

Original Article

# Menstrual Characteristics of Sickle Cell Anaemia Patients of Reproductive Age in North West of Nigeria

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## Article History

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## ABSTRACT

Sickle cell anaemia (SCA) is an inherited autosomal recessive haemolytic anaemia with clinical manifestations of chronic anaemia, haemolysis and vasculopathy. Nigeria is believed to be the most sickle cell anaemia endemic country in sub-Saharan Africa with 2% - 3% of the total population affected. Adolescent girls living with sickle cell anaemia face unique gynecological challenges including delayed puberty marked by a later onset in menarche when compared to adolescent girls without sickle cell anaemia. Vaso-occlusive pain associated with menstrual cycle and abnormal uterine bleeding. This was a cross-sectional comparative study involving SCA and normal women of child bearing age. Following the acquisition of Institutional ethical clearance, a total of 90 respondents (60 HbSS, 30 Hb AA) who were within the reproductive age group were enrolled for this study. Participants were enrolled from the Sickle Cell Clinic and Antenatal Clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. Data on socio-demographics, age at menarche, menstrual cycle (regular vs irregular) and menstrual flow (normal, light and heavy) were collated. The mean±SD ages of the HbSS and HbAA respondents were 26.4±7.5 and 25.6±5.5 years respectively. The HbSS participants had statistically significantly higher ages at menarche compared to the HbAA respondents: (15.6±1.3years versus 14.7±1.6years). The relationship between study group (HbSS vs HbAA) and menstrual cycle (regular vs irregular) was not statistically significant. There was a statistically significant relationship between study group (HbSS vs HbAA) and menstrual flow (normal, light, and heavy): (X<sup>2</sup>=17.980, df=2, p=0.0001)

**Keywords:** Delayed Menarche, Northwest Nigeria, Sickle Cell Anaemia,

## INTRODUCTION

Sickle cell anaemia (SCA) is an inherited autosomal recessive haemolytic anaemia with clinical manifestations of chronic anaemia, haemolysis and vasculopathy. Recurrent episodes of vaso-occlusion and inflammation result in progressive damage to most organs, including the brain, kidneys, lungs, bones, cardiovascular and reproductive systems, which becomes apparent with increasing age.<sup>1</sup> SCA is also contributory to several

obstetric complications and high maternal mortality rates in women of child-bearing age living with SCD in Nigeria.

Nigeria is believed to be the most sickle cell endemic country in sub-Saharan Africa with 2% - 3% of the total population affected.<sup>2</sup> About 150,000 children are born every year with sickle cell disease (SCD) in Nigeria (33% of the global burden) and there are about 4 - 6 million people living with the disease.<sup>3,4</sup> SCD is also contributory to several obstetric

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complications and high maternal mortality rates in women of child-bearing age living with SCD in Nigeria<sup>5</sup>.

Puberty is a pivotal time in the life of a human being, which is characterised by development of secondary sexual characteristics, growth spurt and changes in body image. These changes have immense psychological impact on adolescents generally. Adolescent girls living with sickle cell anaemia face unique gynecological challenges, this includes delayed puberty which is marked by a later onset in menarche when compared to adolescent girls without sickle cell anaemia. They also experience vaso-occlusive pains associated with menstrual cycle and other menstrual abnormalities.<sup>6,7</sup> This has been found to contribute to the lower self-esteem many teenagers with SCD experience, as well as a higher risk for depression, anxiety, social withdrawal, attention deficit and hyperactivity, which may affect how they follow and adhere to their care plan as they work towards a normal life.<sup>8</sup> This may further contribute negatively to their educational and occupational productivity, psychological wellbeing, reproductive health outcomes and their general quality of life.

Some determinant factors associated with delayed menarche in sickle cell anaemia includes, chronic low baseline haemoglobin, high metabolic rate, low body mass index, deficiency and low level of some micronutrients such as zinc, recurrent vaso occlusive episodes and impaired hypothalamic-pituitary-gonadal axis due to chronic hypoxia.<sup>9,10</sup> This can be further impaired in SCA subjects with recurrent blood transfusion need, as endocrine dysfunction is the most common and earliest organ toxicity seen in subjects with chronic iron-induced cellular oxidative damage due to iron overload.<sup>11</sup> The predicted risks of iron overload and endocrine organ failure naturally increases with both the duration of disease requiring transfusion therapy and the number of transfusions.<sup>11</sup> Early initiation of hydroxyurea therapy helps reduce early mortality and normalize growth parameters.<sup>12,13</sup>

Despite the high prevalence of sickle cell anaemia in Nigeria, there is limited studies on the menstrual characteristics of affected women in the North West region. Most available studies focused mainly on the

general clinical manifestations and complications of sickle cell disease. There is a need to give attention to menstrual and reproductive health issues in these women. Understanding the menstrual characteristics of women with sickle cell anaemia will provide valuable information for clinicians in planning and management of reproductive health issues. Early identification of menstrual abnormalities, early interventions, and improving the overall quality of life for women living with sickle cell anaemia.

