Recognizing occult renal disease in managed hypertensives

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Introduction
Occult renal disease (ORD) is a condition that characterizes the early stages of kidney disease, which cannot be detected by routine monitoring such as serum creatinine only. The objective of this study was to determine the prevalence of ORD in managed hypertensives in a tertiary health care center in South Nigeria.

Participants and methods
A cross-sectional retrospective was carried out in 708 managed hypertensives attending the medical outpatient clinic. Data from 826 patients were analyzed, and 706 (85.7%) of these patients were found to have a creatinine value of 1.5 mg/dl and less. These 708 managed hypertensives with a normal serum creatinine value were analyzed, and their estimated glomerular filtration rate (eGFR) calculated with the Chronic Kidney Disease Epidemiology (CKD_EPI) prediction equation.

Results
A total of 218 (30.9%) had an eGFR lower than 60 ml/min,244(34.6%) had an eGFR of 60–89 ml/min, and the remaining 244 (34.6%) had an eGFR of 90 ml/min and above.

Conclusion
ORD has a high prevalence of 31% in treated hypertensive patients with normal serum creatinine values of less than 1.5 mg/dl. There is a need to use eGFR values, in this case, the CKD-EPI to assess GFR, to enable physicians detect chronic kidney disease at an earlier stage than the current practice of using serum creatinine alone. This is important as it appears that serum creatinine alone grossly underestimates the presence of CKD in treated hypertensive patients.

Keywords:
creatinine, estimated glomerular filtration rate, occult renal disease

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Introduction

Occult renal disease (ORD) is a condition that characterizes the early stages of renal failure, which cannot be detected by routine monitoring [1].

Hypertension guidelines recommend screening for chronic kidney disease, and this includes using serum creatinine and urine dipstick [2]. This strategy may lead to a miscalculation, as persons with chronic kidney disease (CKD) missed by the use of serum creatinine but detected by the use of glomerular filtration rate (GFR) measurements have higher risks for death, cardiovascular events, and end-stage renal disease (ESRD) [3].

The main cause of CKD in Nigeria includes hypertension, chronic glomerulonephritis, and diabetes [4]. The treatment of CKD and ESRD in Nigeria is expensive and mostly unaffordable by Nigerians. The cost of renal replacement therapy in Nigeria is prohibitive and virtually but out of reach to the large majority of Nigerian patients with end-stage kidney disease [5]. This is so as there are no government-funded ESRD treatment programs and no government-funded dialysis or assisted transplant programs. The large majority of transplant and dialysis centers are privately operated, and the entire cost burden is on the patient and supportive relations.

Chronic kidney disease is a major health problem in Nigeria [6]. The kidney is a main target of organ damage in hypertension [7]. Studies have shown that the prevalence of renal dysfunction among patients attending cardiology clinics is high [8,9]. In a study done involving 1224 patients from 124 hypertension treatment centers, it was shown that 30% of the study population had moderate to severe renal dysfunction and that only 21% of the study population had normal renal function [10].

In another study of 2686 patients attending a major hypertensive clinic in Europe, 7.6% of the patients studied had renal dysfunction, when a cutoff value of serum creatinine of 1.5 mg/dl was used. This figure

rose to 22.3% of the total managed hypertensives when a 24 h urinary creatinine clearance was used [11].

Increases in serum creatinine, even mild increases, constitute the most important predictor for cardiovascular death and could predate moderate to severe chronic kidney disease and subsequently ESRD [12].

Given the state of kidney care in sub-Saharan Africa and especially Nigeria, early detection of renal damage in managed hypertensive patients is essential. This facilitates earlier referral and management of risk factors. Although serum creatinine may be very effective in that regard, the eGFR has been touted as a more effective tool in diagnosing chronic kidney disease in managed hypertensives even when the serum creatinine is 1.5 mg/dl and less [13].

Participants and methods

This study was done in a tertiary health care center, South-South Nigeria, on 708 managed hypertensives, with a serum creatinine of 1.5 mg/dl and less.

The eGFR was calculated with the Chronic Kidney Disease Epidemiology equation (CKD_EPI). This was done with the following equation programmed on the Microsoft Excel platform.

Equation: $141 \times \min(S.Cr/\kappa,1)^{\alpha} \times \max(S.Cr/\kappa,1)^{-1.209} \times 0.993^{Age} \times 1.159$ (if black)$\times 1.018$ (if female).

(κ is 0.9 for males and 0.7 for females, and α is −0.411 for males and −0.329 for females [14,15]).

The eGFR was calculated using Microsoft Excel. The results were then transferred to the SPSS version 21 (SPSS IBM Incorporated).

Results

Results were set forth as follows.

