

ORIGINAL ARTICLE

An analysis of patients with chronic kidney disease newly referred to a specialized renal service in Sudan

Mazin Shigidi¹, Sahar Ebrahim², Wieam Karrar³

¹College of Medicine, Jouf University, Jouf, Saudi Arabia; ²Faculty of Nursing Sciences, University of Khartoum, Khartoum, Sudan;

³Dr Salma Centre for Kidney Diseases, University of Khartoum, Khartoum, Sudan.

ABSTRACT

Background: Limited data are available regarding the management of chronic kidney disease (CKD) outside the specialized nephrology services in Sudan.

Methods: A retrospective cohort study was conducted at Dr Salma Centre for Kidney Diseases (DSCKD) in Khartoum, Sudan. We aimed to determine the timing and reasons for referral of patients to specialized nephrology services and to evaluate the management of CKD at primary care level. Newly referred adult patients with CKD were recruited between July and September 2018. Information was extracted from the referral notes, from follow-up records at DSCKD and via direct interview of patients. Data analysis was performed using SPSS.

Results: A total of 244 patients were studied. Their mean age was 55 ± 13 years and 210 (86%) were on regular follow-up at primary care level. Hypertensive kidney disease and diabetic nephropathy were the leading causes of CKD. Most patients (78%) were timeously referred with CKD stage 3 or 4. Referrals were mostly due to elevated creatinine levels (35%), non-resolving nephrotic syndrome (27%) and upon patients' request (28%). Most patients (60%) did not require significant modifications to their management; 25 patients (11%) were late referrals and scheduled for urgent dialysis.

Conclusions: The current study reflects a good level of awareness regarding the management of CKD at primary care level and appropriate timing of referrals in most cases.

Keywords: chronic kidney disease; primary health care; Sudan.

INTRODUCTION

The overall prevalence of chronic kidney disease (CKD) in Sudan is estimated to range between 8–11% [1]. It is unlikely that all patients who are diagnosed as having CKD will be followed up by a nephrologist and it is expected that most patients will be cared for at the primary care level [2,3]. However, doctors working at the primary care level are often less aware of existing CKD practice guidelines. Previous reports have demonstrated that the treatment of patients with CKD at the primary care level is associated with a persistent pattern of late referral to nephrology services [4]. Late referral of CKD patients to these specialized services is associated with increased hospital admissions, elevated incidences of

anaemia and CKD mineral bone disorder, and therefore increased morbidity and cost of care [4,5].

Patients with CKD are expected to be referred to specialized nephrology services once their estimated glomerular filtration rate (GFR) reaches around 30 mL/min/1.73 m² [4,6,7]. In many circumstances, the decision of primary care physicians to refer to specialized renal services is influenced by patient factors such as the presence of clinical symptoms, their age, education level, the availability of medical insurance and the proximity to specialized services [6].

Limited data are available from the Sudan regarding the management of CKD patients outside the nephrology

units, as well as the timing of the referral of patients with CKD to specialized services. The current study therefore analysed the patients with CKD who were newly referred to a specialized renal centre to determine the aetiology of their kidney disease, assessed their prior management at the primary care level, and evaluated the timing of and reasons for referral.

METHODS

A retrospective cohort study was conducted at the Dr Salma Centre for Kidney Diseases (DSCKD) in Khartoum, Sudan. The centre is a large, multidisciplinary nephrology department that is linked to the University of Khartoum and accepts referrals from all parts of the country.

All adult patients newly referred to DSCKD with CKD between 1 July and 30 September 2018 were included in the study. We excluded patients who were less than 15 years of age, those with previous follow-up at DSCKD, those referred with acute kidney injury, kidney transplant recipients, patients on maintenance dialysis therapy and those who declined to give consent for enrolment. The diagnosis and staging of CKD were based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria and included the presence of abnormal radiological or histological findings, persistent proteinuria or an eGFR <60 mL/min/1.73 m² [6,7]. Acute kidney injury was ruled out once the kidney damage had been reported to be persistent for more than three months [8]. At DSCKD, urine dipstick testing and urine microscopy were routinely performed for all patients, and overt proteinuria on dipsticks was followed by measurement of the urine protein/creatinine ratio [6,9]. Serum creatinine concentration was determined enzymatically using a cobas c 501 analyser (Roche Diagnostics). Standardised creatinine measurements were reported as the assay was calibrated to isotope dilution mass spectrometry (IDMS)-traceable reference material. Estimation of the GFR used the re-expressed MDRD equation, with-out adjustments for ethnicity. The severity of CKD was graded from stage 1 to stage 5 [7]. Patients were labelled as being referred late if they were referred less than six months prior to the start of dialysis as kidney replacement therapy [10,11].

