eGFR and Chronic Kidney Disease Stages among Newly Diagnosed Asymptomatic Hypertensives and Diabetics Seen in a Tertiary Health Center in Nigeria

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Objectives: Moderate to severe CKD, may be symptomless and therefore may be undetected if effort is not made to assess kidney function. The aim of this study was to determine the eGFR of asymptomatic newly diagnosed hypertensives and diabetics with a view to creating awareness for early screening, evaluation and intervention especially in resource-poor settings where kidney replacement therapy is prohibitive.

Design, Setting, Participants: This is a retrospective study. Records of all hypertensive and diabetic patients referred to the medical clinic were included in the study for analysis. They were considered newly diagnosed if they were just being referred and were not on antihypertensive therapy or had been on therapy only in the last one month. The diagnosis of diabetes mellitus was made according to the guideline of the American Diabetes Association. We included in the analysis patients who had anthropometric measurements and serum creatinine from which we calculated the eGFR.

Main Outcome Measures: Use of eGFR and CKD stage in asymptomatic newly diagnosed hypertensives and diabetics.

Results: Six hundred and twenty eight patients were included in the study. The mean age (SD) for men and women were 50.19 (12.41) and 48.63 (14.43) respectively. A total of 242 (38.5%) had stage CKD stages 3a, 3b and 4 with a predominance of females: 184 (29.6%) vs 58 (9.2%). There was an association between CKD stage, sex ($\chi 2=135.56$, $P<.001$) and age ($\chi 2=30.83$, $P=.01$).

Conclusion: A substantial number of asymptomatic patients with hypertension and diabetes have CKD stages 3 and 4, associated with age and sex, but not with the BP stage. Without a proper evaluation, which includes determination of GFR, significant deterioration of kidney function may be missed and an appropriate intervention may not be instituted. (*Ethn Dis.* 2014;24[2]:220–225)

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Key Words: Screening, eGFR, Newly Diagnosed Hypertensives, Diabetics

Introduction

About 11% of the US adult population has chronic kidney disease (CKD) by the criteria of microalbuminuria, proteinuria and an estimated glomerular filtration rate (eGFR) of 20-30mL/min/1.73m^2.[1] Chronic kidney disease (CKD), like other non-communicable diseases, may be symptomless and therefore may be undetected, especially in resource-poor countries where health care infrastructures for kidney replacement therapy are not widely available. But when detected early, intervention would prevent a significant number of patients from presenting with advanced uremia.[2] A simple and effective way to measure kidney function is estimated glomerular filtration rate (eGFR), and this can be done and reported by the laboratory, given the variability of serum creatinine determinations alone.[3] Chronic kidney disease screening programmes, with a view to making early referrals and institute early interventions, have intensified in the last few years. For example, in the United Kingdom, eGFR is a routine practice where appropriate referrals are made to the nephrologists.[4] Also, International Society of Nephrology Global Outreach Program funds community CKD screening in many developing parts of the world.[5] The National Kidney Early Evaluation Programme (KEEP) is a free community screening programme aimed at early detection of kidney diseases among high – risk individuals. Participating countries include Mexico, United States, and Japan.[6–8]

The aim of our study was to determine the eGFR of asymptomatic newly diagnosed patients with hypertension and diabetes. This provides an opportunity for early detection of CKD and institution of measures to modify the course of the disease.

Study Variables and Statistical Analysis

In this retrospective study, records of all hypertensive and diabetic patients referred to the medical outpatient clinic were included in the study for analysis. They were all considered newly diagnosed if they were just being referred and were not on antihypertensive therapy or had been on therapy only in the last one month. The blood pressure at diagnosis when patient was assessed before commencement of antihypertensives was considered for the diagnosis of hypertension.

