

Pubertal delay in children and adolescents with sickle cell disease in eastern Uganda: a cross-sectional study

Joanilah Nampijja

nampijja.joaner01@gmail.com

Busitema University

Kevin Otoro

Varimetrics Group Limited

Jimmy Patrick Alunyo

Busitema University

David Mukunya

Busitema University

Sarah Kiguli

Makerere School of Public Health

Crispus Tegu

Busitema University

Lisa Rynn

Busitema University

Simon Odoch

Busitema University

Research Article

Keywords: sickle cell disease, pubertal delay, adolescence, tanner staging, growth, Uganda

Posted Date: October 19th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10960024/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Pubertal delay is a neglected complication of sickle cell disease (SCD), particularly in sub-Saharan Africa where disease burden is high and survival into adolescence is increasing. In these setting, we estimated the prevalence and correlates of pubertal delay among children and adolescents with SCD in eastern Uganda.

Methods

We conducted a hospital-based cross-sectional study among patients aged 8–19 years with confirmed SCD attending Mbale Regional Referral Hospital, Uganda. Pubertal development was assessed using Tanner staging and age-specific criteria for delayed puberty. Sociodemographic, nutritional, anthropometric, clinical, and treatment-related data were collected through structured interviews, medical history, and physical examination. Factors associated with pubertal delay were examined using multivariable ordinal logistic regression.

Results

Of 407 participants, 234 (57.5%) were female. Overall, 261 (64.1%) had delayed pubertal development, with higher prevalence among girls than boys (166 [70.9%] of 234 vs 95 [54.9%] of 173). Mean age at menarche was 13.15 years (SD 1.65). In adjusted analysis, male sex (aOR 0.28, 95% CI [0.16–0.47], $p < 0.001$), tall stature (aOR 0.39, 95% CI [0.17–0.90], $p = 0.027$), and intake of at least four fruit varieties per day (aOR 0.30, 95% CI [0.119–0.755], $p = 0.011$) were associated with lower odds of pubertal delay. Treatment status was associated with higher odds of pubertal delay (aOR 6.21, 95% CI [1.24–31.0], $p = 0.026$).

Conclusion

Pubertal delay was highly prevalent among children and adolescents with SCD in eastern Uganda. Routine pubertal, growth, and nutritional assessment should be integrated into comprehensive SCD care.

Background

Sickle cell disease (SCD) comprises a group of inherited haemoglobin disorders caused by mutations in the β -globin gene, resulting in the production of sickle haemoglobin. Its clinical spectrum includes sickle cell anaemia, haemoglobin SC disease, and sickle β -thalassaemia, with sickle cell anaemia being the most common and severe form (Egesa et al., 2022; Kato et al., 2018). Under conditions of deoxygenation, dehydration, acidosis, or infection, sickle haemoglobin polymerises, causing erythrocytes

to become rigid, haemolyse prematurely, and obstruct microvasculature. These processes drive chronic anaemia, recurrent vaso-occlusive pain, infection, progressive organ dysfunction, and substantial morbidity and mortality from early childhood (Kato et al., 2018; Konotey-Ahulu, 1974).

The burden of SCD is rising globally and remains concentrated in sub-Saharan Africa. Between 2000 and 2021, the number of people living with SCD increased by 41.4%, from 5.46 million to 7.74 million, while annual births of infants with SCD increased to approximately 515,000 (Thomson et al., 2023). More than three-quarters of global SCD cases occur in sub-Saharan Africa, where population growth and improving child survival are expected to increase the number of affected children reaching adolescence and adulthood (Thomson et al., 2023). In Uganda, SCD is a major public health problem; national data estimate sickle cell trait and disease prevalence among children at 13.3% and 0.7%, respectively (Ndeezi et al., 2016; Piel, Hay, Gupta, Weatherall, & Williams, 2013). Eastern Uganda, including Mbale, has a substantial SCD burden, and Mbale Regional Referral Hospital contributes 16.7% of patients in the Ugandan Sickle Pan-African Research Consortium Registry (Nsubuga et al., 2024; Okwi et al., 2010).

As survival improves, the clinical focus of SCD care must extend beyond prevention of early mortality to adolescent health, growth, sexual maturation, and quality of life. Puberty is a critical developmental transition marked by activation of the hypothalamic-pituitary-gonadal axis, accelerated linear growth, development of secondary sexual characteristics, and psychosocial maturation. Delayed puberty is commonly defined as absence of breast development by age 13 years in girls or absence of testicular enlargement to at least 4 mL or 2.5 cm by age 14 years in boys (Klein, Emerick, Sylvester, & Vogt, 2017). In young people with SCD, chronic anaemia, recurrent vaso-occlusion, chronic inflammation, nutritional deficiencies, endocrine dysfunction, and organ damage may disrupt normal pubertal timing and progression (Hauschild & Theintz, 2007).

Evidence from African settings suggests that adolescents with SCD experience delayed pubertal onset, impaired growth, and delayed attainment of sexual maturity, with studies from Cameroon and Kenya reporting growth and pubertal delay among affected children and adolescents (Ritha Mbono Betoko et al., 2023; A. Omar, Mutai, & Abdallah, 2019). In Uganda, however, published evidence has mainly focused on disease burden, retention in care, clinical complications, and health-related quality of life, rather than pubertal maturation (Kambasu, Rujumba, Lekuya, Munube, & Mupere, 2019; Ndeezi et al., 2016). At Mbale Regional Referral Hospital, approximately 1400 patients are registered in the sickle cell clinic, most of whom are children and adolescents. Yet local data on the timing, attainment, and correlates of pubertal development among adolescents with SCD remain limited. Addressing this evidence gap is essential for integrating pubertal assessment, nutritional support, counselling, and adolescent-centred care into routine SCD services in eastern Uganda.

Methods

Study design and setting

We conducted a cross-sectional study in 2024 at Mbale Regional Referral Hospital (MRRH) in eastern Uganda. The study was done over a six-month period. MRRH is a major public referral facility located in the central business district of Mbale City, along Pallisa Road, and serves 16 districts in eastern Uganda. The hospital runs a weekly sickle cell clinic with approximately 1400 registered patients, about 68% of whom are children and adolescents.

Study population and eligibility

The study population comprised children and adolescents aged 8–19 years with confirmed sickle cell disease attending care at MRRH. Participants were eligible if they had sickle cell disease, were aged 8–19 years, and provided assent where applicable, with consent obtained from a parent, guardian, or next of kin. Participants were excluded if they were very ill, experiencing severe pain, or had another chronic medical condition, including HIV infection, because such conditions could independently affect growth and pubertal development.

Sample size and sampling

The sample size was calculated using OpenEpi, assuming an unknown population proportion of 50% and a 95% confidence level. The minimum required sample size was 384 participants. After adding 10% to account for non-response, the final target sample size was 422 participants. Participants were recruited consecutively as they attended the sickle cell clinic or after clinical stabilisation during admission, until the target sample size was reached.

Study procedures and data collection

Potential participants and their caregivers were approached during clinic attendance or during admission after the child's condition had improved and they were no longer acutely ill or in severe pain. The study was explained to participants and caregivers, and written informed consent and assent were obtained before enrolment. Participation involved a single study visit lasting approximately 30 minutes.