Data collection used a standardized data capture sheet and involved extraction of data from patients' referral notes and DSCKD's medical records. Patients were also interviewed. Where patients had incomplete records, their referring centres were contacted for more details. Information captured included demographic data, comorbid conditions, aetiology and severity of CKD, details of previous management and reasons for referral. All patients included in the study were followed up at DSCKD for at least six months.

Data were analysed using IBM SPSS Statistics for Windows, version 20 (IBM Corporation, Armonk, NY, USA). Variables were summarized using percentages, means with standard deviations, or medians with interquartile ranges. Chi-square and Student's t-tests were applied for analysis of categorical and numerical variables, respectively. Univariate logistic regression was performed to calculate the relative risk (RR) and confidence intervals (CIs) for patients to be referred with advanced CKD. Statistical significance was set at a P value of less than 0.05.

The study was approved by the Ethics Committee of the Graduate College, University of Khartoum, Sudan. Approval was also obtained from DSCKD. Written consent was obtained from all participants before enrolment.

RESULTS

During the study period, 279 adult Sudanese patients were newly referred to DSCKD with CKD. Among those, 19 patients (6.8%) did not return for follow-up, 15 patients (5%) had incomplete records and their primary physicians could not be reached, and one patient (0.3%) refused to give consent for enrolment; these were all excluded from the study. A total of 244 patients fulfilled the inclusion/exclusion criteria and were enrolled; they included 31 patients (13%) who had their primary treating physicians successfully contacted for additional information. The characteristics of the study cohort are summarized in Table 1. Most patients were referred from urban regions, 125 (51%) were males, 53 (22%) were university graduates, 61 (26%) were secondary school graduates and 162 (66%) were unemployed.

Hypertension, diabetes mellitus and glomerulonephritis were the commonest causes of CKD among the patients studied. A positive family history of CKD was mentioned by 69 patients; the aetiology was determined in 34 cases and was mostly due to polycystic kidney disease and primary glomerulonephritis.

Most patients (210, 86%) were receiving regular follow-up in a government or private primary healthcare facility before being referred. Follow-up was with a general physician in 89 patients (42%), family physician in 17 patients (8%), general practitioner in 83 cases (40%) and was unknown in 21 patients (10%). The mean duration of follow-up was 2.6 ± 2.9 years, with most patients (190, 78%) being referred with CKD stage 3 or 4 (Figure 1).

At DSCKD, the diagnosis was confirmed clinically in 205 patients (84%), and kidney biopsies were performed in 39 patients (16%). Hypertensive nephrosclerosis and diabetic nephropathy were the commonest causes of CKD. Patients with hypertensive nephrosclerosis were found to be at highest risk of being referred with advanced CKD (Table 2).

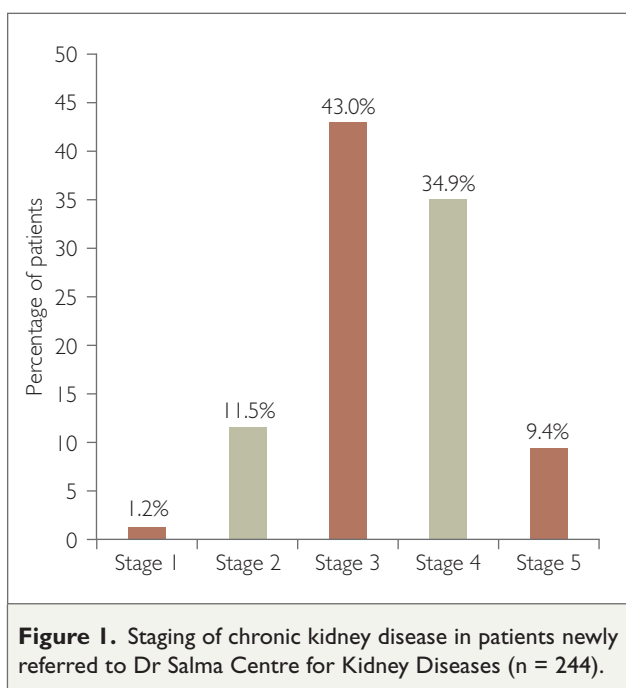
Table 1. Characteristics of patients newly referred with CKD and reasons for their referral (n = 244).