Patient's characteristics such as sex, age, social status, family history of hypertension/diabetes, smoking, and

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alcohol consumption were abstracted from the records. Body mass index (BMI) was calculated using the formula weight/height,^{2}. and was categorized as: underweight $<18.5 kg/m^2$, normal 18.5–24.9kg/m^2, overweight $\geq$25–29.9kg/m^2, and obese $\geq 30 kg/m^2$.[9] Blood pressure readings were extracted from patient records. Hypertension was defined as blood pressure of $\geq$140/90 mm Hg[10] or use of anti-hypertensives, but for such patients the blood pressure when first diagnosed was used. The following blood pressure categories were used: $\leq$120/80 mm Hg, 120–139/80–89 mm Hg, $\geq$140–159/90–99 mm Hg and $\geq$160/100 mm Hg. Patients whose records indicated that they had heart failure, pulmonary edema clinical evidence of uraemia, obstructive uropathy, and clinical diabetic nephropathy, were excluded. Chest x-rays, standard 12-lead ECG, and echocardiography records were also abstracted.

Hypertensive heart disease was clinically diagnosed when an apical impulse was palpable (heaving). However, in all of them an ECG was done and hypertensive heart disease was diagnosed when either left atrial enlargement (P wave duration of .04s and depth of $\geq$1mm or product of $\geq$.04mm sec) or left ventricular hypertrophy (Cornell voltage QRS duration product of $\geq$24440mm sec) was present. A strain pattern ST depression $\geq$1mm in leads 1, aVL, V4–V6 was also taken as a diagnostic feature on ECG. On echocardiography, a left ventricular mass was indicated by wall thickness greater than .45.

Only patients whose diagnosis of diabetes met the criteria of American Diabetes Association were included: symptoms of diabetes mellitus and a random plasma glucose of $\geq$200 mg/dL (11.1 mmol/L) or fasting plasma glucose $\geq$126mg/dL (7.0 mmol/L), or 2-hour post-prandial glucose $\geq$200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT).[11]

Estimated glomerular filtration rate was calculated using the electronic version four-variable MDRD formula provided by National Kidney Foundation.[12] Chronic kidney disease was defined in this study as eGFR $\leq$ 60mL/min/1.73m^2 (stages 3a +3b-5), irrespective of the cause,[13,14] according to the latest guideline.[14] Our records of urine analysis for protein are incomplete and these are not included in the classification.

The patients' demographics and characteristics were summarised with descriptive statistics such as frequencies, mean, percentages, and standard deviations. Continuous variables are expressed as means $\pm$ standard deviation (SD) and Student's *t* test used when analysing paired variables. Chi-square test was used to explore relationship between categorical variables. Multivariate analysis was performed using a stepwise logistic regression model using certain variables associated with eGFR $\leq$60mL/min/1.73m^2, our definition of CKD in this study. All probabilities were considered significant at $P<.05$. Data analysis was done using Statistical Package for Social Sciences (SPSS Inc. Chicago, IL) version 16 for analysis.

RESULTS

A total of six hundred and twenty eight (628) patients were included in the study (Table 1): 306 men and 322 women. The mean ages $\pm$ SD for men and women were 50.2 $\pm$ 12.4 and 48.6 $\pm$ 14.4, respectively. Four hundred and fifty-six (72.6%) of the study population were aged 41–75 years with 62 patients (9.9%) aged >75 years.

Two hundred and thirty one (36.8%) men and 230 (36.6%) women were known hypertensives. Thus, 461 (73.4%) were aware of being hypertensives and 54 (8.6%) were aware that they had diabetes mellitus. The use of alcohol and cigarettes was relatively low in our study population, 103 (16.4%) and 39(6.2%) respectively.

There was no significant sex difference in all blood pressure categories ($P=.28$), however, mean diastolic (DBP) and systolic blood pressure (SBP) were significantly higher in men than in women (88.9 $\pm$ 17.4 vs 85.2 $\pm$ 15.0 mm Hg, $P=.01$; 138.2 $\pm$ 28.3 mm Hg and 133.8 $\pm$ 26.4mm Hg, $P=.04$, respectively). The mean BMI was significantly higher in women when compared to men (28.8 $\pm$ 11.1 vs 26.6 $\pm$ 4.9 kg/m^2, $P<.001$) (Table 1).

