Journal of Clinical and Biomedical Sciences

Original Article

Evaluation of SCORED as a diagnostic tool for early detection of chronic kidney disease (CKD) and End-stage renal disease (ESRD): A hospital-based study

Osama F Mosa[1*]

1. Assistant Professor of Clinical Biochemistry & Laboratory Biomedicine, Department of Public Health, Health Sciences College at Lieth, UQU, Al-Lieth, Makkah KSA.

Abstract

Background: Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD) are significant public health problems characterized by structural or functional anomalies of the kidneys. CKD is considered one of the major non-communicable diseases and its prevalence is increasing rapidly in Saudi Arabia. Early detection of CKD is crucial but is not common as it is generally asymptomatic in the early stages. As a result, many cases are identified at more advanced stages. Aim: Risk assessment of CKD and ESRD epidemic in the Al-Leith Area in correlation with clinical, socioeconomic, and biochemical parameters using the Screening for Occult Renal Disease (SCORED) form.

Material & Methods: A cross-sectional, non-interventional investigation was conducted on every patient admitted to the internal medicine clinic-kidney unit at Al-Leith General Hospital (June-October 2018). The demographic and anthropometric data were obtained using a structured questionnaire, while urine and blood samples were collected and analyzed respectively.

Results: 120 patients were included as divided into 2 groups (Group I-CKD=89 patients, Group II-ESRD=31 patients). A significant difference was found for kidney function, swelling of the limbs, fasting blood glucose, total cholesterol, hemoglobin, Sodium levels, and blood pressure ($P<0.05$). Patients scoring 0-3 for occult renal disease (SCORED) were 73 in Group I (82.02%) and 2 in Group II (6.45%), while a score >4 was observed in 16 (17.98%) and 29 (93.55%), respectively.

Conclusions: Chronic diseases along with lifestyle influences were found to greatly affect CKD progression to ESRD. The use of the SCORED is a good pre-screening tool for CKD as it was effective at identifying patients at risk of kidney disease.

Keywords: SCORED, CKD, ESRD, KDIGO, Risk factors, Al-Lieth, KSA.

Introduction

Chronic kidney disease (CKD) is a condition characterized by progressive loss of renal function over a period of several years.[1, 2] CKD affects around 10% - 13% of the adult population and became a public health challenge due to the considerably increased risks of cardiovascular disease and death among the affected people.[3-5] The early stage symptoms are often non-specific, while the advanced stage symptoms include nausea, vomiting, loss of appetite, fatigue and weakness, sleep problems swelling of feet and ankles, chest pain, shortness of breath and more frequent urination.[6-8]

Among the most common causes of CKD are hypertension, diabetes, cardiovascular diseases and interstitial nephritis. This condition can further cause a decrease in kidney function and leading to uremia, hyperkalemia, hyperphosphatemia and decreased production of erythropoietin. Currently, the conceptual model recommended in 2002 by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) describe the criteria for progression of CKD.[2,9] It is usually defined and diagnosed by measuring serum creatinine levels using glomerular filtration rate (GFR) and While others include proteinuria, serum creatinine and eGFR.

***Corresponding Author**
Dr. Osama F Mosa
Assistant Professor of Clinical Biochemistry & Laboratory Biomedicine, Department of Public Health, Health Sciences College at Lieth, UQU, Al-Lieth, Makkah KSA.
Mobile No : 00966541485058
E-mail : drosama2030@gmail.com
Conflict of Interest: None
Financial Aid: Nil

End-stage renal disease (ESRD) follows CKD and is a condition where kidney function has declined to the stage where kidneys can no longer function on their own. A patient with ESRD must undergo dialysis or kidney transplantation in order to survive for more than a few months or years.[10-13] ESRD has become a severe burden worldwide highly affecting both social and economic future. [14,15] Until now, only three successful clinical trials have shown to delay the onset of the disease.[3, 5, 16] In these trials, ESRD was the only unambiguous endpoint for irreversible kidney failure used in order to gain permission for delaying its progression.[5, 17, 18]

