Original Paper

A Profile of Renal Function in Northern Cameroonians with Essential Hypertension

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Keywords

Essential hypertension · Blood pressure · Kidney function · Creatinine · Glomerular filtration rate · Urine chemistry

Abstract

Background/Aim: The two-way cause and effect relationship existing between high blood pressure and kidney dysfunction is currently a well-documented phenomenon with patients in either category being almost equally predisposed to the other pathology. Our goal was to assess the renal function capacity of hypertensive patients in our setting. **Methods:** This cross-sectional descriptive study involved the determination of blood pressure levels and the collection of blood and urine samples for the measurement of renal function markers. Hypertensive patients who came for medical follow-up constituted the study participants, and were enrolled consecutively into the study from February to May 2015. Data analysis was performed using the SPSS 20.0 software, and significant differences were determined at $p < 0.05$.

Results: The prevalence of elevated creatinine and urea levels were 35 and 27%. Eighty percent of the participants had a decreased glomerular filtration rate (≤ 90 mL/min/1.73 m³), with at least 36% recording less than 60 mL/min/1.73 m³. Proteinuria and glucosuria were recorded in 15% and 8% of the participants, respectively. The mean diastolic pressure was observed to be significantly higher in participants with proteinuria ($p = 0.016$), and participants' weight directly correlated with systolic blood pressure ($p = 0.015$). Furthermore, the mean estimated glomerular filtration rate was relatively lower in participants >60 years compared to those <60

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years ($p < 0.001$). **Conclusion:** Renal function is often perturbed in hypertensive patients, and good blood pressure control may reduce the progression of renal impairment. Thus, a systematic evaluation of renal function in addition to blood pressure control in hypertensive patients is indispensable towards effectively reducing the occurrence of renal events and preventing end-stage renal disease.

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Introduction

Hypertension is a clinical condition associated with chronic elevation of blood pressure (BP), characterized by an arterial BP $>140/90$ mm Hg [1]. It has been observed to record more than 25,000 new cases annually [2] and projected to affect 150 million persons in sub-Saharan Africa by 2015 [3], with reports of increasing prevalence rates over the years in Cameroon [4–6]. Africa, previously known for its high infectious disease rates, currently experiences an upsurge in the prevalence of noncommunicable diseases, thus resulting in a double burden of disease [7]. Noncommunicable diseases have been purported to be a primary cause of deaths in developing countries by 2020 [8], among which diabetes and hypertension assume a lead role, being frequently associated with a variety of co-morbid states and end organ complications including renal impairment and cardiovascular diseases, which result in premature mortality. Hypertension and renal impairment share a two-way cause and effect relationship, with each one being a common etiology of the other. Early diagnosis of kidney disease is vital for an effective management of hypertensive patients. With even moderate reduction of the glomerular filtration rate (GFR) being a predictive risk of cardiovascular diseases and end-stage renal disease [9], there is the need for systematic evaluation of kidney function in order to slow down the progression of kidney disease. We aimed at assessing and ascertaining the renal function capacity of patients with hypertension in a bid to better their management and contribute epidemiologic and clinical data on renal impairment in hypertension.

Methods

Study Design and Sample Collection

This prospective cross-sectional study involving 100 participants was carried out at the General Medicine Services of the Ngaoundere Regional Hospital and the Protestant Hospital, the two reference hospitals in the Adamawa region of Cameroon, spanning the period from February to May 2015. Participants of at least 17 years of age with a diagnosis of hypertension (BP $>140/90$) without any known cause were consecutively enrolled into this study after having obtained adequate information concerning the study and consenting to participate thereafter. Pregnant women and participants diagnosed with diabetes, dyslipidemias, and HIV/AIDS, or who refused to consent to the study, were excluded. A questionnaire was used to collect information on participants' sociodemographic status and clinical history, with communication being principally in the French, English, and Fulfuldé (local) languages. Resting BP and weight measurements were performed per participant after which fasting venous blood samples (5 mL) were collected, part of which was immediately used to measure fasting whole blood glucose and the rest was left in dry tubes to clot for 5–10 min. Blood samples were centrifuged at 2,000 rpm for 3 min, and sera were separated into Eppendorf tubes and frozen at -20°C for a maximum of 7 days prior to weekly laboratory analysis. Early-morning urine samples were subsequently collected, and urine chemistry analysis was performed immediately. All measurements were carried out following pre-established standard operating procedures. This study obtained ethical clearance from the Ngaoundere Regional Hospital Ethical Committee (Ref: 1227/L/RC/RA/DSP/HR/NGD/CLE).

