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IMPACT OF SICKLE CELL DISEASE ON GROWTH / NUTRITIONAL STATUS OF PEDIATRIC POPULATION WITH REFERENCE TO WHO GROWTH STANDARDS

Paediatric Medicine

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ABSTRACT

Introduction: Hereditary hemoglobinopathies are most common group of monogenic disorders in the world. Among them, Sickle Cell Disease(SCD), a progressively debilitating genetic disease, impacts the significant amount of the world's poorest and most vulnerable population. India is estimated to have the second-highest burden of SCD. India accounts for 14.5% of total newborn with SCD. **Objective:** The objective of the study was to observe the impact of sickle cell disease on growth and nutritional status of the children suffering from the disease with reference to WHO growth standards. **Material and Method:** An observational and cross-sectional study was conducted in Index Medical College Hospital and Research Centre, Indore from September 2022 to February 2024. The study enrolled 100 paediatric patients with Sickle Cell Disease between 5 - 18 years age group. The anthropometric variables for all children were recorded and projected on WHO charts 2007 which was expressed in Z-scores and was gender specific. **Results:** The mean(SD) age of the SCD patients was 10.70 (3.38) years. Overall, 60% males and 40% females, about 81% from rural and 19% from urban area participated in the study. The haemoglobin of SCD patients was 6.09(01.79) gm/dl. About 71% population were classified as HbSS and the rest 29% as HbSC and HbS –beta-thalassemia genotype. Stunting was found in 63% of pediatric population suffering from SCD; wasting was found in 60% of pediatric population and severe underweight was found in 15% of the pediatric population. **Conclusion:** SCD is a chronic disease with financial, emotional and social burden on family, thus affecting growth and QOL of children and adolescents with a genetic disadvantage, so it is important as a pediatrician to provide proper social and genetic counselling to promote follow up, quality care, screening, vaccination to improve growth and reducing morbidity and complications.

KEYWORDS

sickle cell disease, nutritional status, growth, children, z-score.

INTRODUCTION

Sickle Cell Disease (SCD) is the most common among hemoglobinopathies. It is a lifelong inherited autosomal recessive blood disorder which impacts the significant amount of the population worldwide. It is resulted by a single nucleotide substitution, converting a glutamic acid codon to a valine codon at position 6th of the beta-globin subunit[1], which changes three dimensional structure, net charge and oxygen affinity of hemoglobin and converts it in an unstable form. This unstable hemoglobin is called Sickle haemoglobin (HbS) which polymerizes due to low oxygen tension and modifies discoid shape of normal red blood cell to crescent (sickle-like) form**.** The sickle shaped Red blood cells interact with endothelium and leucocytes and because of their unusual shape block the small vessels which lead to many clinical complications like haemolytic anemia and vaso-occlusive events[2]

The most common types of Sickle hemoglobinopathy are HbSS, HbS Beta thalassemia and sickle cell trait. When an individual has a pair of sickle gene inherited from both the parent then it forms homozygous sickle cell disease (HbSS). When an individual possesses only one HbS gene from either of the parents then it is called heterozygous condition known as sickle cell trait (SCT) (HbAS). These individuals are carriers of Sickle Cell Disease. The homozygous disease is more serious then heterozygous form and often results in severe complications and mortality[3]. Sickle beta thalassemia is an inherited form of sickle cell disease that affects red blood cells both in the production of abnormal haemoglobin, as well as the decreased synthesis of beta globin chains.

Worldwide, approximately 7% population is affected by this disease. About 300,000-500,000 infants take birth with a hemoglobinopathy per year. It consists of either Sickle cell syndromes or Thalessemia. According to WHO, Sickle cell syndrome accounts for 200,000 (70%) newborn cases globally[4,5]. The SCD is more frequently found in Africa, especially in sub-Saharan Africa (SSA). Half of the global burden of SCD is carried by India, Nigeria and the Democratic Republic of Congo. The second highest burden of the disease is found in India after Nigeria[6]. About 14.5% of the total newborns, born with SCD are found in India[7]. The sickle cell gene has been shown to be prevalent among socioeconomically disadvantaged ethnic groups; scheduled tribe, scheduled caste and backwards castes in India[8]. Madhya Pradesh has the highest prevalence of SCD; about 27 districts fall under sickle cell belt and prevalence of HbS varies from 10-33%.

