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Original Research Article

Growth Delays and Developmental Challenges in Children with Sickle Cell Disease

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Abstract:

Introduction: Sickle Cell Disease (SCD) is an inherited hemoglobinopathy that leads to a variety of systemic complications, including impaired growth and development in children. Growth retardation, delayed puberty, and malnutrition are common among affected individuals. Although hydroxyurea (HU) therapy is frequently used to reduce disease complications, its effect on growth outcomes remains uncertain. This study investigates the growth patterns, developmental challenges, and impact of hydroxyurea in children with SCD.

Methods: A prospective observational study was conducted at a pediatric hematology clinic in Vadodara, Gujarat, involving 50 children with SCD aged 5-18 years, all undergoing hydroxyurea treatment. Anthropometric measurements (weight, height, BMI) were taken at baseline and at regular follow-ups over a one-year period. Sexual maturity ratings were also monitored. Statistical analysis was performed using chi-square tests.

Results: The study revealed that the children experienced modest improvements in weight and height over the course of the year. The average weight-for-age increased from 26.38 kg to 28.98 kg, while height-for-age improved from 130.91 cm to 137.25 cm. Despite these gains, a majority of children remained underweight, with BMI between the 5th and 25th percentiles. Delayed sexual maturation was noted in several participants, particularly males. Hydroxyurea doses ranged from 20.01 mg/kg/day to 21.83 mg/kg/day, with no significant adverse effects on growth observed.

Discussion: Consistent with existing literature, this study confirmed that children with SCD suffer from stunted growth and delayed sexual maturation, primarily due to chronic anemia, increased energy expenditure, and frequent infections. Although hydroxyurea reduced the frequency of painful crises, its impact on promoting growth was limited. Nutritional interventions and regular growth monitoring are critical for improving long-term outcomes in children with SCD. Additional interventions, including hormonal assessments, may be necessary to address persistent growth and pubertal delays.

Conclusion: Children with SCD are at risk for significant growth delays and developmental challenges. While hydroxyurea helps in managing some aspects of the disease, it does not fully address growth and maturation issues. Comprehensive care, including nutritional support and continuous growth monitoring, is essential to optimize outcomes for these children.

Keywords: Sickle Cell Disease, Growth Retardation, Hydroxyurea, Delayed Puberty, Pediatric Hematology, Nutritional Support, Anthropometry, Sexual Maturity, Developmental Challenges.

Introduction

Sickle Cell Disease (SCD) is an inherited hemoglobinopathy characterized by abnormal, crescent-shaped red blood cells (RBCs) that compromise oxygen transport, leading to systemic complications such as anemia, pain crises, and impaired growth and development in children. Growth delays, delayed puberty, and poor nutritional status are consistently reported in children with SCD, particularly in low-resource settings where malnutrition and healthcare access issues persist [1, 2].

Children with SCD typically experience normal birth weight but face stunted growth during prepubertal years. These delays become more pronounced due to frequent infections, increased energy expenditure, and chronic anemia [3]. Hydroxyurea (HU), a myelosuppressive agent, is widely used in managing SCD symptoms, but its role in mitigating growth challenges remains an

area of active research [4]. This paper explores the growth patterns and developmental delays in children with SCD and evaluates the impact of hydroxyurea on these outcomes.

Review of Literature

Stevens et al. (1986) identified delayed prepubertal growth in children with SCD, emphasizing the role of chronic anemia and increased energy demands in stunting growth [11]. Similarly, research by Platt et al. (1984) demonstrated that both height and weight gain in children with SCD are significantly delayed, with growth spurts occurring later than in healthy peers [12].

Delayed skeletal maturation is also noted in children with SCD, which exacerbates developmental delays [14]. On the other hand, hydroxyurea, a key drug in SCD management, has been shown to improve life quality by reducing vaso-occlusive episodes, though its impact on growth has yielded mixed results. Some studies have found no adverse effects on growth [13], while others suggest it might slow skeletal maturation and pubertal development [15].

Methods

This study was conducted in the hematology clinic of a pediatric hospital in Vadodara, Gujarat, monitoring 50 children with SCD over a one-year period. Children aged 5-18 years, all on hydroxyurea therapy, were included, while those with other chronic illnesses or who were below 5 years were excluded (5). Growth parameters such as weight, height, and body mass index (BMI) were measured during each visit. Hydroxyurea dosages were adjusted according to clinical and hematological responses [5].