	Frequency (%)
Referred from urban / rural areas	171 (70%) / 73 (30%)
Male / female ratio	125 (51%) / 119 (49%)
Mean age of patients	
At referral to DSCKD	55 ± 13 years
When first diagnosed with CKD	48.6 ± 16.6 years
Married / unmarried	206 (84%) / 38 (16%)
Literate / illiterate	172 (71%) / 72 (30%)
Employed / unemployed	162 (66%) / 82 (34%)
Family history of CKD	69 (28%)
Risk factors for CKD progression	
Hypertension	186 (83%)
Overt proteinuria	112 (46%)
Diabetes mellitus	108 (44%)
Anaemia	79 (32%)
Dyslipidaemia	77 (32%)
Haematuria or proteinuria	62 (25%)
Ischaemic heart disease	23 (9%)
Smoking	17 (7%)
*Mean serum creatinine	
At referral to DSCKD	345 ± 230 µmol/L
When first diagnosed with CKD	212 ± 221 µmol/L
Median eGFR	
At referral to DSCKD	18 ± 47 mL/min/1.73 m ²
When first diagnosed with CKD	30 ± 35 mL/min/1.73 m ²
#Reasons for referral	
Persistently high serum creatinine	86 (35%)
Patient or family request	67 (28%)
Nephrotic syndrome not resolving	65 (27%)
For further management by a nephrologist	57 (23%)
Rapid deterioration in kidney function	43 (18%)
Planning for kidney replacement therapy	18 (7%)
Other	16 (7%)

*In 61 patients, the initial serum creatinine and eGFR were unknown. #Some patients had multiple reasons for referral. Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

During their follow-up at primary care level, 147 patients (70%) had well-controlled blood pressure on antihypertensive medication and required no further interventions at DSCKD. Furthermore, 112 patients (53%) were maintained on angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for renoprotection.

A significant number of the patients with CKD stages 4 and 5 were being treated with calcium carbonate, vitamin D analogues, iron supplements and erythropoietin therapy (Table 3). However, 34 patients (14%) were not having regular follow-up and were referred to DSCKD via emergency departments.



During the six months follow-up period at DSCKD, no significant changes were made in the management of 146 patients (60%); 25 (11%) were scheduled for vascular access creation, and 17 (7%) were referred for pre-transplant work-up. A total of 54 patients (22%) required a series of modifications in their management plan, including the drugs prescribed to control hypertension, CKD–mineral and bone disorder and anaemia (Table 4). Furthermore, 44 patients (18%) had to be initiated on immunosuppressive therapy for their CKD (Table 5).

DISCUSSION

The current study demonstrates the presence of a good level of awareness of evidence-based guidelines for CKD among primary care practitioners in Sudan, with 78% of the CKD patients received at DSCKD being appropriately referred with CKD stage 3 or 4 [12]. This probably reflects

Table 2. Aetiology of advanced CKD among newly referred patients (n = 244).

Aetiology	Patients			Relative risk (95% CI)	P value
	Stage 1–3 (n = 136)	Stage 4–5 (n = 108)	Total (n = 244)		
Hypertensive nephrosclerosis	28 (21%)	57 (53%)	85 (35%)	2.1 (1.6–2.7)	<0.001
Diabetic nephropathy	25 (18%)	17 (16%)	42 (17%)	0.8 (0.6–1.3)	0.597
Glomerulonephritis	24 (18%)	7 (7%)	31 (13%)	0.45 (0.2–0.8)	0.019
Polycystic kidney disease	18 (13%)	0 (0%)	18 (7%)	0.06 (0–1)	0.038
Lupus nephritis	7 (5%)	5 (5%)	12 (5%)	0.9 (0.5–1.9)	0.855
Interstitial nephritis	9 (7%)	2 (2%)	11 (5%)	0.3 (0.1–1.4)	0.154
Others	17 (13%)	11 (10%)	28 (12%)	0.8 (0.5–1.4)	0.588
Unknown	8 (6%)	9 (8%)	17 (7%)	1.2 (0.7–1.9)	0.421

Abbreviations: CI, confidence interval; CKD, chronic kidney disease.

