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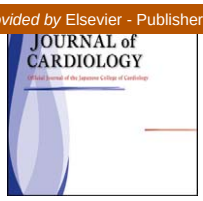

Original article

Arterial blood pressure in adult Nigerians with sickle cell anemia

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KEYWORDS
Arterial blood pressure;
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Summary
Aim and objective: This study was aimed at comparing the arterial blood pressures in steady state adult sickle cell patients with those of age- and sex-matched healthy controls.
Methods: A descriptive cross-sectional study of 62 sickle cell anemia patients and 62 age- and sex-matched healthy controls was carried out in the adult outpatient sickle cell clinics and the cardiac center of the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria. Brachial blood pressures were measured in the right arm in all subjects.
Results: Significant increase in pulse rate was found in the study subjects (87.68 ± 8.91 bpm) compared with the controls (72.13 ± 6.79 bpm) ($p < 0.05$). The mean systolic blood pressure was comparable in the two groups. However, the patients had significantly lower diastolic blood pressure, lower mean arterial blood pressure, as well as a higher pulse pressure than the control subjects. Significant correlations were found between blood pressure indices and hematocrit, body mass index, frequency of crisis, and body surface area.
Conclusion: Relatively lower arterial blood pressure is a significant finding in patients with sickle cell anemia. Hematocrit, frequency of crisis, body mass index, and body surface area are significant determinants of blood pressure indices in sickle cell anemia.

Introduction

Arterial blood pressure has been reported to be typically low in sickle cell anemia and fails to show the age-related rise common in the normal population [1]. Johnson and Giorgio [2] in a retrospective study in Los Angeles reported that blood pressure in sickle cell patients was lower than it was in normal controls. This unusual blood pressure finding in sickle cell anemia has been corroborated by reports from Grell et al. [3] in Jamaica and De Jong et al. [4] in the Netherlands. In a study of 64 adult sickle cell patients with normal creatinine levels by Grell et al. [3], systolic and diastolic pressures were 114 ± 11.0 mm Hg and 65.3 ± 5.3 mm Hg, respectively

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compared with values in the controls of 144.1 ± 22.9 mm Hg and 87.6 ± 13.8 mm Hg.

Although the exact mechanism of the lower blood pressures is unknown, contributing factors could include salt losing sickle cell nephropathy [5], a lowered peripheral resistance [6], alteration in circulating levels of catecholamine, renin, aldosterone, and prostaglandin, or changes in the sensitivity of receptors to these agents [3].

As a group, patients with anemia have lower than expected systolic and diastolic blood pressures [1,2]. However, it has been reported that the blood pressure in patients with sickle cell disease is higher than expected given the severity of their anemia, suggesting the possibility that they have relative hypertension [7]. In a study of 89 sickle cell patients, there was an association between higher blood pressures and stroke. Survival decreased and the risk of stroke increased as blood pressure rose, even though the blood pressure at which these risks increased was below the level defining early hypertension in normal population [7]. Stroke generally occurs in about 4.1% of patients with sickle cell anemia [8]. However, the prevalence increases to over 10% by the age of 50 years [8]. Cerebral ischemia and infarction secondary to vaso-occlusion accounts for 80% of cerebrovascular events [9]. The risk of vaso-occlusive stroke increases with systolic blood pressure [1]. Intermittent hypertension has been described during painful crisis but the frequency or mechanism of this finding is unknown, and hypertension with convulsions has occasionally followed blood transfusions [10,11].

There are few data on this subject from the environment of the study. This study was aimed at comparing the arterial blood pressures in steady state adult sickle cell patients with those of age- and sex-matched normal controls.

Methodology

A descriptive cross-sectional study of 62 sickle cell anemia patients and 62 age- and sex-matched healthy controls was carried out in the adult outpatient sickle cell clinics and the cardiac center of the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria from February to August 2007. The study subjects were drawn from adult patients (age ≥18 years) [12], attending the adult sickle cell clinics of the UNTH Enugu, who had hemoglobin genotype SS on hemoglobin electrophoresis, were in steady state, and consented to participate in the study.

Steady state is defined as absence of any crisis in the preceding 4 weeks, and absence of any symptoms or signs attributable to acute illness. The exclusion criteria for patients were presence of congenital or acquired heart disease, pregnancy and/or inter-current illness, very severe anemia (hematocrit <18%), excessive use of alcohol (more than 16 g daily) [13], and use of tobacco. The controls were healthy subjects selected from students and hospital workers, as well as members of the local community. They were age- and sex-matched with the patients. The eligibility criteria for the controls were: HbAA genotype, absence of congenital or acquired heart disease, consent to participate in the study, absence of pregnancy and/or inter-current illness, and hematocrit level ≥30%. Ethical clearance for the study was obtained from the Ethical Committee of UNTH Enugu.

