Risk factors associated with chronic kidney disease progression: Long-term retrospective analysis from Qatar

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ABSTRACT

Introduction: The risk factors influencing the natural course of chronic kidney disease (CKD) are complex and heterogeneous. Recognizing the factors associated with CKD progression can enable the identification of high-risk patients for more intensive treatment.

Patients and methods: A retrospective evaluation of CKD patients was performed under follow-up between January 1, 2001 and December 31, 2016 at a tertiary health care center.

Results: Among 5370 screened patients, 1020 patients with complete data were included in the analysis. The median follow-up period for the studied patients was 9.3 years. Based on the analysis, 120 (11.8%) patients had reached end-stage kidney disease “ESKD” or death. The study revealed that the risk factors associated with reaching ESKD and/or death using Kaplan–Meier survival curve and log rank test included higher hemoglobin A1c among diabetic patients, higher grade of proteinuria, and non use of renin-angiotensin system blockers. The patients with CKD progression constituted 77.2% of all CKD patients. The study findings indicated that older age, Arab ethnicity, smoking habit, diabetes mellitus and hypertension (presumed as original kidney diseases) are among the significant risk factors associated with a further decline of the estimated glomerular filtration rate (eGFR) and further CKD progression.

Conclusion: This study summarized the demographic and clinical risk factors associated with CKD progression and patients’ outcomes among a unique and heterogeneous population in the state of Qatar. Intensive treatment of modifiable risk factors could be of value in
halting the progression of CKD. However, prospective studies are warranted to confirm our findings.

Keywords: chronic kidney disease, progression risk factors, end-stage kidney disease

INTRODUCTION

The global prevalence of chronic kidney disease (CKD) has been estimated by the Global Burden of Disease Study 2017 as 9.1% of the world population (697.5 million cases). Moreover, CKD resulted in 1.2 million deaths and was the 10th leading cause of death worldwide in 2020.1

The risk factors influencing the natural course of CKD are complex and heterogeneous and there are only a few systematic studies that have focused on this issue.2 The estimated risk factors of CKD progression causing morbidity and mortality have been studied across different ethnic and racial populations, showing important differences between them.3 In the United States, for instance, the rate of renal replacement therapy (RRT) initiation for end-stage kidney disease (ESKD) is disproportionately higher for ethnic minority groups (such as African-American, Hispanic, and Native Americans) when compared to that for Caucasians, despite the similar prevalence for early stages of CKD.4,5

The economic development experienced in Qatar has been associated with inappropriate dietary and lifestyle patterns that led to increased rates of obesity and chronic non communicable diseases. Furthermore, this situation can be associated with a surge in international migration of workers from developing countries, as evidenced by the annual population growth of 18.9% from 2008 onward.6

The present work aimed to study the distribution of CKD in Qatar’s heterogeneous population that has been followed in nephrology clinics to examine the prevalence of risk factors associated with CKD progression as well as to describe the relevant clinical outcomes (such as death or end-stage kidney disease) over a long observation period.

PATIENTS AND METHODS

A retrospective evaluation of CKD patients under follow-up at a tertiary health center (Hamad General Hospital) was conducted. In this study, we reviewed the electronic medical records of all patients visiting the nephrology clinics between January 1, 2001 and December 31, 2016. The estimated glomerular filtration rate (eGFR) for each patient was calculated from the serum creatinine level using the CKD-Epidemiology Collaboration equation.7 Patients diagnosed with CKD of different stages on at least 2 occasions and lasting > 3 months were included. All patients with albuminuria (an albumin-to-creatinine ratio > 3 mg/mmol) or equivalent (protein-to-creatinine ration > 15 mg/mmol or urine protein reagent strip 1+ or more), on at least 2 occasions, lasting > 3 months, were also included. All outpatient eGFR measurements until the end of the study were utilized, excluding the laboratory measurements associated with any hospital admission.

