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Body Mass Index and Sexual Maturation in Adolescent Patients with Sickle Cell Anaemia

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Summary

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Background: Sickle cell anaemia (SCA) is associated with delayed sexual maturation. The Body Mass Index (BMI) or Quetelets Index is closely linked to events of puberty in normal children. We have so far, found no reports on studies on the relationship between BMI and puberty in patients with SCA.

Objectives: To evaluate sexual maturation in patients with SCA, and determine the influence of BMI on the onset of sexual maturation.

Design: A cross-sectional study carried out in Port Harcourt, Rivers State, from June 1999 to June 2000.

Patients and Methods: One hundred and twenty four adolescents with SCA as well as the same number of matched normal controls were evaluated. A structured questionnaire was used to obtain information on personal data and determinants of socio-economic class. Weight, height (HT) and BMI were obtained and sexual maturation assessed.

Results: Fifty-seven (46.0 percent) males and 67 (54.0 percent) females with SCA as well as their matched controls were evaluated. The mean age at onset of sexual maturation was 14.6±1.4 years for males with SCA and 12.1±1.3 years for the controls. Among the females, this was 14.2±1.7 years for the patients and 11.4±0.8 years for the controls. The observed differences were statistically significant ($P<0.05$). The average BMI of SCA patients in Sex Maturity Rating (SMR) 2 was also significantly higher ($P<0.05$) than the average values in SMR I for both sexes.

Conclusion: Sexual maturation is delayed in patients with SCA compared to matched controls. The average BMI obtained at onset of sexual maturation (SMR 2) is significantly higher than values obtained in the prepubertal stages (SMR I) in both sexes. This suggests that, regardless of chronological age, some increase in body fat and size, as reflected in BMI, is associated with onset of sexual maturation in patients with SCA

Key Words : Sexual maturation, Puberty, Sickle cell anaemia, Body Mass Index, Sex Maturity Ratings.

Introduction

SEXUAL maturation involves the transformation of a sexually immature child into an adult capable of reproductive functions as a result of a complex series of hormonal events;[1] this is also referred to as puberty. 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 the reproductive system.[2] The ages at which various puberty changes are observed differ, depending on various genetic and environmental influences.[3] Sickle cell anaemia has been shown in many studies to be associated with delayed sexual development.[4,5] Jimenez *et al* in 1966, reported delayed sexual maturation in their patients with SCA when they noted that females showed no evidence of secondary sexual characteristics by 13 years of age compared to controls, while males by 15-17 years only showed the earliest evidence of secondary sexual characteristics.[6] Emodi in her study

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at Enugu, also reported that by 11 years of age, only 10 percent of females with SCA had reached Sex Maturity Rating (SMR) 2, for pubic hair development compared to 50 percent of controls. By 14 years of age, all females in her control group had achieved SMR 5, while only 50 percent of patients with SCA had achieved this level of development by 16 years of age.[5]

The body mass index (BMI) or Quetelets Index is an indicator of body fat and lean body mass, but has the best correlation with body fat.[7] It is a better indicator of body size than raw height or weight.[8] Weight and BMI have been shown to be significantly reduced in patients with SCA, with absence of the marked increase in BMI which usually occurs at puberty in normal children.[9] Body weight, height and BMI are closely related to events of puberty in normal children.[10,11] After an extensive literature search, we found no studies on the relationship between BMI and puberty in patients with SCA. This study is therefore, designed to evaluate sexual maturation and body mass index in patients with sickle cell anaemia.

Subjects and Methods

This cross-sectional study was carried out in Port-Harcourt, Rivers State over a nine-month period, June to November 1999 and April to June 2000. Ethical clearance was obtained from the Ethical Committee of the University of Port-Harcourt Teaching Hospital (UPTH). Patients with sickle cell anaemia who met the inclusion criteria were consecutively enrolled from the sickle cell clinic and Haematology clinic of the UPTH, as well as the sickle cell clinic of the Nigerian Ports Authority, Port-Harcourt. A total of 124 patients were enrolled, although the minimum sample size required was 70, based on the formula:[12] $n = pq/(E/1.96)$. The haemaglobin genotype of all the subjects had been predetermined in the haematological department of UPTH using cellulose acetate paper for electrophoresis in alkaline medium and all had HbSS electrophoresis. The inclusion criterion was that the subjects must include all adolescents (aged 10–19 years)[13] with sickle cell anaemia, confirmed by Hb electrophoresis, while the exclusion criteria included the following: (i) any adolescent with SCA who also has any other chronic illness that might affect growth and development e.g. tuberculosis, chronic renal failure, or diabetes mellitus, as obtained from the history, physical examination, and case notes, and (ii) any patient whose parents refused to give consent.