The weight and height of each subject were recorded and the surface area determined from a standard formula [14]. The supine brachial and ankle blood pressures were measured separately with the cuff of the mercury sphygmomanometer applied to the right arm and right calf, respectively. The approximate systolic blood pressures were obtained by palpation of the brachial artery. The cuff was deflated and re-inflated to about 10 mm Hg above the approximate systolic value. Phases I and IV Korotkoff's sounds were used as systolic and diastolic blood pressure readings, respectively. The mean arterial blood pressure was taken as the sum of the diastolic blood pressure and one-third of the pulse pressure. Hematological parameters such as hematocrit, reticulocyte count, white blood cell count with differentials, and hemoglobin electrophoresis were obtained.

Data are presented as means ± standard deviation. In order to examine the effect of anemia on the variables, the subjects were classified based on the hematocrit values into four classes in accordance with the World Health Organization classification of anemia as follows: Class 1, normal (hematocrit ≥ 36%); Class 2, mild anemia (hematocrit 30—35.9%); Class 3, moderate anemia (hematocrit 21—29.9%); and Class 4, severe anemia (hematocrit 18—20.9%) [15]. Inter-class differences in blood pressures in the patients were compared by one-way analysis of variance and posthoc multiple comparison of mean using the Tukey's honestly significant difference test. Intra-class differences in parameters between patients and controls in the same hematocrit class were analyzed using the independent Student's *t*-test. All statistical analyses were carried out using the Statistical Packages for Social Sciences (SPSS Inc., Chicago, IL, USA) software version 11.0. Statistical tests with probability values less than 0.05 were considered statistically significant.

Results

Baseline data

The mean ages for patients and controls were 28.27 ± 5.58 (range 18—44) and 28.37 ± 5.91 (range 18—45) years, respectively. There were no statistically significant age and gender differences in patients and controls. The study subjects had statistically significant lower mean values than controls in the measurement of height, weight, body mass index, and body surface area ($p < 0.001$) (Table 1).

Pulse rate and brachial blood pressure

A significant increase in pulse rate was found in the study subjects (87.68 ± 8.91 bpm) compared with the controls (72.13 ± 6.79 bpm) ($p < 0.05$, Table 2). The mean systolic blood pressure was comparable in the two groups. However, the patients had significantly lower diastolic blood pressure, lower mean arterial blood pressure, as well as a higher pulse pressure than the control subjects (Table 2). No significant gender differences in blood pressure indices were found.

Table 1 Age, gender, and anthropometric data.

Parameters	SCA Mean (SD)	Controls Mean (SD)	*t*-Test	*p*-Value
Age (years)	28.27 (5.58)	28.37 (5.91)	0.987	0.924
Gender [frequency (%)]				
Male	31 (50)	31 (50)	0.000	1.00[a]
Female	31 (50)	31 (50)		
Total	62	62		
Weight (kg)	54.97 (10.61)	67.35 (8.37)	7.20	<.001*
Height (m)	1.62 (0.14)	1.72 (0.07)	4.960	<.001*
Body surface area (m^2)	1.62 (0.03)	1.78 (0.14)	3.723	<.001*
Body mass index (kg/m^2)	20.47 (2.73)	23.87 (3.22)	6.181	<.001*

SCA, sickle cell anemia.
* Statistically significant.
[a] Chi-square.

Effects of hematocrit levels on physiologic parameters in patients

Table 3 compares the mean values for the physiologic parameters in the patients in the three separate categories (mild, moderate, or severe anemia) based on their hematocrit levels using analysis of variance.

Significant differences in mean values were observed in brachial systolic blood pressures ($F = 6.029$; $p = 0.004$) and pulse pressure ($F = 5.747$; $p = 0.005$).

Pair wise posthoc multiple comparison of mean using Tukey's honestly significant difference test showed that the observed difference in systolic blood pressure was accounted for by the difference between the moderate and severe anemia group (SE = 3.7128; $p = 0.006$). The mean pulse pressure for patients with mild anemia was significantly different from patients with moderate anemia (SE = 4.40621; $p = 0.0013$).

Comparison of blood pressure indices between patients and controls in the same hematocrit category (hematocrit 30—35.9%) showed no significant difference in mean values (Table 4).

