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ASSESSMENT OF PHYSICAL GROWTH AND SEXUAL MATURATION AMONG ADOLESCENTS WITH SICKLE CELL DISEASE AGED 10-18 YEARS SEEN AT UNIVERSITY OF BENIN TEACHING HOSPITAL, BENIN CITY

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Abstract

Background: Growth restriction and delayed puberty are well- recognized complications of Sickle cell disease (SCD), particularly in sub-Saharan Africa where disease burden is highest. However, data on determinants of sexual maturation among Nigerian adolescents with SCD remain limited**.**

Objective: To assess growth patterns, pubertal development and determinants of sexual maturity among adolescents with SCD compared with age- and sex- matched controls.

Methods: A cross- sectional comparative study was conducted among 150 adolescents with SCD and 80 healthy controls aged 10-18 years attending University of Benin Teaching Hospital (UBTH), Benin City, Edo State. Anthropometric measurements were obtained and body mass index (BMI) calculated. Height-for-age (HAZ) and BMI-for-age (BAZ) Z-scores were generated using WHO Anthro plus. Pubertal assessment was performed using Tanner staging; testicular volume was measured in males and age at menarche documented in females. Disease severity indices and steady-state packed cell volume (PCV) were recorded. Data were analysed using SPSS version 26.0. Statistical significance was set at $p<0.05$.

Results: Adolescents with SCD had significantly lower mean weight, height and BMI compared to controls ($p<0.001$). Mean HAZ (-1.85) and BAZ (-2.10) indicated significant stunting and wasting. A substantial proportion of those aged 13-15 years remained in Tanner stages II-III. Testicular volumes in males aged 13-18 years were significantly below age- specific norms ($p<0.001$). Mean age at menarche was significantly delayed (13.9± 1.6 years; $p<0.001$). Disease severity was significantly associated with lower BMI and delayed puberty. In multivariate analysis, age, BMI and steady-state PCV independently predicted advanced Tanner stage.

Conclusion: Adolescents with SCD exhibit significant growth impairment and delayed sexual maturation. Optimizing nutritional status and haematological control may improve pubertal outcomes

Key words: *Adolescents, Delayed puberty, Growth restriction, Sickle cell disease, Tanner staging, WHO*

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Introduction

Sickle cell disease (SCD) is a chronic hereditary hemoglobinopathy characterized by the production of abnormal haemoglobin S, which leads to recurrent vaso-occlusive crises, chronic haemolytic anaemia and multi-organ complications.[1] Adolescence is a critical developmental stage marked by rapid growth, hormonal changes and the attainment of sexual maturity. Sexual maturation involves the transformation of a sexually immature child into adult capable of reproductive functions because of a series of hormonal events.[2] It is associated with physical, emotional, social and psychological changes. The physical changes include acceleration of growth rate, development of sex specific skeletal characteristics, alteration of body mass and composition as well as development of secondary sexual characteristics and maturation of reproductive system.[3] SCD is associated with inflammatory stress, chronic anaemia and increased energy expenditure-factors that can blunt growth velocity and delay pubertal milestones. This is attributed to chronic illness, recurrent infections, nutritional deficiencies and long-term effects of disease–related complications.[4] Across diverse settings, adolescents with SCD tend to be shorter, lighter and enter/complete puberty later than peers, with downstream psychological effects and potential implications for health and fertility. Understanding the impact of SCD on physical growth and sexual maturity is essential for improving clinical care, psychosocial support and quality of life for these patients.

