International Journal of Science and Healthcare Research
Vol.4; Issue: 4; Oct.-Dec. 2019
Website: www.ijshr.com
Original Research Article *ISSN: 2455-7587*

Assessment of Cormic Index in Sickle Cell Disease Subjects and Its Association with Clinical Severity

Dr. Mainak Bardhan[1], Ipsita Das[2], Romesh Tiwari[3], Dr Dnyanesh Amle[4], Dr Debapriya Rath[5]

[1]House Surgeon, Pt JNM Medical College, Raipur (CG)
[2]Research Scholar, Department of Biochemistry, Pt JNM Medical College, Raipur (CG)
[3]MBBS Final Year, Pt JNM Medical College, Raipur (CG)
[4]Assistant Professor, Department of Biochemistry, AIIMS, Nagpur
[5]Assistant Professor, Department of Biochemistry, Pt JNM Medical College, Raipur (CG)

Corresponding Author: Dr Debapriya Rath

ABSTRACT

Sickle cell anemia is a complex pathophysiologic single gene defect genetic disorder with a wide spectrum in the severity of the disease. Decomposing stature into its major components is a useful strategy to assess antecedents of disease, morbidity, and death in adulthood. CORMIC INDEX is calculated as (Sitting Height / Height) × 100. Leg length relative to total body proportions is a good indicator of overall growth reserve capacity of a person or a group of people. Previous studies in sickle cell patients have shown evidence of growth failure and are associated with delayed puberty. There is no study correlating growth pattern in sickle cell disease patients with the CORMIC index, in our study we tried to do this. The main conclusion in which we arrived is that "there is no significant correlation between the severity of sickle cell anemia and Cormic index", however, sickle cell affects many growth parameters i.e. height, weight, and sitting height.

Keywords: Cormic index, Sickle cell Anemia, Hydroxyurea, Chhattisgarh

INTRODUCTION

Sickle cell disease, one of the world's commonest single-gene disorders, was first described by Herrick in 1910, who linked his patients' symptoms to abnormally shaped erythrocytes in the blood. [1,2] Sickle cell disease (SCD) is a highly variable condition. [3] It is caused by a mutation in the β-globin gene. An Adenine (A) to Thymine (T) substitution (GAG to GTG transversion) in the 6th codon of the β-globin gene specifies the insertion of Valine in place of Glutamic acid. [4]

India is known to be home of over 50 % of global sickle cell disease patients. [5] The World Health Organization (WHO) estimates that hemoglobinopathies cause 3.4% of deaths worldwide in children younger than five years old (2008). In addition to the close geographic correlation between the frequency of the Haemoglobin S gene in populations and the historic incidence of malaria, evidence for the partial resistance of carriers to all forms of Plasmodium falciparum malaria has been reported in many populations. [6,7]

Bone marrow infarction is a well-recognized complication of sickle cell disease. [8-10] Sickle cell disease is also associated with an impaired oxygen delivery system to skeletal muscle that could alter the ATP production process. Exercise induces intramuscular necrosis more in sickle cell disease patients as compared to those not having sickle cell disease. [11] SCD also results in impaired muscle force production and resistance to fatigue, independent of muscle mass. SCD is also associated with high fatigability when exercise intensity is high. [12] There is also the presence of persistent red marrow in the axial and appendicular skeleton, avascular necrosis of femur head, bone infarcts, septic arthritis and tubercular infection of bone in SCD. [13] SCD is associated with microvessel rarefaction, decrease in