ESRD is a clinically significant endpoint that influences both well-being and lifespan. However, when compared with other endpoints such as stroke, myocardial infarction or death. Although there are guidelines on the definition of myocardial infarction and stroke, there are no globally accepted definitions of ESRD.[7, 9, 10] In addition, the often asymptomatic nature of the early stages of CKD, leads to diagnosis only at advanced stages. The SCORED questionnaire consists of a self-reported form on nine variables, where each of them is assigned a specific value. It is a tool that was first published in 2007 by researchers in USA with the aim to identify and test more people at risk of CKD, as the standard test of serum creatinine measurement failed to diagnose many people at risk. It has been used for evaluation of the risk for occult renal disease, but never in an established diagnostic scenario.[19]

Our study was built on the concept that CKD is one of the fastest-growing multifactorial health problems in the world, now reaching an epidemic proportion in Saudi Arabia and other countries as a consequence of lifestyle changes, pollution, and unhealthy diet with increased consumption of processed food products.[20, 21] Taking into account pitfalls in the diagnosis of CKD and ESRD, the present report aims at describing a framework to describe kidney function in connection with CKD and ESRD. The present investigation focuses on the evaluation of the SCORED questionnaire for identifying patients at risk for developing CKD and ESRD , the detection and association with risk factors responsible for CKD and ESRD at Al-Leith Area and evaluation of the diagnostic performance of some routine lab tests.

Methods

1.1 Study area

A hospital-based investigation was conducted at Al-Leith area in the Kingdom of Saudi Arabia during the period from June to October 2018.

1.2 Study population

The study included all inpatients and outpatients registered at the Internal Medicine Clinic and Kidney Unit at Al-Leith General Hospital, after obtaining informed consents. Indeed, Biomedical ethical committee of the Health Sciences College at Lieth and the Hospital Institutional Review Board committee approved the proposal before the start of study under the numbers of CA/012/018 and AGH-JED-01-4-018, respectively. Furthermore, we confirm that our ethical approval was compatible with the Helsinki declaration for human subject research.

1.3 Sampling (sample size & sample technique)

Blood samples were obtained from 120 patients (54 males & 66 females) and classified according to the Kidney Disease: Improving Global Outcomes (KDIGO)-CKD criteria (Figure 1).[22]

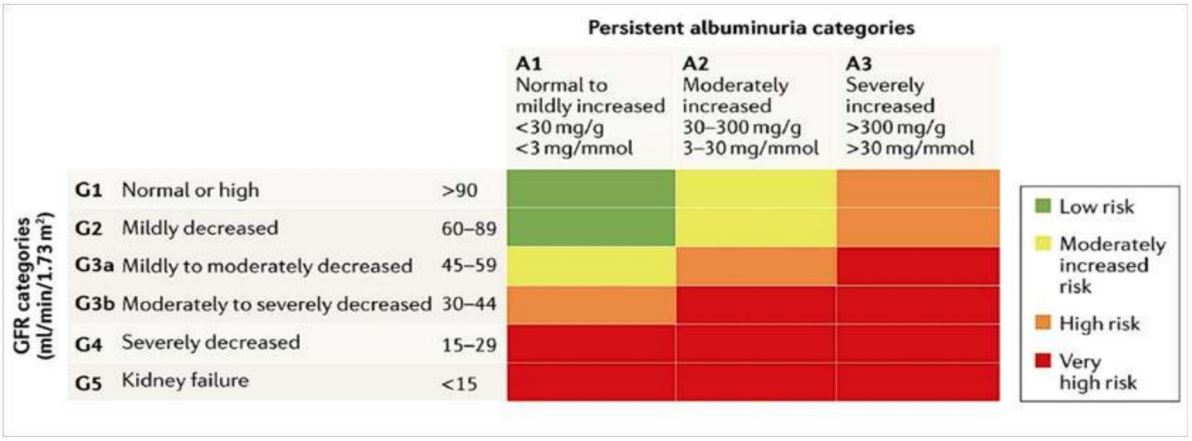

Figure 1 : Prognosis of CKS based on GFR and Albuminuria Levels (CKD– Chronic Kidney Disease) GFR– Glomerular Filtration Rate. (Modified and adapted from KDIGO guideline).[22]