The identified CKD patients were screened for demographic data, including their age, gender, nationality, and ethnicity. Body mass index (BMI) was calculated for each patient as the body weight measured in kilograms, divided by the height squared meter. The date of diagnosis of CKD and eGFR at the time of diagnosis was recorded. Follow-up renal function until the last follow-up visit was performed yearly, and it included yearly registered values of eGFR for any individual patient plus the degree of albuminuria/proteinuria (expressed as urinary albumin or protein/creatinine ratios in mg/mmol). Further categorization of the eGFR and albuminuria grades for each value/year/patient was conducted as per the Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (KDIGO) classification.8

The cause of CKD for each patient was retrieved from the patient’s file as per the primary nephrologist assessment. In addition, the comorbid conditions, including diabetes mellitus, diabetes complications, hypertension, dyslipidemia, cardiovascular diseases, cerebrovascular disease, or peripheral vascular disease, were also assessed.

Inclusion criteria

– Age ≥ 18 years at the time of inclusion.
– All patients diagnosed with CKD according to the KDIGO classification.
– Follow-up period with available laboratory data for ≥ 2 years.

Exclusion criteria

– Follow-up period < 2 years.
– Patients who required initiation of RRT shortly after the presentation.
– Insufficient data, including:
unidentified cause of CKD
unavailable renal function test data for > 2 years during the follow-up

Primary outcomes
Included
- Initiation of RRT in the form of hemodialysis, peritoneal dialysis, or preemptive kidney transplantation
- Patient’s death

Secondary outcome
- eGFR progression:
  Patients were classified as per their eGFR difference between the values at the time of inclusion and the last follow-up, as follows:
  - patients with eGFR decline (CKD progression patients, who show reduced eGFR values over years) and patients without (non progression patients who did not show reduced eGFR values over years).
- eGFR decline expressed in mL/min/per year for those with CKD progression:
  eGFR decline per year was calculated by dividing the eGFR difference (at the time of inclusion and the last follow-up) by the follow-up period in years.
- Albuminuria or proteinuria progression

Statistics
Data were presented as the means ± standard deviation for continuous variables and as the numbers or percentages for categorical variables. Patients were followed in survival analysis from the date of CKD diagnosis until the last follow-up or the occurrence of primary outcome events, including the start of RRT, kidney transplant, eGFR < 10 mL/min/1.73 m², or death. Kaplan–Meier analysis with the log rank test was used to assess the association of primary outcome events with different measured variables. p ≤ 0.05 was considered to indicate statistical significance.

RESULTS
In total, 5370 patients visited the nephrology outpatient department at a tertiary health care center between January 1, 2001 and December 31, 2016. A total of 1369 patients were excluded because they had < 2-year of the follow-up period. Further 2981 patients were excluded for incomplete data. The remaining 1020 patients with complete data were included in the analysis. The mean ± SD and median follow-up periods for the studied patients were 9.6 ± 3.8 and 9.3 years, respectively (range: 2–17 years) (Figure 1).

Table 1 shows the demographic characteristics of the patients. The patients mainly included men (63.6%) of Arab ethnicity (61.3%) and aged > 60 years (55%). Their BMI, class I, II, and III constituted 46.7%. Table 1 also shows CKD, eGFR, and albuminuria grade distribution at the start and progression at the last follow-up. For example, G3b, G4, and G5 constituted 19.9% at the start, which increased to 58.5% at the last follow-up. Similarly, the A3 albuminuria grade progressed from 36.9% at the start to 46.6% at the last follow-up.

Table 2 shows the cause of CKD, which was mainly secondary to DM (18.8%), HTN (15.9%), or both (41.5%). Glomerulonephritis constituted the next most frequent cause (9.2%). Evaluation of the various comorbid conditions associated with CKD revealed that hypertension was the most prevalent disease, detected in 93.5% of the studied patients (57.4% of which were diagnosed as a cause of CKD either alone or in association with DM). The majority of hypertensive patients (69.4%) were maintained on two or more anti-hypertensive medications. The prevalence of DM was 67.2% (60.3% of which were diagnosed as a cause of CKD either alone or in association with HTN). Other comorbidities are described in Table 2.