A total of 708 out of 826 managed hypertensives were found to have a serum creatinine of 1.5 mg/dl and below.

However, other data were incomplete in 2 subjects and they were excluded from the final analysis, and thus 706 subjects were analysed. 293 (41.5%) were males and 413 (58.5%) were females.

218 (30.9%) had an eGFR of <60 and the remaining 488 (69.1%) had an eGFR of 60 mls/min/1.73m2 and above body surface area using the CKD_EPI formula.

Table 1 Group statistics of patients with normal serum creatinine, grouped as male and female

Sex of the patient	*n*	Mean	SD	Significance
Age				
Male	293	56.92	16.742	0.015
Female	413	53.96	15.323	
Systolic BP 1				
Male	293	153.75	21.738	0.005
Female	413	149.48	20.700	
Diastolic BP 2				
Male	293	82.42	13.839	0.704
Female	413	82.84	14.404	
Weight of patient				
Male	293	66.60	8.966	0.012
Female	413	64.80	9.609	
Serum creatinine				
Male	293	1.088	0.297	0.333
Female	413	1.110	0.3137	
Total cholesterol				
Male	293	206.47	45.632	0.384
Female	413	209.76	51.812	
High-density lipoprotein				
Male	293	64.9	40.100	0.261
Female	413	72.52	110.875	
Low-density lipoprotein				
Male	293	116.28	58.327	0.005
Female	413	129.19	62.085	
Triglyceride				
Male	293	105.46	25.616	0.100
Female	413	109.01	29.875	
GFR				
Male	293	90.82	28.551	0.000
Female	413	72.92	27.628	

BP, blood pressure; GFR, glomerular filtration rate.

Table 2 General statistics for patients with normal serum creatinine

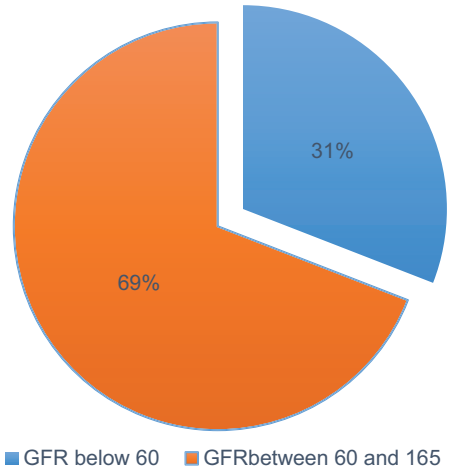
	N	Mean	SD	Minimum	Maximum
GFR	706	80.35	±29.353	39	165
Age	708	55.16	±15.970	18	96
Systolic BP 1	708	151.26	21.267	110	210
Diastolic BP 2	708	82.67	14.167	50	110
Weight of patient	708	65.55	9.378	35	88
Serum creatinine	708	1.101	0.3069	0.5	1.5
Total cholesterol	708	208.43	49.293	101	387
High-density lipoprotein	708	69.30	88.563	25	1320
Low-density lipoprotein	708	123.73	60.793	25	285
Triglyceride	708	107.55	28.182	41	243

BP, blood pressure; GFR, glomerular filtration rate.

Table 3 Sociodemographic distribution with respect to religion

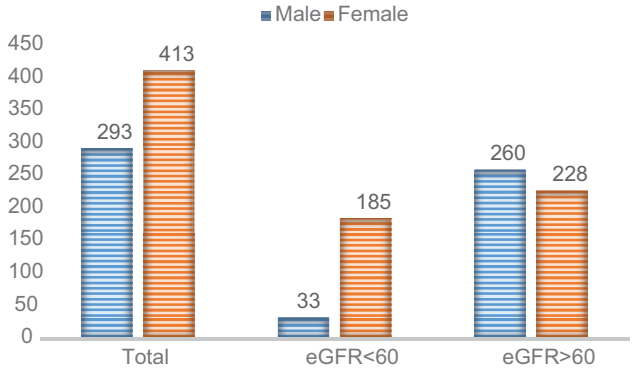
	Frequency	Percentage	Cumulative %
Christianity	614	86.7	86.7
Islam	55	7.8	94.5
Others	12	1.7	96.2
Nil	27	3.8	100.0
	708	100.0	

Figure 1



GFR of Patients with Normal Serum Creatinine

Figure 2



Comparison of GFR Values in patients with Normal Serum Creatinine

Table 4 Sociodemographic distribution with respect to occupation

	Frequency	Percentage	Cumulative %
None	262	37.0	37.0
Civil servant	153	21.6	58.6
Farmer	38	5.4	64.0
Pensioner	84	11.9	75.8
Self employed	171	24.2	100.0
Total	708	100.0	