Data were collected using a structured questionnaire developed specifically for this study based on the study objectives. The questionnaire was administered by the principal investigator and trained research assistants, including two nurses and one clinical officer working in the sickle cell clinic. Research assistants were trained to administer the questionnaire in English, Lumasaba, and Luganda. Data collected included sociodemographic characteristics, medical and treatment history, dietary information, and physical examination findings. The English version of the questionnaire is provided as Supplementary **File 1**.

Anthropometric assessment

Weight, height, and body mass index were measured using standardised procedures. Each anthropometric measurement was taken twice; where measurements differed, a third measurement was taken and the average was recorded. Weight was measured using a calibrated Seca electronic digital scale. Height was measured using a wooden stadiometer with a movable headpiece and recorded to the nearest 0.1 cm.

Weight and height measurements were plotted on age- and sex-specific World Health Organization growth reference charts. Nutritional status was classified using WHO Z-scores: values below -2 SD were classified as underweight or stunted, values from -2 SD to $+2$ SD as normal, and values above $+2$ SD as overweight or obese. Height-for-age Z-scores below -2 SD were classified as stunting.

Pubertal assessment and outcome definition

Pubertal development was assessed using Tanner staging. Examinations were conducted in privacy by same-sex assessors using tanner staging charts; female research assistants assessed girls and male research assistants assessed boys. Testicular assessment in boys was done using an orchidometer.

Pubertal development was classified as early, normal, or delayed. Early puberty was defined as onset of secondary sexual characteristics before age 8 years in girls and before age 9 years in boys. Normal puberty was defined as onset of secondary sexual characteristics, corresponding to tanner stage 2, between ages 8–13 years in girls and 9–14 years in boys. Delayed puberty was defined as absence of breast development by age 13 years or older in girls, and absence of testicular growth to at least 4 mL in volume or 2.5 cm in length by age 14 years or older in boys.

Data quality assurance

The data collection tool was pretested at Budaka Health Centre IV, an independent facility, to assess suitability, practicality, and reliability and to identify potential sources of error before data collection. Content validity was assessed by two paediatricians who reviewed and rated the questionnaire. Research assistants were trained before data collection. Equipment was calibrated before use, and selection criteria and measurement procedures were standardised to improve data quality and reduce measurement error.

Statistical analysis

Data were initially entered and summarized in Microsoft Excel version 16.2, then exported to Stata version 18 for statistical analysis. Categorical variables were summarized using frequencies and percentages. Continuous variables were summarized using means and standard deviations for normally distributed data, and medians with interquartile ranges for skewed data.

Descriptive analyses were used to summarise participant characteristics, pubertal development, and growth-related outcomes. Bivariable analyses were conducted to assess associations between

participant characteristics and pubertal development. Variables with $p < 0.20$ at bivariable analysis, together with biologically plausible variables, were included in the multivariable model. Ordinal logistic regression was used to assess factors associated with pubertal development. Adjusted odds ratios, 95% confidence intervals, and p values were reported. Statistical significance was defined as $p < 0.05$. Effect modification was assessed using interaction terms, including age-by-sex interactions, and tested using likelihood ratio tests. Only statistically significant interactions were retained in the final model.

Results

Participant flow and baseline characteristics

A total of 448 children and adolescents were screened for eligibility. Sixteen did not meet the age criterion, leaving 432 participants who were enrolled. Twenty-five participants were subsequently excluded because of incomplete data, leaving 407 participants in the final analysis.

Social demographic and economic status of the participants

The mean age of participants was 12.07 years (SD 3.15). Overall, 234 (57.5%) participants were female and 173 (42.5%) were male. Most participants were aged 8–13 years (278 [68.3%]), had primary-level education (335 [82.3%]), lived in families of 5–10 members (287 [70.5%]), and had unemployed parents or guardians (314 [77.1%]). Most participants missed fewer than 30 school days in the preceding period (398 [97.8%]).

Participant characteristics

The mean age of the 407 participants was 12.07 years (SD 3.15). Of these, 278 (68.3%) were aged 8–13 years and 129 (31.7%) were aged 14–19 years. Overall, 234 (57.5%) participants were female and 173 (42.5%) were male.

Most participants had attained primary-level education (335 [82.3%]), while 46 (11.3%) had attained secondary education and 26 (6.4%) had never attended school. Most lived in households comprising 5–10 members (287 [70.5%]). Parents or guardians were unemployed for 314 (77.1%) participants, self-employed for 61 (15.0%), and formally employed for 32 (7.9%).

Parents accompanied 243 (59.7%) participants to clinic, whereas 128 (31.4%) attended independently. Twenty-three (5.7%) were accompanied by guardians and 12 (2.9%) by siblings. Overall, 398 (97.8%) participants had missed fewer than 30 school days. See Table 1.

Table 1
Sociodemographic characteristics according to pubertal development status

(Mean, SD)	Pubertal development			Total n (%)
	Early n (%)	Normal n (%)	Delayed n (%)	
N	67 (16.5)	79 (19.4)	261 (64.1)	407 (100.0)
Sex				
Female	12 (17.9)	56 (70.9)	166 (63.6)	234 (57.5)
Male	55 (82.1)	23 (29.1)	95 (36.4)	173 (42.5)
Age in years (12.07,3.15)				
8–13	45 (67.2)	72 (91.1)	161 (61.7)	278 (68.3)
14–19	22 (32.8)	7 (8.9)	100 (38.3)	129 (31.7)
Education level				
Never attended	4 (6.0)	5 (6.3)	17 (6.5)	26 (6.4)
Primary	58 (86.6)	72 (91.1)	205 (78.5)	335 (82.3)
Secondary	5 (7.5)	2 (2.5)	39 (14.9)	46 (11.3)
Family size				
<5	8 (11.9)	12 (15.2)	37 (14.2)	57 (14.0)
5–10	52 (77.6)	53 (67.1)	182 (69.7)	287 (70.5)
>10	7 (10.4)	14 (17.7)	42 (16.1)	63 (15.5)
Employment status				
Employed	4 (6.0)	4 (5.1)	24 (9.2)	32 (7.9)
Self employed	8 (11.9)	17 (21.5)	36 (13.8)	61 (15.0)
Unemployed	55 (82.1)	58 (73.4)	201 (77.0)	314 (77.1)
Parent/guardian's level of education				
No education	15 (22.4)	17 (21.5)	57 (21.8)	89 (21.9)
Primary	29 (43.3)	36 (45.6)	121 (46.4)	186 (45.7)
Secondary	22 (32.8)	21 (26.6)	74 (28.4)	117 (28.7)
University/college	1 (1.5)	5 (6.3)	9 (3.4)	15 (3.7)
Who usually brings you to the clinic				
Guardian	1 (1.5)	3 (3.8)	19 (7.3)	23 (5.7)

(Mean, SD)	Pubertal development			Total n (%)
	Early n (%)	Normal n (%)	Delayed n (%)	
Other	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)
Parent	44 (65.7)	53 (67.1)	146 (55.9)	243 (59.7)
Self	20 (29.9)	21 (26.6)	87 (33.3)	128 (31.4)
Siblings	2 (3.0)	2 (2.5)	8 (3.1)	12 (2.9)
Days of school missed				
<30 days	67 (100.0)	79 (100.0)	252 (96.6)	398 (97.8)
30–90	0 (0.0)	0 (0.0)	6 (2.3)	6 (1.5)
90 + days	0 (0.0)	0 (0.0)	3 (1.1)	3 (0.7)

Prevalence of pubertal development patterns

Of the 407 participants, 261 (64.1%) were classified as having delayed pubertal development, 79 (19.4%) had normal pubertal development, and 67 (16.5%) had early pubertal development.