One hundred and twenty (11.8%) patients reached the primary outcome (ESKD or death) after a mean follow-up of 9.6 years (Table 2).

Table 3 describes the factors that were found to be associated with the decline of eGFR over the studied follow-up period when compared with those who did not experience any reduction of eGFR during the same period. Age > 60 years, Arab ethnicity, and having a smoking habit were identified as the risk factors of CKD progression leading to morbidity and mortality (p < 0.05). Furthermore, DM and/or HTN, as a cause of CKD, was significantly associated with eGFR decline, when compared to other causes (p = 0.0001). For DM, higher hemoglobin A1c acted as a significant risk factor for eGFR decline, while, for HTN, the more the number of anti-hypertensive medications, the greater the ratio of eGFR decline. For all CKD patients, higher albuminuria grade and non use of ACEI/ARBs were significantly associated with more patients...
Figure 1. Study population flowchart and the follow-up period

Table 1. Demographic characteristics of CKD patients

| Age (years): |
|-------------|
| Mean ± SD | 59.8 ± 14.2 |
| Median     | 61.3        |
| More than 60 years | 561 (55%) |
| Equal to or less than 60 years | 459 (45%) |

| Gender: |
|---------|
| Males   | 649 (63.6%) |
| Females | 371 (36.4%) |

| Ethnicity: |
|-----------|
| Arab      | 625 (61.3%) |
| Asian (East, South East) | 336 (32.9%) |
| Indian    | 28 (2.7%)   |
| African   | 26 (2.5%)   |
| Caucasian | 5 (0.5%)    |

| BMI (kg/m²): |
|--------------|
| 18.5 to < 25 (normal weight) | 132 (12.9%) |
| 25 to < 30 (over weight)    | 346 (33.9%) |
| 30 to < 35 (class I obesity) | 260 (25.4%) |
| 35 to < 40 (class II obesity) | 128 (12.5%) |
| 40 (class III obesity)      | 90 (8.8%)   |
| Missing                    | 64 (6.2%)   |

| Smoking |
|---------|
| Yes     | 188 (18.4%) |
| No      | 710 (69.6%) |
| Missing | 122 (11.9%) |

| CKD, at time of diagnosis: |
|----------------------------|
| 1-Grades:                  |
| G1                        | 462 (41.8%) |
| G2                        | 279 (27.4%) |
| G3a                       | 147 (14.4%) |
| G3b                       | 48 (4.7%)   |
| G4                        | 8 (0.8%)    |
| G5                        |             |
| 2-Albuminuria:            |
| A1                        | 386 (37.8%) |
| A2                        | 376 (36.9%) |
| A3                        | 17 (1.7%)   |
| Missing                   |

| CKD, at last follow-up: |
|-------------------------|
| 1-Grades:               |
| G1                      | 60 (5.9%)   |
| G2                      | 169 (16.6%) |
| G3a                     | 180 (17.6%) |
| G3b                     | 238 (23.3%) |
| G4                      | 214 (21%)   |
| G5                      | 145 (14.2%) |
| Missing                  |
| 2-Albuminuria:          |
| A1                      | 135 (13.2%) |
| A2                      | 227 (22.3%) |
| A3                      | 475 (46.6%) |
| Missing                 | 183 (17.9%) |
Table 2. Causes of CKD, associated comorbidities, follow-up period, and outcome

| Cause of CKD: | Number (%) |
|--------------|------------|
| DM and HTN   | 424 (41.5%)|
| DM           | 192 (18.8%)|
| HTN          | 163 (15.9%)|
| GN           | 94 (9.2%)  |
| Autoimmune   | 23 (2.2%)  |
| Neoplasia    | 15 (1.4%)  |
| Obstructive  | 8 (0.7%)   |
| Solitary functioning kidney (dysplastic/surgical removal) | 7 (0.6%) |
| Hereditary   | 2 (0.19%)  |
| Chronic interstitial nephritis | 2 (0.19%) |
| Acquired cystic kidney disease | 1 (0.09%) |
| Cardio renal | 1 (0.09%)  |
| Atrophic kidneys | 88 (8.6%) |

