, comorbidities derived from chart review may have integral limitations in terms of accuracy. Finally, because this study exclusively covers Turkish patients, the results cannot be generalized to other ethnic groups. Also, study subjects may differ from the CKD population in the community because of patients referred to nephrology clinics.

In conclusion, this CKD cohort study would shed light on the natural history and clinical consequences of CKD in the Turkish population. In addition, controllable variables can be found through the data obtained from the study and the renal replacement needs of patients can be reduced by using them to prevent CKD development and poor outcomes.

Declarations

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

This study was approved by the Division of Nephrology, Department of Internal Medicine, Kayseri City Training and Research Hospital, Kayseri (Date 09.09.2021, Decision Number 473)

REFERENCES

1. Bikbov B, Purcell C, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2020;395(10225):709-733.
2. Imai E, Matsuo S, Makino H, Watanabe T, Akizawa T, Nitta K, et al. Chronic Kidney Disease Japan Cohort (CKD-JAC) study: design and methods. Hypertens Res. 2008;31(6):1101-7.
3. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. Lancet. 2013;382(9889):339-52.
4. Li L, Astor BC, Lewis J, Hu B, Appel LJ, Lipkowitz MS, Tet al. Longitudinal progression trajectory of GFR among patients with CKD. Am J Kidney Dis. 2012;59(4):504-12.
5. Astor BC, Matsushita K, Gansevoort RT, van der Velde M, Woodward M, Levey AS, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney Int. 2011;79(12):1331-40.
6. Rucker D, Hemmelgarn BR, Lin M, Manns BJ, Klarenbach SW, Ayyalasomayajula B, et al. Quality of care and mortality are worse in chronic kidney disease patients living in remote areas. Kidney Int. 2011;79(2):210-7.
7. Weiner DE, Krassilnikova M, Tighiouart H, Salem DN, Levey AS, Sarnak MJ. CKD classification based on estimated GFR over three years and subsequent cardiac and mortality outcomes: a cohort study. BMC Nephrol. 2009;10:26.
8. Abboud H and Henrich WL. Clinical practice. Stage IV chronic kidney disease. N Engl J Med. 2010; 362: 56-65
9. Drury PL, Ting R, Zannino D, Ehnholm C, Flack J, Whiting M, et al. Estimated glomerular filtration rate and albuminuria are independent predictors of cardiovascular events and death in type 2 diabetes mellitus: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. Diabetologia. 2011;54(1):32-43.
10. Iimori S, Naito S, Noda Y, Nishida H, Kihira H, Yui N, et al. Anaemia management and mortality risk in newly visiting patients with chronic kidney disease in Japan: The CKD-ROUTE study. Nephrology (Carlton). 2015;20(9):601-8.
11. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351(13):1296-305.
12. Shah R, Matthews GJ, Shah RY, McLaughlin C, Chen J, Wolman M, et al. Serum Fractalkine (CX3CL1) and Cardiovascular Outcomes and Diabetes: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study. Am J Kidney Dis. 2015;66(2):266-73.
13. Shoji T, Emoto M, Shinohara K, Kakiya R, Tsujimoto Y, Kishimoto H, et al. Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. J Am Soc Nephrol. 2001;12(10):2117-2124.
14. Lash JP, Go AS, Appel LJ, He J, Ojo A, Rahman M, et al. Chronic Renal Insufficiency Cohort (CRIC) Study: baseline characteristics and associations with kidney function. Clin J Am Soc Nephrol. 2009;4(8):1302-11.
15. Imai E, Matsuo S, Makino H, Watanabe T, Akizawa T, Nitta K, et al. Chronic Kidney Disease Japan Cohort study: baseline characteristics and factors associated with causative diseases and renal function. Clin Exp Nephrol. 2010;14(6):558-70.
16. Martínez-Castelao A, Górriz JL, Portolés JM, De Alvaro F, Cases A, Luño J, et al. Baseline characteristics of patients with chronic kidney disease stage 3 and stage 4 in Spain: the MERENA observational cohort study. BMC Nephrol. 2011;12:53.
17. Titze S, Schmid M, Köttgen A, Busch M, Floege J, Wanner C, et al. Disease burden and risk profile in referred patients with moderate chronic kidney disease: composition of the German Chronic Kidney Disease (GCKD) cohort. Nephrol Dial Transplant. 2015;30(3):441-51.
18. Kang E, Han M, Kim H, Park SK, Lee J, Hyun YY, et al. Baseline General Characteristics of the Korean Chronic Kidney Disease: Report from the KoreaN Cohort Study for Outcomes in Patients With Chronic Kidney Disease (KNOW-CKD). J Korean Med Sci. 2017;32(2):221-230.
19. Imai E, Horio M, Iseki K, Yamagata K, Watanabe T, Hara S, et al. Prevalence of chronic kidney disease (CKD) in the Japanese general population predicted by the MDRD equation modified by a Japanese coefficient. Clin Exp Nephrol. 2007;11(2):156-163.
20. Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D. Hypertension Prevalence and Control Among Adults: United States, 2015-2016. NCHS Data Brief. 2017;(289):1-8.
21. National Diabetes Statistics Report, 2020, Centers for Disease Control and Prevention, Atlanta, GA:Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services, 2020.
22. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. Ann Intern Med. 2006;144(1):21-8.
23. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Hypertension. 2003;42(5):1050-65.
24. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001;345(12):861-9.

25. De Nicola L, Minutolo R, Chiodini P, Zoccali C, Castellino P, Donadio C, et al. Global approach to cardiovascular risk in chronic kidney disease: reality and opportunities for intervention. Kidney Int. 2006;69(3):538-45.

26. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease: Pathophysiological Insights and Therapeutic Options. Circulation. 2021;143(11):1157-1172.

27. Levey AS, Rocco MV, Anderson S, Andreoli SP, Bailie GR, Bakris GL, et al. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis. 2004;43(5 Suppl 1):S1-290.

28. Duru OK, Li S, Jurkovitz C, Bakris G, Brown W, Chen SC, et al. Race and sex differences in hypertension control in CKD: results from the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2008;51(2):192-8.

29. Agarwal R. Debate: CON Position. People with chronic kidney disease should have a blood pressure lower than 130/80 mm Hg. Am J Nephrol. 2010;32(4):374-6; discussion 377-8.

30. Appel LJ, Wright JT Jr, Greene T, Agodoa LY, Astor BC, Bakris GL, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. N Engl J Med. 2010;363(10):918-29.