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COMPARISON OF ARTERIAL BLOOD PRESSURE IN SICKLE CELL PATIENTS AND NON-SICKLE CELL YOUNG ADULTS IN ZARIA, KADUNA STATE NIGERIA

***[1]Abdulrauf, R. A, [1]Farouk, A., [2]Adamu, J., [3]Nmadu, J. N. and [3]Awwalu, S.**

[1]Department of Human Physiology, Faculty of Basic Medical Sciences, Ahmadu Bello University Zaria
[2]College of Health Sciences, University of Abuja, Gwagwalada, F. C. T.
[3]Department of Haematology and Blood Transfusion, Ahmadu Bello University Teaching Hospital, Shika-Zaria.

*Corresponding authors' email: oluwakemi2016@gmail.com Phone: +2347069197661

ABSTRACT

The current study was aimed at evaluating the arterial blood pressure indices in young adults with (Sickle cell anemia) SCA in comparison to those with normal HbAA age- and sex-matched healthy controls. A sample size of 60 individuals aged 18-30 years were recruited for participation. They were divided into two groups; 30 being sickle cell patients (HbSS) as confirmed by hemoglobin electrophoresis and 30 being the control (HbAA) group. Consent was obtained from both groups and data was collected in a face-to-face administered questionnaire. The blood pressure in both groups were determined using a mercury sphygmomanometer and the results obtained showed that SCA patients had a significantly ($p < 0.05$) lower diastolic pressure and no difference ($p > 0.05$) was observed in systolic blood pressure. The mean arterial pressure was also found to be significantly ($p < 0.05$) lower in SCA patients than the normal. The sickle cell group exhibited a significantly ($p < 0.05$) higher heart rate and pulse pressure than the control group. In conclusion, sickle cell patients have a lower diastolic blood pressure and higher heart rate than non-sickle cell group. Therefore, as SCD patients transition into adulthood, they may not be at risk of hypertension and development of its various complications, but they may be prone to consequences of hypotension and bradycardia such as reduced cardiac output, reduced coronary hypoperfusion and cardiac arrhythmias.

Keywords: Sickle cell anemia, Arterial blood pressure, Comparison

INTRODUCTION

Sickle cell anemia, a hereditary hemoglobinopathy, results from a single nucleotide substitution in the β-globin gene, leading to the production of HbS (Taiwo, 2011). When deoxygenated, HbS molecules aggregate, distorting red blood cells into characteristic sickle shapes. This change in cell morphology contributes to vascular occlusion, hemolysis, and a complex cascade of physiological events (Weisel and Litvinov, 2019). Sickle cell disease applies to all patients with at least a single HbS chain and one other abnormal globin chain, which may be another sickle cell chain (in which case the patient is homozygous, HbSS and by definition has sickle cell anemia), HbSC, or one of the thalassemia's (Hb S-thal) (Piel *et al.*, 2017, Ibrahim *et al.*, 2024).

Sickle cell disease (SCD) is characterized by repeated vaso-occlusion and chronic hemolysis resulting into chronic complications such as pulmonary arterial hypertension (PAH) and early mortality (Ahmed and Ogunlade, 2022). It stands as one of the most prevalent inherited disorders globally, with an especially high incidence in Sub-Saharan Africa, where Nigeria plays a significant role as a region deeply impacted by the disease (Pinto *et al.*, 2021, Epis *et al.*, 2022). Africa accounts for 75% of sickle cell cases worldwide and according to a recent WHO research, 150,000 babies in Nigeria alone are born each year with sickle cell anemia, that is, around 2% of infants in the country are affected (Piel *et al.*, 2017; Ojelabi, 2018; Nwabuko *et al.*, 2022). The prevalence of SCD within the states in Nigeria ranges from 1%-3%. Hb-SS is the predominant hemoglobin variant found in Nigeria while Hb-SC occurs sporadically and has been mostly reported in the south western Nigeria (Nubila *et al*., 2013).

