Observational Study

Medicine®

OPEN

Hypertension in adolescents and young adults referred to a tertiary hypertension clinic in Cape Town, South Africa

Erika S. W. Jones, MBBCh, FCP, PhD, Ilhaam Esack, MBChB, Phetho Mangena, MBChB, FCP, Brian L. Rayner, MBChB, FCP, MMed, PhD*

Abstract

To audit the young patients referred to the Hypertension Clinic at Groote Schuur Hospital that predominately serves the underprivileged communities of Cape Town.

Folders of patients between the ages of 15 and 30 years over a 2 year period were reviewed. The data collected included demographic, clinical and laboratory data, investigations, causes of hypertension, and presence of hypertensive organ damage.

Of the 110 patients reviewed, 61 (55.5%) were females, 22 (20%) Black African, and 88 (80%) of Mixed Ancestry. Eight (7.3%) were found to be normotensive, 16 (14.5%) had a secondary cause and 86 (78.2%) had essential hypertension. Thirty five (31.8%) were current or previous smokers, and 11 (10%) admitted to current or prior use of metamphetamines. A family history of hypertension in a first degree relative was present in 80 (72.7%) patients. Comorbidities present were diabetes in 7 (6.4%) patients, metabolic syndrome in 13 (11.8%), and obesity in 26 (23.6%), but 42.6% had a body mass index (BMI) $<25\,kg/m^2$. Chronic kidney disease (CKD) was present in 29 (26.4%) patients and ECG left ventricular hypertrophy in 56 (50.9%). Overall organ damage was present in 72 (65.5%) patients.

In this cohort of young hypertensives most patients had essential hypertension with a strong family history. Significant organ damage was identified. High risk behavior, including smoking and illicit drug use, and obesity were identified as contributing factors. Secondary causes were identified in 14.2%. These results suggest a targeted approach to the investigation of young hypertensives for secondary causes, and significant opportunities for lifestyle intervention.

Abbreviations: ACR = albumin/creatinine ratio, ARB = angiotensin receptor antagonist, BMI = body mass index, BP = blood pressure, CKD = chronic kidney disease, ECG = electrocardiogram, ENaC = epithelial sodium channel, LVH = left ventricular hypertrophy, MDRD = Modification in Diet in Renal Disease.

Keywords: adolescent, South Africa, young hypertension

1. Introduction

The Global Burden of Disease report showed that hypertension is the "leading risk factor for global mortality" and was the cause of 7% of deaths worldwide in 2010.[1] In the majority there is no known underlying cause of hypertension, but in young people a secondary cause is more likely and more extensive investigation is required.[2] Potential causes are kidney disease, renal artery stenosis, coarctation of the aorta or endocrine causes, amongst others.

In South Africa there has been a dramatic rise in the prevalence of hypertension in young people. According to the 2016 South African Demographic and Health Study 20% of males aged 15 to 24 compared to 7.7% in the 1998 survey and 33% of males aged 25 to 34 compared to 15% in 1998 had hypertension [3,4]. In females, 17% of 15 to 24 year olds compared to 4.2% in 1998 and 27% of 25 to 34 year olds compared to 10.6% in 1998 had hypertension. This has been mirrored in other parts of the world.[5,6] Furthermore, the prevalence of hypertension in low and middle income countries compared to higher income countries is significantly higher: 15.2% vs 10.7% in males and 10.4% vs 4.3 vs in females, respectively.[7] This high and rising prevalence of hypertension, particularly from low to middle income countries, calls for increased attention to the prevention and management of hypertension in adolescents and young adults.

There have been numerous studies demonstrating that the risk factors for hypertension in adolescents are obesity, low birth weight, family history of hypertension and diabetes, and sedentary behavior. The South African National Youth Risk Behavior Surveys conducted in 2002 and 2008 showed that the rate of obesity increased in adolescents (grade 8–11) from 1.6% to 3.3% in males and 5.0% to 7.5% in females respectively.[8]

Editor: Manal Kamel Youssef.

The authors received no funding for this study.

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Division of Nephrology and Hypertension, and Nephrology and Hypertension Research Unit, University of Cape Town, Cape Town, South Africa.

