Prevalence and Associated Factors of Chronic Kidney Disease among Relatives of Hemodialysis Patients in Saudi Arabia

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Chronic kidney disease (CKD) is a serious health issue in the Kingdom of Saudi Arabia (KSA). In KSA, there are currently over 20,000 patients on dialysis and 9,810 patients undergoing follow up after kidney transplantation.1 The combined prevalence of renal replacement therapy in Saudi Arabia is estimated at 294.3 per million population.1

In Saudi Arabia, the age-standardized prevalence of CKD (stages 1–2, stage 3, stage 4, and stage 5, not including renal replacement therapy) is estimated at 9,892 per 100,000, which is higher than the estimates for Western Europe (5,446 per 100,000) and North America (7,919 per 100,000).1 Based on the National Health and Nutrition Examination Survey (NHANES), the prevalence of CKD in adults in the United States of America (US) is 11.7%.3 We found only a single study of the prevalence of CKD among the young Saudi population (mean age of 37.4 ± 11.3 years).3 This study estimated CKD prevalence within this segment of the Saudi population at 5.7% using the modification of diet in renal disease (MDRD)-3 equation and 5.3% using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Individuals at higher risk for the development of CKD include those with a strong family history of CKD.5,11-S3 Studies in the US have confirmed the high prevalence of CKD among relatives of end-stage kidney disease (ESKD) patients with 14% of screened relatives having GFR < 60 ml/min/1.73m² (20-24). First or second-degree relatives of patients with ESKD are 2 to 3 times more likely to develop ESKD and are more likely to be obese and to have undetected hypertension.6,51,54,55 Thus, individuals with a family history of CKD are a high-risk group as are hypertensive, diabetics, and those over 65 years of age.53

Here, we approached the first-degree relatives of 4,500 dialysis patients to assess the prevalence of undiagnosed CKD among first-degree relatives of Saudi hemodialysis patients.

RESULTS

Demographic and Clinical Characteristics

The characteristics of the 5177 relatives (26% of total invited) are shown in Table 1. Relatives presented for CKD screening from all regions of KSA: 23.2%, 20.7%, 28.9 % and 27.2% from the central, eastern, western, and southern regions. The most common relatives screened were offspring (63.7%). The mean age of the screened relatives was 34.3 ± 14.3 years, and mean BMI was 29.6 ± 11.8 kg/m².

In the index patients (Table S1), most had a primary diagnosis for their CKD of DM (45.5%), followed by those of unknown etiology (20.2%) and hypertension (19.8%). Inherited kidney diseases contributed only 0.12% of the total.

Prevalence of Chronic Kidney Disease and Associated Factors

Mean serum creatinine was 80.9 ± 26.4 μmol/l, and the mean eGFR was 96.4 ± 22.6 ml/min/1.73m² (Table 2).
Of all relatives screened, 54.6% had eGFR > 90 ml/min/1.73m², indicative of healthy kidney status, 39.6% had eGFR < 90 ml/min/1.73m², and 5.8% had eGFR of less than 60 ml/min/1.73m². Of the relatives with eGFR between 60 and 90 ml/min/1.73m², 8% had proteinuria. Thus, the prevalence of CKD was 13.8% (5.8% eGFR < 60 ml/min/1.73m² + 8% with proteinuria and eGFR 60 – 90 ml/min/1.73m²). There were 68% in CKD stages 0 – 1 and 32% in stages 2 – 5. The prevalence rates of glycosuria, hematuria, and proteinuria were 9.5%, 17.9%, and 26.5% respectively, among all of the screened individuals.