The distribution differed between girls and boys. Among the 234 girls, 166 (70.9%) had delayed pubertal development, 56 (23.9%) had normal development, and 12 (5.1%) had early development. Among the 173 boys, 95 (54.9%) had delayed development, 23 (13.3%) had normal development, and 55 (31.8%) had early development. See Fig. 2.

Tanner stage 2 analysis

Tanner stage 2 was analysed separately from the primary classification of pubertal development. Using this classification, 211 (51.8%) of 407 participants were classified as having early development, 143 (35.1%) as having normal development, and 53 (13.0%) as having delayed development.

Among boys, 100 (57.8%) were classified as early, 57 (33.0%) as normal, and 16 (9.3%) as delayed using Tanner stage 2. Among girls, 111 (47.4%) were classified as early, 86 (36.8%) as normal, and 37 (15.8%) as delayed.

Table 2
 Pubertal development classified using Tanner stage 2, overall and by sex

Group	Early n (%)	Normal n (%)	Delayed n (%)
Overall (n = 407)	211 (51.8)	143 (35.1)	53 (13.0)
Boys (n = 173)	100 (57.8)	57 (33.0)	16 (9.3)
Girls (n = 234)	111 (47.4)	86 (36.8)	37 (15.8)

Anthropometric and nutritional characteristics

Overall, 92 (22.6%) participants had short stature, 206 (50.6%) had normal height, and 109 (26.8%) had tall stature. Short stature was recorded in 71 (27.2%) participants with delayed pubertal development, nine (11.4%) with normal development, and 12 (17.9%) with early development.

Based on BMI classification, 320 (78.6%) participants were underweight, 84 (20.6%) had normal BMI, and three (0.7%) were overweight.

Ninety-five (23.3%) participants reported consuming fewer than two fruit varieties per day, 274 (67.3%) consumed two to four varieties, and 38 (9.3%) consumed at least four varieties. Among participants with available information on meal frequency, 149 (39.6%) reported consuming three or fewer meals per day and 227 (60.4%) reported more than three meals per day. See Table 3.

Table 3
Anthropometric and nutritional characteristics according to pubertal development status

	Pubertal development			Total n (%)
	Early n (%)	Normal n (%)	Delayed n (%)	
N	67 (16.5)	79 (19.4)	261 (64.1)	407 (100.0)
Current height				
Short stature	12 (17.9)	9 (11.4)	71 (27.2)	92 (22.6)
Normal height	29 (43.3)	49 (62.0)	128 (49.0)	206 (50.6)
Tall stature	26 (38.8)	21 (26.6)	62 (23.8)	109 (26.8)
Current weight				
Under weight	9 (13.4)	9 (11.4)	62 (23.8)	80 (19.7)
Normal weight	20 (29.9)	19 (24.1)	64 (24.5)	103 (25.3)
Over weight	37 (55.2)	48 (60.8)	134 (51.3)	219 (53.8)
Obese	1 (1.5)	3 (3.8)	1 (0.4)	5 (1.2)
BMI				
Underweight	55 (82.1)	62 (78.5)	203 (77.8)	320 (78.6)
Normal weight	10 (14.9)	17 (21.5)	57 (21.8)	84 (20.6)
Overweight	2 (3.0)	0 (0.0)	1 (0.4)	3 (0.7)
Fruit intake				
<2	14 (20.9)	24 (30.4)	57 (21.8)	95 (23.3)
2–4	43 (64.2)	43 (54.4)	188 (72.0)	274 (67.3)
4+	10 (14.9)	12 (15.2)	16 (6.1)	38 (9.3)
Meals per day				
<=3	21 (41.2)	39 (49.4)	89 (36.2)	149 (39.6)
>=3	30 (58.8)	40 (50.6)	157 (63.8)	227 (60.4)

Sickle cell disease-related clinical and treatment characteristics

Painful vaso-occlusive crises were reported by 401 (98.5%) participants. Complications occurred three to six times per year in 257 (63.1%) participants, one to two times per year in 110 (27.0%), less than once per year in 13 (3.2%), and more than six times per year in 27 (6.6%). Frequent infections were reported by

286 (70.3%) participants. Clinic attendance was fewer than three visits for 130 participants, four to six visits for 74, and seven or more visits for 203. Hydroxyurea exposure, current hydroxyurea use, blood transfusion history, and other treatment characteristics according to pubertal-development category are presented in Table 4.

Table 4
Clinical and treatment characteristics according to pubertal development status

Characteristic	Early n (%)	Normal n (%)	Delayed n (%)	Total n (%)
Painful vaso-occlusive crises				
No	2 (3.0)	1 (1.3)	3 (1.1)	6 (1.5)
Yes	65 (97.0)	78 (98.7)	258 (98.9)	401 (98.5)
Frequency of SCD complications				
1–2 times/year	21 (31.3)	29 (36.7)	60 (23.0)	110 (27.0)
3–6 times/year	42 (62.7)	44 (55.7)	171 (65.5)	257 (63.1)
< 1 time/year	2 (3.0)	2 (2.5)	9 (3.4)	13 (3.2)
> 6 times/year	2 (3.0)	4 (5.1)	21 (8.0)	27 (6.6)
Frequent infections				
No	24 (35.8)	20 (25.3)	77 (29.5)	121 (29.7)
Yes	43 (64.2)	59 (74.7)	184 (70.5)	286 (70.3)
Clinic visits				
< 3 times	21 (31.3)	37 (46.8)	72 (27.6)	130
4–6 times	9 (13.4)	12 (15.2)	53 (20.3)	74
≥ 7 times	37 (55.2)	30 (38.0)	136 (52.1)	203
Hydroxyurea use				
No	3 (4.5)	10 (12.7)	16 (6.1)	29
Yes	64 (95.5)	69 (87.3)	245 (93.9)	378
Ever taken hydroxyurea				
No	1 (1.5)	12 (15.2)	15 (5.7)	28
Yes	66 (98.5)	67 (84.8)	246 (94.3)	379
Currently taking hydroxyurea*				
No	4 (6.1)	7 (10.4)	5 (2.0)	16
Yes	62 (93.9)	60 (89.6)	241 (98.0)	363
Blood transfusion history				
< 2 times	38 (74.5)	45 (57.0)	145 (58.9)	228
≥ 3 times	13 (25.5)	34 (43.0)	101 (41.1)	148

Physical examination findings

Mild jaundice was recorded in 206 (50.6%) participants, moderate jaundice in 18 (4.4%), and severe jaundice in one (0.2%). Mild pallor was present in 193 (47.4%) participants and moderate pallor in 22 (5.4%). Mild oedema was recorded in 66 (16.3%) participants and moderate oedema in six (1.5%). Frontal bossing was present in 55 (13.5%) participants. Temperature was within the normal range in 265 (65.1%) participants; 57 (14.0%) had hypothermia and 85 (20.9%) had hyperthermia.