Classic longitudinal work in Jamaica showed significantly later menarche in SCD vs controls (15.4 vs. 13.0 years). Contemporary studies continue to report delayed Tanner staging and later menarche by approx. 2 years in SCD with disease- severity markers linked to delay.[12-15] These delays have psychosocial implications including poor self- esteem, stigmatization and impaired peer relationships.[16-19]

Anthropometric assessment and Tanner staging remain the primary clinical tools to evaluate growth and sexual maturation in adolescents. Height-for-age (HAZ) and BMI-for-age (BAZ) Z- scores based on World Health Organization (WHO) standards[20] are commonly used to quantify stunting and wasting while Tanner staging[10] provides a standardized measure of secondary sexual characteristics. Testicular volume, measured using an orchidometer, is a reliable marker of pubertal onset in males while age at menarche serves as a key indicator of reproductive health in females.

Early identification of growth failure and delayed sexual maturation can prompt timely nutritional support, endocrine evaluation and appropriate management strategies including hydroxyurea therapy and psychosocial interventions. Furthermore, data from Nigerian cohorts can inform regional guidelines, establish local reference standards and serve as benchmark for evaluating the impact of emerging therapies on adolescent development. This study therefore aims to comprehensively evaluate growth patterns, nutritional status and pubertal development among adolescents with SCD attending UBTH, Benin City. Specifically, it seeks to:

1. Evaluate anthropometric indices (height, weight, BMI) in adolescents with SCD in comparison with age-matched controls

2. Assess pubertal development using Tanner staging, testicular volume and age at menarche
3. Examine the association between disease severity and delayed puberty
4. Identify independent predictors of sexual maturation in this population

Method

Study Design

This hospital-based descriptive cross-sectional study was conducted among adolescents with SCD.

Study Area

Benin City is the capital of Edo State in southern Nigeria, with an estimated population of over 1.7 million people. SCD remains a significant public health concern in Nigeria, with an estimated prevalence of 2–3% among newborns. In Edo State, care for children with SCD is primarily provided at secondary and tertiary health facilities, with comprehensive management—including hydroxyurea therapy—largely available at tertiary centres such as UBTH. The study was conducted at the Paediatric Haemato-oncology Clinic of UBTH, a tertiary referral centre located in Benin City, Edo State, Nigeria. UBTH provides comprehensive care for children with SCD, including routine follow-up, laboratory and growth monitoring.

Study Population

All adolescents with SCD and attended the general outpatient clinic of the hospital between July and December 2025 were consecutively recruited.

Inclusion criteria for subjects

- All who granted assent/consent
- No other chronic diseases like chronic kidney disease, chronic liver failure

Inclusion criteria for controls

- Must be HbAA
- All that granted assent /consent
- No other chronic diseases like chronic kidney disease, chronic liver failure

Sample Size Determination

The minimum sample size was calculated using the formula for comparison of two independent proportions in case–control studies[21]:

$$n = \frac{(Z_{\alpha/2}+Z_{\beta})^2\,[P_1(1-P_1)+P_2(1-P_2]}{(P_1-P_2)^2}$$

Where:

- n = minimum sample size per group
- $Z_{\alpha/2}$ = standard normal deviate at 95% confidence level (1.96)
- Z_{β} = standard normal deviate at 80% power (0.84)
- P_1 = prevalence of delayed sexual maturation among adolescents with SCD (40% = 0.40)
- P_2 = prevalence among controls (15% = 0.15)

$$n = \frac{2.88}{0.0625} = 46.1$$

The minimum required sample size per group was therefore approximately 47 participants. However, to improve statistical power, allow subgroup analyses, and account for incomplete data, 150 adolescents with SCD and 80 controls were recruited.

Sampling Technique

A consecutive sampling technique (a non-probability sampling method) was employed. All eligible adolescents with SCD who attended the Paediatric Haemato-oncology Clinic during the study period and met inclusion criteria were consecutively recruited until the required sample size was achieved. Consecutive sampling minimized selection bias by ensuring that every eligible participant within the study period had an equal opportunity for inclusion.

Ethical approval/ consideration

Ethical approval was sought and obtained from the Ethics Committee of UBTH, Benin City (NHREC -UBTH-HREC/24/12/2022B). Informed consent was obtained from the parents and assent from adolescents. The study adhered strictly to the ethical principles outlined in the Declaration of Helsinki on research involving human subjects.