A total of 404 (64.3%) were hypertensives or had hypertensive heart disease, and this was almost equally distributed between the two sexes 200 (male, 31.9%) vs 204 (female, 32.4%). Fifty-eight (9.2%) had a combination of hypertension and type 2 diabetes mellitus. One hundred and forty-six (23.3%) had hypertension and conditions such as arthritis, headaches and anxiety. The mean eGFR was significantly higher in men compared to women (74.3 $\pm$ 17.7 vs 56.6 $\pm$ 13.3 mL/min/1.73m^2, $P<.001$).

Chronic kidney disease stages were analysed by sex, age category, BP classification, and diagnosis at presentation (Table 2). Sixty-two (9.9%) men had CKD stage 1, while 186 (29.6%) of men and 138 women (22.0%) had CKD stage 2. The total number of patients with CKD stages 3a, 3b and 4 was 242 (38.5%). There was an association between sex and CKD stage ($\chi 2=134.84$, $P<.001$) and also between CKD stage and age category though patients in age categories <20 years and >75 years were fewer in number compared to other age categories ($\chi 2=27.73$, $P=.01$).

Sixty-seven (10.7%) and 66 (10.5%) of patients with normal blood pressure had CKD stages 2 and 3a/b, respectively. One hundred and four (16.6%) and 67 (10.7%) of patients with BP of 120/80–139/89 mm Hg had CKD stages 2 and 3a/b, respectively. There was a tendency toward increasing CKD stage with increasing age. There was no association between BP class and CKD stage ($\chi 2 =11.95$, $P=.22$) and also no

Table 1. Patients' sociodemographics

	Male	Female	Total	*P*
Age, mean (SD)	50.2 (12.4)	48.6 (14.4)	49.4 (13.5)	.15
Known hypertensive, yes, *n* (%)	231 (36.8)	230 (36.6)	461 (73.4)	.25
Known diabetic, yes, *n* (%)	26 (4.14)	28 (4.5)	54 (8.6)	.52
Alcohol, yes, *n* (%)	90 (29.4)	13 (4.0)	103 (16.4)	0
Smoking, yes, *n* (%)	34 (11.1)	5 (1.6)	39 (6.2)	0
Blood pressure category, mm Hg, *n* (%)				
≤120/80	60 (9.6)	84 (13.4)	144 (22.9)	.28
120/80–139/89	100 (15.9)	99 (15.8)	199 (31.7)	
140/90–159/99	71 (11.3)	70 (11.1)	141 (22.5)	
≥160/100	75 (11.9)	69 (11.0)	144 (22.9)	
SBP, mm Hg, mean ± SD	138.2 ± 28.3	133.8 ± 26.4	135.9 ± 27.4	.04
DBP, mm Hg, mean ± SD	88.9 ± 17.4	85.0 ± 15.0	87.0 ± 16.3	.01
BMI, kg/m^2, mean ± SD	26.6 ± 4.9	28.8 ± 11.1	27.8 ± 8.7	.00
eGFR, mL/min/1.73m^2, mean ± SD	74.3 ± 17.7	56.6 ± 13.3	65.2 ± 17.9	.00
Diagnosis at presentation, *n* (%)				
Hypertension/HHD	200 (31.8)	204 (32.5)	404 (64.3)	.11
Type 2 diabetes	4 (.6)	3 (.5)	7 (1.1)	
Hypertension and Diabetes	33 (5.3)	25 (4.0)	58 (9.24)	
Cardiomyopathy	9 (1.4)	4 (.6)	13 (2.1)	
Others	60 (9.6)	86 (13.7)	146 (23.3)	

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; eGFR, estimated glomerular filtration rate; HHD, hypertensive heart disease.