Table 5
Physical examination findings

	Pubertal Development in Boys and Girls			
	Early n (%)	Normal n (%)	Delayed n (%)	Total n (%)
N	67 (16.5)	79 (19.4)	261 (64.1)	407 (100.0)
Any Jaundice				
+	33 (49.3)	48 (60.8)	125 (47.9)	206 (50.6)
++	5 (7.5)	3 (3.8)	10 (3.8)	18 (4.4)
+++	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)
0	29 (43.3)	28 (35.4)	125 (47.9)	182 (44.7)
Pallor				
+	31 (46.3)	44 (55.7)	118 (45.2)	193 (47.4)
++	4 (6.0)	6 (7.6)	12 (4.6)	22 (5.4)
0	32 (47.8)	29 (36.7)	131 (50.2)	192 (47.2)
Oedema				
+	8 (11.9)	15 (19.0)	43 (16.5)	66 (16.3)
++	0 (0.0)	0 (0.0)	6 (2.3)	6 (1.5)
0	59 (88.1)	64 (81.0)	211 (81.2)	334 (82.3)
Frontal bossing:				
None	55 (82.1)	59 (74.7)	238 (91.2)	352 (86.5)
Present	12 (17.9)	20 (25.3)	23 (8.8)	55 (13.5)
Temperature				
Hypothermia	8 (11.9)	11 (13.9)	38 (14.6)	57 (14.0)
Normal	45 (67.2)	52 (65.8)	168 (64.4)	265 (65.1)
Hyperthermia	14 (20.9)	16 (20.3)	55 (21.1)	85 (20.9)

Participant-reported growth and pubertal development

Seventy-four (18.2%) participants reported delayed growth. Delayed breast or testicular development was reported by 341 (85.5%) participants and delayed pubic-hair development by 171 (42.9%). Delayed menstruation was reported by 63 participants in the female-specific assessment, while 26 participants reported delayed facial-hair development in the male-specific assessment. See Table 6.

Table 6
Participant-reported growth and pubertal-development characteristics

Characteristic	Population assessed	No, n (%)	Yes, n (%)
Delayed growth	All participants (n = 407)	333 (81.8)	74 (18.2)
Delayed breast/testicular development*	All participants	58 (14.5)	341 (85.5)
Delayed pubic-hair development*	All participants	228 (57.1)	171 (42.9)
Delayed menstruation	Girls only (n = 234)	171 (73.1)†	63 (26.9)†
Delayed facial-hair growth	Boys only (n = 173)	147 (85.0)†	26 (15.0)†

Factors associated with pubertal development

In multivariable ordinal logistic regression, male sex, tall stature, consumption of at least four fruit varieties per day, and reported influence of a specific sickle cell disease treatment on secondary sexual development remained independently associated with pubertal-development category (Table 7). Compared with girls, boys had lower adjusted odds of being in a more delayed pubertal-development category (adjusted odds ratio [aOR] 0.28, 95% CI 0.16–0.47; $p < 0.001$). Tall stature was similarly associated with lower adjusted odds of delayed pubertal development compared with short stature (aOR 0.39, 95% CI 0.17–0.90; $p = 0.027$). Participants who reported consuming at least four fruit varieties per day had lower adjusted odds of delayed pubertal development than those consuming fewer than two varieties per day (aOR 0.30, 95% CI 0.12–0.76; $p = 0.011$).

Participants who reported that a specific treatment for sickle cell disease had influenced their secondary sexual development had higher adjusted odds of being in a more delayed pubertal-development category than those reporting no such influence (aOR 6.21, 95% CI 1.24–30.98; $p = 0.026$).

Age, weight category, BMI, education level, parent or guardian employment status, clinic attendance, hydroxyurea exposure, current hydroxyurea use, blood transfusion frequency, self-reported delayed growth and pubertal characteristics, complication frequency, frequent infections, and pallor were not independently associated with pubertal-development category after adjustment.

Some associations observed in crude analysis were attenuated after adjustment. Current hydroxyurea use was associated with pubertal development in crude analysis (crude odds ratio [COR] 2.81, 95% CI 1.18–6.71; $p = 0.020$) but not after adjustment (aOR 2.24, 95% CI 0.63–7.94; $p = 0.211$). Similarly, frontal bossing was associated with pubertal development in crude analysis (COR 0.43, 95% CI 0.25–0.72; $p = 0.001$), but the adjusted estimate did not meet the prespecified threshold for statistical significance (aOR 0.42, 95% CI 0.17–1.03; $p = 0.059$). See Table 5

Table 7
Multivariable analysis of notable variables and relation to puberty

Variables	COR (95%CI)	p-value	AOR (95%CI)	p-value
Sex				
Female	1	1	1	1
Male	0.38 (0.253–0.569)	< 0.001	0.28 (0.162–0.467)	< 0.001
Age in years				
14–19	2.12 (1.321–3.406)	0.002	0.96 (0.463–1.997)	0.916
Current height				
Normal height	0.54 (0.307–0.935)	0.028	0.65 (0.275–1.511)	0.313
Tall stature	0.39 (0.212–0.716)	0.002	0.39 (0.173–0.9)	0.027
Current weight				
Normal weight	0.47 (0.247–0.911)	0.025	1.01 (0.4–2.565)	0.977
Over weight	0.48 (0.266–0.859)	0.014	0.84 (0.362–1.956)	0.689
Obese	0.18 (0.038–0.81)	0.026	0.29 (0.046–1.793)	0.182
BMI				
Normal weight	1.26 (0.767–2.084)	0.357	1.03 (0.495–2.141)	0.938
Overweight	0.14 (0.012–1.624)	0.115	0.14 (0.009–2.218)	0.162
Education level				
Primary	0.84 (0.372–1.91)	0.681	0.67 (0.206–2.16)	0.50
Secondary	2.77 (0.897–8.567)	0.077	1.78 (0.398–7.942)	0.451
Employment status of Parent/guardian				
Self-employed	0.54 (0.214–1.381)	0.2	0.75 (0.218–2.554)	0.642

Variables	COR (95%CI)	p-value	AOR (95%CI)	p-value
Unemployed	0.6 (0.263–1.37)	0.225	0.73 (0.248–2.144)	0.567
Fruit intake				
2–4	1.33 (0.835–2.127)	0.229	0.93 (0.489–1.775)	0.828
4+	0.51 (0.253–1.028)	0.06	0.3 (0.119–0.755)	0.011
Has any specific treatment for SCD				
YES	2.92 (0.836–10.197)	0.093	6.21 (1.244–30.978)	0.026
Clinic visit				
4–6 times	1.85 (1.021–3.366)	0.043	1.5 (0.517–4.342)	0.456
7 + times	1.42 (0.915–2.189)	0.119	1.55 (0.558–4.302)	0.401
Hydroxyurea use				
Yes	1.23 (0.604–2.509)	0.567	1.83 (0.399–8.414)	0.436
Transfusion times				
3–6 times	1.27 (0.846–1.912)	0.247	1.53 (0.869–2.685)	0.141
7 + times	0.36 (0.02–6.466)	0.491	0.69 (0.022–21.241)	0.83
Are you currently taking hydroxyurea				
Yes	2.81 (1.177–6.706)	0.02	2.24 (0.633–7.941)	0.211
Delayed growth				
Yes	3.03 (1.57–5.84)	0.001	1.96 (0.82–4.702)	0.13
Delayed breast/ testicular development				
Yes	0.91 (0.506–1.622)	0.741	1.32 (0.581–2.981)	0.511
Delayed pubic hair development				

