Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2019, 8(5): 177-182

Etiology of Chronic Kidney Disease (CKD) in Saudi Arabia

Hussain Gadelkarim Ahmed[1,2]*, Faisal Saud Mohammed Alzayed[1], Husam Khalaf Ali Albluwe[1], Ziyad Ali Salem Alosayfir[1], Mohannad Yousef Jarallah Aljarallah[1], Besher Kanan M Alghazi[1] and Mohammed Ali Ghazai Alshammari[1]

[1] *College of Medicine, University of Hail, Hail, Saudi Arabia*

[2] *Department of Histopathology and Cytology, FMLS, University of Khartoum, Khartoum, Sudan*

**Corresponding e-mail: Hussaingad5@gmail.com*

ABSTRACT

The burden of chronic kidney disease (CKD) is increasing each year worldwide due to the increase of its etiological factors. Several conditions have been linked to the evolution of the CKD including diabetes mellitus (DM), hypertension, overweight/obesity, etc. CKD can lead to more harmful conditions such as cardiovascular diseases (CVD). CKD starts with mild kidney damage as stage 1 and progress without treatment to stage 5 (end-stage CKD), which eventually results in kidney failure. The epidemiology of the CKD depends strongly on socio-economic status and comorbidities. Therefore, this review aimed to identify the common etiological factors in Saudi Arabia in light of the available literature from Saudi Arabia. The review mainly focused on the studies devoted to the CKD from Saudi Arabia published up to March 2019. The studies were identified through searches of the Medline database, EMBASE, Web of Science, Scopus, and Google Scholar, using the keywords: chronic kidney disease with DM, hypertension, obesity, glomerulonephritis, nephritis, renal failure, and Saudi Arabia. Only papers in the English language were included.

Keywords: Chronic kidney disease with DM, Hypertension, Obesity, Glomerulonephritis, Nephritis, Renal failure, and Saudi Arabia

INTRODUCTION

Chronic kidney disease (CKD) is globally known as it can complicate to end-stage renal disease (ESRD) and cardiovascular disease (CVD) [1]. As there is a general population aging, the epidemiology of CKD is continuously increasing affecting one out of 10 persons and about 4 per 100,000 reach ESRD. When CKD occurs, it is usually associated with high CVD comorbid diseases, thus detecting CKD at early stages through screening can prevent many individuals to develop ESRD [2].

CKD has changed over time, and the existing international guidelines describe it as declined renal function evidenced by glomerular filtration rate (GFR) of <60 mL/min per 1.73 m^2, or markers of kidney damage, or both, of at least 3-months, irrespective of underline reason [3]. The evolution of CKD or stealing of renal function eventually results in ESRD, which may indicate a massive increase in CVD. As regard to the screening and early diagnosis of CKD, both serum creatinine and proteinuria should be considered as serum creatinine which alone is regarded as inadequate predictors of renal function loss. Proteinuria can proof both kidney damage and loss of function due to the progression of the disease [4].

Although detecting of risk factors designating the necessity for intervention in early stages of CKD can recover the patient, all risk factors for progression of CKD to ESRD have not yet been recognized. However, there were several documented risk factors including DM, hypertension, glomerulonephritis, nephritis, sickle cell nephropathy, hereditary factors, etc. [5]. DM and hypertension are the prime causes of CKD middle and high-income countries and some low-income countries. The epidemiology and progression of CKD greatly vary worldwide by ethnicity, socio-economic and perhaps epigenetic influence [3].

As early detection of CKD permits essential opportunities for effective interventions, which can reduce the probability of progression into ESRD, as well as, reduces the risk of CVD, 299 Saudi were randomly screened for CKD. Variable stages of CKD were identified in 24% of the subjects (38.6% were males, and 61.4% were females) [6]. Another study included 5000 Saudi selected from 30 primary health centers reported an overall prevalence of CKD of 9.4%. Stage V, Stage IV, stage III, and stage IV, were reported in 0.4%, 0.5%, 7.8%, and 0.6%, respectively [7]. Another study investigated 2800 Saudi from 13 towns neighboring Hail city (Northern Saudi Arabia), detected CKD in 7.8% persons (43.8% males and 56.2% females) [8].