capillary tortuosity, and widening of microvessel diameter. There are also changes in fiber type distribution, muscle atrophy, an increase in satellite cell number, and a decrease in the activity of creatine kinase and several oxidative enzymes. [14] As far as genetics are concerned, the occurrence of osteonecrosis in sickle cell disease patients is under the control of some modifier genes. BMP 6 (bone morphogenetic protein) has been reported as associated with osteonecrosis in sickle cell anemia. [15] Osteoporosis (OP) and low bone mineral density (BMD) or osteopenia is now being recognized as a common bone complication in both children and adults with SCD. The prevalence of low BMD in SCD ranges from 30 to 80%. [16-19] Cortical infarction of the diaphyses of the long bones, a well-documented complication of sickle cell anemia in children, leads to gross roentgenographic changes that have been described by many workers. [20-22] Avascular necrosis is an important chronic complication of SCD in developed countries. Hernigou et al (1991) recorded a 32.5% incidence of femoral head involvement in 160 patients with either homozygous or heterozygous SCD. Of this 80 % had pain and impaired function, with secondary osteoarthritis in 30%; 16% had undergone surgery. [23]

Decomposing stature into its major components is proving to be a useful strategy to assess the antecedents of disease, morbidity, and death in adulthood. [24-27] Human leg length (femur + tibia), sitting height (trunk length + head length) and their proportions, for example, (leg length/stature), or the sitting height ratio (sitting height/stature × 100), among others, are associated with epidemiological risk for overweight (fatness), coronary heart disease, diabetes, liver dysfunction, and certain cancers. [23]

Sitting height when measured alongside standing height can provide information about the body's relative proportion. Some studies suggest that the proportions of leg and trunk length can be affected by socio-economic status and growth in childhood. Impaired growth in childhood reduces growth in a way that has a disproportionate effect on leg length. Individuals from the lower socio-economic backgrounds, which would more likely include individuals who are less well-nourished and have a poorer diet, as a consequence have a proportionately shorter leg compared with well-nourished individuals from a higher socioeconomic background.

Human beings follow a cephalo-caudal gradient of growth, the pattern of growth common to all mammals. A special feature of the human pattern is that between birth and puberty the legs grow relatively faster than other post-cranial body segments. [24]

CORMIC INDEX is calculated as (Sitting Height / Height) × 100. It defines the percentage of total stature that is comprised of head and trunk. The remaining portion of the body will be the length of the legs. The lower the CORMIC INDEX the relatively longer the legs are.

CORMIC INDEX allows individuals with different heights to be compared in terms of the percentage of the body that is composed of the relative length of legs. Because it is Sitting Height dependent, this measure can be overestimated in individuals with high levels of gluteal-femoral fat, therefore underestimating the relative contribution of the lower limb to total stature. [23] There are international references [24] that allow the comparison of any values and the conversion of CORMIC INDEX raw data into percentiles and z-scores.

Eveleth and Tanner [28,29] published data for body proportions and leg length, estimated via the sitting height ratio, from dozens of human populations, distributed across most geographic regions of the world. The CORMIC INDEX is a commonly used measure of body proportion.

Mean CORMIC INDEX for populations of adults varies from minimum

values, *i.e.*, relatively longest legs for Australian Aborigines (CORMIC INDEX = 47.3 for men and 48.1 for women) to the maximum CORMIC INDEX values, *i.e.*, relatively shortest legs for Guatemala Maya men and Peruvian women (CORMIC INDEX = 54.6 and 55.8). [20]

It has been shown experimentally that mice and other non-human mammals raised in warmer temperatures experience greater bone tissue growth and longer limb bones. The usual explanation for this is greater vascularization, allowing for greater oxygen and nutrient perfusion. [30] Iodine deficiency during infancy and childhood results in reduced leg length, especially the distal femur, the tibia, and the foot. [31]

Plasticity refers to the concept that the development of the phenotype of an organism is responsive to variations in the quality and quantity of environmental factors required for life. [32] Human growth is highly plastic during the years of growth and development, responding to the overall quality of living conditions. [33] From the perspective of developmental plasticity, leg length, both in terms of absolute size and relative to total stature, is an indicator of the quality of the environment for growth during infancy, childhood and the juvenile years of development. [39] Improved nutrition during infancy and childhood result in a greater increase in Leg Length than in total height or weight. [34]