Arterial blood pressure (ABP) is the force of blood pushing against the walls of the arteries as the heart pumps blood. If this pressure rises and stays high over time, it can damage the body through its effect on the bodily organs in many ways (Ajayi *et al.*, 2013). Elevated ABP, particularly hypertension, is a well-established risk factor for cardiovascular diseases, including coronary artery disease, stroke, and heart failure (Ramón *et al.*, 2023). Uncontrolled hypertension can lead to structural and functional changes in the arterial walls, promoting atherosclerosis and increasing the risk of adverse cardiovascular events (William, 2003). Arterial blood pressure (ABP) serves as a fundamental measure of cardiovascular health and is recognized as a key indicator for assessing the risk of hypertension and related vascular issues. Systemic and pulmonary hypertension (PH) is a major risk factor for early death in SCD (Desai *et al.,* 2022). There have been conflicting findings on blood pressure parameters in sickle cell patients, while some studies conducted in Nigeria have highlighted the elevated risk of hypertension (Oluseyi *et al.*, 2021), others studies have reported low blood pressure in patients with homozygous sickle cell disease (SCD) and have sought various hypotheses on the mechanism of this finding (Ajayi *et al.,* 2013; Elfaki *et al*., 2023). Ajayi *et al.,* 2013 reported from the findings of their study that systolic and diastolic blood pressures are lower in SCA patients in stable state (compared with control, HB AA subjects) but are relatively higher during crisis while diastolic blood pressure is significantly higher in HB AS than HB AA and HB SS subjects in crisis while Lopes *et al.,* 2022 who studied cardiovascular complications in patients with sickle cell and other hemoglobinopathies reported that Dilatation of the cardiac chambers, left and right ventricular hypertrophy, pulmonary hypertension, diastolic dysfunction, mitral regurgitation and tricuspid regurgitation are more prevalent in SCA than in the other hemoglobinopathies considered. Elfaki *et al*., 2024 also reported increased prevalence of 29% of pulmonary hypertension in sickle cell patients.

ABP is influenced by several variables that contribute to its measurement and interpretation such as Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Pulse Pressure (PP), Mean Arterial Pressure (MAP), Rate-Pressure

Product (RPP). The conflicting results from previous studies underscore the need for a comprehensive analysis by comparing ABP profiles in steady-state sickle cell patients and non-sickle cell young adults, this will provide insights into the potential influence of SCD on these variables and their association with hypertension risk, making the research pivotal in establishing a clearer understanding of the relationship between sickle cell disease and ABP. There is a notable research gap regarding assessment of ABP in steady-state sickle cell young adult in Zaria, as compared to non-sickle cell young adults, hence the choice of young adults as the study population. Existing studies on this topic within our geographical context are limited, if not absent. To the best of our knowledge, this is the first study comparing ABP profiles in steady-state sickle cell patients and non-sickle cell young adults in Zaria. The study will measure and compare the heart beat rate, the systolic and diastolic blood pressure values in sickle cell and non-sickle cell groups and also identify certain risk factors associated with the development of hypertension such as age, weight and height to blood pressure variation.

MATERIALS AND METHODS

Mercury sphygmomanometer, Stethoscope, Stopwatch, Participant questionnaires, Informed consent forms, Anthropometric measuring tools (height, weight)

Study Area

Zaria is a metropolitan city in Nigeria which lies within four local government areas in Kaduna State; it is the capital city to the Zazzau Emirate Council, and one of the original seven Hausa city-states and a major city in the state. The local government areas that made up of the city of Zaria includes: Zaria Local Government, Sabon Gari Local Government, Giwa Local Government and Soba Local Government areas in Kaduna state, Nigeria. From the 2006 population census, Zaria was estimated to have 736,000 people. It is located at 11.066667 (latitude decimal degrees), 7.7 (longitude decimal degrees).

The study was conducted at the Ahmadu Bello University Teaching Hospital sickle cell anemia clinic and the department of Human Physiology, Ahmadu Bello University, Zaria.

Study Population

The target population consisted of two groups: steady-state sickle cell patients and non-sickle cell young adults in Zaria. The steady-state sickle cell young adults were recruited from the Ahmadu Bello University Teaching Hospital (ABUTH) sickle cell clinic, while the non-sickle cell young adults were recruited from the undergraduate students of Department of Human Physiology, Ahmadu Bello University Zaria. Both groups were within the age range of 18-30 years.

Inclusion and Exclusion Criteria

The inclusion criteria for sickle cell patients include: Confirmed diagnosis of sickle cell disease, aged between 18-30 years,), attending the adult sickle cell clinics of the ABUTH, who had hemoglobin genotype SS on hemoglobin electrophoresis and were in steady state, (Steady state is defined as absence of any crisis in the preceding 4 weeks without blood transfusion in the last three months, and absence of any symptoms or signs attributable to acute illness) and willingness to participate and provided informed consent. For the control group (non-sickle cell) young adults: HbAA genotype, absence of congenital or acquired heart disease, consent to participate in the study, absence of pregnancy and/or inter-current illness.

Exclusion Criteria

The exclusion criteria for sickle cell patients:

i. Patients who are on antihypertensive medications,
ii. Patients who are taking anxiolytics (medications for anxiety), SCA patients who are currently participating in clinical trials involving investigatory therapeutic products.

Exclusion criteria for (control group) non-sickle cell patients:

i. Individuals with history of substance abuse (alcohol and tobacco),
ii. Participants with a history of congenital or acquired heart disease, pregnancy and/or inter-current illness.