| Comorbidities: | Number (%) |
|---------------|------------|
| HTN           | 954 (93.5%)|
| Number of Anti-hypertensive medications: | |
| 1             | 292 (30.6%)|
| 2             | 378 (39.6%)|
| 3             | 216 (22.6%)|
| 4             | 66  (6.9%) |
| 5             | 2  (0.2%)  |
| DM            | 686 (67.2%)|
| Hemoglobin A1c %: | |
| < 6           | 55  (8%) |
| >6 and <= 8   | 400 (58.3%)|
| >8 and <= 10  | 174 (25.3%)|
| >10           | 57  (8.3%) |
| Diabetic Retinopathy | 341 (33.4%) |
| Diabetic Neuropathy | 183 (17.9%) |
| Diabetic foot  | 109 (10.6%)|
| Coronary artery disease | 281 (27.5%) |
| Congestive heart failure | 182 (17.8%) |
| Peripheral artery disease | 91 (8.9%) |
| Cerebrovascular Stroke | 65 (6.3%) |
| HCV           | 28  (2.7%) |
| HBV           | 11  (1%)  |
| HIV           | 1   (0.09%)|

| Follow-up period (years): | Number (%) |
|---------------------------|------------|
| Mean ± SD                 | 9.6 ± 3.8  |
| Median                    | 9.3        |
| Outcome:                  | Number (%) |
| living on regular follow-up | 900 (88.2%)|
| Expired                   | 20 (2%)    |
| Hemodialysis              | 73 (7.2%)  |
| Peritoneal dialysis        | 24 (2.4%)  |
| kidney transplant          | 3  (0.3%)  |

DM: diabetes mellitus  
HTN: hypertension  
GN: glomerulonephritis  
HCV: hepatitis C virus infection  
HBV: hepatitis B virus infection  
HIV: Human immunodeficiency virus infection

DISCUSSION

In this study, a long follow-up period associated with informative electronic medical files allowed the investigators to identify the clinical risk factors associated with CKD progression and those associated with ESKD/patient death over a prolonged period when compared to other similar studies. Among our studied group of CKD patients, CKD progression was found to be associated with patients' certain demographics and disease–related risk factors. Patient–related factors in our study included older age (particularly >60 years), Arab ethnicity, or being a smoker. Older age is associated with the occurrence and higher progression of CKD by multiple studies.9,10 Regarding the Arab racial preponderance, although non communicable diseases including diabetes, hypertension, and obesity are highly prevalent in the Arab world, there is very limited data available on the exact prevalence of various kidney diseases in the Arab population.11 One recent report from Palestine showed that CKD is highly prevalent among type 2 diabetic adults and that comorbidity hypertension, smoking, and older age increase the risk of developing CKD.12 For patients with CKD, there has been a lack of
Table 3. Factors affecting eGFR decline among the studied patients