Table 1. Characteristics of first-degree relatives of hemodialysis patients in Saudi Arabia

| Regional distribution in Saudi Arabia | N (%) |
|---------------------------------------|-------|
| Central                               | 1187  (23.2%) |
| Eastern                               | 1068  (20.7%) |
| Western                               | 1479  (28.9%) |
| Southern                              | 1329  (27.2%) |

| Relationship to index patient         | N (percent) |
|---------------------------------------|-------------|
| Offspring                             | 3130 (63.7%) |
| Sibling                               | 1307 (26.6%) |
| Parent                                | 477  (9.7%)  |

Demographics

| Age in mean ± SD (range) years        | 34.3 ± 14.3 (01 – 95) |
|---------------------------------------|-----------------------|
| Male                                  | 2802 (50.9%)          |
| Female                                | 2510 (49.1%)          |

Medical History

| History of hypertension               | 731 (14.3%)          |
| History of diabetes mellitus          | 1196 (23.4%)         |

| Previous pregnancy                    | 91 (31.1%) of married women |

Table 2. Markers of chronic kidney disease in first-degree relatives of hemodialysis patients

| Measured parameter                  | N (percent) or mean ± SD (range) |
|--------------------------------------|----------------------------------|
| Glycosuria                           | 484 (9.5%)                      |
| Hematuria                            | 912 (17.9%)                     |
| Proteinuria                          | 1353 (26.5%)                    |

| eGFR (ml/min/1.73m²)                 | 96.4 ± 22.6 (1.7 – 267)         |
| eGFR < 90 ml/min/1.73m²              | 1987 (39.6%)                    |
| eGFR < 60 ml/min/1.73m²              | 291 (5.8%)                      |
| eGFR 60 – 90 ml/min/1.73m² with proteinuria | 401 (8%)                  |
| CKD = eGFR < 60 ml/min/1.73m² + GFR of | 692 (13.8%)                     |
| 60 – 90 ml/min/1.73m² with proteinuria|                                   |
| CKD Stages 0 – 1                     | 3306 (68%)                      |
| CKD Stages 2 – 5                     | 1566 (32%)                      |
| BMI (kg/m²)                          | 29.6 ± 11.8 (7.0 – 85)          |
| BMI ≥ 25                             | 3313 (66.2%)                    |
| BMI > 30                             | 2069 (39.8%)                    |
| Mean systolic blood pressure (mm Hg) | 123.5 ± 18.1 (100 – 190)        |
| Mean diastolic blood pressure (mm Hg)| 77.6 ± 11.2 (58 – 110)          |
| Systolic blood pressure > 130 mm Hg  | 1435 (28.1%)                    |
| Diastolic blood pressure > 90 mm Hg  | 439  (8.6%)                     |

Of relatives with BMI > 30 kg/m², indicative of overweight, constituted 39.8% of the total. An even higher fraction (66.2%) had BMI > 25 kg/m², indicative of obesity. Mean SBP was 123.5 ± 18.1 mm Hg and diastolic blood pressure was 77.6 ± 111.2 mm Hg. Although only 14.3% reported a history of hypertension, we found that 28.1% had systolic hypertension and 8.6% had diastolic hypertension, suggesting that undiagnosed hypertension was common.

We compared the frequency of hypertension, obesity, and potentially uncontrolled DM in the relatives with CKD and those without CKD (Table S2). Systolic hypertension was more common in the relatives with CKD (35.9%) compared to those without (29.2%). Of the relatives studies, > 30% had a BMI of

Table 3. Risk factors for more severe kidney disease among the relatives of hemodialysis patients

| Stage          | Stages 0 – 1 | Stages 2-5 | Total = 1506 |
|----------------|-------------|-----------|-------------|

| N (percent) | (68%) | (32%) | P value |
|-------------|-------|-------|---------|
| Age (years) | 31.3 ± 12.8 | 40.9 ± 15.0 | 0.0001 |
| Male        | 1840 (49.6%) | 804 (51.7%) | 0.1 |
| Glycosuria  | 258 (7.8%)   | 198 (12.7%) | 0.0001 |
| Hematuria   | 579 (17.5%)  | 286 (18.4%) | 0.5 |
| Proteinuria | 836 (25.3%)  | 442 (28.4%) | 0.015 |
| History of hypertension | 354 (10.7%) | 291 (18.7%) | 0.0001 |
| History of DM | 655 (19.8%) | 434 (27.9%) | 0.0001 |
| Family History of CKD | 202 (6.1%) | 109 (7.0%) | 0.002 |
| Body mass index > 30 kg/m² | 2089 (63.2%) | 1103 (70.9%) | 0.0001 |
| Systolic blood pressure > 130 mm Hg | 912 (27.6%) | 504 (32.4%) | 0.0003 |
| Diastolic blood pressure > 90 mm Hg | 314 (9.5%) | 202 (13.0%) | 0.0002 |
| Primary diagnosis of the index cases: | | | |
| Hypertension | 634 (20.7%) | 229 (19.2%) | 0.7 |
| Glomerulonephritis | 155 (4.7%) | 75 (4.8%) | |
| Diabetes | 1498 (45.3%) | 720 (48.3%) | |
| Chronic tubulointerstitial nephritis | 132 (4.0%) | 72 (4.6%) | |
| Other causes | 202 (6.1%) | 68 (4.4%) | |