The Reserve Capacity Hypothesis posits that during human growth and development, the somatic and cognitive systems usually "overshoot" their minimally necessary capacity for sustaining a life of the individual. By overshooting this necessary capacity, an individual has reserve capacity which may be channelled into greater growth, better health, more successful reproduction, social and economic success, and lower rates of senescence. Leg length relative to total stature may be one indicator of overall reserve capacity of a person or a group of people. [35-37]

Previous studies of sickle cell disease patients have demonstrated clear evidence of growth failure, in terms of height as well as weight in sickle cell disease patients associated with delayed puberty. In one study, the decline in growth was unrelenting throughout childhood and adolescence for males, especially for weight and BMI, whereas for females, growth status in length/height and weight declined during childhood and some recovery occurred with the onset of puberty. [38]

There have been many studies about growth and growth failure in sickle cell disease, but studies correlating growth in sickle cell disease patients with CORMIC INDEX, which is a good tool for indicating growth patterns have not been conducted yet. Our study tried to correlate CORMIC INDEX with growth in sickle cell disease patients.

MATERIALS & METHODS

This was an Observational, analytical case-control study with cross-sectional data collection conducted in the Department of Biochemistry, Pt. J.N.M. Medical College, Raipur, and Dr. B. R. Ambedkar Memorial Hospital, Raipur and OPD of Sickle Cell Institute Chhattisgarh, Raipur.

Ethical clearance was obtained from the Institutional Ethical Committee of Pt. J.N.M. Medical College, Raipur C.G. Subjects in this study includes the patients with SCD, visiting the OPD of Sickle Cell Institute Chhattisgarh, Raipur. Our study is a continuous response variable from independent control and experimental subjects with 1 control(s) per experimental subject. They were divided in

Study groups:

Group 1-Haemoglobin SS subjects without Hydroxyurea therapy (n=40)

Group 2-Haemoglobin SS subjects undergoing Hydroxyurea therapy (n=40)

Group 3- Haemoglobin AS subjects (n=40)

Group 3-Healthy control subjects (Haemoglobin AA) (n=40)

Inclusion criteria:

- Age 5 years to 15 years.
- Confirmed Haemoglobin SS by electrophoresis and HPLC.
- Subjects who are in steady-state, that is, absence of any crisis in the preceding four weeks, no recent drop in the hemoglobin level, and absence of any symptoms or signs attributable to acute illness.
- Children who were not taking medications known to affect growth, for example, steroids.
- Signed, informed consent of the caregiver.

Exclusion criteria:

- Children with a congenital cardiac abnormality, chronic renal disease, or abnormal chest wall deformity or chronic respiratory disorder.
- Children with postural deformity.
- Children with a history of cerebrovascular accident.
- Sickle cell anemia patients with a history of long-term transfusion therapy.
- Refusal of consent.

Data collection

After obtaining informed written consent from the guardian/ parents, a detailed history of all the subjects participating in the study was elicited and their thorough clinical examination was done.

5ml of peripheral venous blood was obtained from each subject after overnight fasting through phlebotomy. 2 ml of blood was separated in a vial containing EDTA for performing haematological test and rest 3 ml of blood without any anticoagulant was used for performing biochemical test.

Biochemical tests: Biochemical analysis was performed on ILAB 600 Clinical chemistry analyzer, Werfen (Belgium) as per manufacturer protocol Total bilirubin (T bilirubin), conjugated/direct bilirubin (D bilirubin), Aspartate transaminase (AST), Alanine transaminase (ALT), alkaline phosphatase (ALP), serum sodium and potassium were performed.

Hematological tests: The diagnosis of the of sickle cell disease (Haemoglobin SS), sickle cell trait (Haemoglobin AS) and normal controls (Haemoglobin AA) were established by performing hemoglobin electrophoresis and High-performance liquid chromatography (HPLC) using Haemoglobin Variant ® (Bio-Rad Laboratories, Hercules, CA, USA).