| Estimated GFR | Decliners | Non decliners | P value |
|---------------|-----------|---------------|---------|
| **Total = 1020** | Number = 788 (77.2%) | Number = 232 (22.7%) | |
| **Gender:** | | | |
| Male | 502 (77.3%) | 147 (22.7%) | 0.491 |
| Female | 286 (77.1%) | 85 (22.9%) | |
| **Age (years), last follow-up** | | | 0.001* |
| Mean ± SD | 61.8 ± 13 | 52.9 ± 16 | |
| More than 60 years | 471 (83.9%) | 90 (16.1%) | 0.0001* |
| Equal or less than 60 years | 317 (69.1%) | 142 (30.9%) | |
| **Ethnicity:** | | | 0.001* |
| Arab | 504 (80.6%) | 121 (19.4%) | |
| Others | 284 (71.8%) | 111 (28.2%) | |
| **BMI:** | | | |
| BMI at study entry | 31.7 ± 6.0 | 29.7 ± 5.4 | 0.176 |
| BMI at last follow-up | 31.0 ± 6.8 | 30.2 ± 6.0 | 0.161 |
| **Smoking:** | | | 0.013* |
| Yes | 160 (85.1%) | 28 (14.9%) | |
| No | 533 (75.1%) | 177 (24.9%) | |
| **Cause of CKD:** | | | |
| DM and HTN | 366 (86.1%) | 59 (13.9%) | |
| DM | 162 (84.4%) | 29 (15.2%) | |
| HTN | 116 (71.2%) | 47 (28.8%) | |
| Others | 144 (59.8%) | 97 (40.2%) | 0.0001* |
| **Albuminuria, at time of diagnosis:** | | | 0.015* |
| Mean ± SD | 27.3 ± 53.1 | 14.6 ± 23.1 | |
| **Grade:** | | | |
| A1 | 166 (68.9%) | 75 (31.1%) | |
| A2 | 308 (79.8%) | 78 (20.2%) | |
| A3 | 302 (80.3%) | 74 (19.7%) | 0.001* |
| **Hemoglobin A1c:** | | | |
| At time of diagnosis of CKD | 7.8 ± 2.3 | 6.7 ± 2.0 | 0.0001* |
| At last follow-up | 7.1 ± 1.8 | 6.4 ± 1.5 | 0.0001* |
| Duration of hypertension, years | 12.6 ± 7.7 | 10.3 ± 6.5 | 0.14 |
| **Number of anti-hypertensive medications** | | | |
| 1 | 207 (70.9%) | 85 (29.1%) | |
| 2 | 299 (79.1%) | 79 (20.9%) | |
| 3 | 178 (82.4%) | 38 (17.6%) | 0.0001* |
| 4 | 63 (95.5%) | 3 (4.5%) | |
| **Use of ACEI/ARBs** | | | |
| Yes | 458 (74.1%) | 166 (25.9%) | |
| No | 330 (82.1%) | 72 (17.9%) | 0.002* |
| **Co morbidities:** | | | |
| Diabetes Mellitus | YES | 576 (84%) | 110 (16%) | 0.0001* |
| No | 212 (63.7%) | 121 (36.3%) | |
| Diabetic retinopathy | YES | 303 (88.9%) | 38 (11.1%) | |
| No | 485 (71.4%) | 194 (28.6%) | 0.0001* |
| Diabetic Neuropathy | YES | 169 (92.3%) | 14 (7.7%) | |
| No | 619 (14 %) | 218 (26%) | 0.0001* |
### Table 3 – continued

| Estimated GFR                        | Decliners | Non decliners | P value |
|-------------------------------------|-----------|---------------|---------|
| **Diabetic foot**                   |           |               |         |
| Yes                                 | 97 (88%)  | 12 (11%)      |         |
| No                                  | 691 (75.9%) | 220 (24.1%)  | 0.001*  |
| **Hypertension**                    |           |               |         |
| Yes                                 | 758 (79.5%) | 196 (20.5%)  |         |
| No                                  | 30 (45.5%)  | 36 (54.5%)    | 0.0001* |
| **Congestive heart failure**        |           |               |         |
| Yes                                 | 162 (89%)  | 20 (11%)      |         |
| No                                  | 626 (74.7%) | 212 (25.3%)  | 0.0001* |
| **Coronary artery disease**         |           |               |         |
| Yes                                 | 246 (87.5%) | 35 (12.5%)   |         |
| No                                  | 542 (73.3%) | 197 (26.7%)  | 0.0001* |
| **Peripheral vascular disease**     |           |               |         |
| Yes                                 | 82 (90.1%)  | 9 (9.9%)      |         |
| No                                  | 706 (76.1%) | 222 (23.9%)  | 0.001*  |
| **Cerebrovascular Accident**        |           |               |         |
| Yes                                 | 55 (84.6%)  | 10 (15.4%)    |         |
| No                                  | 733 (76.8%) | 221 (23.2%)  | 0.094   |