**Objective:** To study the age at menarche and characterize the menstrual cycle of subjects with sickle cell anaemia.

## **MATERIALS AND METHODS**

This was a cross-sectional comparative study involving women of child bearing age. A total of ninety (90) respondents (60 HbSS, 30 Hb AA) who were within the reproductive age group were enrolled for this study. Participants were enrolled from the Sickle Cell Clinic and Antenatal Clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. Data on socio-demographics, age at menarche, menstrual cycle (regular vs irregular) and menstrual flow (normal, light and heavy) were collated.

### **Inclusion criteria**

All consenting HbSS and HbAA participants 18 years and above who consented to the study were enrolled. Venous blood samples were collected from respondents with undocumented haemoglobin electrophoresis result.

### **Exclusion criteria**

Respondents with co-morbidities, primary amenorrhea, postmenopausal, those on hormonal therapy and those who did not consent were excluded in the study.

### **Data analysis**

Data was summarized using Jefferys Amazing Statistical Package Version 0.16.4 {JASP (University of Amsterdam)}. Qualitative data were summarized as frequencies and percentages. Quantitative data were summarized as mean and standard deviation. Means were compared using student T-test while Mid-P exact were used to assess

relationships between study groups and qualitative variables. Level of statistical significance was set at  $p \leq 0.05$ .

### Ethical Considerations

Ethical clearance was obtained from the health research ethics committee, Ahmadu Bello University Teaching Hospital (ABUTH) Shika. All questionnaires were coded and all data generated were confidential. Computers were password-protected using alpha-numeric codes. All study participants who were found to require treatments/interventions were referred appropriately. Refusal to participate or withdrawal from the study did not compromise the status of care offered to patients.

### RESULTS

The mean $\pm$ SD ages of the HbSS and HbAA participants were 26.4 $\pm$ 7.5 and 25.6 $\pm$ 5.5 years respectively. Marital and educational status is summarized in Fig 1, 2. The HbSS participants had statistically significantly higher ages at menarche compared to the HbAA participants: (15.6 $\pm$ 1.3 years versus 14.7 $\pm$ 1.6 years, t-statistic=3.052,  $p=0.003$ ).

The relationship between study group (HbSS vs HbAA) and menstrual cycle (regular vs irregular) was not statistically significant ( $p=0.593$ ). The Petos Odds Ratio for HbSS participant having irregular menstrual cycles compared to HbAA participant was 1.73 (95% CI 0.41, 7.40). There was a statistically significant relationship between study group (HbSS vs HbAA) and menstrual flow (normal, light, and heavy): ( $X^2=17.980$ ,  $df=2$ ,  $p=0.0001$ ).