Sample Size Determination

Sample size was calculated using the below formula

$n = \frac{z^2pq}{d^2}$

Where,

N = desired sample size

Z = standard normal deviation = 1.96

P = prevalence = 2%, 2/100=0.02

Q = (1-p) = (1-0.02) = 0.98

D = precision = 0.05

$N= \frac{(1.96)^2 \times 0.02 \times 0.98}{(0.05)^2}$

$N= 30.118144 \approx 30$

But for the purpose of this work, the sample size was taken up to 60 in order to obtain better results. With matched ages and gender, we have;

SCA: 30 = 15 males, 15 females, non-SCA: 30 = 15 males, 15 females.

Ethical Consideration

Ethical clearance was obtained from the Ahmadu Bello University Health Ethical Committee at Ahmadu Bello University Teaching Hospital Shika Zaria, reference number of NHREC/TR/ABUTH-NHREC/01/02/23, informed consent was sought from individual subjects before the commencement of the research work.

Data Collection

Data was collected using a structured questionnaire administered in face-to-face interviews. Additionally, blood pressure measurements were taken using the 2021 Erka meter 3000 manual calibrated sphygmomanometers, a stopwatch of 15 seconds for the heart rate and a stethoscope for auscultation. Subjects body weight and height was measured using the ZT-120 health scale.

Measurement of the Blood Pressure

Standard methodology as recommended by the Fourth report on diagnosis, evaluation and treatment of high blood pressure in children and adolescents was used to measure blood pressure. Blood pressure (BP) measurement was taken by an indirect method using a mercury sphygmomanometer of appropriate cuff size attached to the arm. The blood pressure was measured after the subject have rested in a seated position for 5 minutes, legs uncrossed and flat on the floor and arm resting on a table at the same level with the heart; using ERKA 3000 sphygmomanometer (Charles, 1997). The blood pressure was measured three times at an interval of 3 minutes and the mean recorded. All were carried out by the same investigator.

Pulse Pressure (PP) was calculated using the formula: PP = SBP– DBP.

Mean Arterial Pressure (MAP) was calculated using the formula MAP = DBP + 1/3(PP)

Rate Pressure Product (RPP) was calculated

Anthropometry

All patients enrolled in the study were weighed, wearing light clothing. Height was taken barefooted to the nearest 0.1cm. Both weight and height were measured using electronic body Tes-200 RC scale. Height and weight for control group was measured using minimeter portable device and electronic body scale, respectively. Body mass index (BMI) was calculated for all subjects based on the formula: BMI: Weight in kilogram /Height (in meter^2)

as the product of SBP and heart rate (Ahmed and Ogunlade, 2022).

Data Analysis

The collected data were analyzed using SPSS window version 22. All the readings were presented as a mean ± standard deviation. Descriptive statistics was used to summarize demographic information, blood pressure values and other relevant variables. The independent sample t-test was used to determine the significant difference between two groups. A p-value of < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

Blood pressure parameters in sickle cell and non- sickle cell individuals

A significantly higher heart rate was found in the SCA group (89.57 ± 12.37 bpm) compared with the controls (79.27 ± 10.61 bpm) ($p < 0.05$, Table 1). The mean systolic blood pressure was statistically insignificant in the two groups. However, the sickle cell group had significantly lower diastolic blood pressure, lower mean arterial blood pressure, as well as a higher pulse pressure than the control subjects (Table 1).

Table 1: Blood pressure parameters in sickle cell and non- sickle cell individuals

	Groups	Mean	Std. Deviation	p value
Diastolic (mmHg)	HbSS/SC	66.83	11.27	0.00**
	HbAA	79.73	6.58	
Systolic (mmHg)	HbSS/SC	108.37	13.29	0.07
	HbAA	114.27	11.1	
Pulse Pressure	HbSS/SC	41.53	11.41	0.01**
	HbAA	34.53	9.19	
Mean Arterial Pressure	HbSS/SC	80.68	10.71	0.00**
	HbAA	91.24	7.15	
Heart Rate (bpm)	HbSS/SC	89.57	12.37	0.00**
	HbAA	79.27	10.61	
Rate-Pressure Product	HbSS/SC	9717.4	1963.876	0.13
	HbAA	9036.07	1377.183	

Values with asterisks (**) showed statistical significance. HbSS/ SC- Sickle cell hemoglobin, HbAA- Normal or non-sickle cell hemoglobin

Association of Demographic, anthropometric and other risk factors and Blood pressure parameters

The mean ages for patients and controls were 22.97 ± 3.73 and 23.83 ± 2.3 (years), respectively. There were no statistically significant age and gender differences in patients and controls. The SCA group had statistically significant lower mean values than controls in the measurement of height, weight and body mass index ($p < 0.05$) (Table 2). No association was found between the blood pressure and risk factors assessed.