** Correspondence: Brian L. Rayner, E13 Groote Schuur Hospital, Observatory, Cape Town 7925, South Africa (e-mail: brian.rayner@uct.ac.za).*

How to cite this article: Jones ES, Esack I, Mangena P, Rayner BL. Hypertension in adolescents and young adults referred to a tertiary hypertension clinic in Cape Town, South Africa. Medicine 2020;99:48(e23137).

Received: 8 April 2020 / Received in final form: 25 August 2020 / Accepted: 14 October 2020

http://dx.doi.org/10.1097/MD.0000000000023137

Childhood and adolescent obesity is one of the strongest predictors of adult hypertension.[9] On the other hand, mean blood pressure (BP) levels as well as the prevalence of elevated BP and hypertension among US children and adolescents have declined during the past decade despite no reduction in body mass index, and this may be associated with a change in dietary factors.[10]

There is also a familial influence on high BP with studies showing an increased prevalence in children with a family history of hypertension when compared to children from normotensive families, possibly suggesting an underlying genetic predisposition.[11]

Investigation of young adults is advocated by all major guidelines for evidence of secondary causes and organ damage.[2] Predictors of secondary causes for hypertension include young age (<30 years) with no risk factors, resistant hypertension, severe hypertension (>180/110 mm Hg), non-dipping status, and hypertension mediated organ damage.[2] The currently recommended assessment for a young patient with hypertension ("full workup") includes an ECG, echocardiogram, 24-hour ambulatory BP monitoring, renal function tests, electrolyte tests, endocrine tests, CT angiography and renal ultrasound to detect secondary causes and organ damage.[12] However, due to the dramatic rise in hypertension in adolescents and young adults, it is questionable as to whether all these tests are necessary in all cases, and the beneficial impact needs to be balanced against costs, risk of procedures, patient burden and incidental diagnosis.[2] More research is needed to define the clinical approach to investigation of adolescents and young adults with suspected hypertension, especially from poorer socio-economic communities in developing countries where resources are limited.

2. Methods

2.1. Aim

The aim of the study was to conduct an audit of young hypertensives referred to our clinic to determine their clinical characteristics and underlying causes to guide policy in regard to assessment and investigation of these patients.

2.2. Setting

Groote Schuur Hospital Hypertension Clinic is a regional tertiary referral hospital located in Cape Town. It provides services for young hypertensives, patients with resistant hypertension or with complicated hypertension, mainly for public sector patients, predominantly from underprivileged communities without medical insurance. Patients are mainly referred from primary care clinics serving the uninsured population of Cape Town. Folders of all patients between the ages of 15 and 30 years over a 2 year period (2014–2016) were reviewed. No patients were excluded. The data collected included clinical and laboratory data, investigations, causes of hypertension, and hypertension mediated organ damage. The study was a retrospective cohort study describing young patients with hypertension and was approved by the University of Cape Town Human Research Ethics Committee (055/2015)

2.3. Assessments

BP was measured using a validated automated device (Dinamap Carescape Monitor, Woodley Equipment Company Ltd, UK) in accordance with South African Hypertension Practice Guideline.[13] The measurements were taken using the appropriate cuff size with the patient was seated after 5 minutes rest in a quiet environment by a specialist hypertension nurse. An average of the last 3 readings was used and staged according to the South African Hypertension Practice Guideline.[14]] Hypertension was defined as a BP ≥140/90 mm Hg.

All new assessments were performed by Nephrology and Hypertension specialist in training. This included a comprehensive medical history, examination including fundoscopy and urine analysis. All cases were reviewed in a joint consultation by the consultant in charge (BR, EWJ) to stage the hypertension, define hypertensive mediated organ damage and decide on further investigations for secondary causes. A written comprehensive medical report was compiled from which most of the data was obtained. The data was extracted from the medical records under the supervision of a nephrology and hypertension specialist in training (PM).

2.4. Demographic data

Age at first visit, smoking status, drug use, duration of hypertension, family history of diabetes and hypertension, presence of diabetes mellitus, number of anti-hypertensives used and hypertension diagnosis (essential hypertension or a secondary cause). Anthropomorphic data, including height, weight and waist circumference were measured. BMI was calculated: weight (kg)/height^2 (m^2), and was categorised as underweight: <20; ideal weight: 20–24; overweight: 25–30; obesity: 30–35; morbid obesity: >35 kg/m^2.