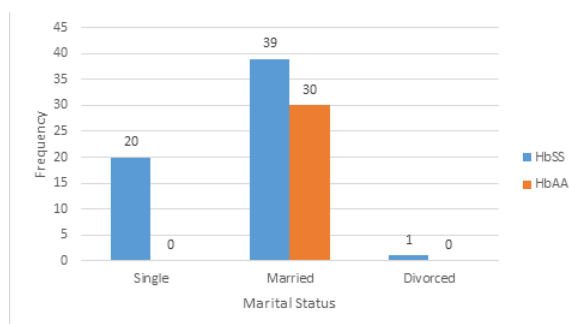


Figure 1: Marital patterns of the study subjects

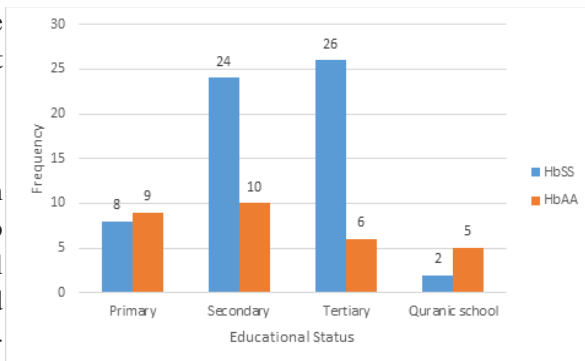


Figure 2: Educational status of the study subjects

### DISCUSSION

Our study compared the menstrual characteristics of women with SCA with that of their HbAA counterpart. The determinants of age at menarche includes genetics, socioeconomic factors, nutritional status and general health. Studies have shown the age at menarche in girls to be between the ages of 10 to 16 years, while menarche is said to be delayed by the age of 16.<sup>14</sup> Our study recorded the age at menarche among the SCA and HbAA women as 15.6 $\pm$ 1.3 years and 14.7 $\pm$ 1.6 years respectively. This is similar to the report by Mohammed-Durosinlorun et al. (2021) in North West Nigeria and Mbamagnoua et al. (2023) in Brazzaville that the age at menarche in normal and sickle cell patients is 15.2 years and 15.9 years respectively.<sup>15,16</sup> A study by Betoko et. al., (2023) in Cameroon, reported a prevalence of 27.3% delayed puberty in girls with SCA, with the median age of menarche delayed by 2 years when compared to girls without SCA with a lower body mass index which was also recorded in the girls with SCA.<sup>17</sup> This is contrary to the study by Zemel et al., where the median age at menarche of SCA subjects was 13.2 years, despite a delayed puberty of 1 to 2 years.<sup>18</sup> This is also expected as the mean age at menarche in that environment is 12.25 years.<sup>19</sup> We cannot discount the immense effect of environment, socio economic status and nutrition on menarche and puberty at large. Interestingly, Singhal et al., reported the age at menarche in girls with HbSS as 15.4 (1.3) years, which was significantly later than girls with HbSC disease (13.7 (1.7) years) and those with HbAA haemoglobin (13.1 (1.3) years).<sup>20</sup> This may be attributed to the lower haemoglobin levels in HbSS as some studies have shown that decreased growth velocity in

children with SCA is independently associated with decreased haemoglobin concentration.<sup>10</sup>

Delayed physical and sexual characteristics in SCA patients is attributed to deficiencies and dysregulation in gonadal hormone levels.<sup>17</sup> El - Hazmi et al. (1992) noted a decrease in follicle stimulating hormone (FSH) and luteinizing hormone (LH) during early pubertal development among SCA patients which was associated with late puberty and therefore late menarche<sup>21</sup>

Most of the respondents (90%) had regular menstrual cycle of about 21 - 35days. Most of the SCA group had light menstrual flow rate when compared with HbAA group. This is similar to a study by Yoong et al., (2002) with 87% of SCA women having light to normal flow.<sup>22</sup> Mohammed-Durosinlorun et al. (2021) reported light menstrual flow in 71% of the SCD respondents.<sup>15</sup> This may be a protective compensatory mechanism developed to prevent blood loss in the already existing chronic anaemic state.

Interestingly, our study population showed a higher literacy rate among the SCA women compared to the HbAA women. This may be attributed to the poor prospect of marriage and employment due to the frequent ill health, stigmatization and its social consequences, largely resulting from the ignorant perception of SCD in the society. Bulgin *et al* (2018) reported that individuals living with SCA experience negative reactions and stigmatization from family and society at large.<sup>9</sup> This may contribute to the need for better educational qualifications so as to improve their chances in the labour market and in marriage. Moreover, the highly educated SCA patients are more likely to seek specialist care in our study center, being a tertiary hospital with a sickle cell clinic and easily accessible multi- specialist care.

## CONCLUSION

This study showed that individuals with sickle cell anaemia have delayed menarche compared to their HbAA counter parts. This may contribute to the psychological stress experienced in puberty by adolescent girls with sickle cell anaemia. However, the delay in menarche and in puberty generally may be of some advantage to these adolescent girls with Sickle cell anaemia, as menarche is viewed as a sign

of maturity and fertility in women. A delay in menarche may therefore delay early marriage and early sexual exposure, and increase the chances of further education.

## Recommendations

Early childhood commencement of sickle cell disease modifying drugs such as hydroxyurea, found to be positively associated with increased haemoglobin concentration, may improve growth velocity in these children, normalize growth parameters, thereby having a positive impact on puberty and menarche.

## Study Limitations

This study was carried out in a tertiary hospital; therefore, there may be some selection bias, and the findings may not fully represent what is obtainable in the community.

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## Conflicts of interest

There are no conflicts of interest.

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