Clinical and Biochemical Measurements

Blood Pressure

BP measurements were performed using an automated BP monitor (OMRON-HEM-712CN2, serial number: 64167999LF, USA) after having instructed patients to rest for at least 15 min upon arrival. Paired measurements were done on both the right and left arms per patient with a time lapse of maximum 5 min, and the average systolic and diastolic BPs were calculated and recorded. BP was classified as “normal” for a systolic BP <140 mm Hg and a diastolic BP <90 mm Hg.

Blood Parameters

Biochemical markers were measured using commercially acquired kits. Fasting blood sugar (FBS) measurements were performed on whole blood prior to centrifugation using a glucometer (EasyTouch ET-101, serial number: 1012A002911; Biopitik Technology Inc., Taiwan) with reference values stated at 75–120 mg/dL. Determination of serum creatinine and urea concentrations were done by spectrophotometry using a Semi Auto Chemistry Analyser (Mindray BA-88, serial number: BH7AB2710; China), following the Jaffe (Cromatest, Ref: 1123010, Lot: 15060X) and Berthelot (Cromatest, Ref: 11556015, Lot: 15153) methods, respectively. Normal values were considered 0.7–1.4 mg/dL for males and 0.5–1.1 mg/dL for females for serum creatinine and 10–50 mg/dL for serum urea. All measurements were performed following the manufacturer’s procedures. GFRs were estimated using both the Cockcroft-Gault (CG) formula [10] and the modification of diet in renal disease (MDRD) formula as derived by Levey et al. in 1999 (revised in 2011) [11, 12]. Considering the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) recommendations for the classification of chronic kidney disease (CKD) [13], participants were classified into stage 1 (estimated GFR [eGFR] >90 mL/min/1.73 m³), stage 2 (eGFR: 60–89 mL/min/1.73 m³), stage 3 (eGFR: 30–59 mL/min/1.73 m³), stage 4 (eGFR: 15–29 mL/min/1.73 m³), and stage 5 (eGFR <15 mL/min/1.73 m³).

Urine Parameters

Urine chemistry was performed following the dipstick method and using URIT 11V strips (Lot: 56140110–20150912; URIT medical electronic Co, China), and the presence of the following parameters was determined: blood, leucocytes, bilirubin, urobilinogen, protein, glucose, ketones, ascorbic acid, specific gravity (SG), pH, and nitrates.

Quality Assurance

Standard specimen collection, processing, storage, transport procedures, and the use of appropriate glass and plastic ware were ensured. Calibration of the spectrophotometer was by the use of the CALIMAT multiparameter calibrator (Reference: 62321, Lot: 1003001280; Biomérieux, France). FBS measurements for the first 20 participants were measured using both the glucometer and GOD-PAP colorimetry and were compared for variations. Likewise, BP measurements between the automated BP monitor and a manual sphygmomanometer were compared. In the same line, the reproducibility of results of biochemical measurements for these initial 20 samples was assessed using a second semiautomated spectrophotometer (SECOMAM Basic/70V B0358, serial number 1790). Furthermore, analytical quality and validation of results of biochemical measurements was carried out using the LYOTROL™ N control serum (Reference: 62373, Lot: 1003001280; Biomérieux, France).

Ethical Consideration

Information on the aim, merits, and demerits of this study was fully disclosed to the participants in the language best understood by them prior to obtaining a written consent and enrollment into the study. Participation was voluntary, and the will to discontinue participation was free and without sanctions. Above all, participants’ information was kept strictly confidential, and those with abnormal results were referred to a nephrologist.

Data Management and Analysis

Data recorded in Microsoft excel spreadsheet was checked for concordance with the source data and analyzed following international standard references for clinical and biochemical measurements using the statistical package for social sciences (SPSS) version 20.0. The results were compared with those obtained using R version 3.0.2 software. Prevalence rates were calculated as percentages: the ANOVA and Mann-Whitney U tests were used to compare the means and mean ranks in normally and non-normally distributed sub-data sets, respectively, and likewise, the Pearson and Spearman correlation tests for the investigation of relationships. Statistical significance was considered at $p < 0.05$.