For each enrolled patient, a structured questionnaire was used to obtain information on personal data and other determinants of socio-economic class. Socio-economic class was assigned as upper, middle and lower using the classification proposed by Olusanya *et al.*[14] The following were also obtained: weight, height, and

Table I

Age and Sex Distribution of Patients with Sickle cell Anaemia

Age (Years)	*Males*	*Females*	*Total*
10	7	8	16
11	6	7	13
12	4	6	10
13	5	7	12
14	7	8	15
15	7	7	14
16	7	7	14
17	6	6	12
18	4	5	9
19	4	6	10
Total	57	67	124

Table IIA

Mean Ages of Males and SMR Stages for Genitals*

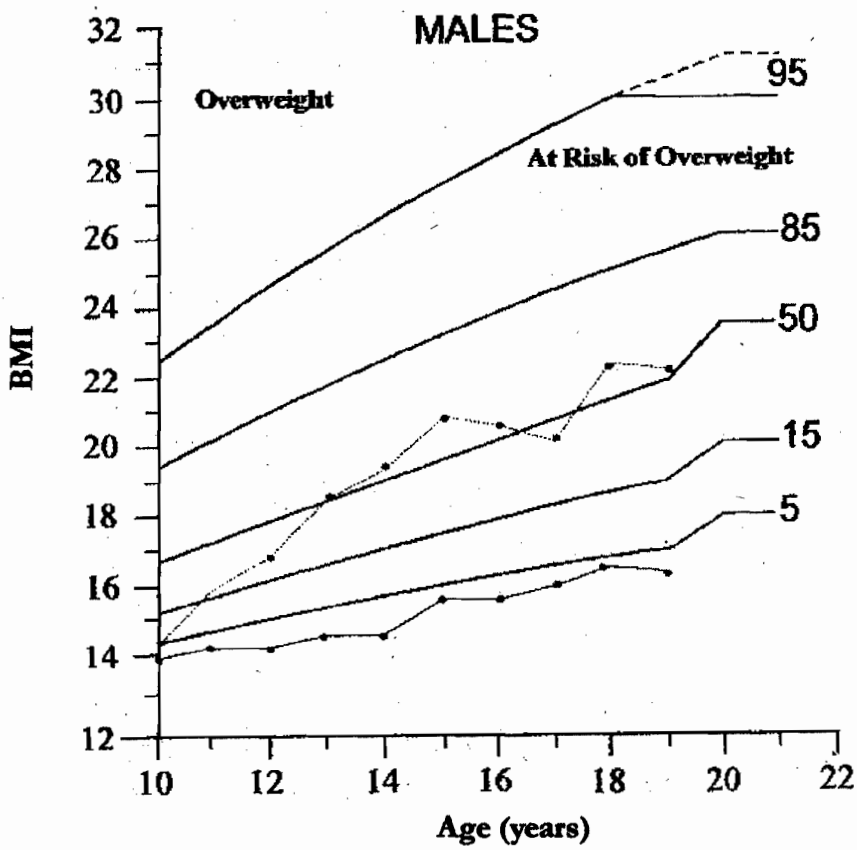
SMR	*Patients (n = 57)*		*Controls (n =57)*		*'t' Value*	*p*
(Genitals)	*No.*	*Mean Age ± SD (years)*	*No.*	*Mean Age ± SD (years)*		
Stage 1	26	12.2 ± 2.2	9	10.3 ± 0.5	4.17	<0.05
Stage 2	15	14.6 ± 1.4	11	12.1 ± 1.3	4.69	<0.05
Stage 3	7	16.4 ± 1.5	10	13.7 ± 1.0	4.16	<0.05
Stage 4	6	17.0 ± 0.8	10	15.2 ± 0.8	4.36	<0.05
Stage 5	3	18.7 ± 0.6	17	16.8 ± 1.2	4.20	<0.05