Haematological analysis like haemoglobin concentration, RBC count, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Corpuscular Haemoglobin (MCH), Red blood cell Distribution Width (RDW), Total Leukocyte Count (TLC), Haematocrit and Platelet Count were performed on Auto Haematology Analyzer BC-3000 Plus (Mindray).

Measurement of height- Stadiometers are devices specifically designed for the accurate measurement of height, and when used with care yield data of the highest quality. All anthropometric measurements were made by one observer. Stature was measured with a stadiometer, with the subject standing erect, heels together, and line of vision directed horizontally.

Measurement of weight- Subjects' weights were measured barefooted and wearing light clothing on a single bathroom weighing scale.

Measurement of Sitting Height- Sitting height was measured using the sitting-height table, with the subject sitting with their back straight, head in the sagittal plane positioned in the Frankfort horizontal plane, the shoulders relaxed and upper surface of the thighs horizontal. A right angle was formed between the thighs and the backs of the calves. The head plate was brought into firm contact with the vertex. Sitting height will be measured from the vertex of the head to the seated buttocks. The various linear measurements will be taken three times and the mean will be recorded.

Derivation of Subischial Leg Length- It is expressed as the difference between height/length and sitting height.

Derivation of Body Mass Index- The body mass index is expressed as weight in Kg/height in metre^2 (Kg/m^2).

Derivation of CORMIC Index- It is expressed as (Sitting height/height) × 100

Investigation (as described in sample collection):

- Solubility test
- Haemoglobin Electrophoresis
- HPLC
- Routine hematology parameters
- Routine biochemical parameters

Statistical Analysis

A proper statistical analysis was done at the end of the test. Data are expressed as mean±S.D. and range, Kolmogorov-Smirnov analysis was used to assess if the data was parametric or non-parametric. To compare frequency distribution in various groups chi-square test or Fischer's exact probability tests were used. To compare categorical variables in various groups ANOVA followed by post hoc Tukey's HSD test were used. P-value <0.05 are treated as statistically significant. SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA were used to perform the statistical analysis.

RESULT

Out of 160 patients who took part in the study majority(53.6%) were from 6 to 10years of age group followed by 11 to 15years and </=5 years.

		Group				Total
	Age (years)	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	HbAS	HbAA	
	</=5	4	2	1	0	7
		10.0%	5.0%	2.5%	.0%	4.4%
	6-10	20	22	25	19	86
		50.0%	55.0%	62.5%	47.5%	53.8%
	11-15	16	16	14	21	67
		40.0%	40.0%	35.0%	52.5%	41.9%
Total		40	40	40	40	160
		100.0%	100.0%	100.0%	100.0%	100.0%

Table-1 Age distribution in study groups was compared using Chi-square test, no significant difference was found in the distribution indicating that groups were matched for age distribution

		Gender		Total
	Group	F	M	
	HbSS (Without hydroxyurea)	26	14	40
		28.3%	20.6%	25.0%
	HbSS (With hydroxyurea)	20	20	40
		21.7%	29.4%	25.0%
	HbAS	18	22	40
		19.6%	32.4%	25.0%
	HbAA	28	12	40
		30.4%	17.6%	25.0%
Total		92	68	160
		100.0%	100.0%	100.0%

Table 2- Gender distribution in study groups was compared using Chi square test, No significant difference was found n the distribution indicating that groups were matched for gender.