Table 3. Chronic medications prescribed for patients while on regular follow-up at primary healthcare facilities (n = 210).

Medications	Number and percentages of patients				
	Stage 1 (n = 3)	Stage 2 (n = 28)	Stage 3 (n = 97)	Stage 4 (n = 68)	Stage 5 (n = 14)
ACEi / ARBs	3 (100%)	6 (21%)	38 (39%)	53 (78%)	12 (86%)
Calcium carbonate	0 (0%)	2 (7%)	46 (47%)	62 (91%)	14 (100%)
Vitamin D analogues	0 (0%)	0 (0%)	31 (32%)	36 (53%)	9 (64%)
Iron supplements	0 (0%)	0 (0%)	16 (17%)	64 (94%)	14 (100%)
Erythropoietin	0 (0%)	0 (0%)	0 (0%)	18 (29%)	7 (50%)
Loop diuretics	0 (0%)	6 (21%)	2 (2%)	31 (46%)	8 (57%)

Abbreviations: ACEi, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CKD, chronic kidney disease.

Table 4. Changes in the management of newly referred patients with CKD (n = 224).

Modifications	Number and percentages of patients					
	Stage 1 (n = 3)	Stage 2 (n = 28)	Stage 3 (n = 105)	Stage 4 (n = 85)	Stage 5 (n = 23)	Total patients (n = 224)
None	3 (100%)	9 (32%)	80 (76%)	49 (58%)	5 (22%)	146 (60%)
Antihypertensive drugs added	0 (0%)	0 (0%)	7 (7%)	19 (22%)	13 (57%)	39 (16%)
ACEi added	0 (0%)	14 (50%)	21 (20%)	6 (7%)	0 (0%)	41 (17%)
Calcium carbonate added	0 (0%)	0 (0%)	5 (5%)	32 (38%)	9 (39%)	46 (19%)
Vitamin D analogues added	0 (0%)	0 (0%)	0 (0%)	23 (27%)	7 (30%)	32 (13%)
Iron supplements added	0 (0%)	0 (0%)	2 (2%)	21 (25%)	9 (39%)	32 (25%)
Erythropoietin initiated	0 (0%)	0 (0%)	0 (0%)	35 (41%)	16 (70%)	51 (21%)
Loop diuretics stopped	0 (0%)	0 (0%)	0 (0%)	15 (18%)	6 (26%)	21 (9%)
Kidney biopsy requested	0 (0%)	19 (68%)	25 (24%)	0 (0%)	0 (0%)	44 (18%)
Referred for transplant work-up	0 (0%)	0 (0%)	0 (0%)	8 (9%)	9 (39%)	17 (7%)
Scheduled for dialysis access creation	0 (0%)	0 (0%)	0 (0%)	8 (9%)	17 (74%)	25 (11%)

Abbreviations: ACEi, angiotensin converting enzyme inhibitors; CKD, chronic kidney disease.

Table 5. Immunosuppressive therapies prescribed for newly referred patients (n = 44).

Therapy	Number of patients (%) and diagnoses						Total
	FSGS (n = 15)	MPGN (n = 9)	MCD (n = 6)	MN (n = 3)	LN (n = 6)	No biopsy (n = 5)	
Tacrolimus	1 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Cyclosporine	3 (20%)	0 (0%)	0 (0%)	3 (100%)	0 (0%)	0 (0%)	6 (14%)
Prednisone and MMF	0 (0%)	6 (67%)	0 (0%)	0 (0%)	6 (100%)	0 (0%)	12 (27%)
Prednisone and AZA	5 (33%)	3 (33%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	9 (20%)
Prednisone	6 (40%)	0 (0%)	5 (83%)	0 (0%)	0 (0%)	5 (100%)	16 (36%)

Abbreviations: FSGS, focal segmental glomerulosclerosis; MPGN, membranoproliferative (mesangiocapillary) glomerulonephritis; MCD, minimal change disease; MN, membranous nephropathy; LN, lupus nephritis (classes iii, iv, v); MMF, mycophenolate mofetil; AZA, azathioprine.

the attentiveness of the treating physicians towards progressive declining kidney function. Because 28% of referrals were at the request of patients or family members, it also reflects their concern regarding their kidney health. Timely referral of patients with CKD to nephrology services allows for optimizing the management and slowing the progression of the disease, planning kidney replacement therapy, and results in improved survival [10,13].