* Sex maturity rating

Table IIB

Mean Ages of Males in SMR Stages for Pubic Hair

SMR (Pubic Hair)	*Patients (n = 57)*		*Controls (n =57)*		*'t' Value*	*p*
	No.	*Mean Age ± SD (years)*	*No.*	*Mean Age ± SD (years)*		
Stage 1	27	12.3 ± 2.2	10	10.4 ± 0.5	4.20	<0.05
Stage 2	14	14.7 ± 1.3	10	12.2 ± 1.3	4.60	<0.05
Stage 3	7	16.4 ± 1.5	9	13.7 ± 1.0	4.10	<0.05
Stage 4	8	17.7 ± 0.8	12	15.8 ± 0.8	5.20	<0.05
Stage 5	1	19.0 ± 0.0	16	16.7 ± 1.0	9.20	<0.05



Controls ----------
Patients _____

Fig 1 Mean BMI by Age in Male Patients and Controls

BMI^9= Wt. (in Kg/Ht (in metres)^2. The stages of sexual maturation were assessed using the sex maturity rating as proposed by Tanner. Descriptions and photographs of the various stages were available for comparison.[15] The controls for the study were students selected from Community Secondary School, Okoro-nu-odu, Obio-Akpor, Port-Harcourt. The students, matched for age, sex, and socio-economic class with the patients, were selected by stratified random sampling. The haemaglobin genotypes of the controls were determined as were their sex maturity ratings and BMI; none had the SS genotype.

Results

One hundred and twenty four adolescents with sickle cell anaemia were evaluated. Fifty-seven (46.0 percent) were males and 67 were females. The same number of

Table IIIA

Mean Ages of Females in SMR Stages for Breast Development

SMR (Breast)	Patients (n = 57)		Controls (n =57)		't' Value	p
	No. (years)	Mean Age ± SD	No. (years)	Mean Age ± SD		
Stage 1	23	11.9 ± 2.5	10	10.2 ± 0.4	3.17	<0.05
Stage 2	16	14.4 ± 1.8	11	11.6 ± 0.7	5.63	<0.05
Stage 3	10	15.2 ± 2.2	10	13.2 ± 0.6	2.77	<0.05
Stage 4	11	16.1 ± 1.9	10	14.3 ± 0.5	3.03	<0.05
Stage 5	7	18.0 ± 1.2	26	16.6 ± 1.3	2.69	<0.05

Table IIIB

Mean Ages of Females in SMR Stages for Pubic Hair

SMR (Pubic Hair)	Patients (n = 57)		Controls (n =57)		't' Value	p
	No.	Mean Age ± SD (years)	No.	Mean Age ± SD (years)		
Stage 1	24	11.8 ± 2.5	8	10.3 ± 0.7	2.64	<0.05
Stage 2	18	14.2 ± 1.7	13	11.4 ± 0.8	6.11	<0.05
Stage 3	10	15.0 ± 2.0	10	13.2 ± 0.6	3.63	<0.05
Stage 4	11	16.7 ± 1.4	11	14.6 ± 0.5	4.69	<0.05
Stage 5	4	18.8 ± 0.5	25	17.1 ± 1.3	4.79	<0.05

Table IV

Mean BMI of Females and Males in SMR 1 and 2

		SMR I		SMR 2		't' Value	p
		No.	Mean BMI/SD	No.	Mean BMI/SD		
Females:	Patients	24	13.4±0.9	18	15.4±0.8	7.62	<0.05
	Controls	8	14.4±1.2	13	16.3±1.4	3.57	<0.05
Males:	Patients	26	14.2±0.8	15	15.0±0.9	2.85	<0.05
	Controls	9	15.3±1.1	11	16.8±1.2	2.91	<0.05

appropriately matched controls was also evaluated. The age and sex distribution of the patients with SCA patients is shown in Table 1. Tables IIA and IIB show the mean ages of males in each SMR stage for the genitals and pubic hair development, respectively. The mean age of onset of sexual maturation in male patients was 14.6±1.4 years for the genitals and 14.7±1.3 years for pubic hair development. Among controls, onset of maturation was noted at a mean age of 12.1±1.3 years for the genitals and 12.2±1.3 years for pubic hair development. The mean ages of the male patients in all SMR stages were significantly higher than those of controls for both genitals and pubic hair development ($p < 0.05$).