		N	Mean	S.D.	P value
No. of BT	HbSS (Without hydroxyurea)	40	2.325	5.00967	
	HbSS (With hydroxyurea)	40	2.7	6.96217	0.004
	HbAS	40	0	0	
	HbAA	40	0	0	
	Total	160	1.2562	4.43293	

Table 3

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Sig.
No. of BT	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	-0.4	1.0
		HbAS	2.3	0.1
		HbAA	2.3	0.1
	HbSS (With hydroxyurea)	HbAS	2.70000*	0.0
		HbAA	2.70000*	0.0
	HbAS	HbAA	0.0	1.0

Table 4

Table 3-4 Comparison of no. of blood transfusion was performed between study groups significant difference was found between frequency of blood transfusions between groups. Further on post hoc analysis it was found that frequency of blood transfusion was significantly higher in HBSS with hydroxyurea compared to HbAS and Hb AA (p<0.0001 for both).

		N	Mean	S.D	P-Value
Height (cm)	HbSS(Without hydroxyurea)	40	121.40	19.27	
	HbSS(With hydroxyurea)	40	124.22	16.86	
	HbAS	40	121.50	9.21	<0.0001
	HbAA	40	134.30	12.51	
	Total	160	125.36	15.75	

Table 5

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Sig.
Ht (cm)	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	-2.8	0.8
		HbAS	-0.1	1.0
		HbAA	-12.90000*	0.0
	HbSS (With hydroxyurea)	HbAS	2.7	0.8
		HbAA	-10.07500*	0.0
	HbAS	HbAA	-12.80000*	0.0

Table 6

Table 5,6A comparison of mean height was performed between study groups significant difference was found in mean height between groups. Further on post hoc analysis, it was found that mean height was significantly less in HBSS with hydroxyurea and Hb SS without hydroxyurea therapy and HbAS compared to that in HbAA subjects (p<0.0001 for all).

		N	Mean	S.D	P-Value
Sitting Height (cm)	HbSS (Without hydroxyurea)	40	62.58	10.46	0.003
	HbSS (With hydroxyurea)	40	63.33	7.03	
	HbAS	40	64.78	5.53	
	HbAA	40	69.70	4.85	
	Total	160	65.09	7.74	

Table 7

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Sig.
Sitting Ht (cm)	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	-0.8	1.0
		HbAS	-2.2	0.5
		HbAA	-7.12500*	0.0
	HbSS (With hydroxyurea)	HbAS	-1.5	0.8
		HbAA	-6.37500*	0.0
	HbAS	HbAA	-4.92500*	0.0

Table 8

Table 7,8 Figure 2 A comparison of sitting height was performed between study groups significant difference was found between sitting height in study groups. Further on post hoc analysis it was found that sitting height was significantly less HBSS with hydroxyurea and Hb SS without hydroxyurea therapy and HbAS compared to that in HbAA subjects (p<0.0001 for all).

		N	Mean	S.D	P-Value
Weight (Kg)	HbSS (Without hydroxyurea)	40	22.20	8.96	
	HbSS (With hydroxyurea)	40	22.43	7.63	
	HbAS	40	19.85	4.11	<0.00001
	HbAA	40	25.95	7.64	
	Total	160	22.61	7.56	

Table 9

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Sig.
Wt (Kg)	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	-0.2	1.0
		HbAS	2.4	0.5
		HbAA	-3.8	0.1
	HbSS (With hydroxyurea)	HbAS	2.6	0.4
		HbAA	-3.5	0.1
	HbAS	HbAA	-6.10000*	0.0

Table 10

Table 9,10, A comparison of weight was performed between study groups significant difference was found between mean weight of study groups. Further on post hoc analysis it was found that mean weight was significantly lower in HbAS subjects compared to HbAA (p=0.001).

		N	Mean	S.D	P-Value
Cormic index	HbSS (Without hydroxyurea)	40	51.54	2.30	
	HbSS (With hydroxyurea)	40	51.15	1.86	
	HbAS	40	53.30	1.87	<0.0001
	HbAA	40	52.04	2.41	
	Total	160	52.01	2.26	

Table 11

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Sig.
Cormic index	HbSS (Without hydroxyurea)	HbSS (With hydroxyurea)	0.4	0.9
		HbAS	-1.76500*	0.0
		HbAA	-0.5	0.7
	HbSS (With hydroxyurea)	HbAS	-2.14750*	0.0
		HbAA	-0.9	0.2
	HbAS	HbAA	1.26000*	0.0

Table 12

Table 11,12:A comparison of cormic index was performed between study groups significant difference was found between cormic index of study groups. Further on post hoc analysis it was found that cormic index was significantly lower in HbSS without hydroxyurea and HbSS with hydroxyurea compared to HbAS ($p<0.0001$ for both). Also, Cormic index was significantly lower in HbAS subjects compared to HbAA ($p<0.0001$).