Data collection procedures

Two research assistants (1 registrar and 1 house officer) were trained to assist in this study with administration of the questionnaires and examinations of the participants.

The patients and their parents/caregivers were given clear and adequate information in English and/or Bini Languages and allowed to make an informed decision.

Data Collection Tools

Anthropometry was assessed for SCD subjects and controls but tanner staging and reproductive assessment could only be done for the SCD subjects as the controls did not grant consent for this.

- A questionnaire- capturing demographic data, clinical history, frequency of crises, transfusion, hospital admissions and complications (severity of disease)
- Anthropometry measurement of height and weight were done. Body mass index (BMI) was calculated as weight (Kg) divided by height in meter squared (m^2) and compared with WHO growth charts. Anthropometric standardization was performed using WHO Anthro plus software to generate Heigh-for age Z-scores (HAZ) and BMI- for- age (BAZ). Stunting and wasting were defined as Z- scores less than -2SD according to WHO standards.
- Pubertal Assessment was done using Tanner staging for breast and pubic hair development in girls, genital and pubic hair development in boys
- Reproductive health assessment was done using age at menarche for females, testicular volume assessment for males

Tanner Staging[10]

a. Male.

Male genitalia were examined, pubic hair distribution was noted, and testicular volume was determined using the Prader orchidometer. The genitalia and pubic hair distribution were staged using the staging below. Testicular volume was compared with normative values.

Genitalia

- Stage 1(prepubertal): testes, scrotum and penis are childlike; testicular volume is <4ml or length of <2.5cm
- Stage 2(Early puberty): enlargement of scrotum and testes, scrotal skin reddens and thins; testicular volume 4-6ml or length or 2.5-3.2cm

- Stage 3: Growth of penis (length), further scrotal/testicular enlargement; testicular volume 6-12ml or length of 3.3-4cm
- Stage 4: Further penis growth (especially diameter), development of glans; scrotal skin darkens; testicular volume 12-20ml or length of 4.1-4.5cm
- Stage 5(Adult maturity): adult genitalia. Testicular volume >20-25 ml or length of ≥ 4.5-5cm

Pubic hair

- Stage 1: no pubic hair
- Stage 2: sparse, long, slightly pigmented hair at base of penis
- Stage 3: darker, coarser, curlier hair spreading sparsely
- Stage 4: Adult- type hair, not yet spread to medial thighs
- Stage 5: adult hair distribution extending to thighs/abdomen

Testicular Volume: Normal Reference Values

- 1-9 years (prepubertal): 1-3ml
- 9-11 years: 3-4ml
- 11-12 years:4-6ml
- 12-13 years:6-10ml
- 13-14 years:10-15ml
- 14-16 years:15-20ml
- ≥ 16 (adult ref): 20-25ml

b. Females

The female breasts were examined and their pubic hair distribution was noted. Staging of both was done as below;

Breast Development (Thelarche)

- Stage 1 (prepubertal): only papilla (nipple) is elevated, no glandular tissue
- Stage 2: breast bud forms (small mound of breast and papilla), areola begins to enlarge
- Stage 3: breast and areola enlarge further but no separation of contours
- Stage 4: areola and papilla form a secondary mound above the breast; distinction between breast and areola become visible
- Stage 5: mature breast contour; areola recessed to general contour of breast; only papilla projects

Pubic Hair Development

- Stage 1(prepubertal): no pubic hair
- Stage 2: sparse long, lightly pigmented hair, straight or slightly curled mainly along labia majora
- Stage 3: hair becomes darker, coarser, curlier; spreads sparsely over mons pubis
- Stage 4: Adult- type hair, denser, curled but covering smaller area than adults (not yet on thighs)
- Stage 5(Adult pattern): adult- type hair in quantity and distribution, forming an inverse triangle; extends to medial thighs.