Tables IIIA and IIIB show the mean ages of females at various SMR stages. Pubic hair development

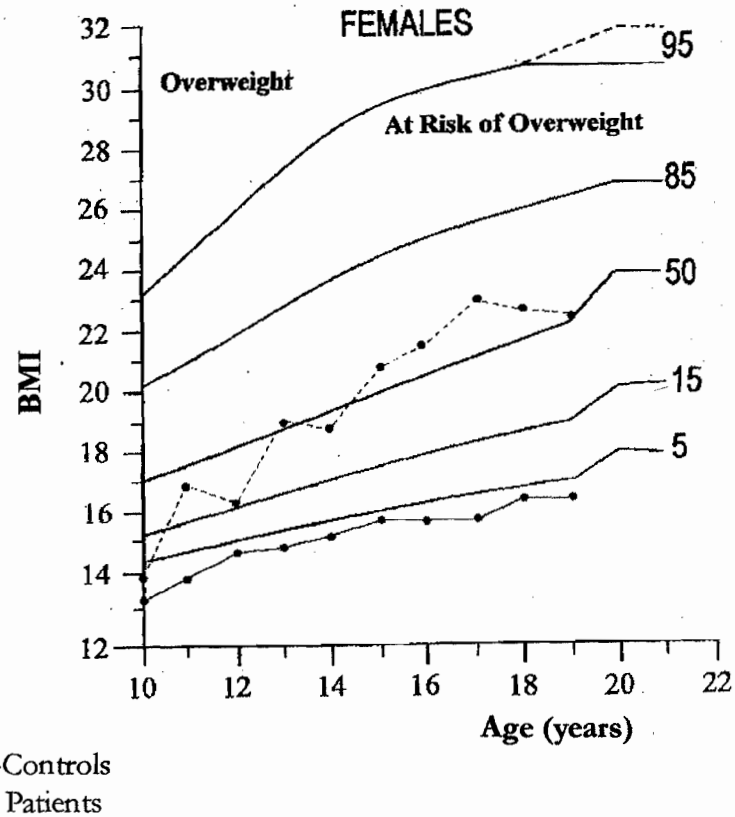


Fig 2: Mean BMI by Age in Female Patients and Controls

was the first sign of puberty observed in most females at a mean age of 14.2±1.7 years for patients with SCA, and a mean age of 11.4 ± 0.8 years in the controls. The mean ages of the female patients were significantly higher than those of controls in all the SMR stages ($p<0.05$). The average BMI of males with SCA was 15.03 while that of controls was 19.15. The average BMI of females with SCA was 15.03 while that of the controls was 19.8. These differences were statistically significant with "t" values of 9.48 and 9.23 respectively, and $p<0.05$. Fig. 1 compares the BMI of male patients and controls, while Fig. 2 compares that of the females. There were no significant differences in BMI between male and female subjects with SCA ($P>0.05$).

The influence of BMI on the onset of development of genitals in males and pubic hair in females was assessed since these were the first signs of sexual maturation observed in the respective sexes. The average BMI values of patients in the prepubertal stages (SMR I) were compared with those of patients at onset of puberty (SMR 2) for both males and females (Table IV). The average BMI of subjects in SMR I (prepubertal) was significantly lower than those at onset of puberty (SMR 2; $p<0.05$).

Discussion

The results obtained in the present series show that both onset and completion of sexual maturation are delayed in patients with sickle cell anaemia. These findings are in keeping with earlier reports from both within and outside Nigeria.[4-6] The mean age at onset of puberty observed in males with SCA in this study is close to the mean age of 14.2±1.3 years reported earlier by Olambiwonnu *et al.*[16] The mean age at onset of pubic hair development in males in this study is however, lower than that reported by Oyedeji where the earliest age of pubic hair development in males was 20 years.[4] However, Oyedeji had only six males aged 13 years and above, in his study population and this may have limited his findings. The mean age of completion of pubic hair development noted in this study differs remarkably from that reported by Abassi *et al* in which pubic hair maturation was uncompleted even at a mean age of 26.6 years.[17] Abassi *et al's* results have been criticized for reflecting the bias of one with a well known interest in hypogonadism; he may thus have used a group of more severely affected patients. Among the females, the delayed onset of sexual maturation is also in keeping with the findings by Emodi[5] who observed that by 13 years of age, only 40

percent of the females with SCA had reached SMR 2 for breast development; this was unlike in the controls where 50 percent of the females were already at SMR 4 at this age. Platt *et al* reported median ages of 11.8 years and 12 years for the onset of breast and pubic hair development, respectively.[18]

The reason for the observed delay in sexual maturation in patients with SCA have however, remained elusive. Implicated factors include hormonal, haematological, socio-economic, nutritional, medicare, infections, trace elements and vitamin deficiencies.[19] Weight, height, body mass index and body build may also be contributory factors. Body mass index has been shown in this study to be significantly lower in patients with SCA compared to controls. The lower BMI value in patients with SCA is a reflection of their low body fat. It also reflects the greater increase in height than weight usually seen in adolescents with SCA.