GFR: glomerular filtration rate  
BMI: body mass index  
CKD: chronic kidney disease  
DM: diabetes mellitus  
HTN: hypertension  
ACEI: angiotensin-converting enzyme inhibitors  
ARBs: angiotensin receptor blockers

### Table 4. Degree of eGFR decline among patients with progressive CKD

| Factors                              | Degree of eGFR decline ml/min/1.73 m²/year | P value |
|--------------------------------------|------------------------------------------|---------|
| **Cause of CKD:**                    |                                          |         |
| DM and HTN                           | 3.2 ± 4.3*                               |         |
| DM                                   | 2.4 ± 2.0                                |         |
| HTN                                  | 2.2 ± 1.8                                |         |
| Others                               | 2.3 ± 2.5                                | 0.001   |
| **Albuminuric, at time of diagnosis:** |                                      |         |
| Grading                              |                                          |         |
| A1                                   | 1.6 ± 1.5*                               |         |
| A2                                   | 2.7 ± 4.4*                               |         |
| A3                                   | 3.2 ± 2.4                                | 0.0001  |
| Hemoglobin A1c %, at time of diagnosis |                                       |         |
| ≤ 6                                   | 2.2 ± 2.1                                |         |
| >6 and ≤ 8                           | 2.4 ± 2.0                                |         |
| >8 and ≤ 10                          | 2.8 ± 2.0                                |         |
| >10                                   | 4.1 ± 6.2*                               | 0.0001  |
| Use of ACEI/ARBs                     |                                          |         |
| Yes                                  | 2.3 ± 2.9                                | 0.0001  |
| No                                   | 3.3 ± 3.7                                |         |

GFR: glomerular filtration rate  
CKD: chronic kidney disease  
DM: diabetes mellitus  
HTN: hypertension  
ACEI: angiotensin-converting enzyme inhibitors  
ARBs: angiotensin receptor blockers
studies on the association between smoking and CKD progression, and the limited literature has yielded conflicting results. However, in a recent prospective cohort study involving Korean CKD patients, smoking was found to be associated with a significantly higher risk of worsening kidney function.13

In a systematic review and meta-analysis with a follow-up duration of 1.5–16 years, it was found that being male, having substantial proteinuria, and having diabetes were associated with increased hazards of progression to ESRD.14 In our study, there was no gender effect on CKD progression. Some previous studies have indicated no gender differences in the progression of nephropathy among patients with diabetes.15 Other studies have shown that the male gender predicted the progression of renal disease in patients with diabetes,16 while others reported a detrimental effect of the female gender on the progression of diabetic nephropathy.17

Disease-related factors, associated with CKD progression in the current study, included having type 2 diabetes and hypertension (diagnosed as the causes of original kidney disease), diabetic retinopathy, diabetic neuropathy, diabetic foot, cardiovascular disease, or advanced CKD at the time of diagnosis. Furthermore, diabetes mellitus was found to be associated with greater CKD progression when associated with a higher Hb A1C. Intensive glucose control has previously been demonstrated to be associated with a significant reduction in renal events in patients with type 2 diabetes in the Action in Diabetes and Vascular Disease study.18 However, in contrast to our findings, the present finding mainly suggested the development of micro or macro albuminuria, with no effect on doubling the serum creatinine level. Other relatively small-sized studies reported no association between the baseline HbA1c level and renal outcomes.19 Therefore, a relatively long-term follow-up of our patients might have shown the long-term effect of Hb A1C in association with rising serum creatinine levels.

In our study, hypertension was found to be associated with greater CKD progression when the patient was treated with more numbers of antihypertensive medications.