Table 4. Logistic regression analysis of factors for an association with stages 2 – 5 CKD in relatives of hemodialysis patients

| Risk factor | P value |
|-------------|---------|
| Age         | 0.000   |
| Center      | 0.000   |
| Proteinuria | 0.029   |
| Systolic Hypertension | 0.035 |
| Gender      | 0.12798 |
| Family History of Hypertension | 0.1452 |
| Degree of Relation (parent = 3, sibling = 2, offspring = 1) | 0.57782 |
| Glycosuria  | 0.71490 |
| Hematuria   | 0.81479 |
| Family History of Diabetes mellitus | 0.81576 |
It was noteworthy that the prevalence of CKD among the screened relatives of patients from the southern region was between 2 to 4-fold higher than the prevalence in other regions. Although the relatives from the southern region had significantly higher prevalence of CKD, the prevalence of diabetes among the relatives and their index cases was the lowest among the four regions. The opposite characteristics were observed in the relatives from the eastern region, which had the highest prevalence of DM and the lowest prevalence of CKD. These geographic differences suggested that the family history of CKD is caused by something other than familial diabetes. Consanguineous marriages are common within Saudi families (57%), but there is no evidence that is more common in the South.7 Thus, the geographic data suggested a possible autosomal dominant inherited kidney disease was prevalent in the South.

In the Saudi population of the same age bracket as our screened relatives, the prevalence of diabetes is 12.1%,3 which was almost half the prevalence of the relatives reporting a history of diabetes (23.4%). On the day of screening, only 9.5% of the cohort had glycosuria. This low proportion compared to the self-reported history information could be at least partially due to the 5.1% who reported taking antidiabetic medication. Alternatively, the self-reporting regarding a history of DM could be inaccurate. We found no positive association between the prevalence of DM and CKD in the relatives among the different regions. Indeed, in the eastern and southern regions, these conditions were negatively correlated.

Among relatives with CKD, the prevalence of systolic hypertension was significantly higher than among the relatives without CKD (p = 0.03). This is consistent with previous reports.5 On the day of screening, 28.1% of the relatives had systolic hypertension, even though only 14.3% reported a history of hypertension. Thus, our resulted suggested a frequency of undiagnosed hypertension of 13.8%. There was diastolic hypertension in 8.6%. Our findings are consistent with another study from Saudi Arabia, which reported 15.2% of adult Saudis were hypertensive and 57.8% unaware of this diagnosis.56

We found that in the screened relatives, the prevalence of obesity (BMI of > 30 kg/m²) was 39.8%, which is higher than reported for the general Saudi population (28.7%).57 A higher prevalence of obesity was also observed in the relatives with stages 2–5 CKD (70.9 %) compared with those in stages 0–1 (63.2%). This is in keeping with previous reports showing that obesity among incident dialysis patients was independently associated with a family history of CKD. This raises the possibility of adiposity-related genes being a cause of CKD.54

In conclusion, the overall combined prevalence of CKD was 13.8% and was highest in the southern region.
of Saudi Arabia. Reduced kidney function was more likely in older relatives and those with systolic hypertension, glycosuria, or proteinuria. Many relatives had undiagnosed hypertension and undiagnosed or poorly managed diabetes. Nationwide screening programs need to be established to forecast strategic health plans to deal with the escalating cost burden of CKD in the Kingdom.

DISCLOSURE
All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL
Supplementary File (Word)
Supplementary Method
Supplementary Results
Supplementary References

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