Variables	COR (95%CI)	p-value	AOR (95%CI)	p-value
Yes	1.52 (1.006–2.304)	0.047	0.98 (0.527–1.804)	0.937
Delayed menstruation for female				
Yes	1.86 (1.039–3.342)	0.037	1.77 (0.676–4.621)	0.245
Delayed facial hair growth				
Yes	2.19 (0.804–5.945)	0.125	2.82 (0.715–11.131)	0.138
Complication frequency				
Occasionally (1–2 times a year)	0.65 (0.42–1.009)	0.055	1.04 (0.458–2.357)	0.927
Rarely (less than once a year)	1.12 (0.342–3.694)	0.848	1.45 (0.239–8.849)	0.684
Frequently (more than 6 times a year)	1.84 (0.721–4.671)	0.203	0.83 (0.257–2.668)	0.752
Frequent infections				
Yes	1.1 (0.714–1.699)	0.663	1.28 (0.725–2.266)	0.393
Pallor				
++	0.79 (0.342–1.839)	0.589	0.85 (0.251–2.881)	0.794
0	1.27 (0.844–1.917)	0.251	1.06 (0.59–1.888)	0.854
Frontal bossing				
Present	0.43 (0.253–0.721)	0.001	0.42 (0.173–1.034)	0.059

COR=crude odds ratio. aOR=adjusted odds ratio. SCD=sickle cell disease. CI=confidence interval.

Discussion

This study assessed pubertal development and associated factors among children and adolescents aged 8–19 years with sickle cell disease attending care at Mbale Regional Referral Hospital in eastern Uganda. Delayed pubertal development was common, affecting 64.1% of participants, and was more frequent among girls than boys. In the adjusted analysis, male sex, tall stature, and consumption of at least four fruit varieties per day were associated with lower odds of being in a more delayed pubertal-

development category, whereas reported influence of a specific sickle cell disease treatment on secondary sexual development was associated with higher odds. These findings provide context-specific evidence on pubertal maturation, growth, nutrition, and clinical characteristics among young people with sickle cell disease in a high-burden setting.

The high prevalence of delayed pubertal development is consistent with previous reports of impaired growth and delayed sexual maturation among children and adolescents with sickle cell disease (Akiibinu et al., 2020; R. M. Betoko et al., 2023; J. Omar, 2021; Soliman, De Sanctis, & Elalaily, 2014). Chronic anaemia, inflammation, recurrent illness, increased metabolic demands, nutritional deficiencies, and endocrine dysfunction have all been implicated in altered pubertal timing in sickle cell disease. These mechanisms are plausible in the present population, although they were not measured directly. The observed burden supports routine assessment of growth and pubertal progression as part of adolescent sickle cell disease care.

The separate Tanner stage 2 analysis yielded a lower proportion classified as delayed: 13.0% overall, 15.8% among girls, and 9.3% among boys. This analysis should be interpreted separately from the primary age-specific classification because the two approaches apply different criteria to pubertal development and are therefore not interchangeable. Nevertheless, both analyses showed a higher proportion of delayed development among girls than boys. Reporting the Tanner stage 2 findings separately provides additional information on attainment of a key pubertal milestone without replacing the primary study outcome.

Girls had a higher prevalence of delayed pubertal development than boys, with 70.9% of girls and 54.9% of boys classified as delayed in the primary analysis. Previous studies have reported later menarche and slower pubertal progression among girls with sickle cell disease than among unaffected peers (Gomes et al., 2017; Soliman et al., 2014). The higher prevalence among girls in this study may reflect differences in the timing and clinical expression of sex-specific pubertal milestones, as well as nutritional, endocrine, or disease-related influences. These findings support systematic assessment of breast development, menstrual history, growth, and nutritional status during follow-up of girls with sickle cell disease.

Delayed pubertal development was also common among boys. Delayed testicular enlargement and slower progression through Tanner stages have previously been described in boys with sickle cell disease, with variation according to disease severity, nutritional status, and genotype (Soliman et al., 2014; Zemel, Kawchak Da Fau - Ohene-Frempong, Ohene-Frempong K Fau - Schall, Schall Ji Fau - Stallings, & Stallings, 2007). More than half of the boys in this study were classified as having delayed pubertal development, indicating that pubertal assessment in sickle cell disease should not focus on girls alone. Age-appropriate assessment of testicular and genital development should form part of routine adolescent clinical review.

Growth abnormalities were common in the study population. Short stature occurred more frequently among participants with delayed pubertal development, while underweight was common across the cohort. However, weight category and BMI were not independently associated with pubertal-

development category after adjustment. The association with stature was more consistent: participants with tall stature had lower adjusted odds of being in a more delayed pubertal-development category than those with short stature. Growth impairment in sickle cell disease has been linked to chronic anaemia, increased energy expenditure, recurrent illness, inflammation, and nutritional deficiencies (Mandese et al., 2019; Soliman et al., 2014). Height therefore remains a useful component of longitudinal assessment, although the cross-sectional design of this study does not establish whether growth pattern precedes or follows delayed pubertal development.

Consumption of at least four fruit varieties per day was associated with lower adjusted odds of delayed pubertal development. This finding should not be interpreted as evidence of a direct protective effect of fruit intake. Fruit diversity may instead represent broader dietary quality, micronutrient availability, household food security, caregiver support, or socioeconomic conditions that were not fully captured in the analysis. Nutritional factors, including vitamin and micronutrient deficiencies, have been implicated in impaired growth and pubertal development in children with chronic illness and sickle cell disease (Soliman et al., 2014; Vilela, Fisberg, Ferrari, & Braga, 2025). Further studies incorporating validated dietary measures and biochemical assessment of micronutrient status are needed to clarify this association.

Clinical morbidity was substantial. Almost all participants reported vaso-occlusive crises, and recurrent infections were common. Neither complication frequency nor frequent infections remained independently associated with pubertal-development category after adjustment. The absence of an independent association should be interpreted cautiously because these exposures were highly prevalent, limiting contrast between participants. Chronic haemolysis, tissue hypoxia, inflammation, and recurrent illness remain biologically plausible contributors to impaired growth and pubertal maturation in sickle cell disease (Rees et al., 2010), but the present study was not designed to establish these pathways.

Hydroxyurea exposure was not independently associated with pubertal-development category in the adjusted analysis. Current hydroxyurea use showed an association in crude analysis, but this association was attenuated after adjustment. Hydroxyurea is established in the management of sickle cell disease because of its effect on vaso-occlusive morbidity and other clinical outcomes, but evidence on its relationship with growth and pubertal timing is less consistent and may depend on age at initiation, duration of treatment, adherence, and underlying disease severity (Nottage et al., 2016; Thornburg et al., 2012; Wang, Kavanagh, Little, Holliman, & Sprinz, 2011). The present findings do not support attributing delayed pubertal development to hydroxyurea exposure.