Only 35% of the Sudanese population is urban; however, 70% of the patients studied were from urban regions, which have better primary healthcare facilities, better transportation, and are near specialized health services [14-16].

Most referred patients had received at least some formal education and had access to medical insurance coverage and family financial support. Educated patients are expected to have better incomes, are often aware of common health problems and tend to seek medical care early [1,17]. On the other hand, around 30% of our patients were illiterate and were mostly from rural areas and more likely to be referred late. It is likely that illiterate patients had more limited understanding of their illness and often sought medical advice late [1,18].

More than one third of patients studied were unemployed, a much higher rate than that of the general population,

which is estimated at 18% [19]. Most patients related their unemployment to their physical disability; however, interviews conducted by the renal social worker suggested that the main reasons were their psychological unwillingness to seek employment, over-protective families and family financial support, which is highly prevalent in the Sudanese culture.

Variations were seen in the clinical practices and management of CKD in individual primary healthcare centres. Overall, the median eGFR reported at the time of referral was 18 mL/min/1.73 m² with few patients being referred early (CKD stages 1 and 2). Deferring referral of early stages avoids overwhelming the limited specialist renal services. Urine dipstick tests and urine microscopy were routinely performed for all patients during their follow-up at primary healthcare centres. The urine protein/creatinine ratio was mostly determined for those with more than 2+ protein on urine dipsticks and those with hypoalbuminaemia. Testing for microalbuminuria is not routine at primary healthcare level. This might lead to early CKD being underdiagnosed [20].

Hypertension, diabetes mellitus and glomerulonephritis were the main causes of CKD; those are the commonly reported causes in Sudan. The most common indication for performing a kidney biopsy was nephrotic syndrome; primary focal segmental glomerulosclerosis (FSGS) was the most common lesion diagnosed. In Sudan, FSGS and membranoproliferative (mesangiocapillary) glomerulonephritis have consistently been reported as the commonest causes of primary glomerulonephritis. Patients who refuse a kidney biopsy are therefore often treated empirically for these conditions [21].

The patients who were referred late were mostly those with long-standing hypertension who had adhered poorly to therapy and did not follow up regularly. Late referral is associated with reduced survival on dialysis and less chance of having a kidney transplant [7,13]. Most of the patients with a family history of CKD were aware of the implications of the condition and were often referred to DSCKD upon request and with CKD stage 2 or 3.

On reviewing the management at primary care level, it appeared that around 60% of hypertensives had well-controlled blood pressure and did not require changes in therapy. Furthermore, CKD renoprotection strategies, treatment of anaemia and CKD-mineral and bone disease control guidelines were implemented in similar percentages of patients. These findings probably reflect efforts to enhance CKD awareness and promote clinical practice guidelines among primary care physicians, with the Sudan National Centre for Kidney Diseases and Surgery (NCKDS) playing an important role in this regard.

Our study is limited by the relatively short study period, and the low numbers of patients enrolled from rural areas. The numbers of patients referred to specialized health services from rural areas often drop dramatically during the rainy and harvesting seasons. Longer-term, multicentre, prospective studies with the involvement of primary health-care practitioners are therefore essential to confirm the validity of the conclusions of the study reported here.

CONCLUSIONS

There is a good level of awareness regarding the management of CKD stages 3 and 4 at primary healthcare level and most patients are well managed and timeously referred. Improving the awareness and management of CKD at the primary care level is expected to lead to better outcomes for individual patients as well as benefits for the healthcare system.