2.5. Organ damage

All patients had an electrocardiogram (ECG) performed, and the presence of left ventricular hypertrophy (LVH) was determined using Sokolow-Lyon criteria (S in V1 plus R in V5 or V6 ≥35) and/or Cornell voltage criteria ((R in avL + S in V3 + 6 in females) x QRS duration) > 2440 mm/ms)[14]

Fundoscopy is routinely performed to diagnose retinopathy and the grade was recorded (grade 1: silver wiring, grade 2: AV nipping, grade 3: haemorrhages and/or exudates, grade 4: papilloedema).

Chronic kidney disease (CKD) was staged based on estimated GFR using the Modification in Diet in Renal Disease (MDRD) formula not adjusted for ethnicity.[15] Microalbuminuria was defined as albumin/creatinine ratio (ACR) of 3–30 mg/mmol and macroalbuminuria as an ACR > 30 mg/mmol.

Presence of ischaemic heart disease, cerebrovascular accidents and peripheral arterial disease was also recorded.

2.6. Laboratory data

The following laboratory tests were routinely performed: serum potassium, creatinine and calculation of the estimated GFR using MDRD formula, fasting glucose and lipogram, plasma renin concentration, plasma aldosterone concentration, aldosterone to renin ratio, urine ACR and genetic analysis for the R536Q variant of the β-chain of the epithelial sodium channel (ENaC).[16]. Primary aldosteronism was indicated by an aldosterone > 500 pmol/L and an aldosterone to renin ratio >70, and a Liddle phenotype if the R563Q mutation was positive and/or renin was suppressed and aldosterone ≤100 pmol/L.

Further special investigations, such as abdominal/renal ultrasound, renal CT angiogram, and endocrine tests (with the exception of the renin/aldosterone ratio) were only done at the discretion of the consultant in the clinic when there was a suspicion of an underlying secondary cause.

The data were captured onto a spreadsheet. Normally distributed data were summarised using means and standard deviations, otherwise continuous data were summarised using medians and interquartile ranges. A *t*-test was used to compare normally distributed data. Categorical data were summarised using frequencies and percentages. Categorical variables were analysed using the Chi-Squared test, provided there were enough responses per independent variable category; in cases where there were not enough responses per category not be met, Fishers exact test was used. In all tests used, a *P* value of .05 was considered statistically significant. All data were analyzed using SPSS version 25 IBM SPSS Statistics for Macintosh, Version 25.0, 2017.

3. Results

One hundred ten patients were identified with a mean age of 23.1 years. (Table 1) Sixty one (55.5%) were female and 49 (44.5%) were male with 88 (80%) of mixed ancestry and 22 (20%) of African ethnic origins. The mean duration of hypertension before referral was 17.5 months. Twenty five percent of the patients were obese, but 42.6% had a BMI $< 25\,kg/m^2$. Thirty eight point one percentage and 8.1% were current or former smokers, or abusers of metamphetamine respectively, and 13.1% of females were using oestrogen containing oral contraceptives. Family history of a first degree relative with hypertension or diabetes was present in 74.8% and 33.4% respectively, and 6.4% had underlying type 2 diabetes. The mean uric acid was 0.32 mmol/L and 15 (13.6%) patients had a level >0.40 mmol/L. The R563Q mutation of the ENaC that causes a Liddle like syndrome was present 6.8% of the 88 patients tested, and overall 17 (15.5%) had a Liddle phenotype based on renin and aldosterone levels and/or presence of R563Q mutation.

Table 1

Demographic data of the patients.

Parameter	Result
Mean age (years, s.d.)	23.1
Male (%)	49 (44.5%
Female (%)	61 (55.5%)
Hypertension duration (months, s.d.)	17.5
Smoking (%)[+]	
Current	24 (26.1)
Former	11 (12)
Never	57 (62)
Metamphetamine abuse (%)	
Current	5 (4.5)
Former	4 (3.6)
Never	101 (92)
Oral contraceptive use	8 (13.1)
Diabetic	7 (6.4)
BMI (kg/m^2, %)*	
<25	46 (42.6)
25–30	35 (32.4)
30-–35	13 (12)
>35	14 (13)
Family history of hypertension (%)	80 (72.7)
Family history of diabetes	35 (33.7)
R563Q mutation positive[#]	6 (6.8%)
Liddle phenotype	17 (15.5)

Legend - [+] n=92, [*] n=108, [#] n=88. BMI = body mass index, s.d. = standard deviation.