![Image: Survival Functions](Image)

**Figure 2. Impact of albuminuria grade on the primary outcome events (ESKD and death)**

| Group | Chi-Square | df | Sig. |
|-------|------------|----|-----|
| Log Rank (Mantel-Cox) | 37.057 | 2 | .000 |

Test of equality of survival distributions for the different levels of Albuminuria/Proteinuria grade.
medication (reflecting more severe hypertension) and if antihypertensives were not including ACEIs or ARBs. This finding is supported by several studies demonstrating the beneficial effects of blood pressure control and other benefits with the use of ACEs/Arbs in reducing renal events.\(^\text{20,21}\)

The association between kidney disease progression and cardiovascular disease (CVD) risk was assessed among patients with type 2 diabetes and CKD in a UK primary healthcare setting to reveal that progression of CKD is possibly associated with CVD risk, in which increased risk of cardiovascular events was noted among those with the fastest rate of eGFR decline, most predominantly in heart failure cases.\(^\text{22}\)

In our study, greater eGFR decline was found to be associated with having both diabetes and hypertension ($-3.2 \pm 4.3 \text{ mL/min/1.73 m}^2/\text{year}$) as original kidney disease, to have a higher grade of albuminuria ($-3.2 \pm 2.4 \text{ mL/min/1.73 m}^2/\text{year}$), high HbA1c (>10% was associated with an eGFR decline of $-4.1 \pm 6.2 \text{ mL/min/1.73 m}^2/\text{year}$) and not being on any medication for renin-angiotensin system block ($-3.3 \pm 3.7 \text{ mL/min/1.73 m}^2/\text{year}$).

Similarly, on assessing factors associated with reaching primary outcome events, including death and reaching ESKD, it was found that higher albuminuria, high HbA1c, and the non use of renin-angiotensin system blockers were associated with higher statistical significance. On the other hand, having type 2 diabetes and hypertension as the primary causes of CKD were found to be associated with death/ESRD, albeit without significance.

**Figure 3. Impact of hemoglobin A1c at the time of diagnosis of CKD on the primary outcome events (ESKD and death)**

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**Overall Comparisons**

| Test of equality of survival distributions for the different levels of the A1c category at the start. | Chi-Square | df | Sig. |
| --- | --- | --- | --- |
| Log Rank (Mantel-Cox) | 9.823 | 3 | .020 |

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Limitations and strengths
Limitations included that this study was observational and hence its results cannot be used to suppose causality. In addition, being in a country with such a diverse population, the studied group was heterogeneous. However, there are many strengths of this study. For instance, it included a patient selection process, which resulted in a representative CKD patient cohort as well as a long observation period with a high number of follow-up visits, which allowed the identification of risk factors for kidney and patient outcomes.

CONCLUSIONS
Our findings showed that the risk factors associated with reaching ESKD and/or death included high A1c among diabetic patients, a high grade of proteinuria, and the non use of renin-angiotensin system blockers. Furthermore, the study revealed that older age, Arab ethnicity, smoking habit, diabetes mellitus and hypertension (presumed as original kidney diseases) are among the significant risk factors associated with greater eGFR decline and CKD progression.

Financial Disclosure
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Ethical Approval and Patients’ Consent
The study was approved by the local ethical committee of the Hamad Medical Corporation research center, under research study number #17195/17 in accordance with the relevant guidelines and regulations. Patients’ consent was inapplicable as the study was designed to be a retrospective evaluation of preexisting medical data from registries and electronic medical reports with no
human interventions. Patients’ confidentiality was preserved.

**Availability of Data and Materials**
Available

**Competing Interests**
None to disclose

**Authors’ Contributions**
Contributing authors have shared in data collection and manuscript review.

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**REFERENCES**

1. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
2. Tsai WC, Wu HY, Peng YS, et al. Risk factors for development and progression of chronic kidney disease: a systematic review and exploratory meta-analysis. *Med (Baltim).* 95:e3013;2016.
3. Hounkpatin HO, Fraser SDS, Honney R, Dreyer G, Brettie A, Roderick PJ. Ethnic minority disparities in progression and mortality of pre-dialysis chronic kidney disease: a systematic scoping review. *BMC Nephrol* 21:217;2020.
4. Renal Data System (USRDS) Annual Data Report. Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2008.
5. Fischer MJ, Hsu JY, Lora CM et al. CKD Progression and mortality among hispanics and non-hispanics. *J Am Soc Nephrol.* 27:3488 – 3497; 2016.
6. Al Malki, H., Rashed, AH, Asim M. Renal replacement therapy in Qatar—past, present and future. *Open J Nephrol.* 8:42-55;2018.
7. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). *Ann Intern Med.* 5;150:604 – 612;2009.