Participants who reported that a specific sickle cell disease treatment had influenced their secondary sexual development had higher adjusted odds of being in a more delayed pubertal-development category. This association requires cautious interpretation. The measure was based on participant perception and does not identify a specific treatment effect. It might reflect underlying disease severity, treatment intensity, developmental concerns that prompted treatment, or other unmeasured

characteristics associated with both treatment experience and pubertal development. The cross-sectional design also precludes establishing whether treatment exposure preceded the developmental outcome. Longitudinal studies incorporating treatment timing, adherence, disease severity, and serial pubertal assessments would be better suited to evaluating this relationship.

Participant perceptions also highlighted the psychosocial dimension of delayed maturation. Some adolescents reported delayed growth, pubic-hair development, menstruation, or facial-hair development. These concerns are clinically relevant because physical maturation is closely linked to body image, peer comparison, privacy, and social functioning during adolescence. Chronic illness and delayed puberty can adversely affect self-esteem and quality of life (Rees, Williams Tn Fau - Gladwin, & Gladwin, 2010). Pubertal assessment in sickle cell disease clinics should therefore be accompanied by age-appropriate counselling and psychosocial support, particularly for adolescents concerned about differences in physical development.

Jaundice, pallor, oedema, and frontal bossing were also documented in the cohort. Frontal bossing was associated with pubertal-development category in crude analysis, but the association was attenuated after adjustment and did not reach the prespecified threshold for statistical significance. It should therefore not be interpreted as an independent correlate of pubertal delay. Nevertheless, these clinical findings remain relevant to the broader assessment of chronic sickle cell disease, in which anaemia, haemolysis, and marrow expansion can contribute to skeletal and growth abnormalities (Gupta, Shrivastava, & Kumar, 2025).

Taken together, these findings demonstrate a substantial burden of delayed pubertal development among children and adolescents with sickle cell disease in eastern Uganda, particularly among girls. The observed associations with sex, stature, dietary diversity, and perceived treatment-related influence highlight areas that warrant further investigation. Routine sickle cell disease care for adolescents should incorporate longitudinal assessment of growth and pubertal progression, nutritional evaluation, and timely referral for those with suspected developmental delay.

Strengths and limitations

This study has several strengths. It addresses an important evidence gap in adolescent sickle cell disease care in Uganda. It included a relatively large sample from a major regional referral hospital serving a high-burden population. Pubertal development was assessed using Tanner staging rather than self-report alone, and anthropometric measurements were collected using standardised procedures. The study also assessed sociodemographic, nutritional, clinical, treatment-related, and perception-based factors, allowing a broad interpretation of pubertal development in this population.

The study also has limitations. The cross-sectional design limits causal inference and prevents assessment of temporal relationships between exposures and delayed puberty. Consecutive sampling may have introduced selection bias because adolescents attending clinic or admitted to hospital may differ from those not engaged in care. Some pubertal milestones, dietary information, and clinical

histories relied on recall, which may have introduced recall bias. Hormonal assays and detailed endocrine evaluation were not performed, limiting mechanistic interpretation. The absence of a healthy comparison group from the same setting limits direct comparison with adolescents without sickle cell disease. Finally, because this was a referral hospital-based study in Mbale City, findings may not be fully generalisable to all adolescents with sickle cell disease in Uganda.

Conclusion

Delayed pubertal development was highly prevalent among children and adolescents with sickle cell disease attending care at Mbale Regional Referral Hospital, affecting approximately six in ten participants, with a higher prevalence among girls than boys. The findings indicate that pubertal delay in this population is associated with growth and nutritional factors and may also reflect the broader influence of chronic disease burden, treatment-related factors, psychosocial concerns, and unmeasured endocrine or socioeconomic characteristics.

Male sex, tall stature, and consumption of at least four fruit varieties per day were associated with lower odds of being in a more delayed pubertal-development category, whereas reported treatment-related influence on secondary sexual development was associated with higher odds. The treatment-related association should be interpreted cautiously because it may reflect underlying disease severity or other unmeasured factors rather than a direct effect of treatment.

Recommendations

Routine assessment of growth and pubertal development should be integrated into the clinical care of children and adolescents with sickle cell disease. Height, weight, body mass index, Tanner stage, and age-appropriate pubertal milestones should be assessed during routine follow-up. Adolescents with delayed pubertal development, impaired growth, undernutrition, or psychosocial concerns should receive appropriate counselling and timely referral for paediatric or endocrine evaluation when indicated.

Nutritional assessment and counselling should be strengthened within sickle cell disease services. Given the high prevalence of underweight in the study population and the association between greater fruit diversity and lower odds of delayed pubertal development, dietary counselling should emphasise balanced dietary diversity and access to micronutrient-rich foods. Nutritional supplementation should be guided by clinical assessment and established indications rather than fruit intake alone. Further studies incorporating biochemical measures are needed to clarify the contribution of specific micronutrient deficiencies to pubertal development in children and adolescents with sickle cell disease.

Sickle cell disease services should also adopt adolescent-centred approaches that address both physical maturation and psychosocial wellbeing. Counselling on growth and puberty, caregiver education, age-appropriate psychosocial support, and linkage with school or community support services should be incorporated where feasible, particularly for adolescents experiencing delayed maturation or concerns about body image and peer comparison.

At policy and programme level, growth, nutrition, pubertal development, and adolescent psychosocial care should be incorporated into comprehensive sickle cell disease guidelines and routine service delivery. Facilities providing adolescent sickle cell disease care should be equipped with appropriate anthropometric tools and supported with trained health workers, standardised approaches to pubertal assessment, nutritional counselling, and clear referral pathways for specialist evaluation.

Future research should prioritise longitudinal studies that follow children with sickle cell disease through adolescence to establish the timing and progression of pubertal development. Such studies should incorporate hormonal assessments, nutritional biomarkers, genotype, measures of disease severity, treatment initiation and duration, adherence, and socioeconomic characteristics. Longitudinal evaluation would also help clarify the observed association between perceived treatment-related influence and delayed pubertal development and distinguish treatment effects from differences in underlying disease severity.

Abbreviations

aOR	Adjusted odds ratio
BMI	Body mass index
CI	Confidence interval
COR	Crude odds ratio
HIV	Human immunodeficiency virus
MRRH	Mbale Regional Referral Hospital
NCDs	Non-communicable diseases
SCD	Sickle cell disease
SD	Standard deviation
WHO	World Health Organization

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Busitema University Faculty of Health Sciences Research Ethics Committee (Approval No. **BUFHS-2024-202**) and the Uganda National Council for Science and Technology. Administrative clearance was obtained from Mbale Regional Referral Hospital before commencement of the study. All study procedures were conducted in accordance with the approved protocol and the principles of the Declaration of Helsinki.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Funding

This study received no funding.

Author Contribution

JN conceived and led the study, coordinated data collection, performed the initial data analysis, and drafted the initial manuscript. JPA and DM contributed to the study design, supported data analysis, and co-led the interpretation of findings and manuscript development. JPA, KO, and LR supported field implementation, data acquisition, and drafting of selected sections of the manuscript. CT and SO supervised the study, provided scientific oversight, and made substantial contributions to manuscript writing and critical revision for intellectual content. All authors reviewed the manuscript.