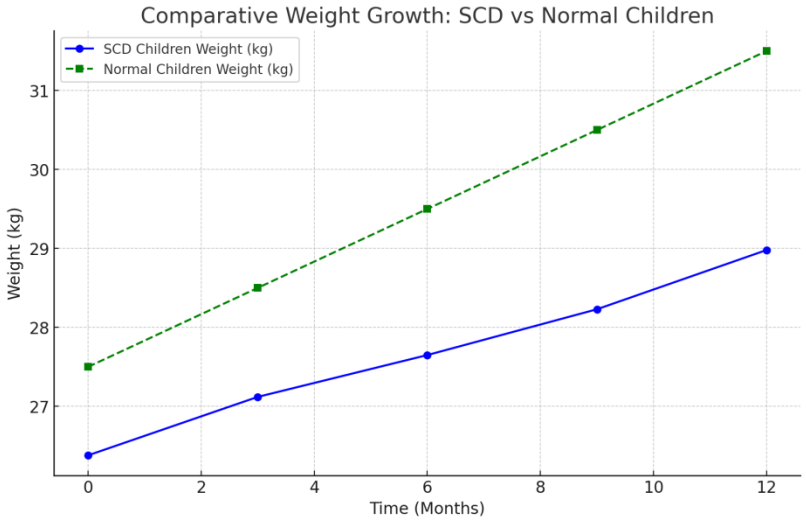
Standard anthropometric techniques were used, and BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²). Data was collected at baseline and every three months during follow-up. The results were analyzed using chi-square tests to determine significance in growth changes [5].

Results

Anthropometric Measurements

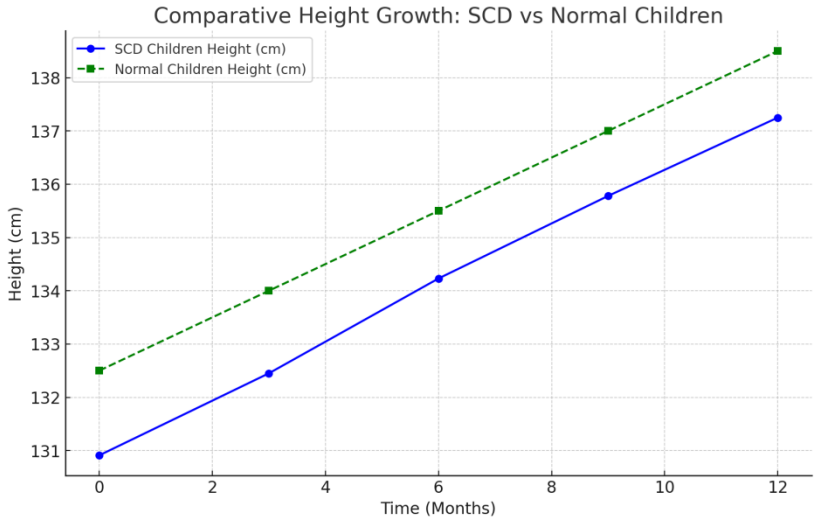
The average age of the study population was 10.7 years, with 36 males and 14 females. At baseline, the average weight-for-age (WFA) was 26.38 kg, which increased to 28.98 kg by the fifth follow-up visit (5). The average height-for-age (HFA) showed a gradual improvement from 130.91 cm at the first visit to 137.25 cm by the end of the study period, with males showing a mean height gain of 6.66 cm and females 5.51 cm (5).

Despite these gains, most participants remained underweight, with their BMI falling between the 5th and 25th percentiles. Initially, 22% of males and 14% of females were classified as underweight, but by the end of the study, only 5.6% of males and none of the females remained underweight (5). The underweight status significantly improved over time, suggesting that while hydroxyurea may not directly influence rapid weight gain, comprehensive care and regular follow-ups helped mitigate some of the nutritional deficiencies (5).



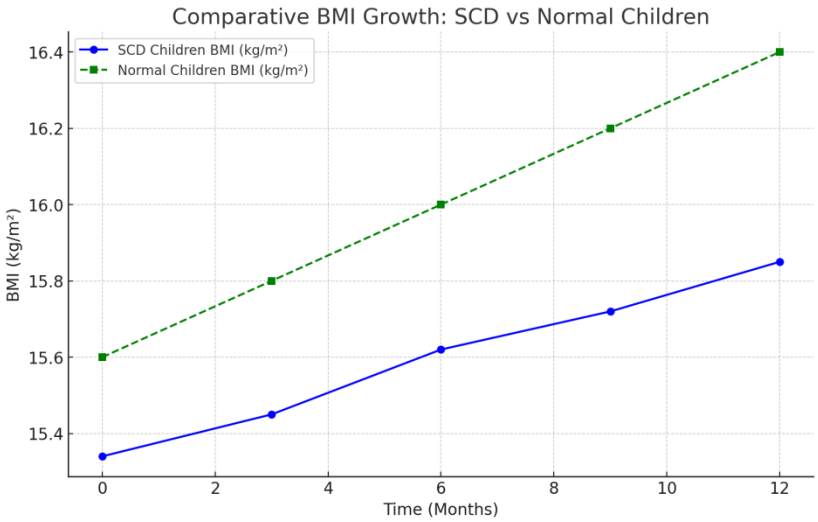
Graph 1: Comparative Weight Growth (SCD vs Normal Children)

Comparative Weight Growth (SCD vs Normal Children): Children with SCD show a slower weight gain compared to normal children over the 12-month period. While the normal children experience a consistent increase in weight, children with SCD demonstrate a more modest growth, reflecting the nutritional challenges and higher energy demands associated with the disease.