Table 1. Correlation (*r*) between selected parameters in the male, female, and general study population

General study population					
parameter	age	weight	SBP	DBP	FBS
Age	–	–0.015	0.164	0.082	0.198*
Weight	–0.015	–	0.243*	0.139	–0.033
Creatinine	0.080	–0.080	0.077	0.019	0.141
Urea	0.225*	–0.189	0.124	–0.042	0.139
eGFR-CG	–0.277*	0.105	–0.137	–0.119	–0.071
eGFR-MDRD	–0.474**	0.569**	–0.019	–0.036	–0.088
SG	–0.104	–0.156	–0.123	–0.197*	–0.086
Female population					
parameter	age	weight	SBP	DBP	SG
Weight	0.034	–	0.342**	0.342**	–0.032
Creatinine	0.049	–0.059	0.075	0.020	0.171
Urea	0.143	–0.131	0.200	–0.092	0.284*
eGFR-CG	–0.225	0.102	–0.150	–0.129	–0.037
eGFR-MDRD	–0.422**	0.506**	0.013	0.032	–0.046
Male population					
parameter	age	weight	SBP	DBP	FBS
Weight	–0.142	–	0.045	–0.134	–0.143
Creatinine	0.341*	–0.252	0.075	0.052	0.142
Urea	0.341*	–0.388*	–0.015	0.057	0.387*
eGFR-CG	–0.385*	0.325*	–0.108	–0.102	–0.033
eGFR-MDRD	–0.545**	0.718**	–0.068	–0.188	–0.039

eGFR, estimated glomerular filtration rate; CG, Cockcroft-Gault; MDRD, modification of diet in renal disease; SG, specific gravity; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar. * $p < 0.05$, ** $p < 0.05$.

Results

One hundred participants were enrolled into this study comprising 31 males and 69 females (sex ratio M/F: 0.45) with age ranging from 17 to 93 years and the mean age being 56.06 ± 15.53 . Housewives (58%) and farmers (24%) constituted the most prevalent occupation encountered in this study.

Among these participants, the frequency of raised creatinemia and uremia was recorded at 35 and 27%, respectively. Decreased eGFR (≤ 90 mL/min/1.73 m³) was found in 79% (CG) and 80% (MDRD), with 36% (CG) and 51% (MDRD) recording ≤ 60 mL/min/1.73 m³, respectively. Subsequent clinical staging of CKD following the KDIGO guidelines revealed proportions of 20%, 29%, 38%, 5%, and 5% of participants at stage 1, stage 2, stage 3, stage 4, and stage 5, respectively. Furthermore, following urine chemistry analyses, 15% and 8% of the participants had proteinuria and glucosuria, respectively, and it was noted that all participants with glucosuria also presented with proteinuria.

Following correlation analyses in the general study population, our results demonstrated that participants' ages varied directly with FBS and serum urea, and indirectly with eGFR levels. Weight correlated with systolic BP and eGFR-MDRD, while diastolic BP was observed to vary inversely with urine SG (Table 1).

Table 2. Comparison of the means and mean ranks of selected parameters between the age groups

Parameter	Age, years	n	Mean ± SD	p value
SBP, mm Hg	<60	61	160.70±28.39	0.217
	>60	39	168.36±32.51	
DBP, mm Hg	<60	61	96.07±20.74	0.651
	>60	39	97.92±18.61	
FBS, mg/dL	<60	61	98.61±29.09	0.009*
	>60	39	114.93±37.52	
Creatinine, mg/dL	<60	61	1.39±2.01	0.316
	>60	39	1.83±2.28	
Urea, mg/dL	<60	61	47.51±32.21	0.048*
	>60	39	63.64±48.45	

Parameter	Age, years	n	Mean rank	Sum of ranks	p value
eGFR-CG, mL/min/1.73 m ³	<60	61	56.59	3,452.00	0.009*
	>60	39	40.97	1,598.00	
eGFR-MDRD, mL/min/1.73 m ³	<60	61	61.62	3,759.00	<0.001*
	>60	39	33.10	1,291.00	

SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; eGFR, estimated glomerular filtration rate; CG, Cockcroft-Gault; MDRD, modification of diet in renal disease. * $p < 0.05$.

Among female patients, participants' weight was observed to positively vary with both systolic and diastolic BP and eGFR-MDRD. Likewise, urine SG varied directly with serum urea levels.

In male participants, on the other hand, the relationships between serum urea, eGFR levels and age, and weight and eGFR levels were replicated. Age further correlated with serum creatinine, while, serum urea varied directly with FBS, and inversely with weight (Table 1).

Comparing means of parameters, GFR recorded significant lower mean ranks of eGFR-CG ($p = 0.009$) and eGFR-MDRD ($p < 0.001$) in participants older than 60 years, as well as higher mean FBS ($p = 0.009$) and serum urea ($p = 0.048$), compared to those 60 years and younger (Table 2).