REFERENCES

1. Abu-Aisha H, Elhassan EAM, Khamis AH, Abu-Elmaali A. Chronic kidney disease in police forces households in Khartoum, Sudan: Pilot Report. *Arab J Nephrol Transplant*. 2009; 2(2):21-26.
2. Sharif MU, Elsayed ME, Stack AG. The global nephrology workforce: Emerging threats and potential solutions! *Clin Kidney J*. 2016; 9(1):11-22.
3. Johnson DW, Atai E, Chan M, Phoon RKS, Scott C, Toussaint ND, et al. KHA-CARI Guideline: Early chronic kidney disease: detection, prevention and management. *Nephrology (Carlton)*. 2013; 18(5):340-350.
4. Martinez-Ramirez HR, Jalomo-Martinez B, Cortes-Sanabria L, Rojas-Campos E, Barragan G, Alfaro G, et al. Renal function preservation in type 2 diabetes mellitus patients with early nephropathy: a comparative prospective cohort study between primary health care doctors and a nephrologist. *Am J Kidney Dis*. 2006; 47(1):78-87.
5. Smart NA, Titus TT. Outcomes of early versus late nephrology referral in chronic kidney disease: a systematic review. *Am J Med*. 2011; 124(1):1073-1080.e2.
6. Gaitonde DY, Cook DL, Rivera IM. Chronic kidney disease: detection and evaluation. *Am Fam Physician*. 2017; 96(12):776-783.
7. Levin A, Stevens P, Bilous RW, Coresh J, de Francisco ALM, De Jong PE, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013; 3(1):1-150.
8. Thomas ME, Blaine C, Dawney A, Devonald MAJ, Ftouh S, Laing C, et al. The definition of acute kidney injury and its use in practice. *Kidney Int*. 2015; 87:62-73.
9. Kaminska J, Dymicka-Pekarska V, Tomaszewska J, Matowicka-Karna J, Koper-Lenkiewicz OM. Diagnostic utility of protein to creatinine ratio (P/C ratio) in spot urine sample within routine clinical practice. *Crit Rev Clin Lab Sci*. 2020; 57(5):345-364.
10. Smart NA, Dieberg GD, Ladhani M, Titus T. Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. *Cochrane Database Syst Rev*. 2014; 18(6):CD007333.

11. Baer G, Lameire N, Van Biesen W. Late referral of patients with end-stage renal disease: an in-depth review and suggestions for further actions. *NDT Plus*. 2010; 3(1):17-27.
12. Rosenberg M, Kalda R, Kasiulevicius V, Lember M. Management of chronic kidney disease in primary health care: position paper of the European Forum for Primary Care. *Qual Prim Care*. 2008; 16(4):279-294.
13. Grapsa E, Kiousi E. The role of an out-patient renal clinic in renal disease management. *J Transl Int Med*. 2015; 3(1):3-7.
14. Sudan population. World Population Prospects 2019 Revision. Available at <https://www.worldometers.info/world-population/sudan-population>.
15. Allender S, Foster C, Hutchinson L, Arambepola C. Quantification of urbanization in relation to chronic diseases in developing countries: a systematic review. *J Urban Health*. 2008; 85(6):938-951.
16. Bello AK, Hemmelgarn B, Lin M, Manns B, Klarenbach S, Thompson S, et al. Alberta Kidney Disease Network. Impact of remote location on quality care delivery and relationships to adverse health outcomes in patients with diabetes and chronic kidney disease. *Nephrol Dial Transplant*. 2012; 27(10):3849-3855.
17. Patrice HM, Joiven N, Hermine F, Yves BJ, Francois KF, Gloria AE. Factors associated with late presentation of patients with chronic kidney disease in nephrology consultation in Cameroon – a descriptive cross-sectional study. *Ren Fail*. 2019; 41(1):384-392.
18. Salman B, Tahir M, Qureshi R, Dhrolia MF, Ahmad A, Imtiaz S. Factor causing late referral of CKD patients to nephrology care. *Arch Renal Dis Manag*. 2017; 3(1):26-29.
19. The World Bank. International Labor Organization, ILOSTAT database. Available at <https://data.worldbank.org/indicator/SL.UEM.TOTL.ZS>.
20. Bello AK, Ronksley PE, Tangri N, Kurzawa J, Osman MA, Singer A, et al. Quality of chronic kidney disease management in Canadian primary care. *JAMA Netw Open*. 2019; 2(9):e1910704.
21. Nadium WK, Abdelwahab HH, Ibrahim MA, Shigidi MM. Histological pattern of primary glomerular diseases among adult Sudanese patients: A single center experience. *Indian J Nephrol*. 2013; 23:176-179.