Correlation analysis of blood pressure indices and anthropometric and physiologic variables in the patients showed significant correlations between: (1) systolic blood pressure and hematocrit ($r = 0.263$; $p = 0.039$), weight ($r = 0.448$; $p < 0.001$), body mass index ($r = 0.321$; $p = 0.011$), body surface area ($r = 0.276$; $p = 0.03$); (2) mean arterial pressure and frequency of crisis ($r = 0.267$; $p = 0.036$); (3) pulse pressure and weight ($r = 0.331$; $p = 0.009$). These correlation coefficients remained statistically significant even after controlling for the effect of hematocrit, (Tables 5 and 6).

Discussion

The brachial systolic blood pressure in sickle cell anemia patients from this study was not significantly different from that of the controls, but the diastolic blood pressure was found to be significantly lower in the patients than in the controls.

Ayuo et al. [16] reported similar findings in his study, in Kenya, of 52 sickle cell anemia patients in steady state, 13—27 years of age (mean age 18.9 years) and mean hemoglobin concentration of 8.5 ± 1.4 g/dl; in which the systolic blood pressure of 114.9 ± 9.9 mm Hg was found to be comparable with that of the controls, while the diastolic blood pressure of 64.6 ± 10 mm Hg was significantly lower than that of the controls. However Grell et al. [3] in a study of 64 Jamaican sickle cell anemia patients with ages ranging from 30 to 69 years, reported statistically significant lower levels of systolic and diastolic blood pressures of 114.6 ± 11.0 mm Hg and 65.3 ± 5.3 mm Hg, respectively compared with values in the controls of 144.1 ± 22.9 mm Hg and 87.6 ± 13.8 mm Hg. The mean ages and hemoglobin concentration were not specified. The apparent significant difference observed in the Jamaican study could be

Table 2 Physiologic data in patients and controls.

Parameters	SCA Mean (SD)	Controls Mean (SD)	*t*-Test	*p*-Value
Pulse rate (bpm)	87.68 (8.91)	72.13 (6.79)	11.062	<.001*
Brachial systolic BP (mm Hg)	119.50 (11.70)	121.2 (8.97)	0.527	0.599
Brachial diastolic BP (mm Hg)	64.867 (8.95)	76.88 (6.18)	8.629	<.001*
Brachial pulse pressure (mm Hg)	54.63 (12.87)	44.31 (10.91)	4.735	0.001*
Mean brachial arterial BP (mm Hg)	81.18 (12.65)	91.71 (5.47)	5.850	<.001*
Hematocrit (%)	24.07 (3.10)	38.65 (1.97)	30.589	<.001*

BP, blood pressure; SCA, sickle cell anemia.
* Statistically significant.

Table 3 Physiologic parameters in sickle cell anemia; comparison with hematocrit levels.

Parameters	Values; mean (SD) Hematocrit levels			*F*-statistic	*p*-Value
	Mild	Moderate	Severe		
Age	26.11 (3.59)	23.60 (5.35)	25.18 (7.48)	0.922	0.402
Pulse rate	90.89 (13.57)	86.45 (8.36)	89.54 (5.54)	1.214	0.304
Brachial SBP	115.11 (13.57)	122.85 (9.34)	110.91 (13.75)	6.029	0.004*
Brachial DBP	69.78 (12.21)	64.60 (8.84)	61.87 (4.05)	2.083	0.134
Pulse pressure	45.33 (10.28)	58.25 (12.19)	49.09 (12.21)	5.747	0.005*
MAP	74.53 (28.58)	83.42 (6.82)	78.49 (6.39)	2.210	0.119

DBP, diastolic blood pressure; SBP, systolic blood pressure; MAP, mean arterial blood pressure.
* Statistically significant.

Table 4 Comparison of age and blood pressure indices in subsets of patients and controls with hematocrit level between 30 and 35.9%.

Parameters	Values; mean (SD)		*t*-Test	*p*-Value
	SCA	Controls		
Age	26.11 (3.59)	22.82 (3.82)	1.972	0.064
Pulse rate	90.89 (13.57)	72.19 (5.33)	4.213	0.001*
Brachial SBP	115.11 (13.57)	124.55 (12.93)	1.588	0.130
Brachial DBP	69.78 (12.22)	78.18 (5.60)	2.043	0.056
Pulse pressure	45.33 (10.28)	46.36 (14.16)	0.182	0.857
MAP	74.53 (28.58)	92.73 (3.89)	2.101	0.056

SCA, sickle cell anemia; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial blood pressure.
* Statistically significant.

Table 5 Effect of clinical parameters on blood pressure indices in sickle cell anemia; a correlation analysis.