1.4 Data collection method

A well-designed questionnaire was used to collect anthropometric, sociodemographic and clinical data along with routine lab test results. Estimated GFR (eGFR) was calculated by using the Modification of Diet in Renal Disease (MDRD) formula:

GFR (mL/min/1.73 m^2) =175 × (SCr.)-1.154 × (Age)-0.203 × (0.742 if female) × (1.212 if African).[23]

1.4.1 Sociodemographic and anthropometric data

The sociodemographic and clinical data were collected using a structured questionnaire. Moreover, anthropometric (height, weight, Body Mass Index (BMI), blood pressure and smoking index) were analyzed by referring to standard protocols. Height and weight were measured using a digital balance with the attached height scale. BMI was calculated as weight in kilograms divided by the square of height in meters. Blood pressure analysis was performed in triplicates after a gap of 5 min. Patients were classified to have either a normal blood pressure, if both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were normal or as having mild, moderate and severe hypertension when SBP or DBP were mildly, moderately and severely raised, respectively.[7, 11, 15] The SCORED Questionnaire was used to screen for occult renal disease.[19]

1.5 Blood specimen collection and laboratory analysis

Five ml of fasting venous blood sample were collected from each patient. Serum was separated from whole blood by following standard protocols to analyze serum glucose, serum creatinine, total cholesterol, albumin, Sodium, Potassium, Calcium and the Blood Urea Nitrogen (BUN) tests.

1.6 Data analysis

Data were analyzed using SPSS software package version 20.0 (IBM, NY, USA). Qualitative data were described using the number and percentage. A comparison between different groups regarding categorical variables was performed using the Chi-square test. Quantitative data were described using mean and standard deviation for normally distributed data. For normally distributed data, a comparison between two independent populations was done using an independent t-test. Significance test results are quoted as two-tailed probabilities. The significance of the obtained results was examined at the 5% level.

Declarations

Ethical approval: Under the numbers of CA/012/018 and AGH-JED-01-4-018.

Results

Out of 120 patients, 89 were distributed under group I category who met criteria of CKD (74.2% and 31 under group II who met the criteria of ESRD (25.8%). The distribution of demographic data in relation to diagnosis is summarized in Table 1. Interestingly, age in group I ranged from 39-62 years with a mean value of 45.6±7.25 years and in group II ranged from 41-65 years with a mean value of 53.5±8.1 years exhibiting a significant difference ($P<0.05$) , while there was no statistical significance regarding gender, residence, occupation and onset date of diabetes. Weight in group I ranged from 65-95 kg (mean value 79.8±10.3 kg) and in group II ranged from 69-102 kg (mean value 91.2±9.65 kg). BMI in group I ranged from 24.0-33.9 with a mean value 27.8±2.01 and in group II ranged from 26.8-35.2 with a mean value 30.1±1.98. These differences were found to be statistically significant between the two groups for both features ($P<0.05$), whereas this was not the case for height measurement ($P>0.05$) (Table 2).

The prevalence of risk factors for CKD in the patients enrolled in the study are presented in Table 3. There were 5 cases with liver disease in group I (5.62%) and 12 in group II (38.71%) while the number of cases without liver disease was 84 (94.38%) and 19 (61.29%), respectively. A significant difference was noticed between the studied patients regarding liver disease ($P<0.05$) while there was no significance regarding smoking ($P>0.05$).

Our study revealed a significant difference ($P<0.05$) regarding early medical signs of kidney disease. Foams in urine was observed in 6 patients in group I (6.74%) and 7 patients (22.58%) in group II, while proteinuria was present in 12 (13.48%) and 18 (58.06%) patients, respectively. Thirty patients from group I exhibited swelling in the limbs (33.71%) as opposed to 22 (70.97%) patients in group II. Elevated blood pressure was observed in 19 patients in group I (21.35%) and 20 patients in group II (64.52%), while 62 (69.66%) and 26 (83.87%) patients, respectively, experienced increased night urination as shown in Table 4 and Figure 2.