Normative Data/ Reference Points

- Onset of puberty(thelarche): typically between 8-13 years
- Menarche: Usually occurs at Tanner stage 3-4 (average age 12-13 years)
- Delayed puberty in girls: absence of breast development by age 13 years or absence of menarche by age 15 years

Data Analysis

The data was entered into the Excel spreadsheet. IBM Statistical Package for Social Sciences (SPSS) version 26.0 was used to analyse the data. Continuous variables such as age, weight, height, BMI, testicular volume were summarized using means and standard deviation. Categorical variables including age groups, BMI categories, Tanner stages, disease severity categories were summarized using frequencies and percentages. Independent t-test was used to compare mean age, weight, height, BMI and Z-scores between SCD adolescents and controls. One sample t-test was used to compare mean testicular volume and mean age at menarche with established reference values. Chi-square test was used to compare proportions, including BMI categories and prevalence of delayed puberty across disease severity groups. ANOVA was used to compare mean BMI across disease severity categories. Spearman's rank correlation coefficient was used to assess associations between Tanner stage and continuous variables. Ordinal logistic regression analysis was performed to determine independent predictors of Tanner stage. A p-value of <0.05 was considered statistically significant.

Results

Demographic Characteristics of study population

One hundred and fifty SCA were recruited (80 males and 70 females) with Male: Female ratio of 1.1:1. Fifty-six (37.3%) were aged 13-15 years. More than half of the subjects (64.0%) had normal weight. See table I

Comparative Analysis of mean age and anthropometry of SCA and Control

Mean age was similar between both groups. The SCA group demonstrated significantly lower weight, height and BMI compared to the control group (p< 0.0001). see table II

Anthropometric Standardization (WHO Z-Score Analysis) for SCA and Controls

Using WHO Anthroplus algorithm**,** The SCA group has a mean HAZ of -1.85 and BAZ of -2.10 suggesting stunting and wasting respectively and this was statistically significant (p<0.001) when compared with the controls. See table III

Tanner Staging in SCD Adolescents by Age Group

Of the subjects aged 10-12, majority (72.4%) were pre-pubertal, while of those 13-15 years, 7% were pre-pubertal, while a significant proportion of SCA adolescents aged 13-15 years (66.3%) are in Tanner stages II and III while those between 16-18years 71.8 % were Tanner stages IV and V and none was pre-pubertal. See table IV

Comparison of testicular volume (TV) in male adolescents with SCA with age- specific normative values

Significant reductions in testicular volume were observed in adolescents aged 13-18 years consistent with delayed pubertal progression and this is statistically significant (p <0.001). See table V

Comparison of mean age of menarche of SCD females and reference mean

The mean age of menarche (13.9 years) is significantly delayed (p<0.001) compared to the standard reference age of 12.4 years. The SCA adolescents aged 13-15 years have 7.8 RR of having delayed menarche. See table VI

Impact of Disease Severity on BMI and Pubertal Delay

There is statistically significant association between disease severity, BMI and delayed puberty. See table VII

Determinants of Sexual maturity in Adolescents with SCA

Age and BMI showed strong positive associations while PCV demonstrated a moderate but significant association. SES was not significantly correlated. See table VIII

Independent determinants of Tanner stage in Adolescents with SCA

Ordinal Logistic Regression (Multivariate) showed that higher BMI and PCV significantly increased the likelihood of advanced pubertal staging independent of age. See table IX

Table I: Age distribution and BMI status of study population

	SEX CONTROLS		SCA	
Variable	**Male (N=40)**	**Female (N=40)**	**Male (N=80)**	**Female (N=80)**
Age (years)				
10 - 12	17 (42.5%)	16 (40.0%)	30 (37.5%)	23 (32.9%)
13 - 15	13 (32.5%)	13 (32.5%)	28 (35.0%)	28 (40.0%)
16 - 18	10 (25.0%)	11 (27.5%)	22 (27.5%)	19 (27.1%)
BMI Status				
Underweight	1 (2.5%)	2 (5.0%)	28 (35.0%)	21(30.0%)
Normal Weight	32 (80.0%)	34 (85.0%)	50 (62.5%)	46 (65.7%)
Overweight	7 (17.5%)	4 (10.0%)	2 (2.5%)	3 (4.3%)