Table 2

Baseline BP and use of antihypertensive drugs.

Parameter	Result
Mean systolic BP in mm Hg (s.d.)	134.1 (15)
Mean diastolic BP in mm Hg (s.d.)	86.5 (13.7)
Mean number of antihypertensives (s.d.)	1.6 (1.2)
Class of antihypertensive (n, %)	
Thiazide diuretic	57 (51.8)
Loop diuretic	4 (3.6)
B-blocker	16 (14.5)
Calcium channel blocker	41 (56.4)
ACE inhibitor/ARB	43 (39.4)
Aldosterone antagonist	3 (2.7)
α-blockers	1 (0.9)
Number of drugs (n, %)	
0	21 (19.1)
1	32 (29.1)
2	33 (31.8)
3 or more	22 (20)

ARB = angiotensin receptor antagonist, s.d. = standard deviation, BP = blood pressure.

The mean BP at presentation was 134.1/86.5 mm Hg and the mean number of antihypertensives used was 1.6. (Table 2) The most commonly used antihypertensive drugs were ACE inhibitors/Angiotensin receptor blockers (39.4%), calcium channel blockers (56.4%) and thiazide diuretics (59.4). Only 19.1% were untreated and 20% were receiving 3 or more antihypertensives at baseline. There was no difference in antihypertensive use between males and females.

Of the 110 patients referred 2 (1.8%) and 6 (5.5%) were found to be normotensive (<130/80 mm Hg) or have high normal BP (130–140/80–90 mm Hg) respectively. Essential hypertension was present in 74.5% and secondary causes in 16 (14.5%). (Table 3) The main secondary causes were renal artery stenosis in 7 (due to Takayasus arteritis) and renal parenchymal disease in 7. Patients with and without secondary causes for their hypertension were compared. (Table 4) The key differentiating features were that patients with essential hypertension were more overweight, had significantly increased waist circumference (87.9 cm vs 77.4 cm, $P = .011$), were more likely to have a family history of hypertension (74.5% vs 62.5%) and had less evidence of target organ damage. ECG LVH was present in 45.7% with essential hypertension vs 81.3% ($P = .031$) with secondary causes and evidence of CKD in 19.1% vs 68.8% ($P < .0001$) respectively.

Table 3

Causes of hypertension.

Cause	N (%)
Hypertension	102 (92.7)
Primary hypertension	82 (74.5)
Renal artery stenosis	7 (6.4)
Renal parenchymal disease	7 (6.4)
Primary hyperaldosteronism	1 (0.9)
Gordon syndrome	1 (0.9)
Incomplete data	4 (3.6)

Table 4

Comparison of patients with and without secondary causes for hypertension.

	No secondary cause	Secondary cause	
	N (%)	N (%)	*P* value
Family History of hypertension	70 (74.5)	10 (62.5)	.043
LVH on ECG	43 (45.7)	13 (81.3)	.031
CKD	18 (19.1)	11 (68.8)	<.0001
Any target organ damage	58 (61.3)	14 (87.5)	.05
	Mean ± SD	Mean ± SD	*P* value
Weight (kg)	75.0 ± 18.6	65.7 ± 12.7	.064
Waist circumference (cm)	87.9 ± 14.6	77.4 ± 12.7	.011
Body Mass Index (kg/m^2)	30.7 ± 33.5	23.4 ± 4.0	.403

CKD = chronic kidney disease, LVH = left ventricular hypertrophy, ECG = electrocardiogram.

Four patients (2 with stroke and 2 with peripheral arterial disease) had established cardiovascular disease. CKD was present in 29 (26.4%) patients, defined by eGFR < 60 ml/minutes and/or increased urine albumin creatinine ratio, and ECG left ventricular hypertrophy in 56 (50.9%). Grade 1 retinopathy was present in 33 (30%), grade 2 in 8 (7.2%) and grade 4 in 1 (0.9%). Overall, organ damage was present in 72 (65.5%) patients.

4. Discussion

The findings of this study have important implications for the investigation and management of hypertension in adolescents and young adults. Firstly, the majority (78.2%) of referred patients had essential hypertension, 14.5% had a secondary cause, 5.5% had borderline or high normal BP, and < 2% were considered truly normotensive. Furthermore, patients with essential hypertension were more likely to have a family history of hypertension, more likely to be overweight with increased waist circumference, and less likely to have hypertensive organ damage especially CKD. This implies that a targeted approach to extensive investigation should be considered based on history, physical examination and basic investigations. Nearly 90% of the secondary causes were of renal origin, either Takayasus arteritis or renal parenchymal disease, which could be suggested by urine dipsticks, impaired kidney function, abnormal renal ultrasound findings and discrepant pulses/bruits present on physical examination.