In a related context, blood pressure (systolic and diastolic), fasting blood glucose (FBG), total cholesterol, hemoglobin (Hb) and Na levels differed significantly between the two groups. Conversely, triglycerides (TG) and other electrolytes (K, Ca) did not show any significant difference. Measured kidney function tests (including serum creatinine, GFR and BUN test) exhibited a significant relevance between the two different groups and are summarized in Table 5.

The incidence of autoimmune diseases between the two groups was diverse for different diseases and between the two groups. More specifically, there were 78 patients with Type I diabetes (DMI) in group I (87.64%) and 31 in group II (100%), and 15 (16.85%) and 6 (19.35%) patients, respectively, for rheumatoid arthritis (RA). Similar rates were recorded for systemic lupus erythematosus (SLE) with 22 patients in group I (24.72%) and 7 in group II (22.58%), while scleroderma was observed in 10 (11.24%) and 4 (12.90%) patients, respectively. These differences were significant for DMI, RA, SLE and scleroderma (P<0.05) but not for Lupus Nephritis (P>0.05).

Figure 3 presents a summary of treatments administered to patients for chronic diseases that could retard the deterioration of renal disease pathogenesis (P<0.05). Insulin was administered in 55 patients in group I (61.80%) *vs* 15 patients in group II (48.39%). Forty two patients in group I were taking oral hypoglycemic agents (47.19%) as opposed to 19 in group II (61.29%). The percentage of patients in the two groups under lipid lowering drugs was almost threefold in group II compared to group I (22 (70.97%) and 24 (26.97%) respectively), while antihypertensive drugs were taken by 36 patients in group I (40.45%) and 20 in group II (64.52%).

The SCORED questionnaire was also used to evaluate patients at risk of CKD and ESRD. Individuals who score >4 have higher chances of developing CKD and, thus, should be further tested for CKD markers.[19] A score of 0-3 indicates a low risk of developing the disease. In our study, 73 patients in group I had a score from 0-3 (82.02%) while there were only 2 patients with this score in group II (6.45%). Conversely, a score > 4 was found in16 patients in group I (17.98%) as opposed to the majority of patients in group II (22 patients corresponding to 93.55%) (P<0.05) (Table 6).

Table 1: Distribution of the studied patients regarding demographic data in relation to diagnosis.

	Group I "CKD" n=89		Group II "ESRD" n=31		P value
Age **Range** **Mean** **S.D.**	39-62 45.6 7.25		41.0-65.0 53.5 8.1		0.032*
Gender **Male** **Female**	35 54	39.33 % 60.67%	19 12	61.29% 38.71%	0.136
Residence **Rural** **Urban**	42 47	47.19% 52.81%	15 16	48.39% 51.61%	0.107
Occupation **Unemployed** **Employed** **Retired**	30 41 18	33.71% 46.07% 20.22%	10 15 6	32.26% 48.39% 19.35%	0.098
Onset date of diabetes **<5 yrs** **5-10 yrs** **10+ yrs**	35 30 24	39.33% 33.71% 26.97%	10 12 9	32.26% 38.71% 29.03%	0.177

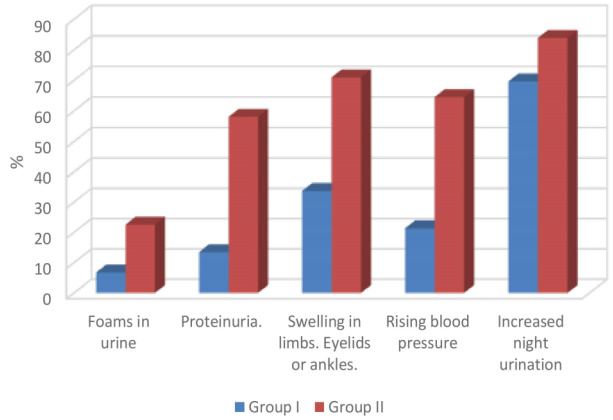

Figure 2 : Distribution of the studied patients regarding early signs of kidney disease.