Gender-based comparisons portrayed significant differences in mean age and serum creatinine between men and women as presented in Table 3.

Furthermore, we compared the means and mean ranks of selected parameters by treatment protocol, and it was observed that participants on multidrug therapy had higher mean systolic and diastolic BPs, and mean pH rank (Table 4).

Interestingly, the mean DBP was observed to be significantly higher in participants with proteinuria compared to those without (106.94 ± 26.07 vs. 94.56 ± 17.65 ; $p = 0.012$).

Discussion

Hypertension represents a pertinent and persistent risk factor for the development and progression of kidney and other target organ diseases particularly in the absence of appropriate BP control measures. Related data portray systemic hypertension as being second only to diabetes mellitus as a cause of end stage renal disease (ESRD). Our records of a higher prevalence of decreased eGFR compared to that of increased serum creatinine correlates with

Table 3. Comparison of the means of selected parameters between the sexes

Parameter	Gender	n	Mean ± SD	p value
Age, years	Male	39	59.90 ± 15.43	0.048*
	Female	61	53.61 ± 15.21	
Weight, kg	Male	39	68.41 ± 15.09	0.238
	Female	61	66.02 ± 16.85	
SBP, mm Hg	Male	39	165.28 ± 28.37	0.675
	Female	61	162.67 ± 31.40	
DBP, mm Hg	Male	39	95.00 ± 18.20	0.474
	Female	61	97.93 ± 20.92	
FBS, mg/dL	Male	39	114.77 ± 37.39	0.069
	Female	61	98.20 ± 20.91	
Creatinine, mg/dL	Male	39	1.50 ± 0.78	0.001*
	Female	61	1.60 ± 2.65	
Urea, mg/dL	Male	39	59.44 ± 34.27	0.060
	Female	61	50.20 ± 43.00	
SG	Male	39	1.019 ± 0.008	0.299
	Female	61	1.024 ± 0.037	
pH	Male	39	5.97 ± 0.51	0.927
	Female	61	6.04 ± 0.64	
eGFR-CG, mL/min/1.73 m ³	Male	39	61.32 ± 30.17	0.384
	Female	61	66.99 ± 32.46	
eGFR-MDRD, mL/min/1.73 m ³	Male	39	70.31 ± 25.36	0.913
	Female	61	70.95 ± 30.18	

SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; SG, specific gravity; eGFR, estimated glomerular filtration rate; CG, Cockcroft-Gault; MDRD, modification of diet in renal disease. * $p < 0.05$.

Table 4. Comparison of the means and mean ranks of selected parameters between the participants on single- and multi-drug therapy

Parameter	Treatment protocol	<i>n</i>	Mean ± SD	<i>p</i> value
SBP, mm Hg	Monodrug	41	153.61±24.06	0.005*
	Multidrug	49	173.33±33.53	
DBP, mm Hg	Monodrug	41	91.88±16.45	0.021*
	Multidrug	49	102.14±22.31	
Creatinine, mg/dL	Monodrug	41	1.52±2.18	0.084
	Multidrug	49	1.64±2.26	
Urea, mg/dL	Monodrug	41	52.68±38.26	0.679
	Multidrug	49	54.73±40.44	

Parameter	Age, years	<i>n</i>	Mean rank	Sum of ranks	<i>p</i> value
pH	Monodrug	41	38.99	1,598.50	0.019*
	Multidrug	49	50.95	2,496.50	
eGFR-CG, mL/min/1.73 m ³	Monodrug	41	51.38	2,106.50	0.051
	Multidrug	49	40.58	1,988.50	
eGFR-MDRD, mL/min/1.73 m ³	Monodrug	41	48.63	1,994.00	0.298
	Multidrug	49	42.88	2,101.00	

SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; CG, Cockcroft-Gault; MDRD, modification of diet in renal disease. * $p < 0.05$.