Our results have thus shown a significant relationship between BMI and sexual maturation in patients with SCA. The mean BMI in patients and controls at onset of puberty (SMR 2) were significantly higher than the mean BMI at the prepubertal stages (SMRI). This tends to suggest that regardless of chronological age, some increase in body fat, and thus size, may be required for pubertal development to occur. This tends to agree with the findings by Frisch and Revelle in females,[20] and by Eletu in males.[11] The effect of BMI on sexual maturation will however, be best elucidated in a longitudinal study.

References

1. Swerdloff RS. Physiological control of puberty. Symposuim on the brain and the endocrine system. *Med Clin N Am* 1978; **62**:351-65.
2. Savage DCL, Evan J. Puberty and Adolescence. In: Forfar JO, Arneil GC, eds. Textbook of Paediatrics. London: Churchill Livingstone, 1984: 366-71.
3. Zacharias L, Rand WM, Wurtman RJ. A prospective study of sexual development and growth in American girls. The statistics of menarche. *Obstet Gynaecol Survey* 1976; **31**: 325-7.
4. Oyedeji GA. Delayed sexual maturation in sickle cell anaemia patients- observation in one practice. *Ann Trop Paediatr* 1995; **15**:197-201.
5. Emodi I. Physical and Sexual Development in Children with Sickle cell Anaemia. Dissertation: National Postgraduate Medical College of Nigeria, 1989: 30-56.
6. Jimenez CT, Scott RB, Henry WL, Sampson CC, Ferguson AD. Studies in sickle cell anaemia XXVI. The effect of homozygous sickle cell disease on the onset of menarche, pregnancy, fertility, pubescent changes and body growth in Negro subjects. *Am J Dis Child* 1966; **111**:497-504.
7. Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services: recommendation from an expert committee. *Am J Clin Nutri* 1994; **59**:307-16.
8. Rolland-Cachera MF, Cole TJ, Semepe M, Tichet J, *et al.* Body Mass Index Variations: Centiles from birth to 87 years. *Euro J Clin Nutri* 1991; **45**:13-21.
9. Emodi IJ, Kaine WN. Weights, heights and Quetelet indices of children with sickle cell anaemia (sicklers). *Nig J Paediatr* 1996; **23**:37-41.
10. Fakeye O, Fagbule D. Age and anthropometric status of Nigerian girls at puberty: implications for the introduction of sex education into secondary schools. *W Afr J Med* 1990; **9**:226-31.
11. Eletu OB. An evaluation of nutritional status of secondary school adolescents in relation with pubertal status in male subjects, in Mushin LGA of Lagos State. Dissertation: West African Postgraduate Medical College, 1986: 51-80.
12. Osibogun A. Research Project: Designs and Implementation. Presented at the West African Training Workshop on Operational Research, 1998.
13. WHO. 'Young people', 'Adolescents' and 'Youth'. A picture of health. Geneva, 1995.
14. Olusanya O, Okpere E, Ezimokhai M. The importance of social class in voluntary fertility control in a developing country. *W Afr J Med* 1995; **4**:205-12.
15. Litt FI, Vaughan CV. Growth and Development during Adolescence. In: Bergman RE, Vaughan VC, eds. Nelson Textbook of Pediatrics. Philadelphia: WB Saunders, 1992: 20-1.
16. Olambiwonnu NO, Penny R, Frasier SD. Sexual maturation in subjects with sickle cell anaemia: Studies of serum gonadotropin concentration, height, weight and skeletal age. *J Pediatr* 1975; **87**:459-64.
17. Abassi AA, Prasad AS, Ortega J, *et al.* Gonadal function abnormalities in sickle cell anaemia. Studies in adult male patients. *Ann Intern Med* 1976; **85**:601-5.
18. Platt OS, Rosenstock W, Espeland MA. Influence of sickle haemoglobinopathies on growth and development. *N Eng J Med* 1984; **311**:7-12.
19. Sergeant GR. Physical and sexual development. In: Sergeant GR, ed. Sickle Cell Disease. Oxford: Oxford University Press, 1985: 269-80.
20. Frisch RE, Revelle R. Height and weight at menarche and a hypothesis of menarche. *Arch Dis Child* 1971; **46**:695-701.