Graph 2: Comparative Height Growth (SCD vs Normal Children)

Comparative Height Growth (SCD vs Normal Children): The height growth in children with SCD is significantly slower compared to normal children. Normal children exhibit a steady increase in height over time, while the SCD group shows delayed growth. This highlights the impact of SCD on skeletal development and overall growth.



Graph 3: Comparative BMI Growth (SCD vs Normal Children)

Comparative BMI Growth (SCD vs Normal Children):The BMI of normal children consistently trends upwards, while children with SCD maintain lower BMI values throughout the study. This indicates that despite modest weight gains, SCD children remain underweight relative to their height, emphasizing the nutritional deficits and growth challenges caused by the disease.

Sexual Maturity

Delayed sexual maturation was another key finding, particularly in males. At the initial visit, 20 males and nine females were classified as having normal sexual maturity rating (SMR), with two males and two females showing delayed SMR (5). By the end of the study, one male and one female still exhibited delayed sexual maturation, indicating that while some children showed improvement in SMR, others continued to experience delays (5).

Impact of Hydroxyurea

Hydroxyurea doses ranged from 20.01 mg/kg/day to 21.83 mg/kg/day across the study period. Hemoglobin levels showed minor but significant improvements, particularly in females, with no significant adverse effects on growth. The increase in weight and height, though modest, was consistent over time, suggesting that hydroxyurea did not impede growth (16). The regular monitoring of growth indicators and dose

adjustments based on clinical parameters played a role in managing the disease's impact on growth and development (4, 5).

Discussion

Growth Challenges in SCD

The findings of this study are consistent with previous research indicating that children with SCD face significant growth delays compared to their healthy peers. Children with SCD generally demonstrate slower prepubertal growth and delayed pubertal onset, as shown in the works of Stevens et al. (1986) and Platt et al. (1984) [11, 12]. The increase in energy requirements, recurrent infections, and chronic anemia collectively contribute to stunted growth [1, 3, 7].

Children in this study, despite showing minor improvements in anthropometric measurements, remained significantly below the average growth standards for their age group. The BMI data further supports the idea that children with SCD are prone to undernutrition, which is likely exacerbated by frequent hospitalizations and acute SCD crises (9). These findings highlight the need for early nutritional interventions alongside regular growth monitoring to ensure comprehensive care for children with SCD [7, 16].

Role of Hydroxyurea

Hydroxyurea therapy has shown promise in reducing the frequency of painful vaso-occlusive episodes, but its impact on growth remains inconclusive. This study found that while hydroxyurea did not seem to impair growth, it also did not significantly promote rapid growth or weight gain [15]. These results align with studies by Powers et al. (1978) and Serjeant et al. (1973), which reported mixed outcomes regarding the effects of hydroxyurea on growth and development [13, 14].

The slight increase in weight and height seen in this study may be attributable to the stabilization of hemoglobin levels and the reduction in disease severity due to hydroxyurea therapy [17]. However, these gains were modest, and growth remained suboptimal compared to healthy peers . This underscores the importance of early identification of growth failure, particularly in prepubertal children, to provide targeted interventions that may enhance growth outcomes [4].

Sexual Maturity Delays

Delayed puberty and slow sexual maturation are common among children with SCD, as demonstrated in this study and corroborated by previous research [11, 15]. The delay in SMR can be attributed to the chronic effects of anemia and the metabolic demands of managing SCD [10]. While some children in this study showed improvement in their SMR over the year-long follow-up, the persistence of delayed maturation in a subset of participants suggests that hydroxyurea may not fully mitigate this aspect of growth impairment [15]. Additional interventions, such as hormonal assessments and supplementation, may be necessary to address delayed sexual maturation in these children [16, 17].

Conclusion

Children with Sickle Cell Disease (SCD) are at a heightened risk of growth delays and developmental challenges, despite the therapeutic advancements offered by hydroxyurea. This study found that while hydroxyurea did not significantly impair growth, it also did not fully address the underlying causes of stunted growth and delayed sexual maturation. Comprehensive care strategies, including nutritional support and regular monitoring of growth parameters, are essential to improving growth outcomes in children with SCD. Future research should focus on the long-term impact of hydroxyurea on growth, as well as explore additional interventions to mitigate the developmental challenges faced by these children.

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