It was observed that such community-based studies are only available from Northern Saudi Arabia. Reports from other Saudi regions were pertaining to disease associated risk factors or comorbid conditions. Thus the present review focused on the possible CKD risk factors in light of literature from Saudi Arabia.

Diabetes Mellitus (DM)

Saudi Arabia is an epidemic with type 2 DM. Saudi Arabia ranked as the 2nd highest prevalence of DM in the Middle East and the 7th highest worldwide [9,10]. Study of 6024 Saudi subjects identified DM in 30% patients (the prevalence in males was 34.1% vs. 27.6% in females) [11]. Another study found an overall prevalence of DM in Hail (northern Saudi Arabia) was 31.1%. The prevalence of male was 32.6% and female was 29.6% ($p<0.0001$) [12].

One of the most encountered factors associated with the growing prevalence rates of CKD worldwide is growing numbers of individuals in developing nations suffering from DM, which is a major risk factor of CKD. A prevalence of 21.8% of CKD was identified among diabetic patients, and CKD was significantly associated with longer duration of DM [13].

In a study from Saudi Arabia, 54,670 with type 2 DM were selected from the Saudi National Diabetes Registry (SNDR) and were analyzed for the presence of diabetic nephropathy. The general prevalence of diabetic nephropathy was 10.8%, allocated into 1.2% microalbuminuria, 8.1% macroalbuminuria and 1.5% ESRD [14]. In a study by the Saudi diabetic kidney disease (SAUDI-DKD) to understand the insinuations of chronic diabetic kidney disease, of the 427 patients with nephropathy, 43 had microalbuminuria, 19% had macroalbuminuria, and 37% had ESRD [15]. Another study from Saudi Arabia confirmed that it contributes significantly to ESRD [16]. A study from Saudi Arabia found a prevalence of 69% of DM among 200 CKD patients and concluded that the role of diabetes as a risk factor for CKD and ESRD is higher than it has been estimated in previous studies in other regions in Saudi Arabia. Females are at a higher risk of CKD and eventually ESRD than males [17]. In a study of a diabetic outpatient clinic, 12.8% of patients had dipstick proteinuria, and of the remaining patients, 41.3% had microalbuminuria [18]. The 2 major factors that influence the CKD status are the very high rate of diabetic nephropathy and shift in age demographics [19].

Hypertension

Hypertension is the leading preventable cause of premature death worldwide. Global hypertension discrepancies are enormous and growing. Combined efforts are immediately required to fight the evolving hypertension burden in low and middle-income countries. In 2010, 31.1% of the world's adults had hypertension; 28.5% in high-income countries and 31.5% in low and middle-income countries. From 2000 to 2010, the age-standardized prevalence of hypertension decreased by 2.6% in high-income countries but increased by 7.7% in low and middle-income countries [20].

In a community-based survey involved 5000 Saudi from Northern Saudi Arabia, the overall prevalence of hypertension was 30.2%, and the incidence in males was 30.8% vs. 29.6% in females. The risk of hypertension increases with the increase of age, as well as, with increasing Body mass index (BMI) and this was found to be statistically significant $p<0.0001$ [21]. Another study investigated 2800 Saudi for the presence of hypertension and reported a prevalence of 33.4% (50.9% were males, and 49.1% were females) [8]. Another study from Saudi Arabia has reported a prevalence of 25.5% of hypertension [22]. A recent study from Saudi Arabia has stated that the incidence of prehypertension was 66.1%, 48.1% and 54.9% in male, female and all subjects, respectively [23]. Many studies have shown that the increasing prevalence of CKD is strongly associated with hypertension as a cause and as a risk factor leads to a progression of CKD [24]. Uncontrolled hypertension in CKD patients has been known as one of the chief factors contributing to the progression of CKD and an elevated risk for CVD, since >50% of patients with CKD have hypertension (blood pressure >140/90 mm Hg) [25].