Secondly, contributing factors to the development of hypertension were found in a high percentage of cases. Overweight/obesity was found in 57.4% of cases, 8.1% were currently or formerly using metamphetamines, and 8% were taking an oestrogen containing oral contraceptive. Eight percent had already established type 2 diabetes. These findings suggest that educational programmes addressing lifestyle issues in young people to prevent obesity and hypertension are crucial. Education regarding the dangers of abuse of metamphetamines that is widespread in Cape Town, is another important factor, and routine screening for urinary amphetamines is advised. We have previously reported the link between amphetamines, malignant hypertension and CKD.[17]

Medical practitioners prescribing oral contraceptives should also be advised to check their subjects BP after initiation. Although smoking does not cause hypertension, there was a very high prevalence of current or past smoking (38.1%) that is certain to amplify the risk of adverse CV events in the future.

Obesity is generally considered one of the major contributing factors to hypertension in young people. However, in our cohort over 40% patients had a normal weight, suggesting other environmental or genetic factors are playing a significant role.

Thirdly, a high percentage of patients had evidence of organ damage in the form of LVH based on ECG criteria (50.9%), CKD (26.4%), and overall 65.5%. Currently there are no trials addressing pharmacological treatment in young people, but current guidelines recommend pharmacological treatment in the presence of organ damage to prevent future CV events and progression of CKD, and thus the majority of our patients require pharmacological treatment. Recommendations for antihypertensives use in young women of childbearing potential should bear in mind the teratogenicity of ACE inhibitors and angiotensin receptor blockers.

Fourthly, this study confirmed the importance of the Liddle phenotype in our population, which is considered part of spectrum of low renin essential hypertension. The R563Q mutation of the ENaC was present in 6.8% of patients and a further 15.5% had a Liddle phenotype based on renin and aldosterone levels. This confirms the previous work we published that showed a prevalence of 5% of the R563Q mutation amongst adult hypertensives in South Africa and the presence of the Liddle phenotype in 20% in a study from 4 African countries.[16,18] A targeted approach to treatment of these patients with amiloride may improve BP control and long-term outcomes.[18] Unfortunately, amiloride, a World Health Organisation essential drug, is not available in South Africa.[19]

There were several limitations of the study. Firstly, the role of ECG in determining LVH in young people has not been well established, and the true prevalence of LVH in this population may have been overestimated.[20] Furthermore, echocardiography is not routinely available in our hospital for assessment of hypertensive organ damage due to resource constraints. Secondly, the study was not prospective, and some data were not available from the files. Thirdly, we do not have data on the long-term BP control and outcome of this cohort, but this was not the objective of the study. Fourthly, highly specialised testing such as CT renal angiography was only performed when indicated by a clinical suspicion, rather than based on protocol, and further secondary cases may have been missed. On the other hand, aldosterone and renin were performed routinely on all patients to detect primary aldosteronism, which is a common secondary cause.[2] Fifthly there may have been referral bias in the number

of patients with Takayasus disease. However, it is the commonest form of vasculitis in adults in Africa.[21]

In conclusion, in this cohort of young patients from predominately underprivileged communities of Cape Town, most patients had essential hypertension with a strong family history. A Liddle phenotype like syndrome was seen in 15.5%. Significant organ damage was identified. High risk behaviour, including smoking and illicit drug use, was identified, and oral contraceptive use and obesity were contributing factors. However, over 40% of patients were non-obese. Secondary causes were identified in 14.5% with the most common secondary causes being renovascular and renal parenchymal disease. These results suggest a targeted approach to the investigation of young hypertensives for secondary causes, although this strategy needs to be tested in a prospective study. There are significant opportunities for lifestyle intervention, and most require pharmacological intervention.