The objective of the study was to observe the impact of sickle cell disease on growth and nutritional status of the children suffering from the disease.

MATERIALS AND METHOD

An observational and cross-sectional study was conducted in the Paediatrics department of a tertiary care hospital during the period of 18 months from September 2022 to February 2024. The enrolled paediatric population was consisted of male and female children between 5 to 18 years of age group with confirmed clinical and laboratory diagnosis of SCD attending OPD, IPD and PICU of the hospital.

Inclusion criteria:

1. Known cases or recently diagnosed cases of sickle cell disease in children of age group 5-18 years of either sex attending OPD, IPD and PICU.
2. Children whose parents gave informed consent to participate by signing in consent form.

Exclusion criteria:

1. Cases of nutritional deficiency anaemia, thalassemia and other haemoglobin abnormalities.
2. Patients with chronic kidney and liver disease.
3. Patients with co-morbidities like congenital or rheumatic heart disease and chromosomal abnormalities.

A self-structured questionnaire was used to obtain the socio-demographic characteristics. For growth assessment height, weight and BMI were measured. The anthropometric variables for all children

were projected on WHO charts 2007 which was expressed in Z-scores and was gender specific.

HAZ (Height for age Z-score):
This reflected the growth achieved in height while standing at a particular age. This score was used to determine stunting. For a Z-score of <-3SD, stunting was noted as severe. Z-score between -3 to -2SD was noted as mild stunting; -2 to +2 was considered normal and more than +2SD was noted as very tall.

WAZ (Weight for age Z-score):
This reflected body weight in a particular age. This score showed if a child was underweight or severely underweight. Between -3 to -2SD, it was underweight. When this Z –score was < -3SD, it was called severe underweight. For children more than 10 years, WAZ score could not be computed because WHO charts were only for children younger than 10 years of age.

BMIZ (BMI for age):
The BMI for age was calculated from weight and height of child and plotting the given value on WHO chart. Severe underweight was considered for < -3SD; underweight was noted between -3 to -2SD and normal between -2 to +2SD.

The statistical analyses were performed using the Statistical Package SPSS-20. P-value for frequency percentage comparison was calculated (chi-square test). P-value<0.05 was considered statistically significant. The Ethical approval was obtained from the Institutional Ethics Committee.

RESULTS

The mean (SD) age of the pediatric population with confirmed diagnosis of SCD was 10.70 (03.38) years. Overall, 60% males and 40% females about 81% from rural area and 19% from urban area were participated in this study. The socioeconomic status of 92% population was low (Table-1). The mean (SD) haemoglobin of SCD population was 6.09(01.79) gm/dl. About 40% of the pediatric population had diagnostic confirmation since two to five years, while 60% population were screened first time for SCD after clinical examination and hospitalization and only 15% of the families had known patient history of SCD. Out of total pediatric population about 71% children and adolescents with SCD were classified as HbSS and the rest 29% were associated with HbAS and sickle–beta thalassemia phenotype (Table-1).

Table 1:Socio-demographic Characteristics Of The Study Pediatric Population

S.NO.	PARAMETERS	PATIENTS WITH SCD(N=100)
1	**Age** mean (SD) years	 10.70(03.38)
2	**Gender** (I) Male (%) (II Female (%)	 60.00 40.00
3	**Socioeconomic status** (I) High (%) (II) Middle (%) (III) Low (%)	 - 8.00 92.00
4	**Caste** (I)Scheduled Tribe (%) (II)Scheduled Caste (%) (III)Other Backward Castes (%) (IV) Other (%)	 58.49 15.09 20.75 05.66
5	**Place of residence** (I) Urban (%) (II) Rural (%)	 19.00 81.00
6	**Haemoglobin** Mean (SD)	 06.09(01.79)
7	**Diagnosis** (I)Pre diagnosed (II)Diagnosed recently	 40.00 60.00
8	**Phenotype** (I) Sickle cell disease (II) Sickle cell trait (III) Sickle beta thalassemia	 71.00 14.00 15.00