Acknowledgements

We acknowledge the management of Mbale Regional Referral Hospital and the staff of the Sickle Cell Clinic for facilitating participant recruitment and supporting data collection for this study. We are also grateful to the children and adolescents living with sickle cell disease, together with their parents and caregivers, for their time and participation. Additionally, we also greatly appreciate the support from Enhancing Research capacity for Sickle Cell Disease and related NCDs across the Lifespan in Uganda, Enrich Project under Grant No. D43TW012466.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

References

1. Akiibinu MO, Omiwole MO, Akinola F, Akinola SS, Garuba HM, Ogunmodede TY, Uzamot KA. Endocrine and Growth disorders in children with Haemoglobin-SS. *Afr J Health Sci.* 2020;33(1):14–22.
2. Betoko RM, Sap S, Alima AY, Chelo D, Nengom JT, Simon D, Ndombo PK. (2023). Pubertal patterns in children with sickle cell anemia: A case-control study in Cameroon. (1769-664X (Electronic)).
3. Betoko RM, Sap S, Alima AY, Chelo D, Nengom JT, Simon D, Ndombo PK. Pubertal patterns in children with sickle cell anemia: A case–control study in Cameroon. *Archives de Pédiatrie.* 2023;30(7):466–70.
4. Egesa WI, Nakalema G, Waibi WM, Turyasiima M, Amuje E, Kiconco G, Asiimwe D. (2022). Sickle cell disease in children and adolescents: a review of the historical, clinical, and public health perspective of sub-saharan africa and beyond. *International Journal of Pediatrics,* 2022.
5. Gomes ICP, Melo HN, Melo SIA, Menezes NVd, Dantas TVP, Cipolotti R. Growth and puberty in a prospective cohort of patients with sickle-cell anaemia: an assessment over ten years. *J Hum Growth Dev.* 2017;27(1):91–8.
6. Gupta P, Shrivastava S, Kumar R. Musculoskeletal complications in sickle cell disease: Pathophysiology, diagnosis and management. *Best Pract Res Clin Rheumatol.* 2025;39(2):102033.
7. Hauschild M, Theintz G. Severe chronic anemia and endocrine disorders in children. *Revue Medicale Suisse.* 2007;3(107):988–91.
8. Kambasu DM, Rujumba J, Lekuya HM, Munube D, Mupere E. Health-related quality of life of adolescents with sickle cell disease in sub-Saharan Africa: a cross-sectional study. *BMC Hematol.* 2019;19(1):9. 10.1186/s12878-019-0141-8.
9. Kato GJ, Piel FB, Reid CD, Gaston MH, Ohene-Frempong K, Krishnamurti L, Vichinsky EP. Sickle cell disease. *Nat Rev Dis Primers.* 2018;4:18010. 10.1038/nrdp.2018.10.
10. Klein DA, Emerick JE, Sylvester JE, Vogt KS. Disorders of puberty: an approach to diagnosis and management. *Am Family Phys.* 2017;96(9):590–9.
11. Konotey-Ahulu FI. The sickle cell diseases. Clinical manifestations including the sickle crisis. *Arch Intern Med.* 1974;133(4):611–9.
12. Mandese V, Bigi E, Bruzzi P, Palazzi G, Predieri B, Lucaccioni L, Iughetti L. Endocrine and metabolic complications in children and adolescents with Sickle Cell Disease: an Italian cohort study. *BMC Pediatr.* 2019;19(1):56. 10.1186/s12887-019-1423-9.
13. Ndeezi G, Kiyaga C, Hernandez AG, Munube D, Howard TA, Ssewanyana I, Ware RE. Burden of sickle cell trait and disease in the Uganda Sickle Surveillance Study (US3): a cross-sectional study. *Lancet Global Health.* 2016;4(3):e195–200.

14. Nottage KA, Ware RE, Aygun B, Smeltzer M, Kang G, Moen J, Helton KJ. Hydroxycarbamide treatment and brain MRI/MRA findings in children with sickle cell anaemia. *Br J Haematol*. 2016;175(2):331–8.
15. Nsubuga M, Mutegeki H, Jjingo D, Munube D, Namazzi R, Opoka R, Kiguli S. The Ugandan sickle Pan-African research consortium registry: design, development, and lessons. *BMC Med Inf Decis Mak*. 2024;24. 10.1186/s12911-024-02618-9.
16. Okwi AL, Byarugaba W, Ndugwa CM, Parkes A, Ocaido M, Tumwine JK. An up-date on the prevalence of sickle cell trait in Eastern and Western Uganda. *BMC Blood Disord*. 2010;10:5. 10.1186/1471-2326-10-5.
17. Omar A, Mutai B, Abdallah F. (2019). CHARACTERISTICS AND GROWTH AND PUBERTAL PATTERNS AMONG PATIENTS WITH SICKLE CELL DISEASE AT KENYATTA NATIONAL HOSPITAL, NAIROBI. *East Afr Med J*, 96(7).
18. Omar J. Gonadotropin-releasing hormone stimulation test and diagnostic cutoff in precocious puberty: a mini review. *Annals of Pediatric Endocrinology & Metabolism*; 2021.
19. Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010–2050: modelling based on demographics, excess mortality, and interventions. *PLoS Med*. 2013;10(7):e1001484. 10.1371/journal.pmed.1001484.
20. Rees DC, Williams Tn Fau - Gladwin, M. T., Gladwin MT. (2010). Sickle-cell disease. (1474-547X (Electronic)).
21. Soliman A, De Sanctis V, Elalaily R. Nutrition and pubertal development. *Indian J Endocrinol Metabol*. 2014;18(Suppl 1):S39–47.
22. Thomson AM, McHugh TA, Oron AP, Teply C, Lonberg N, Tella VV, Aboagye RG. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000–2021: a systematic analysis from the Global Burden of Disease Study 2021. *Lancet Haematol*. 2023;10(8):e585–99.
23. Thornburg CD, Luo FBF, Luo Z, Fau - Z, Miller ST, Miller St Fau - Kalpatthi, Kalpatthi R, Iyer RF, Iyer R, Fau R, Seaman P, Wang WC. (2012). Impact of hydroxyurea on clinical events in the BABY HUG trial. (1528-0020 (Electronic)).
24. Vilela TdS, Fisberg M, Ferrari G, Braga JAP. Vitamin D deficiency in a pediatric population with sickle cell disease. *Pediatr Hematol Oncol*. 2025;42(2):92–103.
25. Wang CJ, Kavanagh PL, Little AA, Holliman JB, Sprinz PG. Quality-of-care indicators for children with sickle cell disease. *Pediatrics*. 2011;128(3):484–93.
26. Zemel BS, Ohene-Frempong KDF, Ohene-Frempong K, Fau - K, Schall JI, Schall Ji Fau - Stallings, V. A., Stallings VA. (2007). Effects of delayed pubertal development, nutritional status, and disease severity on longitudinal patterns of growth failure in children with sickle cell disease. (0031-3998 (Print)).