Table 2. CKD stages by certain characteristics

Stage	1	2	3a	3b	4	Total
Sex, *n* (%) [a]						
Male	62 (9.9)	186 (29.6)	33 (5.3)	21 (3.3)	4 (6)	306 (48.7)
Female	0 (0)	138 (22.0)	121 (19.3)	55 (8.8)	8 (1.3)	322 (51.3)
Age category, years, *n* (%)[b]						
<20	0 (0)	1 (.2)	1 (.2)	0 (0)	0 (0)	2 (.3)
21–40	14 (2.2)	60 (9.6)	26 (4.1)	8 (1.3)	0 (0)	108 (17.2)
41–60	33 (5.3)	144 (22.9)	58 (9.2)	30 (4.8)	6 (1.0)	271 (43.2)
61–75	15 (2.4)	96 (15.3)	46 (7.3)	23 (3.7)	5 (8)	185 (29.5)
>75	0 (0)	23 (3.7)	23 (3.7)	15 (2.4)	1 (.2)	62 (9.9)
BP category, mm Hg, *n* (%) [c]						
≤120/80	11 (1.8)	67 (10.7)	40 (6.4)	26 (4.1)	0 (0)	144 (22.9)
120/80–139/89	21 (3.3)	104 (16.6)	49 (7.8)	18 (2.9)	7 (1.1)	199 (31.7)
140/90–159/99	15 (2.4)	75 (11.9)	36 (5.7)	12 (1.9)	3 (.5)	141 (22.5)
≥160/100	15 (2.4)	78 (12.4)	29 (4.6)	20 (3.2)	2 (.3)	144 (22.9)
Diagnosis at presentation, *n* (%) [d]						
Hypertension/HHD	48 (7.6)	210 (33.4)	89 (14.2)	51 (8.1)	6 (1.0)	404 (64.3)
Type 2 diabetes	2 (.3)	3 (.5)	2 (.3)	0 (0)	0 (0)	7 (1.1)
Hypertension/diabetes	4 (.6)	28 (4.5)	19 (3.0)	5 (.8)	2 (.3)	58 (9.2)
Cardiomyopathy	1 (.2)	7 (1.1)	2 (.3)	3 (.5)	0 (0)	13 (2.1)
Others	7 (1.1)	76 (12.1)	42 (6.7)	17 (2.7)	4 (.6)	146 (23.2)

CKD, chronic kidney disease; BP, blood pressure; HHD, hypertensive heart disease.
[a] $\chi^2 = 135.56$ $P = .00$
[b] $\chi^2 = 30.83$ $P=.01$.
[c] $\chi^2 = 17.06$ $P=.15$.
[d] $\chi^2 = 12.29$ $P=.42$.

In our study, a significant number of asymptomatic hypertensive and diabetic patients had at least CKD stages 3a, 3b and 4 with a lower mean eGFR for the female participants.

association between CKD stage and diagnosis at presentation (χ^2 =12.29, *P*=.42).

A stepwise multivariate logistic regression analysis to predict eGFR <60mL/min showed that the odds ratio for having an eGFR <60mL/min was 6.71 for females and 2.72 for age category >65 years (Tables 3 and 4).

Table 3. Step 1 Logistic regression to predict eGFR <60mL/min

	Odds Ratio	95% Confidence Interval	*P*
Sex			
Male, reference	1.00		
Female	6.60	4.43, 9.84	<.001
Age, years			
18–39, reference	1.00		
40–64	1.51	.95, 2.42	.08
≥65	2.91	1.57, 5.40	.01
BMI, kg/m^2			
18.5–24.9, reference	1.0		.34
>25–29.9	1.24	.77, 1.98	.37
>30	1.42	.88, 2.26	.14
BP category, mm Hg			
≤120/80, reference	1.00		.67
120/80–139/89	.75	.44, 1.27	.29
140/90–159/99	.74	.40, 1.36	.34
≥160/100	.70	.38, 1.30	.26
Diagnosis at presentation			
Hypertension/HHD, reference	1.00		.56
Hypertension/diabetes	.55	.07, 4.00	.56
Cardiomyopathy	1.10	.51, 2.38	.80
Others	1.39	.38, 5.11	.62

eGFR, estimated glomerular filtration rate; BMI, body mass index; HHD, hypertensive heart disease.