Table 2: Association of anthropometric and other risk factors and cardiovascular parameters

	Groups	Mean	Std. Deviation	p value
Age (years)	HbSS/SC	22.97	3.73	0.28
	HbAA	23.83	2.3	0.28
Height (meters)	HbSS/SC	1.63	0.09	0.04**
	HbAA	1.68	0.1	
Weight (kilogram)	HbSS/SC	50.23	7.13	0.00**
	HbAA	64.77	15.58	
Salt intake	HbSS/SC	2.17	0.75	0.61
	HbAA	2.27	0.79	
No. of water sachets (per day)	HbSS/SC	6.67	2.19	0.95
	HbAA	5.6	2.66	
Body mass Index	HbSS/SC	18.90	2.73	0.00**
	HbAA	22.93	5.34	
Sleep (hours)	HbSS/SC	5.97	1.63	0.58
	HbAA	5.77	1.14	
Physical activity (mins)	HbSS/SC	54.73	56.14	0.13
	HbAA	74.67	42.18	0.13
Gender (Male and females)	HbSS/SC	1.5	0.51	1.00
	HbAA	1.5	0.51	

Discussion

This study compared systemic BP of young adults with SCA attending clinic in Ahmadu Bello University Teaching hospital Zaria, Kaduna state Nigeria with those of non-sickle cell counterparts. Many studies on children and adolescents with SCA have shown conflicting results and Cardiopulmonary complications remain a leading cause of morbidity and mortality in sickle cell disease (SCD) (Desai *et al.*, 2022; Galadanci *et al*., 2022). A number of studies document that SCD is associated with lower systemic blood pressures than controls and with a lower prevalence of systemic hypertension.

The mean diastolic and mean arterial pressures were found to be lower while pulse pressure was significantly higher in SCA individuals than control. These findings were comparable with earlier studies of Oguanobi *et al*., 2010 and Hussain and Hassan, 2017 among others who also reported that the systolic BP (SBP) and diastolic BP (DBP) curves of patients with SCA showed lower levels than control group for all age groups. Potential mechanisms for the lower blood pressures in SCD patients include obstruction of the vasa recta in the kidney and repeated ischemia to the renal medulla, resulting in a distal renal tubular concentrating defect and hyposthenuria, lower body mass index in patients with SCD, and lower arterial stiffness (Elfaki *et al.,* 2023). It has also been attributed to systemic vasodilation mediated by the cardiovascular autonomic dysfunction as well as renal tubular defect that causes the increased sodium and water excretion among SCA individuals. Other factors attributed to these findings were compensatory mechanism to overcome the detrimental effects of vaso occlusive crisis, disease salt-losing sickle cell nephropathy, lower peripheral resistance, low body mass index, zinc deficiency which resulted in alteration of circulating levels of catecholamine, renin, aldosterone and prostaglandin or changes in the sensitivity of receptors to these agents (Hassan & Hussain 2017).

Previous reports from Ajayi *et al.,* 2013 showed increased diastolic blood pressures in heterozygote HB AS and HB SS during crisis underscore the possible contributory role of the S-gene in cardiovascular functions. Patients with SCA have been associated with left ventricular diastolic dysfunction as an independent risk factor for mortality (Hankins *et al.,* 2010), and several postulations have been made to explain this effect which include increase body iron burden due to repeated transfusions and continuous haemolysis, increased cardiac activity and possibly increased angiotensin production (Ajayi *et al.,* 2013). The increase in heart rate seen in SCA patients is mostly a compensatory response to the chronic anemia causing decreased oxygen and thus heart rate is increased to improve oxygenation. The increase in the pulse pressure can be attributed to endothelial vascular dysfunction which causes increased arterial stiffness and resultant increase in PP (Novelli *et al.,* 2012). All risk determinants; salt intake, dehydration, physical activity and hours of sleep were all observed to have no effect on the blood pressure indices when compared in both groups.

This study has enhanced a clearer understanding of the relationship between ABP parameters and SCD and this is crucial for assessing the cardiovascular health of individuals living with this genetic disorder. The findings of this study have also directed the focus of the clinician when managing sickle cell patients, the focus should be on managing the decreased diastolic pressure which could result in reduced cardiac output despite the increased heart rate, coronary and peripheral organ hypoperfusion especially since the vasopressor effect of angiotensin II on blood vessels, is not as effective in correcting hypovolaemia and low blood pressure in individuals with SCA. The pulse pressure should also be given attention to as increased pulse pressure has been shown to predict cardiac morbidity in studies carried out among diabetic and hypertensive individuals.

CONCLUSION

In conclusion, our findings support previous reports of relatively lower arterial blood pressure and mean arterial pressure with high pulse pressure in individuals with sickle cell anemia in steady state when compared with age and sex matched young adults with normal hemoglobin type.

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