Table 5 Sociodemographic distribution with respect to education

	Frequency	Percentage	Cumulative %
None	137	19.4	19.4
Primary	162	22.9	42.2
Secondary	233	32.9	75.1
Tertiary	176	24.9	100.0
Total	708	100.0	

Table 6 Sociodemographic distribution with respect to marital status

	Frequency	Percentage	Cumulative %
Single	85	12.0	12.0
Married	523	73.9	85.9
Widowed	98	13.8	99.7
Divorced	1	0.1	99.9
Separated	1	0.1	100.0
Total	708	100.0	

Table 7 Sociodemographic distribution with respect to sex

	Frequency	Percentage	Cumulative %
Male	293	41.4	41.5
Female	413	58.6	100.0
	708	100.0	

In those with eGFR <60mls/min, 33 (15.1%) were males and 185 (84.9%) were females.

Of the total group, males were significantly older than the females, *P*=0.015, and had a higher systolic Bp, *P*=0.005. Males also had a higher weight, *P*=0.012.

Females had a significantly lower eGFR p<0.05. There were no significant differences in High Density Lipoprotein (HDL), Triglyceride, Total cholesterol and serum creatinine.

Tables 1–7 and Figs. 1 and 2.

Discussion

Detecting patients who are hypertensives and who have ORD is very important in routine clinical practice. This is because they are said to have more cardiovascular risk factors than those with normal renal function.

In Nigeria, hypertensive renal damage is a cause of chronic kidney disease. Given the enormous implications of managing CKD in Nigeria, simple cost-effective methods are needed to recognize CKD early. Serum creatinine is relatively easy to measure, but as this and other studies show, it does not sufficiently diagnose cases in which there is already a significant decrease in the GFR. Prediction equations such as the modification of diet in renal disease, Cockcroft-Gault, Revised Bedside Schwartz, and the CKD_EPI equation are all easy to calculate.

This study found a prevalence of 31% (218) of ORD among treated hypertensives in this population, of which 178 had a GFR of 45–49 ml/min and the remaining 40 had a GFR of below 44 ml/min, even though they had a normal serum creatinine value of less than 1.5 mg/dl.

In a study involving primary care patients, Otero and colleagues using the modification of diet in renal disease equation detected a prevalence of ORD of 13% in a population of 1059 patients older than 18 years.

Duncan and colleagues detected a prevalence of ORD in 15.2% of 2781 Canadian patients using the Cockcroft-Gault method.

In similar studies, the percentage of patients with ORD varied from 10.4 to 43.5% according to the study population. This figure in this study is higher than the 15.2% found by Duncan and colleagues. Part of the reason may be that they used a GFR cutoff point of 50 ml/min. This study used a GFR cutoff point of 60 ml/min.

This present study used the CKD-EPI equation and detected a prevalence of ORD in 31% of 708 hypertensive patients with a serum creatinine value less than 1.5 mg/dl.

There were no significant differences in the mean serum creatinine between male and female patients P=0.333, but female subjects had a significantly lower eGFR than male subjects P<0.01.

This is in keeping with the studies by Facila L, Bertomeu-Gonzalez V, Bertomeu V, Gonzalez-Juanatey JR, Mazon P and Morillas P [1], who showed that 29.1% of subject polulation had eGFR<60ml/min (25% of the males and 31.4% of the females, P=0.37) using the C-G equation, and the study by FT Perez-Durillo, AB Villarejo-Villar, J Perez-Durillo, AI Ribes-Bautista and C Macias-Ortiz de Galisteo [16] which also indicated females having a lower eGFR than males. While all these studies including ours, showed the females had a lower eGFR, the difference in our study was that the females had a significantly lower eGFR using the CKD_EPI equation [1].

The difference may lie in the prediction equation used. Cockcroft-Gault equation was used in the reference study and the CKD_EPI equation in this study.

In hypertensive patients, a GFR of less than 60 ml/min is an independent cardiovascular risk factor. Earlier detection of ORD is of particular importance in Nigeria and sub-Saharan Africa. This will enable doctors to establish correct treatment and apply treatments that will slow down the progression of renal disease.

It has been stated that early detection and application of preventive strategies need to be the focus of kidney care in Nigeria.

Conclusion

There is a very high prevalence of ORD in our treated hypertensive patients. This is despite the fact that their serum creatinine was less than 1.5 mg/dl.

Overall, 218 (31%) patients of this group of treated hypertensives had a GFR of less than 60 ml/min.

It is important to screen patients with 24 h creatinine clearance or the use of reliable eGFR prediction equations so as to identify patients with ORD.

There is need to do more extensive similar studies in others centers and immediately identify patients with ORD so that steps can be taken earlier stage to slow down the progression of renal disease in hypertensive patients.

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Conflicts of interest
There are no conflicts of interest.

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