DISCUSSION

In our study, a significant number of asymptomatic hypertensive and diabetic patients had at least CKD stages 3a, 3b and 4 with a lower mean eGFR for the female participants. Because the patients were asymptomatic and presented with no clinical evidence of kidney damage, it would be easy to miss significant kidney damage and deterioration of kidney function. At these stages of CKD, steps should be taken to slow progression of disease. Sex and age, which are non-modifiable risks factors, showed the highest association for CKD stage and they were also the strongest predictive factors for eGFR <60mL/min/1.73m^2. Blood pressure stage and diagnosis at presentation did not show these associations. This may be a reflection of the fact that the mean ± SD SBP and DBP on presentation was 135.90 ± 27.43 and 87.02 ± 16.26, respectively, and probably because some of the patients had been on antihypertensive medications. Therefore, without a determined and deliberate effort to screen for kidney damage, most patients with progressive kidney disease will be missed, with implications for subsequently inadequate treatment. Less than half the total number of study participants had blood pressure ≥140/90 mm Hg. In the face of a BP that is not in the hypertension range and lack of symptoms, there may be laxity in instituting interventions that slow progression of kidney disease. It has been demonstrated that in sub-Saharan Africa, patients often present late for care, and prognosis and survival are poor in such patients.[15,16] Kidney disease may progress with or without obvious clinical features and this may partly explain why patients present late, especially where routine kidney evaluation is not done as in many developed nations. As in our study, where 43.2% of the study population was aged 41–60 years, a significant proportion of those so affected are in the economically productive age group. There have been arguments about the usefulness of routine screening for CKD in the general population as compared to screening a targeted population, but we are

Table 4. Step 5 Logistic regression to predict eGFR <60mL/min

	Odds Ratio	95% Confidence Interval	*P*
Sex			
Male, reference	1.00		
Female	6.71	4.57, 9.86	<.001
Age, years			
18–39, reference	1.00		
40–64	1.45	.93, 2.26	.105
≥65	2.72	1.50, 4.94	.001

eGFR, estimated glomerular filtration rate.

concerned about patients who are seen in the hospital and miss the opportunity for care. More than one third of our study population had at least CKD stage 3a and 3b by eGFR determination and this is in keeping with previous studies.[17] Even though it has been demonstrated that patients who were selected only on the basis of impaired GFR, when followed up for 4.2 years, did not demonstrate a greater loss of GFR than the general population with normal GFR,[18] nonetheless, a reduction in GFR would prompt more screening for evidence of kidney damage and these would include urinalysis. While it may be true that, "the failure to take into account the normal age- and sex-associated decline in GFR and the lack of a requirement for other evidence of kidney disease in CKD stage 3 leads to erroneous categorization of large numbers of most elderly and female subjects as having an intermediate stage of a lethal disease,"[19] it would be desirable to screen for a disease that most developing nations are unable to cope with if allowed to progress. Age and sex are strong predictive factors of eGFR $\leq$60mL/min/1.73m^2 and older patients may benefit from further assessment and screening once the eGFR suggests that there is a reduction in kidney function. This is one of the reasons for including proteinuria in the most recent KDIGO guideline on CKD.[14] In our study, females were at higher risk of CKD than men, and this has also been reported in a large prospective study of men and women in a US study.[20] In the study, the adjusted hazard ratio of developing CKD among women was higher across blood pressure classes than in men.

Therefore, it may be necessary to identify patients who have a combination of albuminuria, a decreased GFR, and other modifiable risk factors.[1] While eGFR may not be sufficient for making a clinical decision,[21–22] may increase the workload of nephrologists unnecessarily, and cause patients to be referred to tertiary health centers when they could well be managed and followed up in secondary health centres, asymptomatic hypertensive, diabetic and older patients who are a high risk group should have a high priority for screening.[23] Indeed, automatic reporting of GFR by laboratories has been recommended to identify asymptomatic kidney dysfunction and also because it correlates well with complications of CKD.[24]

One limitation of our study is our lack of data on proteinuria/albuminuria, but recent guideline recognises CKD stages based on eGFR.[14]

CONCLUSION

We conclude that asymptomatic hypertensive and diabetic patients, and indeed all patients who are at risk of developing CKD, may have substantial deterioration of kidney function as measured by eGFR, and should have a complete targeted screening at the primary level of care to exclude structural kidney damage with a view to early intervention. All physicians should be sensitized in this regard.

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