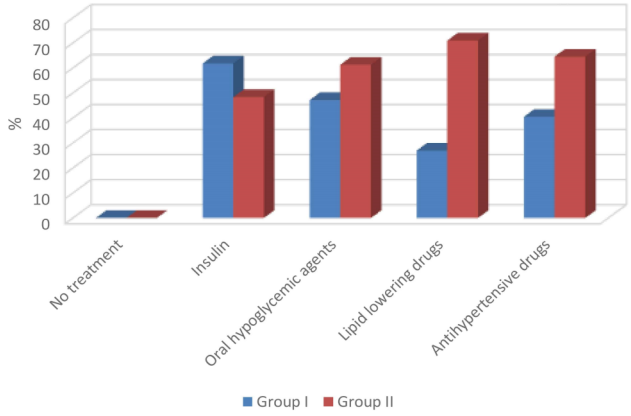

Figure 3: Methods of treatment used in the two studied group for other chronic diseases.

Table 2: Distribution of the studied patients regarding routine anthropometric data in relation to diagnosis.

	Group I "CKD" n=89	Group II "ESRD" n=31	P value
Height (cm)			
Range	156-178	155-177	
Mean	169.2	168.0	0.107
S.D.	16.5	14.3	
Weight (kg)			
Range	65-95	69-102	
Mean	79.8	91.2	0.016*
S.D.	10.3	9.65	
BMI			
Range	24.0-33.9	26.8-35.2	
Mean	27.8	30.1	0.001*
S.D.	2.01	1.98	

Table 3: Distribution of the studied patients regarding risk factors.

	Group I "CKD" n=89		Group II "ESRD" n=31		P value
	No.	*%*	*No.*	*%*	
Smoking					
Yes	25	28.09	10	32.26	0.66
Liver disease					
	5	5.62	12	38.71	0.001*
Yes	84	94.38	19	61.29	

Table 4: Distribution of the studied patients regarding medical early signs of kidney disease.

	Group I "CKD"		Group II "ESRD"		P value
	No.	%	No.	%	
Foams in urine	6	6.74	7	22.58	0.021*
Proteinuria	12	13.48	18	58.06	0.011*
Swelling in limbs	30	33.71	22	70.97	0.006*
Rising blood pressure	19	21.35	20	64.52	0.003*
Increased night urina-	62	69.66	26	83.87	0.001*

Table 5: Kidney function tests in the two studied groups.

Kidney function	Group I "CKD" n=89	Group II "ESRD" n=31	P value
Serum creati-nine **Range** **Mean** **S.D.**	 1.2-10.3 5.65 2.98	 3.2-11.9 7.11 3.65	0.001*
GFR **Range** **Mean** **S.D.**	 42.5-68.0 58.2 7.98	 4.0-13.0 9.0 3.88	0.041*
BUN **Range** **Mean** **S.D.**	 12-65 49.25 16.2	 20.0-113.0 72.6 20.6	0.003*

Table 6: Comparison between the two studied groups regarding the screening for occult renal disease (SCORED).

SCORED	Group I "CKD" n=89		Group II "ESRD" n=31	
	No.	%	No.	%
0-3	73	82.02	2	6.45
More than 4	16	17.98	29	93.55
P value	0.0001*			

Discussion

CKD is the causing factor for progressive uremia along with a decline in renal function that often triggers the onset of renal dialysis indicating ESRD outbreak. The syndrome of symptomatic uremia is tough to define but facile to recognize at the bedside.[8] In our study, about 55% of CKD patients were female and the majority of these patients were unemployed or retired. This is a normal indication since most of the study sample were relatively old (mean = 45.6±7.25 years). A recent cohort study conducted in the Canadian province of Manitoba reported that more women than men were observed to have CKD, and more than half of the reported CKD cases were 65 years old or older.[1] In another study, CKD prevalence was higher in females (52.6%) compared to males (47.4%) with higher incidence in patients aged between 40-64 years than those older than 64 years.[24] This might explain how age predisposes to renal impairment in such away.