Table 2: Anthropometric Parameters Of The SCD Pediatric Population

S.NO	PARAMETERS	FREQUENCY
1	WEIGHT - mean (SD) kg	26.47 (10.41)
2	HEIGHT - mean (SD) cm	129.02 (18.51)
3	BMI – mean (SD) kg/m^2	15.31(02.42)

Anthropometric Indices Of Pediatric Population
In paediatric population with SCD, the mean (SD) values were 26.47(10.41) kg, 129.09 (18.51) cm, and 15.31(02.42) kg/m^{2}for weight, height, and BMI respectively as shown in Table-2.

Height For Age Z-score (HAZ):
In this series, stunting was found in 63 % of pediatric population suffering from SCD, where 16% population was severely stunted with height-for-age (HAZ) score less than -3 SD. About 47% population was stunted with HAZ score between -3 to -2 SD (p value <0.0001). Only 35% population was found normal with HAZ score between -2 to +2 SD; whereas 2% population was tall with HAZ score between +2 to +3 SD (Table -3; Graph-1A).

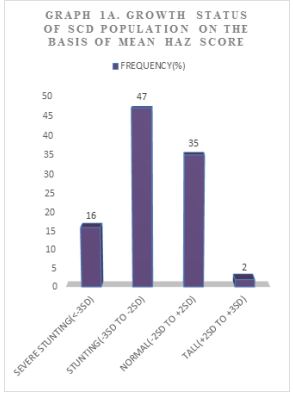
Weight For Age Z-score (WAZ):
In the present study, wasting was found in 60 % of pediatric population with SCD, where 20% population was severely underweight with weight-for-age (WAZ) score less than -3 SD. About 40% population was underweight with WAZ score between -3 to -2 SD (p value < 0.0001). About 40% population was found normal with WAZ score between -2 to +2 SD; whereas no one in the pediatric population had a weight for age score WAZ between +2 to +3 SD or more than +3SD (indicating overweight/obesity) no matter the age (Table-3; Graph-1B).

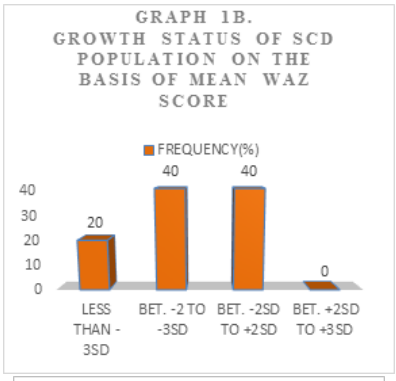
BMI For Age Z-score (BMIZ):
In this series, severe underweight was found in 15 % of SCD population with BMIZ scores less than -3SD. Only 14% of the population were underweight (p value<0.0001). A large number of populations about 71% were normal having BMIZ scores between -2 to +2 SD. In this study no one had BMI score more than +2SD indicator of overweight or obesity (Table -3; Graph-1C).

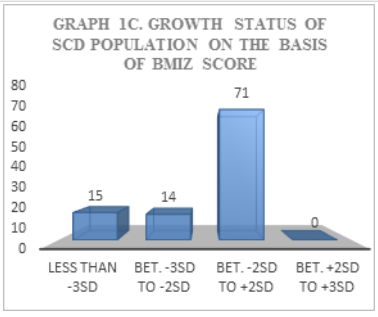
Table 3: Growth/nutritional Status Of The Pediatric Population With SCD (mean Z-scores).

S.NO	VARIABLES (Z SCORES)	PATIENTS WITH SCD N%	P VALUE
1	**HEIGHT FOR AGE (HAZ)** (i) Severe stunting (< -3) (ii) Stunting (-3 to-2) (iii) Normal (-2 to +2) (iv) Tall (+2 to +3)	 16 47 35 2	 <0.0001
2	**WEIGHT FOR AGE(WAZ)** (i) Severe underweight (<-3) (ii) Underweight (-3 to -2) (iii) Normal (-2 to +2) (iv) Overweight (+2 to +3) (v) Obese (>+3)	 20 40 40 0 0	 <0.0001
3	**BMI FOR AGE (BMIZ)** (i) Severe under weight (<-3) (ii) Underweight (-3 to -2) (iii) Normal (-2 to+2) (iv) Overweight (+2 to +3) (v) Obese(>3SD)	 15 14 71 0 0	 <0.0001

Number of cases- 100 *WAZ presented for children upto 10 years (n-52).