Clinical parameters	Blood pressure indices				
	Systolic BP	Diastolic BP	MAP	Pulse pressure	Pulse rate
Hematocrit					
r	0.263*	0.225	0.017	0.085	0.089
p	0.039	0.078	0.898	0.192	0.493
Frequency of crisis					
r	−0.121	−0.140	−0.267*	−0.016	0.064
p	0.342	0.279	0.036	0.903	0.624
Weight					
r	0.448*	0.114	0.230	0.331*	−0.134
p	<0.0001	0.378	0.072	0.009	0.298
BMI					
r	−0.321*	0.128	0.123	0.205	0.054
p	0.011	0.320	0.341	0.110	0.678
BSA					
r	0.276*	0.144	0.226	0.153	−0.001
p	0.030	0.266	0.077	0.235	0.992
Age					
r	0.099	0.056	0.037	0.099	0.118
p	0.445	0.664	0.775	0.444	0.361
Sex					
r	−0.087	0.137	0.149	−0.174	−0.159
p	0.501	0.289	0.549	0.176	0.218

BP, blood pressure; MAP, mean arterial pressure; BMI, body mass index; BSA, body surface area.
* Statistically significant.

Table 6 Partial correlation analysis of clinical parameters and blood pressure indices while controlling for the effect of hematocrit in sickle cell anemia patients.

Clinical parameters	Blood pressure indices				
	Systolic BP	Diastolic BP	MAP	Pulse pressure	Pulse rate
Age					
r	−0.076	0.035	0.036	0.043	−0.128
p	0.562	0.789	0.786	0.740	0.326
Sex					
r	−0.069	0.159	0.151	−0.169	0.167
p	0.596	0.222	0.245	0.194	0.199
Frequency of crisis					
r	−0.084	−0.107	−0.268*	−0.002	0.079
p	0.520	0.412	0.037	0.988	0.543
BMI					
r	0.259*	0.061	0.124	0.189	0.027
p	0.044	0.642	0.340	0.147	0.838
Weight					
r	0.381*	0.012	0.250	0.329*	−0.198
p	0.002	0.926	0.052	0.009	0.126
BSA					
r	0.238	0.105	0.228	0.140	−0.019
p	0.065	0.422	0.078	0.283	0.885

BP, blood pressure; MAP, mean arterial pressure; BMI, body mass index; BSA, body surface area.
* Statistically significant.

accounted for by the slightly elevated systolic blood pressures in the controls.

We observed higher systolic blood pressure and pulse pressure in sickle cell anemia patients with moderate anemia when compared to patients with severe anemia. Several factors could contribute to this effect. Firstly, the combined effect of certain variables in the patients on blood pressure parameters could be quite significant. This study identified some factors that might be determinants of blood pressure indices in sickle cell anemia. These include frequency of crises, weight, body mass index, body surface area, as well as following blood transfusion [10,11,17]. However, the extent to which these factors affect blood pressure indices is yet to be determined. Secondly, the circulatory response to anemia with resultant reduced peripheral vascular resistance and fall in blood pressure is more pronounced in patients with severe anemia.

Our finding of significantly increased pulse rate in the patients when compared with the controls in the same hematocrit category may be related to the increased background inflammatory and oxidative stress associated with sickle cell anemia [18]. Besides, it is likely that the sickle cell anemia patients had a significant variable severity of anemia which may not be properly represented by a single hematocrit measure as used for data analysis in this study.

We noted significant correlations between blood pressure indices and hematocrit, body mass index, frequency of crisis, and body surface area. After controlling for the effect of anemia (hematocrit) significant correlations were still observed in the last three variables. These results confirm previous findings by Pegelow et al. [1] who reported significant correlation between blood pressure indices and body mass index, hematocrit, renal function, age, and sex. However, our study did not demonstrate any significant correlation of blood pressure with age or sex probably due to the preponderance of younger subjects in this study. Sickle cell anemia patients with frequent crisis and increased hyper-hemolysis states have been found to have increased prevalence of elevated systolic blood pressure and pulmonary hypertension [19].

The significantly lower diastolic blood pressure and increased pulse pressure noted in the patients in this study could be as a result of the hemodynamic circulation from chronic anemia, since these differences were not observed when the effect of anemia was accounted for by comparing patients and controls with mild anemia (hematocrit 30−35.9%).

However, increased pulse pressure has been shown to predict cardiac morbidity in studies carried out in diabetic and hypertensive patients [20,21]. Its relevance in patients with sickle cell anemia is yet to be explored.

In conclusion, our findings support previous reports of relatively lower arterial blood pressure in patients with sickle cell anemia. Hematocrit, frequency of crisis, body mass index, and body surface area are significant determinants of blood pressure indices in sickle cell anemia. Blood pressure in these patients should be evaluated relative to the lower values expected for patients with sickle cell anemia.

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