Figures

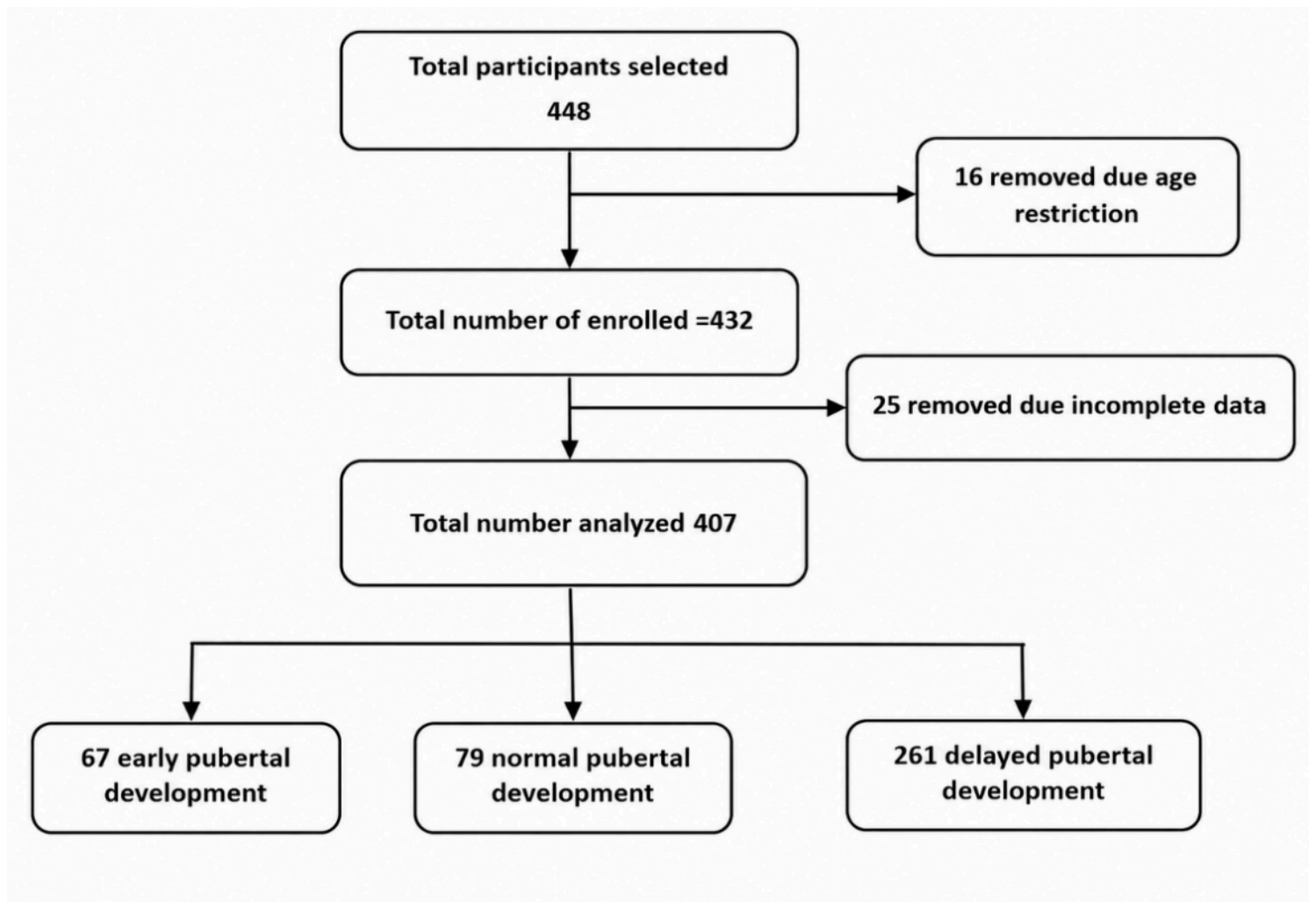


Figure 1

Study participant flow

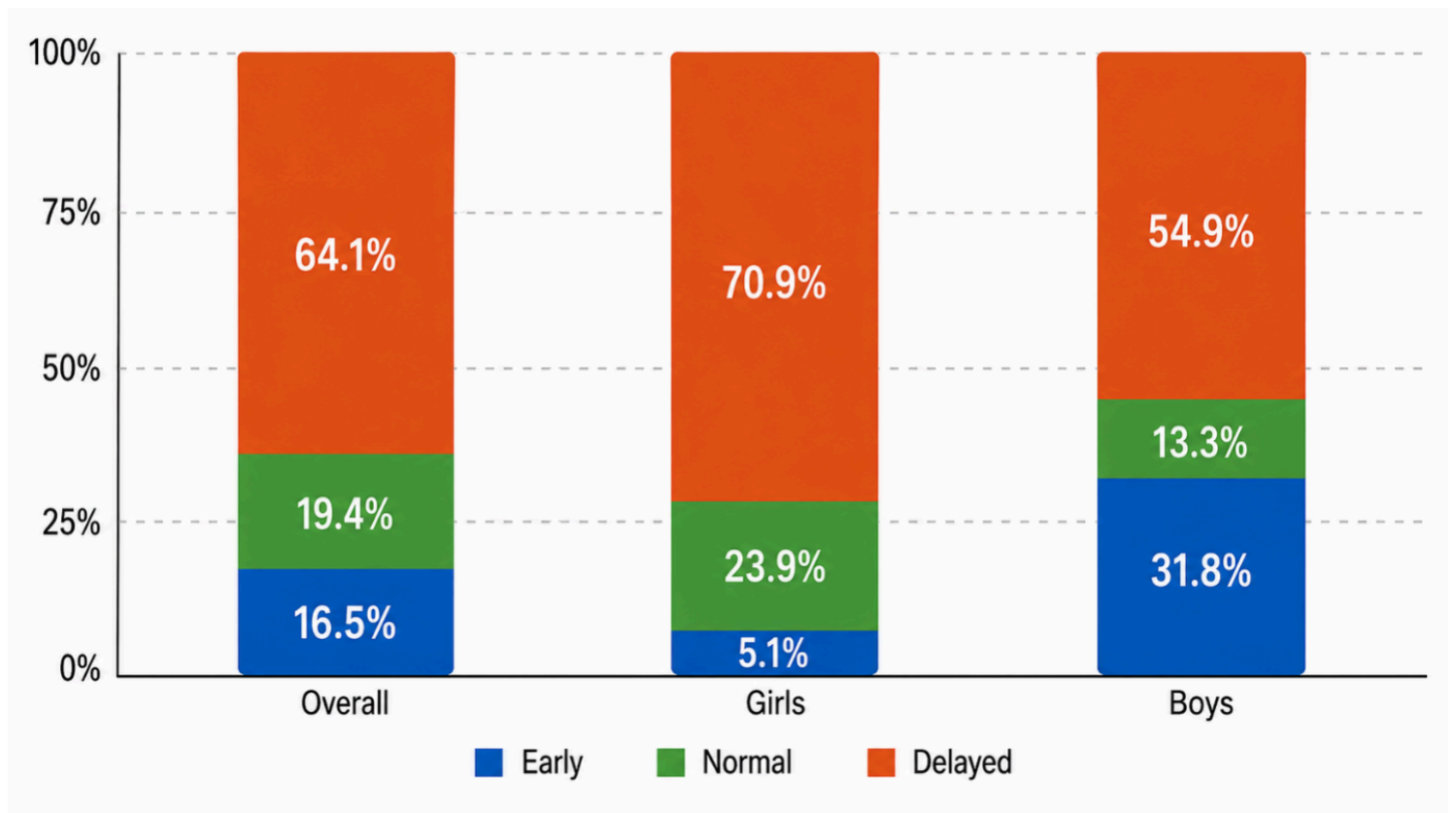


Figure 2

Distribution of early, normal, and delayed pubertal development overall and by sex

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [File1.pdf](#)