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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).[2] 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).[4] 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,S1-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/1.73m^2 (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,S1,S4,S5] Thus, individuals with a family history of CKD are a high-risk group as are hypertensive, diabetics, and those over 65 years of age.[S3]

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/m^2.

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/1.73m^2 (Table 2).

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

Regional distribution in Saudi Arabia N (%)	
Central	1187 (23.2%)
Eastern	1059 (20.7%)
Western	1479 (28.9%)
Southern	1329 (27.2%)
Relationship to index patient	
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	2602 (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

Of all relatives screened, 54.6% had eGFR > 90 ml/min/1.73m^2, indicative of healthy kidney status, 39.6% had eGFR < 90 ml/min/1.73m^2, and 5.8% had eGFR of less than 60 ml/min/1.73m^2. Of the relatives with eGFR between 60 and 90 ml/min/1.73m^2, 8% had proteinuria. Thus, the prevalence of CKD was 13.8% (5.8% eGFR < 60 ml/min/1.73m^2 + 8% with proteinuria and eGFR 60 – 90 ml/min/1.73m^2). 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 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%)
Mean serum creatinine (μmol/l)	80.9±26.4 (28– 596)
eGFR (ml/min/1.73m^2)	96.4 ± 22.6 (1.7– 267)
eGFR < 90 ml/min/1.73m^2	1987 (39.6%)
eGFR < 60 ml/min/1.73m^2	291 (5.8%)
eGFR 60 – 90 ml/min/1.73m^2 with proteinuria	401 (8%)
CKD = eGFR < 60 ml/min/1.73m^2 + GFR of 60 – 90 ml/min/1.73m^2 with proteinuria	692 (13.8%)
CKD Stages 0 – 1	3306 (68%)
CKD Stages 2 – 5	1556 (32%)
BMI (kg/m^2)	29.6 ± 11.8 (7.0 – 85)
BMI > 25	3313 (66.2%)
BMI > 30	2089 (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%)

eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; BMI, body mass index.

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

	Stages 0 – 1 Total = 3306 (68%)	Stages 2-5 Total = 1556 (32%)	P value
Age (years)	31.3 ± 12.8	40.9 ± 15	0.0001
Male	1640 (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/m^2	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 (46.3%)	
Unknown etiology	641 (19.4%)	332 (20.7%)	
Chronic tubulointerstitial nephritis	132 (4.0%)	72 (4.6%)	
Other causes	202 (6.1%)	68 (4.4%)	

DM, Diabetes mellitus; CKD, chronic kidney disease

Relatives with BMI > 30 kg/m^2, indicative of overweight, constituted 39.8% of the total. An even higher fraction (66.2%) had BMI > 25 kg/m^2, 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 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	0.14524
Degree of Relation (parent = 3, sibling = 2, offspring = 1)	0.57762
Glycosuria	0.71490
Hematuria	0.81479
Family History of Diabetes mellitus	0.81576

> 30 kg/m^2 and 40.5 % on anti-diabetic medication had glycosuria, which could indicate uncontrolled DM.

We observed significant regional differences among the screened relatives in terms mean BMIs, being highest in the Eastern region (34.2) and lowest in the Southern region (25.7). On the other hand, there were more relatives with CKD from the Southern region (11.7%) than in the other regions (3.1% in the central region, 2.7% in the eastern region, and 5.3% in the Western region).

To evaluate risk factors that were associated with more severe kidney disease, we compared the characteristics of the relatives with stages $0-1$ disease to those with stages $2-5$ disease (Table 3). The relatives with stages 0-1 were significantly younger (31.3 ± 12.8 years) that those in the later stages (40.9 ± 15 years) and had a higher prevalence of a history of hypertension or DM and a BMI > 25 ($P = 0.0001$).

Using logistic regression analysis, we found that relatives with stages $2-5$ had the following independently associated risk factors: age, region, proteinuria and systolic hypertension (Table 4).

Among this subset of the relatives screened, 860 (17.1%) said that they are on medication with 5.1% taking antidiabetic medications, 2.7% on antihypertensive medications, and 1.3% on nonsteroidal anti-inflammatory drugs (NSAIDs). The patients in the Southern region had the lowest rate of medication use, including antidiabetic medication and NSAIDs (Table S3).

DISCUSSION

In this study, we screened more than 5000 first-degree relatives of Saudi patients on hemodialysis. The subjects consisted of equal proportions from the four geographical regions of Saudi Arabia and had an equal distribution between males and females. The respondents constituted 26% of the total number of relatives approached. The prevalence of CKD among the relatives screened was 13.8%, which is 2.6 times that reported in the Saudi population for similar age group.[4] Other reports have also shown higher prevalence of CKD among hemodialysis patient families that in the general population from different parts of the world.[5,6,S1] The relatives screened in our study tended to be young (mean age 34.3 years). It is conceivable that as they age, the prevalence of CKD among them will be substantially higher. Other limitation of our study related to capturing proteinuria on a urinalysis, which is subject to inaccuracies due to high or low urine specific gravity.

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.[S6]

We found that in the screened relatives, the prevalence of obesity (BMI of > 30kg/m^2) was 39.8%, which is higher than reported for the general Saudi population (28.7%).[S7] 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.[S4]

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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