Table II: Comparative Analysis of mean age and anthropometry of SCD and Controls

Parameter	**Control Group (N=80)**	**SCA Group (N=150)**	**Difference (95% CI)**	**P-Value**
Age (Years)	13.6 ± 2.5	13.9 ± 2.4	-0.3 (-0.9 to 0.3)	0.35(NS)
Weight (kg)	51.2 ± 10.4	37.4 ± 9.1	+13.8 (11.2 to 16.4)	<0.0001*
Height (cm)	158.4 ± 11.2	148.1 ± 10.8	+10.3 (7.8 to 12.8)	<0.0001*
BMI (kg/m²)	20.1 ± 2.6	16.8 ± 2.4	+3.3 (2.6 to 4.0)	<0.0001*

Table III: Anthropometric Standardization (WHO Z-Score Analysis) for SCD and Controls

Parameter (Z-Score)	Control Mean (SD)	SCA Mean (SD)	Mean Difference (95% CI)	t-statistic	P-Value
Height-for-Age (HAZ)	-0.24 (0.9)	-1.85 (1.1)	-1.61 (-1.9 to -1.3)	11.4	<0.001*
BMI-for-Age (BAZ)	+0.15 (1.0)	-2.10 (1.2)	-2.25 (-2.5 to -1.9)	14.2	<0.001*

Table IV: Tanner Staging in SCD Adolescents by Age Group

Tanner Stage	10-12 Years *n (%)*	13-15 Years *n* (%)	16-18 Years *n (%)*	Total (*N*=150)
Stage I (Pre-pubertal)	42 (72.4)	7 (13.2)	0 (0.0)	**49**
Stage II	14 (24.1)	18 (34.0)	3 (7.7)	**35**
Stage III	2 (3.5)	15 (28.3)	8 (20.5)	**25**
Stage IV	0 (0.0)	10 (18.9)	17 (43.6)	**27**
Stage V	0 (0.0)	3 (5.6)	11 (28.2)	**14**
Total	58(100)	53 (100)	39 (100)	**150**

Table V: Comparison of testicular volume (TV) in male adolescents with SCD against age- specific normative values

Age Group in years	SCA Mean TV (mL)	Normal Range (mL)	p-value (One-Sample t)
10-12	3.2 ± 0.4	2 – 5	0.12 (NS)
13-15	6.8 ± 3.1	10 – 15	<0.001*
16-18	14.5 ± 5.6	20 – 25	<0.001*

Table VI: Comparison of mean age of menarche for SCD females with reference mean

Group	Mean Age (Years)	95% Confidence Interval	Reference Mean	*t - test*	*p*-value
SCA Females	13.9 ± 1.6	13.3 – 14.5	12.4	5.93	< 0.001*

Table VII: Impact of Disease Severity on BMI and Pubertal Delay

Disease Severity	Mean BMI (kg/m²)	ANOVA(F)	*p*-value	% with Delayed Puberty (≥ 14 yrs)	Chi-Square (X^2)	*p*-value
Mild	18.4 ± 2.1	8.34	0.002*	12.50%	31.83	0.038*
Moderate	17.1 ± 2.4			28.30%		
Severe	16.2 ± 1.8			66.70%		

Table VIII: Determinants of Sexual maturity in Adolescents with SCD

Variable 1	Variable 2	Correlation (ρ)	P-Value
Tanner Stage	Age	0.74	<0.001
	BMI	0.52	<0.001
	Steady-state PCV	0.31	0.002
	SES	0.11	0.28