DISCUSSION

Sickle Cell Disease resulted in long lasting anemia with blood vessels occlusion. Thus it affected many systems including underweight, small height, retarded growth, and increased diameter of chest along with pain in fingers and protruding facial bones[9]. Endocrine dysfunction and nutritional deficiencies are the other cause which retarded the growth in one or more of the anthropometric indices like BMI, height and weight[10, 11]. Growth retardation concerns weight as well as height in mostly 50% of children with SCD.

Our objective was to measure growth in form of anthropometric measurements like height, weight and BMI of paediatric population with SCD. In our study, WHO growth charts were taken for z-score references. Fadhil *et al*[12] also defined stunting, wasting and underweight as HAZ, WAZ and BMIZ scores < -2 SD from the median WHO standard.

In paediatric population, about of 63 % population was found to be stunted, 60% undernourished and 29% were underweight. Similar results as in our study population was also observed by Kazadi *et al*[13] (stunting 10.5%, wasting 50.3% and underweight 47.7%) in Congo. Esezobor *et al*[14] (11.6%) in Nigeria and Charlotte *et al*[15] (9.1%) in Cameroon observed relatively low frequencies of stunting. These findings were different from our data.

Under nutrition was represented by stunting (63%) in the present study, out of which 16% were severely stunted. It was concordant with the study of Charlotte *et al*[15]. Children in Ghana (25.8)[16] and the USA (stunting 22%)[17] were the other examples of high percentage of stunting.

Male gender and age group (08-12years) were the most affected in terms of growth retardation. Cox *et al*[18] in their study found the same pattern responsible for growth retardation. The study of Chawla *et al*[19], Esezobor *et al*[14] and Islam *et al*[20] concluded that there is a significant difference noticed between SCD population and healthy population. With weight specifically being affected at an earlier age in female and height at an earlier age in male. This result may be attributed to the delay in pubertal attainment in children with SCD[21,22]. Malnutrition is characterised by retarded growth which has a negative impact on pubertal growth[18, 19]. Kazadi *et al*[13]noticed that population with SCD suffered from chronic form of malnourishment hence resulted in smaller size, lower weight for height or BMI.

Underweight was the next criteria to estimate nutritional status. In this series, 20% were severely undernourished. According to WAZ, wasting was found in more than half (60%) in our study population. This result is similar to previous study by Kazdi*et al*[13]. In SCA population underweight percentage (61.5%) was higher than trait group (35.7%), while it was lower than sickle beta thalassemia group (71.4%). High percentage of underweight (22 to 50%)[13,14,17,21] was also noticed by many authors. Children with SCA (HbSS) and sickle beta-thalassemia have the most severe impairment in growth[14]. According to BMI, underweight were noted in 29 % of SCD population. The sickle beta thalassemia percentage of underweight was higher (46.7%) as compared to children with SCA (35.7 %). Kazadi *et al*[13] in Democretic Republic of Congo, and Kamgaing *et al*[23] in Gabonese children reported more stunting percentage in male gender.

CONCLUSIONS

In central India, particularly in Madhya Pradesh, low number of diagnostic facilities or dedicated sickle cell disease clinics exist in public health establishment. Most of the tribal population with SCD rely on the primary health care facilities in rural and often remote areas. There is insufficient knowledge about the disease, its severity and its impacts on growth in general. Therefore, measuring the nutritional status in children with sickle cell disease might provide the degree of severity and significant attention to the health outcome so that the burden of SCD patients and their families to achieve as normal life as possible, can be minimize.

The advent of new born screening, newer oral medication and better general medical care in regards of safer blood transfusion and antibiotics will add in decreasing the rate of recurrence and severity of the SCD related complications and hence decrease the cost for health care.

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