The anthropometric measurements we used revealed an increase in the weight and BMI in both groups, with patients in the ESRD group exhibiting higher levels than the CKD group. Similar results were observed while analyzing chronic disease burden associated with obesity in Ireland.[25]

Blood pressure in the ESRD group was significantly higher than in the CKD group, pinpointing the possibility of hypertension. FBG levels exhibited a significant increase in the ESRD group compared to the CKD. These results are in accordance with a study that concluded that high blood pressure is a strong independent risk factor for ESRD.[26] Other studies conducted in the USA, Caribbean, Iran, Saudi Arabia, Egypt, Jordan and Palestine showed that hypertension and diabetes mellitus (DM) are the most common causes of ESRD.[27-32] Indeed, significant correlation was observed between patients who have DM and hypertension and the onset of ESRD. This phenomenon can be explained on the light of rapid urbanization and increased prevalence of a sedentary lifestyle.[33]

Lipid profile levels were found to be significantly higher in the ESRD group than the CKD. However, dyslipidemia was relatively higher in female CKD patients compared to male patients. The higher pervasiveness of dyslipidemia in female CKD patients may be witnessed by the higher cut off of <50 mg/dl used to diagnosed low HDL compared to a lower value of < 40 mg/dl used in males. Also, estrogen which is considered to be protective against dyslipidemia by boosting the levels of HDL-C in premenopausal females is generally low in CKD female patients.[34, 35] Impressively, almost all of the studied patients were anemic in accordance with previous study that revealed that CKD and ESRD patients probably suffer from anemia.[36] eGFR is an ideal predictor of ESRD risk. During a period of follow-up for 2 years, eGFR more strongly associates with future ESRD risk than magnitude of past eGFR decline, but both contribute substantially to the potential risk of ESRD, especially at eGFR<30 ml/min per 1.73 m^2.[13, 14] CKD is characterized by poor outcomes and high costs, and its increasing worldwide prevalence represents a significant public health challenge. Although most of patients with CKD have early-stage disease, patients with late-stage disease and especially, those with ESRD suffer from an increasingly high risk of co-morbid conditions and possess extremely poor economic background with lack of healthy diet. It is, thus, important to focus interventions, such as efforts to slow kidney progression and preparation for the transition to ESRD, on patients who are most prone to experience a progressive disease course. Recent studies have emphasized the importance of eGFR and albuminuria as measures of kidney disease severity, which can be assessed at the point of clinical contact, used to classify patients into various stages of CKD and form the basis of clinical interventions. However, many other factors influence the rate of progression, including age, co-morbid conditions, such as diabetes mellitus or hypertension, race, ethnicity and genetic mutations.[37,38] Nonetheless, these factors do not account for the observed variability in kidney disease progression.[39,40] While comparing the percentages of people residing in rural regions and the main urban region, it was observed that CKD cases in some rural regions appear to be under represented.[1]

Conclusion

The identification of risk factors for the progression of CKD and ESRD is recommendable for prognosis and early management of the disease. Our study showed that chronic diseases together with rigid lifestyle patterns and environmental conditions in the Al-Leith area are key risk factors for the progression of CKD and ESRD. However, renal function tests, Lipid profile, FBG, TC, Hb and BP levels were significantly augmented in the ESRD group than the CKD ($P<0.05$).The SCORED questionnaire was effective in our scenario and it seems to be a fast, simple, non-invasive screening tool for detecting people at high risk of CKD and ESRD, especially in rural settings where resources are limited. A delicate management of CKD patients at and advanced stage (stage G3) of the disease in primary care will prevent rapid renal decline and prevent the progression to worse complications, like ESRD.