In a piloted study which included 299 Saudi, 64.3% of the patients with different stages of CKD were found

hypertensive [6]. Congenital causes of CKD embody the leading etiology of CKD in children living in the western province of Saudi Arabia. Significant risk factors for renal replacement therapy comprise congenital CKD, Saudi nationality, and hypertension. Hypertension is also a predictor of mortality in children with CKD [26].

Obesity and Overweight

Obesity and overweight are responsible for over 3.4 million deaths, more than 3.9% of years of life lost, and 3.8% of disability worldwide. The increase in obesity has resulted in widespread calls for systematic monitoring of deviations in overweight and obesity prevalence in all populations [27]. The obesity epidemic is a global health catastrophe of the astounding part. Extra body weight is a leading risk factor for the development of CVD [28].

Obesity is prevalent in Saudi Arabia, and it was reported that the overall prevalence of obesity and overweight in Hail region (northern Saudi Arabia) was 63.6% (the prevalence of males was 56.2% vs. 71% of females) [29]. Another study from Northern Saudi Arabia reported prevalence rates of obesity and overweight in 4 provinces; Hail, Baqaa, Ash Shinan, and Ghazala as 64%, 70%, 69%, and 55%, respectively [30]. Other reports from Saudi Arabia showed that the prevalence rates of overweight were 27%, and obesity was 40.23% [31]. The adapting of westernized life over the few past years in Saudi Arabia has led to the highest prevalence rates of overweight and obesity, which place the population at increased risk on non-communicable diseases including CKD [32].

CKD is an emerging non-communicable disease worldwide. Obesity is associated with an increased risk of developing stage 3 CKD, which was no longer significant after adjustment for known CVD risk factors. The relationship between obesity and stage 3 CKD may be mediated through CVD risk factors [33]. However, a high BMI predicts the onset of albuminuria without CKD stages 1-2 as well as CKD stages 3 and higher, the effect being significant only in obese individuals [34].

The Arab countries have a high prevalence of CKD risk factors, e.g., diabetes, obesity and hypertension [35]. A study from Saudi Arabia found that overweight and obesity represent 82.7% of those with CKD [36]. However, there was a lack of data regarding the direct association between CKD and obesity or/and overweight from Saudi Arabia.

Glomerulonephritis

Focal and segmental glomerulosclerosis (FSGS) and membranoproliferative glomerulonephritis (MPGN) were the most common forms of primary glomerulonephritis in adult patients in Saudi Arabia. This study included 6 big referral hospitals from diverse areas of Saudi Arabia contributed to the registry. Biopsy reports and clinical data of 1294 renal biopsies were attained. There were 782 renal biopsies because of glomerulonephritis (GN) constituting for 77.2% of the overall biopsies. About 587 (72.6%) were primary glomerulonephritides, focal and segmental glomerulosclerosis (FSGS) (21.3%), and membranoproliferative glomerulonephritis (MPGN) (20.7%). Membranous glomerulonephritis (MGN) was existing in 10.6% of the patients. IgA nephropathy was instituted in 6.5% of the patients [37]. Another study from Saudi Arabia, reported that minimal change disease and focal segmental glomerulosclerosis were the commonly encountered primary glomerular diseases (20.1% and 19.5% respectively), mesangioproliferative glomerulonephritis IgM nephropathy (14.8%), IgA nephropathy (10.7%), postinfectious glomerulonephritis (9.5%), MGN (7.1%), MPGN (5.9%) and mesangioproliferative glomerulonephritis with negative immunofluorescence (5.9%) [38]. Another study from Saudi Arabia found that the most common primary GN in 102 biopsies from adult patients with a mean age of 28.9 ± 13.6 years and 40.2% female, was focal and FSGS (35.3%). Among 64 patients with systemic lupus erythematosus associated nephritis, of whom most (82.8%) were female, lupus nephritis (LN) 4 (46.9%), and (LN) 3 (32.8%) were the most common lupus nephritis classes [39].