Table IX: Independent determinants of Tanner stage in Adolescents with SCD

Predictor	Odds Ratio (OR)	95% Confidence Interval	P-Value
Age (per year)	3.24	2.10 – 4.98	<0.001
BMI (per kg/m²)	1.45	1.12 – 1.88	0.004
Steady-state PCV (per %)	1.18	1.02 – 1.36	0.028
SES (Upper vs Lower)	1.3	0.65 – 2.50	0.45

Discussion

The Sickle cell group demonstrated significantly lower weight, height and BMI compared to controls. This finding is consistent with multiple Nigerian studies by Adekile et al.[23], Ezenwosu et al.[24], Olowoyeye et al.[25] showing growth impairment among children and adolescents with SCA. Studies from Lagos and Ilorin reported significantly lower mean weight and height in SCA subjects compared to age-matched controls.[23,25] Similarly, a study in Enugu found increased prevalence of under-nutrition and stunting among adolescents with SCA.[24] Chronic haemolysis, increased metabolic demand, chronic inflammation, recurrent infections, reduced appetite, nutritional deficiencies and endocrine dysfunction have been implicated as major contributors to poor somatic growth in affected children[4,26]. The WHO Z- score analysis from this study showed significant stunting (mean HAZ of -1.85) and wasting (BAZ of -2.10) among SCA adolescents compared to controls. These findings indicate chronic undernutrition and long-standing growth faltering. Comparable findings were reported in a Tanzanian cohort where children with SCA had significantly lower height-for-age and BMI-for age Z-scores than controls.[23] Growth retardation in SCA tends to worsen during adolescence due to the additive effects of delayed puberty and chronic anaemia. The degree of growth deficit in African cohorts is often more pronounced than that reported in high-income countries, likely due to nutritional limitations from poverty and limited access to disease-modifying therapies such as hydroxyurea.[5,26]

While most African studies report significant growth deficits, some studies from high-income countries have shown less pronounced differences, particularly among adolescents receiving comprehensive care and hydroxyurea therapy. For example, Rhodes et al.[14] reported partial catch-up growth during late adolescence among participants enrolled in the Cooperative Study of Sickle Cell Disease in the United States. Similarly, Barden et al.[9] observed that although children with SCD had lower lean body mass, BMI differences were attenuated after adjustment for delayed

pubertal timing. These contrasting findings suggest that improved disease control and nutritional support may mitigate growth impairment.

A significant proportion of adolescents aged 13-15 years were in Tanner stages II and III indicating delayed pubertal progression relative to expected age norms. Delayed puberty in SCA has been consistently reported in Nigeria and African populations.[22,24,27] A study from Lagos documented delayed secondary sexual characteristics in both males and females with SCA compared to controls.[22] Similarly, research from Enugu demonstrated delayed pubertal milestones particularly in mid-adolescence.[22] Chronic anaemia/hypoxia, nutritional deficiency, hypogonadotropic hypogonadism and repeated vaso-occlusive crises affecting endocrine organs have been implicated[5,26].

However, not all studies demonstrate uniform pubertal delay. Marshall and Tanner[15] noted considerable physiological variation in pubertal timing even among healthy populations, indicating that part of the observed delay may reflect constitutional delay rather than solely disease pathology. Additionally, Lee[18] emphasized that chronic illness does not invariably result in hypogonadism, particularly when anaemia is adequately controlled. This highlights the importance of distinguishing pathological delay from constitutional variation.

The finding of significantly reduced testicular volume in male adolescents aged 13-18 years in this study align with earlier Nigerian studies showing delayed gonadal maturation in males with SCA[22,27]. Testicular volume is a reliable marker of pubertal onset and progression. Chronic hypoxia and recurrent microvascular occlusion in the testes, and priapism may impair Leydig cell function leading to delayed testosterone production and slower progression through Tanner stages.[5,26] Similar findings have been documented in Ghana and Tanziana.[23,28] Seventy-eight percent (78%) of SCA females aged 13-15 years were pre-menarchal, conferring a relative risk of 7.8 for delayed menarche.