the findings of Kannapiran et al. [14] who observed 29.1% prevalence of glomerular filtration ≤ 60 mL/min/1.73 m² (MDRD) and 17.5% of increased serum creatinine [14], suggesting a possible under-representation of a diminishing renal capacity with the use of serum creatinine only as the tool for evaluating renal function [15, 16]. This is probably a direct effect of the processes of creatinine generation, secretion and extrarenal excretion [14, 17, 18]. In addition, the use of the CG formula to estimate GFR may be subject to further misrepresentation of renal function status in our setting compared to the MDRD formula, owing to its limitation in adjusting for racial variations and its relatively low performance [11, 12, 19]. Furthermore, results of urine chemistry analyses portrayed a 15% proteinuria prevalence, quite close to the 13.4% of albuminuria (>300 mg/L) reported by Addo et al. [20] in a Ghanaian hypertensive population. An 8% prevalence of glucosuria was also obtained herein, and interestingly, it was noted that all participants with glucosuria also presented a proteinuria, most likely due to advanced-stage renal impairment rather than an increase in the plasma glucose concentration above renal threshold level. In this study, we also recorded a significantly high mean diastolic BP in participants with proteinuria, perhaps reiterating the phenomenon of increased renal perfusion and progression of renal dysfunction with increasing BP, thus reaffirming the utility of proteinuria as a predictor of renal and cardiovascular events [21–23].

The increased mean FBS, urea, and decreased eGFR in participants aged >60 years could be attributed to the gradual decline in the glucose metabolism capacity and GFR with age. Moreover, participants' age varied directly with FBS, serum creatinine and urea concentrations, and inversely with GFR levels, corroborating with previous findings [24].

In the general study population, systolic BP was observed to vary directly with weight, and likewise, among females, both systolic and diastolic BP followed the same pattern, thus highlighting the role of overweight and/or obesity in the onset and progression of hypertension [25]. On the other hand, diastolic BP recorded an inverse relationship with urine SG among study participants, suggesting the production of dilute urine with increasing BP, and seemingly indicating a diuretic effect. The means of systolic and diastolic BP and pH recorded higher values in participants on multidrug therapy, which could be a direct outcome of high arterial BP at baseline, necessitating the treatment protocol choice in the first place. Furthermore, nonadherence to antihypertensive therapy could be a factor wherefore the high cost of multiple drugs compared to a single drug favors therapeutic discontinuity [26, 27]. An increase in BP has been previously reported to initiate a diuretic phase in renal function mediated by atrial natriuretic peptide, thus producing dilute sodium-rich urine [28–31]. On another hand, about 50% of our participants were on diuretic therapy, and with the kidneys being the major excretory organ for most drug metabolites, an increase in the number of drug metabolite derivatives excreted may inadvertently induce a change in the urine volume, SG and pH.

The direct association between serum urea levels and urine SG among female participants suggests that urine concentration increases with increasing serum urea levels. This is supported by the well-documented evidence that hyperuremia is a possible outcome of dehydration states even in the absence of renal impairment. In addition, the correlation between serum urea levels and FBS in the male subpopulation corroborates with previous literature on the impact of dehydration on hyperuremia and hyperglycemia, thus their role in widely used standardized osmolarity calculations [32–34]. As expected, serum creatinine and urea levels further demonstrated direct proportionality with age among male hypertensives. Urea levels increased with decreasing weight in the same subpopulation, contradicting the established notion of a partial positive dependence of serum urea levels on the body mass index. Surprisingly, the mean serum creatinine level was observed to be higher in females compared to male participants, concurring with the findings of Ofori and Odia [35] who observed higher serum creatinine and urea levels in female hypertensives compared to males. Conversely,

Ruilope et al. [36] recorded high serum creatinine levels predominantly in males ($p < 0.0001$), as well as Kurata et al [37] who equally found that creatinine clearance and serum creatinine levels in male hypertensive patients were significantly higher compared to those of females ($p < 0.0001$).

Finally, this study failed to demonstrate an association between reduced eGFR and BP level, nor was high BP associated with eGFR status, corroborating with the observations from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 [23].

Limitations

The principal limitation experienced in this study was the verification of participants' self-reported data on the practice of good therapeutic adherence and the use of indigenous antihypertensive therapy (traditional medicine). In addition, the distance from the study sites rendered it impossible to collect 24-h urine samples for urine chemistry.

Conclusions and Perspectives

Most of our study participants presented with varying degrees of renal impairment owing to data on eGFR levels, indicating that the use of serum creatinine and urea only, underestimates renal function capacity. Thus, in-depth analyses are required for regular systematic assessment and management of hypertensive patients. Further studies are needed to investigate cost-effective methods in predicting and preventing renal dysfunction in resource constrained settings.

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Statement of Ethics

All participants provided written consent prior to enrollment into this study, which obtained approval from the Ngoundere Regional Hospital Ethical Committee (Ref: 1227/L/RC/RA/DSP/HR/NGD/CLE), a regional arm of the Cameroon National Ethics Committee among others.

Disclosure Statement

The authors declare that there are no conflicts of interest to disclose.

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