Although the risk of GN as an etiological for CKD was well established [40,41], there was a lack of literature from Saudi Arabia in this context.

Hereditary or Cystic Diseases

Hereditary cystic kidney diseases comprise a complex group of genetic disorders representing one of the most common causes of ESRD in childhood. Within the last years, genetic efforts have brought tremendous progress for the molecular understanding of hereditary cystic kidney diseases identifying more than 70 genes [42]. Hereditary conditions include autosomal dominant polycystic kidney disease, medullary cystic kidney disease, von Hippel-Lindau disease, and tuberous sclerosis [43]. Cystic kidney diseases often are discovered at the time of initial workup

of renal failure through ultrasound or family history, or incidentally at the time of an imaging test [44]. Cystic kidney disease is a common cause of ESRD. It is estimated that the prevalence of cystic kidney disease is 4.81% in the Arabian Gulf countries; hence, hereditary and congenital disease prevalence is 4.43% [45].

Other Conditions

There are many conditions evidenced to have a role in the etiology of CKD, such as plasma cell dyscrasias, sickle cell nephropathy, schistosomiasis, tuberculosis, and contrast nephropathy. These conditions are thought to contribute to 19.59% of the prevalence of CKD [45,46].

CONCLUSION

CKD is prevalent in Saudi Arabia. Many risk factors have been associated with increased risk of CKD with most common, DM, hypertension, and overweight and obesity. Many other miscellaneous risk factors require more investigations among the Saudi population.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Iseki, K. "Epidemiology of CKD in Japan." *Nihon rinsho. Japanese Journal of Clinical Medicine,* Vol. 66, No. 9, 2008, pp. 1650-56.

[2] Noel, D., and P. Landais. "Epidemiology of chronic kidney disease." *La Revue du Praticien,* Vol. 62, No. 1, 2012, pp. 38-42.

[3] Webster, Angela C., et al. "Chronic kidney disease." *The Lancet,* Vol. 389, No. 10075, 2017, pp. 1238-52.

[4] Brandenburg, V., and J. Floege. "Early diagnosis of chronic kidney disease. New insights into creatinine and proteinuria." *Medizinische Klinik, Munich, Germany: 1983,* Vol. 101, 2006, pp. 158-62.

[5] Khanna, Ramesh. "Clinical presentation and management of glomerular diseases: hematuria, nephritic and nephrotic syndrome." *Missouri Medicine,* Vol. 108, No. 1, 2011, p. 33.

[6] Ginawi, Ibrahim Abdelmajeed, et al. "Population screening for chronic kidney disease and its associated risk factors: a survey in Hail region, KSA." *Journal of Public Health and Epidemiology,* Vol. 5, No. 7, 2013, pp. 285-90.

[7] Ahmed, Hussain Gadelkarim, Ibrahim Abdelmajeed Ginawi, and Awdah M. Al-Hazimi. "Prevalence Estimates of Chronic Kidney Disease in Hail Region, KSA: in a Comprehensive Survey." *International Journal of Science and Research,* Vol. 3, No. 7, 2014, pp. 252-56.

[8] Ahmed, Hussain Gadelkarim, et al. "Distribution of CKD and Hypertension in 13 Towns in Hail Region, KSA." *Egyptian Academic Journal of Biological Sciences,* Vol. 6, No. 2, 2014, pp. 39-45.

[9] Alwin Robert, Asirvatham, et al. "Type 2 diabetes mellitus in Saudi Arabia: major challenges and possible solutions." *Current Diabetes Reviews,* Vol. 13, No. 1, 2017, pp. 59-64.

[10] Fawzy, Manal S., et al. "Factors associated with diabetic foot among type 2 diabetes in the Northern area of Saudi Arabia: a descriptive study." *BMC Research Notes,* Vol. 12, No. 1, 2019, p. 51.

[11] Alqurashi, Khalid A., Khalid S. Aljabri, and Samia A. Bokhari. "Prevalence of diabetes mellitus in a Saudi community." *Annals of Saudi Medicine,* Vol. 31, No. 1, 2011, p. 19.