The mean age of menarche (13.9 years) was significantly delayed compared to the reference age (12.4 years). This mirrors 13.2±1.7 years from a study in the United States of America[29] and other Nigerian studies reporting delayed menarche in females with SCA, often occurring 1-2 years later than controls.[22,24] In Enugu, the mean age of menarche among adolescents with SCA was approximately 14 years, significantly higher than that of the controls. Comparable delays have been reported in Ghana and Tanzania.[23,28]

The current study demonstrated a significant association between disease severity, lower BMI and higher prevalence of delayed puberty. Adolescents with severe disease had the lowest BMI (16.2± 1.8kg/m^2) and the highest proportion of delayed puberty. Similar observations were reported in Nigerian cohorts where increased frequency of crises and hospitalizations correlated with poorer growth parameters. In Tanzania, disease severity indices were significantly associated with lower anthropometric measures and delayed maturation.[28]

Age and BMI showed strong positive correlations with Tanner stage while steady-state PCV had a moderate association. BMI appear to play a critical role in pubertal progression. Adequate body fat is necessary for activation of the hypothalamic- pituitary- gonadal axis and low BMI

delays pubertal onset. The significant association between PCV and Tanner stage highlights the role of chronic anaemia in delaying maturation.[30] These findings align with African data indicating that improved haemoglobin levels and better nutritional status predict improved growth and pubertal outcomes.[22,24] The multivariate analysis identified BMI and PCV as independent predictors of advanced Tanner stage even after adjusting for age. These findings emphasize that nutritional status and haematologic stability are modifiable factors influencing pubertal outcomes in SCA[31]. Interestingly, socioeconomic status was not significantly associated with pubertal staging, consistent with findings in some Nigerian studies where disease biology had a stronger influence than socioeconomic factors once patients were already receiving tertiary care.

The findings of this study have important public health implications. First, growth monitoring and pubertal assessment should be integrated into routine SCD clinic visits, particularly during early adolescence. Secondly, nutritional interventions and optimization of haemoglobin levels may represent modifiable targets to improve developmental outcomes. Finally, delayed puberty has psychosocial consequences including low self-esteem, social withdrawal and stigmatization, which necessitate incorporation of adolescent-friendly counselling services into SCD care models. At policy level, strengthening access to hydroxyurea therapy and comprehensive SCD care may reduce long-term endocrine and growth complications. These findings support the inclusion of pubertal surveillance indicators in national SCD management guidelines.

Recommendations

Based on the findings of this study, we recommend:

1. Routine anthropometric and Tanner staging assessments during adolescent SCD clinic visits.
2. Early nutritional evaluation and intervention for adolescents with BMI-for-age Z-score < −2.
3. Optimization of steady-state haemoglobin levels through adherence to hydroxyurea therapy and appropriate transfusion protocols.
4. Early referral for endocrine evaluation in adolescents with absent pubertal signs beyond recommended age thresholds.
5. Longitudinal multicentre studies in Nigeria to establish local pubertal reference standards and evaluate long-term reproductive outcomes.

Conclusion

This study demonstrated that adolescents with SCD in Nigeria experience significant growth impairment and delayed pubertal maturation compared with age- and sex-matched controls. Disease severity was significantly associated with lower BMI and higher prevalence of delayed puberty. Furthermore, BMI and steady-state PCV emerged as independent predictors of advanced Tanner staging even after adjusting for age.

Limitations

1. Inability to perform genital examination among the control group as most controls declined consent for genital evaluation

2. Testicular volume and menarche comparisons were made using standard reference values rather than locally derived normative data. Ethnic and regional differences in pubertal timing may affect precision of comparisons.
3. The cross-sectional nature of this study limits the ability to establish causal relationships between disease severity, BMI, PCV and pubertal delay.

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Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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