8. KDIGO 2012 Clinical Practice Guideline for the evaluation and management of chronic kidney disease, *Kidney Int Suppl.* 3:1 – 150;2013.

9. Arora P, Jalal K, Gupta A, Carter RL, Lohr JW. Progression of kidney disease in elderly stage 3 and 4 chronic kidney disease patients. *Int Urol Nephrol.* 49:1033 – 1040;2017.

10. Sesso R, Prado F, Vicioso B, Ramos LR. Prospective study of progression of kidney dysfunction in community-dwelling older adults. *Nephrology (Carlton).* 13:99 – 103;2008.

11. Farag YMK, Kari JA, Singh AK. Chronic kidney disease in the Arab world: a call for action. *Nephron Clin Pract* 121:c120-c123;2012.

12. Nazzal Z, Hamdan Z, Masri D, Abu-Kaf O, Hamad M. Prevalence and risk factors of chronic kidney disease among Palestinian type 2 diabetic patients: a cross-sectional study. *BMC Nephrol* 21:484;2020.

13. Sangmi L, Shinchan K, Young S, et al. Smoking, smoking cessation, and progression of chronic kidney disease: results from KNOW-CKD Study. *Nicotine Tob Res.* 23;2021.

14. Tsai WC, Wu HY, Peng YS, Ko MJ, Wu MS, Hung KY, et al. Risk factors for development and progression of chronic kidney disease: a systematic review and exploratory meta-analysis. *Med (Baltim).* 95: e3013;2016.

15. Breyer JA, Bain RP, Evans JK, et al. Predictors of the progression of renal insufficiency in patients with insulin-dependent diabetes and overt diabetic nephropathy. The Collaborative Study Group. *Kidney Int.* 50:1651–1658;1996.

16. Gall MA, Hougard P, Borch-Johnsen K, et al. Risk factors for development of incipient and overt diabetic nephropathy in patients with non-insulin dependent diabetes mellitus: prospective, observational study. *BMJ.* 314:783–788;1997.

17. Holl RW, Grabert M, Thon A, Heinze E. Urinary excretion of albumin in adolescents with type 1 diabetes: persistent versus intermittent microalbuminuria and relationship to duration of diabetes, sex, and metabolic control. *Diabetes Care.* 22:1555–1560;1999.

18. ADVANCE Collaborative Group, Patel A, MacMahon S, Chalmers J, Neal B, Billot L, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med.* 358:2560–2572;2008.

19. Lorenzo V, Saracho R, Zamora J, Rufino M, Torres A. Similar renal decline in diabetic and non-diabetic patients with comparable levels of albuminuria. *Nephrol Dial Transplant.* 25:835 – 841;2010.

20. Van den Belt SM, Heerspink HJL, Gracchi V, de Zeeuw D, Wühl E, Schaefer F, ESCAPE Trial Group. Early proteinuria lowering by angiotensin-converting enzyme inhibition predicts renal survival in children with CKD. *J Am Soc Nephrol.* 29:2225–2233;2018.

21. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A metaanalysis of patient-level data. *Ann Intern Med.* 135:73 – 87;2001.

22. Cabrera CS, Lee AS, Olsson M, Schnecke V, Westman K, Lind M, et al. Impact of CKD progression on cardiovascular disease risk in a contemporary UK cohort of individuals with diabetes. *Kidney Int Rep.* 5:1651 – 1660;2020.

23. Turin TC, James M, Ravani P, Tonelli M, Manns BJ, Quinn R, et al. Proteinuria and rate of change in kidney function in a community-based population. *J Am Soc Nephrol.* 24:1661 – 1667;2013.