[12] Ahmed, HG, et al. "Current Burden of diabetes in Kingdom of Saudi Arabia in an epidemiological survey." *Egyptian Academic Journal of Biological Sciences*, Vol. 6, No. 2, 2014, pp. 85-91.

[13] Damtie, Shewaneh, et al. "Chronic kidney disease and associated risk factors assessment among diabetes mellitus patients at a tertiary hospital, Northwest Ethiopia." *Ethiopian Journal of Health Sciences,* Vol. 28, No. 6, 2018, p. 691.

[14] Al-Rubeaan, Khalid, et al. "Diabetic nephropathy and its risk factors in a society with a type 2 diabetes epidemic: a Saudi National Diabetes Registry-based study." *PloS One,* Vol. 9, No. 2, 2014.

[15] Al-Rubeaan, Khalid, et al. "The Saudi diabetic kidney disease study, Saudi-DKD: clinical characteristics and biochemical parameters." *Annals of Saudi Medicine,* Vol. 38, No. 1, 2018, p. 46.

[16] Qari, Faiza A. "Profile of diabetic patients with end-stage renal failure requiring dialysis treatment at the King Abdulaziz University Hospital, Jeddah." *Saudi Journal of Kidney Diseases and Transplantation,* Vol. 13, No. 2, 2002, p. 199.

[17] Alghaythi, SalehMuflih, et al. "Prevalence of diabetes among patients with chronic kidney disease in Hail region." *The Egyptian Journal of Hospital Medicine,* Vol. 71, No. 2, 2018, pp. 2434-43.

[18] Alzaid, Aus A., S. Sobki, and V. De Silva. "Prevalence of microalbuminuria in Saudi Arabians with non-insulin-dependent diabetes mellitus: a clinic-based study." *Diabetes Research and Clinical Practice,* Vol. 26, No. 2, 1994, pp. 115-20.

[19] Al-Sayyari, Abdulla A., and Faissal A. Shaheen. "End-stage chronic kidney disease in Saudi Arabia. A rapidly changing scene." *Saudi Medical Journal,* Vol. 32, No. 4, 2011, pp. 339-46.

[20] Mills, Katherine T., et al. "Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries." *Circulation,* Vol. 134, No. 6, 2016, pp. 441-50.

[21] Ahmed, Hussain Gadelkarim, I. A. Ginawi, and A. M. Al-hazimi. "Prevalence of hypertension in hail region, KSA: In a comprehensive survey." *International Journal of Sciences: Basic and Applied Research,* Vol. 17, No. 2, 2014, pp. 288-96.

[22] Hadlaq, Emad M., et al. "Early screening of diabetes and hypertension in primary care dental clinics at King Saud University in Riyadh, Kingdom of Saudi Arabia." *The Journal of Contemporary Dental Practice,* Vol. 18, No. 8, 2017, pp. 652-59.

[23] Aldiab, Abdurrahman, et al. "Prevalence of hypertension and prehypertension and its associated cardioembolic risk factors; a population-based cross-sectional study in Alkharj, Saudi Arabia." *BMC Public Health,* Vol. 18, No. 1, 2018, p. 1327.

[24] Pugh, Dan, Peter J. Gallacher, and Neeraj Dhaun. "Management of hypertension in chronic kidney disease." *Drugs*, 2019, pp. 1-15.

[25] Barletta, Gina-Marie, et al. "Is blood pressure improving in children with chronic kidney disease? A period analysis." *Hypertension,* Vol. 71, No. 3, 2018, pp. 444-50.

[26] Kari, Jameela A., et al. "Predictors of renal replacement therapy and mortality in children with chronic kidney disease." *Saudi Medical Journal,* Vol. 36, No. 1, 2015, p. 32.

[27] Ng, Marie, et al. "Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013." *The Lancet,* Vol. 384, No. 9945, 2014, pp. 766-81.

[28] Lahey, Ryan, and Sadiya S. Khan. "Trends in obesity and risk of cardiovascular disease." *Current Epidemiology Reports,* Vol. 5, No. 3, 2018, pp. 243-51.