Author contributions

Conceptualization: Erika Wilshire Jones, Phetho Mangena, Brian Lindsay Rayner.
Data curation: Erika Wilshire Jones, Ilhaam Esack, Brian Lindsay Rayner.
Formal analysis: Erika Wilshire Jones, Phetho Mangena, Brian Lindsay Rayner.
Investigation: Erika Wilshire Jones, Ilhaam Esack, Phetho Mangena, Brian Lindsay Rayner.
Methodology: Erika Wilshire Jones, Ilhaam Esack, Phetho Mangena, Brian Lindsay Rayner.
Project administration: Ilhaam Esack, Brian Lindsay Rayner.
Resources: Erika Wilshire Jones, Ilhaam Esack.
Supervision: Erika Wilshire Jones, Brian Lindsay Rayner.
Validation: Erika Wilshire Jones, Phetho Mangena.
Writing – review & editing: Erika Wilshire Jones, Ilhaam Esack, Phetho Mangena.
Writing – original draft: Brian Lindsay Rayner.

References

[1] Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet (London, England) 2012; 380:2224–60.
[2] Thomas C, Hinton ZHA, Baker Richard P, et al. Investigation and treatment of high blood pressure in young people too much medicine or appropriate risk reduction. Hypertension (Dallas, Tex: 1979) 2019;75: 16–22.
[3] Day C, Groenewald P, Laubscher R, et al. Monitoring of non-communicable diseases such as hypertension in South Africa: challenges for the post-2015 global development agenda. S Afr Med J 2014; 104:680–7.
[4] South African Demographic and Health Study 2016. www.health.gov.za, accessed 22 June 2020).
[5] Assadi F. The growing epidemic of hypertension among children and adolescents: a challenging road ahead. Pediatr Cardiol 2012;33: 1013–20.
[6] Dong B, Wang HJ, Wang Z, et al. Trends in blood pressure and body mass index among Chinese children and adolescents from 2005 to 2010. Am J Hypertens 2013;26:997–1004.
[7] Mills KT, Bundy JD, Kelly TN, et al. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. Circulation 2016;134:441–50.
[8] Reddy SP, Resnicow K, James S, et al. Rapid increases in overweight and obesity among South African adolescents: comparison of data from the South African National Youth Risk Behaviour Survey in 2002 and 2008. Am J Public Health 2012;102:262–8.
[9] Tu W, Eckert GJ, DiMeglio LA, et al. Intensified effect of adiposity on blood pressure in overweight and obese children. Hypertension (Dallas, Tex: 1979) 2011;58:818–24.
[10] Xi B, Zhang T, Zhang M, et al. Trends in elevated blood pressure among us children and adolescents: 1999-2012. Am J Hypertens 2016;29: 217–25.
[11] Sinaiko AR. Hypertension in children. N Engl J Med 1996;335: 1968–73.
[12] Rao G. Diagnosis, epidemiology, and management of hypertension in children. Pediatrics 2016;138:00.
[13] Reinders A, Reggiori F, Shennan AH. Validation of the DINAMAP ProCare blood pressure device according to the international protocol in an adult population. Blood Press Monit 2006;11:293–6.
[14] Seedat YK, Rayner BL, Veriava Y. South African hypertension practice guideline 2014. Cardiovasc J Afr 2014;25:288–94.
[15] Madala ND, Nkwanyana N, Dubula T, et al. Predictive performance of eGFR equations in South Africans of African and Indian ancestry compared with (9) (9) mTc-DTPA imaging. Int Urol Nephrol 2012; 44:847–55.
[16] Jones ES, Owen EP, Rayner BL. The association of the R563Q genotype of the ENaC with phenotypic variation in Southern Africa. Am J Hypertens 2012;25:1286–91.
[17] Jones ES, Rayner BL. Hypertension, end-stage renal disease and mesangiocapillary glomerulonephritis in methamphetamine users. S Afr Med J 2015;105:199–201.
[18] Akintunde A, Nondi J, Gogo K, et al. Physiological phenotyping for personalized therapy of uncontrolled hypertension in Africa. Am J Hypertens 2017;30:923–30.
[19] Rayner BL, Spence JD, Bryer A, et al. Registration of amiloride in South Africa: cutting the gordian knot. S Afr Med J 2019;109:632–4.
[20] Rijnbeek PR, van Herpen G, Kapusta L, et al. Electrocardiographic criteria for left ventricular hypertrophy in children. Pediatr Cardiol 2008;29:923–8.
[21] Genga E, Oyoo O, Adebajo A. Vasculitis in Africa. Curr Rheumatol Rep 2018;20:4.