Acknowledgements

The author appreciates the head of Al-Leith Kidney Unit (AKU) and executive head of Al-Leith General Hospital, Makkah, Saudi Arabia for their valuable support and assistance.

References

1. Chartier MJ, Tangri N, Komenda P, Walld R, Koseva I, Burchill C, McGowan KL, Dart A. Prevalence, socio-demographic characteristics, and comorbid health conditions in pre-dialysis chronic kidney disease: results from the Manitoba chronic kidney disease cohort. BMC Nephrol 2018; 19(1):255.
2. Levey AS, Coresh J. Chronic kidney disease. The lancet. 2012; 379(9811):165-80.
3. Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J, Chen M, He Q, Liao Y, Yu X, Chen N. Prevalence of chronic kidney disease in China: a cross-sectional survey. The Lancet. 2012; 379(9818):815-22.
4. 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.
5. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS. Prevalence of chronic kidney disease in the United States. Jama 2007; 298(17):2038-47.
6. Khan YH, Sarriff A, Adnan AS, Khan AH, Mallhi TH. Chronic kidney disease, fluid overload and diuretics: a complicated triangle. PLoS One. 2016; 11 (7).
7. Mosa OF, Binmahfouz A, Agrawal A, Al-Shehri RA, Al-Afifi BM, Al-Omari KK, Al-Yazidi MS. Magnitude and determinants of Diabetes mellitus (DM) and diabetic nephropathy (DN) in patients attending Al-Leith General Hospital. Indian J Basic Appl Med Res 2018; 7(2):486-494.
8. Agarwal R. Defining end-stage renal disease in clinical trials: a framework for adjudication. Nephrol Dial Transpl 2016; 31(6):864-7.
9. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol 2018; 72(18):2231-64.
10. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MS, George MG, Hamdan AD, Higashida RT, Hoh BL. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013; 44(7):2064-89.
11. Mohammed AE, Shenkute TY, Gebisa WC. Diabetes mellitus and risk factors in human immunodeficiency virus-infected individuals at Jimma University Specialized Hospital, Southwest Ethiopia. Diabetes Metab Syndr Obes 2015; 8:197.
12. Tomonaga Y, Risch L, Szucs TD, Ambuehl PM. The prevalence of chronic kidney disease in a primary care setting: a Swiss cross-sectional study. PLoS One 2013; 8(7).
13. Nelson RG, Grams ME, Ballew SH, Sang Y, Azizi F, Chadban SJ, Chaker L, Dunning SC, Fox C, Hirakawa Y, Iseki K. Development of risk prediction equations for incident chronic kidney disease. Jama 2019; 322(21):2104-14.
14. Kovesdy CP, Coresh J, Ballew SH, Woodward M, Levin A, Naimark DM, Nally J, Rothenbacher D, Stengel B, Iseki K, Matsushita K. Past decline versus current eGFR and subsequent ESRD risk. J Am Soc Nephrol 2016; 27(8):2447-55.
15. Rosa TT, Palatini P. Clinical value of microalbuminuria in hypertension. J Hypertens 2000; 18 (6):645-54.
16. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. N Engl J Med 1993; 329(20):1456-62.
17. Brenner BM, Cooper ME, De Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S. 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.
18. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345 (12):851-60.
19. Bang H, Vupputuri S, Shoham DA, Klemmer PJ, Falk RJ, Mazumdar M, Gipson D, Colindres RE, Kshirsagar AV. Screening for Occult Renal Disease (SCORED): A Simple Prediction Model for Chronic Kidney Disease. Arch Intern Med 2007 Feb 26;167(4):374-81.
20. Lew QL, Jafar TH, Koh HW, Jin A, Chow KY, Yuan JM, Koh WP. Red meat intake and risk of ESRD. J Am Soc Nephrol 2017;28(1):304-12.
21. Cianciaruso B, Pota A, Bellizzi V, Di Giuseppe D, Di Micco L, Minutolo R, Pisani A, Sabbatini M, Ravani P. Effect of a low-versus moderate-protein diet on progression of CKD: follow-up of a randomized controlled trial. Am J Kidney Dis 2009; 54 (6):1052-61.
22. Kidney Disease Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. KidneyInter2013; 3:1-150.

23. Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clin Chem 2007; 53(4):766-772.
24. Otero A, De Francisco A, Gayoso P, García F, EPIRCE Study Group. Prevalence of chronic renal disease in Spain: results of the EPIRCE study. Nefrología 2010; 30(1):78-86.
25. Kearns K, Dee A, Fitzgerald AP, Doherty E, Perry IJ. Chronic disease burden associated with overweight and obesity in Ireland: the effects of a small BMI reduction at population level. BMC Public Health 2014; 14(1):143.
26. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J. Blood pressure and end-stage renal disease in men. N Engl J Med 1996; 334(1):13-8.
27. USRDS: The United States Renal Data System. Excerpts from the USRDS 2009 annual data report: Atlas of end-stage renal disease in the United States. Am J Kidney Dis 2010, 55(Suppl 1):S1.
28. Soyibo AK, Barton EN. Caribbean renal registry data. West Indian Med J 2007; 5:45-51.
29. Beladi Mousavi SS, Hayati F, Talebnejad M, Mousavi M. What is the Difference between Causes of ESRD in Iran and Developing Countries? SEMJ 2012; 2:13.
30. Al-Khader AA. Impact of diabetes in renal diseases in Saudi Arabia. Nephrol Dial Transplant 2001; 16(11):2132–5.
31. Barsoum R. Nephrology in Egypt: A Forecast of the Upcoming Century. http:// www.health.egnet.net/health/esn/forecast.html. Accessed. 2003
32. Almdal Almdal, T T, Scharling H, Jensen JS, Vestergaard H. The independent effect of type 2 diabetes mellitus on ischemic heart disease, stroke, and death: a population-based study of 13,000 men and women with 20 years of follow-up. Arch Intern Med 2004; 164:1422–6.
33. Zelmer JL. The economic burden of ESRD in Canada. Kidney Int 2007; 72:1122-9.
34. Adejumo OA, Okaka EI, Ojogwu LI. Lipid profile in pre-dialysis chronic kidney disease patients in southern Nigeria. Ghana Med J. 2016; 50(1):44-9.
35. Adejumo OA, Okaka EI, Madumezia G, Okwuonu CG, Ojogwu LI. Assessment of some cardiovascular risk factors in predialysis chronic kidney disease patients in Southern Nigeria. Nigerian Med J 2015; 56(6):394.
36. Cianciolo G, De Pascalis A, Di Lullo L, Ronco C, Zannini C, La Manna G. Folic acid and homocysteine in chronic kidney disease and cardiovascular disease progression: which comes first. Cardiorenal Med 2017; 7(4):255-66.
37. Seferović J, Ležaić V. Classification of patients at risk for chronic kidney disease by use of eGFR and albuminuria. Biomedicinska Istraživanja 2015; 6 (1):28-36.
38. Kim S, Lim CS, Han DC, Kim GS, Chin HJ, Kim SJ, Cho WY, Kim YH, Kim YS. The prevalence of chronic kidney disease (CKD) and the associated factors to CKD in urban Korea: a population-based cross-sectional epidemiologic study. J Korean Med Sci 2009; 24(Suppl 1):S11-21.
39. Obrador GT, García-García G, Villa AR, Rubilar X, Olvera N, Ferreira E, Virgen M, Gutiérrez-Padilla JA, Plascencia-Alonso M, Mendoza-García M, Plascencia-Pérez S. Prevalence of chronic kidney disease in the Kidney Early Evaluation Program (KEEP) Mexico and comparison with KEEP US. Kidney Int 2010; 77:S2-8.
40. Cavallari LH, Mason DL. Cardiovascular pharmacogenomics - implications for patients with CKD. Adv Chronic Kidney Dis 2016; 23(2):82-90.