[29] Ahmed, Hussain Gadelkarim, et al. "Prevalence of obesity in Hail region, KSA: in a comprehensive survey." *Journal of Obesity,* 2014.

[30] Ginawi, Ibrahim Abdelmajeed, et al. "Prevalence rates of diabetes and obesity in 4 provinces in Hail Region, KSA." *Egyptian Academic Journal of Biological Sciences,* Vol. 6, No. 2, 2014, pp. 47-53.

[31] Alshaikh, Mashael K., et al. "Women in Saudi Arabia and the prevalence of cardiovascular risk factors: a systematic review." *Journal of Environmental and Public Health,* 2016.

[32] DeNicola, Erica, et al. "Obesity and public health in the Kingdom of Saudi Arabia." *Reviews on Environmental Health,* Vol. 30, No. 3, 2015, pp. 191-205.

[33] Foster, Meredith C., et al. "Overweight, obesity, and the development of stage 3 CKD: the Framingham Heart Study." *American Journal of Kidney Diseases,* Vol. 52, No. 1, 2008, pp. 39-48.

[34] Garofalo, Carlo, et al. "A systematic review and meta-analysis suggest obesity predicts the onset of chronic kidney disease in the general population." *Kidney International,* Vol. 91, No. 5, 2017, pp. 1224-35.

[35] Farag, Youssef MK, Jameela A. Kari, and Ajay K. Singh. "Chronic kidney disease in the Arab world: a call for action." *Nephron Clinical Practice,* Vol. 121, No. 3-4, 2012, pp. 120-23.

[36] Aljabri, D. "Prevalence of chronic kidney disease and it's risk factors in Saudi adults." *Journal of Medical Practice and Review*, Vol. 2, No. 10, 2018.

[37] Huraib, S., et al. "The spectrum of glomerulonephritis in Saudi Arabia: the results of the Saudi registry." *Saudi Journal of Kidney Diseases and Transplantation,* Vol. 11, No. 3, 2000, p. 434.

[38] Jalalah, Sawsan M., and Awatif A. Jamal. "Childhood primary glomerular diseases in the western region of Saudi Arabia." *Saudi Journal of Kidney Diseases and Transplantation,* Vol. 20, No. 4, 2009, p. 608.

[39] AlMatham, Khalid I., et al. "Glomerulonephritis disease pattern at Saudi tertiary care center." *Saudi Medical Journal,* Vol. 3, No. 11, 2017, p. 1113.

[40] Singh, Gurmeet R. "Glomerulonephritis and managing the risks of chronic renal disease." *Pediatric Clinics,* Vol. 56, No. 6, 2009, pp. 1363-82.

[41] Haider, Dominik G., et al. "Kidney biopsy in patients with glomerulonephritis: is the earlier the better?" *BMC Nephrology,* Vol. 13.1, 2012, p. 34.

[42] König, Jens Christian, et al. "Network for early onset cystic kidney diseases-A comprehensive multidisciplinary approach to hereditary cystic kidney diseases in childhood." *Frontiers in Pediatrics,* Vol. 6, 2018, p. 24.

[43] Katabathina, Venkata S., et al. "Adult renal cystic disease: a genetic, biological, and developmental primer." *Radiographics,* Vol. 30, No. 6, 2010, pp. 1509-23.

[44] Correas, J. M., et al. "Renal failure and cystic kidney diseases." *Journal de Radiologie,* Vol. 92, No. 4, 2011, pp. 308-22.

[45] Hassanien, Amal A., et al. "Epidemiology of end-stage renal disease in the countries of the Gulf Cooperation Council: a systematic review." *JRSM Short Reports,* Vol. 3, No. 6, 2012, pp. 1-21.

[46] Khanna, Ramesh. "Clinical presentation and management of glomerular diseases: hematuria, nephritic and nephrotic syndrome." *Missouri Medicine,* Vol. 108, No. 1, 2011, p. 33.