DISCUSSION

CORMIC INDEX allows individuals with different heights to be compared in terms of the percentage of the body that is composed of the relative length of legs [40]

There are international references [24] that allow the comparison of any values and the conversion of CORMIC INDEX raw data into percentiles and z-scores.

Cormic index was chosen because other anthropometric parameters do not give an appropriate amount of information about development.

Study groups were matched for age and gender and there was no significant difference in age and gender between study groups.

A comparison of mean height was performed between study groups. A significant difference was found in height between groups. Mean height was significantly less in Hb SS with hydroxyurea and Hb SS without hydroxyurea therapy and Hb AS compared with Hb AA subjects.

A comparison of weight was performed between study groups; a significant difference was found between mean weight of study groups. It was found that mean weight was significantly lower in HbAS subjects compared to Hb AA.

A comparison of sitting height was performed between study groups; a significant difference was found between sitting height in study groups. It was found that sitting height was significantly less in Hb SS with hydroxyurea therapy, Hb SS without hydroxyurea therapy and Hb AS compared to that in Hb AA subjects.

A comparison of Cormic index was performed between study groups; significant difference was found between Cormic index of study groups. It was found that Cormic index was significantly lower in Hb SS without hydroxyurea and HbSS with hydroxyurea compared to Hb AS, also Cormic index was significantly lower in HbAS subjects compared to Hb AA.

Correlation analysis of the severity of SCD and Cormic index was performed using Pearson's correlation analysis. No significant correlation was found between the two parameters.

CONCLUSION

In conclusion, it was found that height, weight, sitting height, Cormic index was significantly lower in subjects with Hb SS with hydroxyurea, Hb SS without hydroxyurea and Hb AS compared to that of control group i.e. Hb AA. The correlation between the severity of sickle cell disease and Cormic index was not found to be significant. Furthermore, studies can be conducted to find correlation between severity of sickle cell disease and other anthropometric or biochemical parameters. Improving the nutritional status and growth

parameters could have a favorable impact on clinical course & prognosis of the children with sickle cell disease. The findings of this study may help to take steps in improving anthropometric growth parameters in children suffering from sickle cell disease.

REFERENCES

1. Nathan D. Book Review Disorders of Hemoglobin: Genetics, Pathophysiology, and Clinical Management Edited by Martin H. Steinberg, Bernard G. Forget, Douglas R. Higgs, and Ronald L. Nagel. 1266 pp., illustrated. New York, Cambridge University Press, 2001. $275. 0-521-63266-8. New England Journal of Medicine. 2001;344(20):1560-1561.
2. Schrier S. Sickle Cell Disease: Basic Principles and Clinical Practice.Stephen H. Embury, Robert P. Hebbel , Nara Mohandas , Martin H. Steinberg. The Quarterly Review of Biology. 1995;70(4):541-542.
3. Rees D, Williams T, Gladwin M. Sickle-cell disease. The Lancet. 2010;376(9757):2018-2031.
4. Stuart MJ, Nagel RL. Sickle-cell disease. The Lancet. 2004;364(9442):1343–60.
5. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. The Indian journal of medical research. 2015 May;141(5):509.
6. Williams T, Mwangi T, Wambua S, Alexander N, Kortok M, Snow R et al. Sickle Cell Trait and the Risk of Plasmodium falciparum Malaria and Other Childhood Diseases. The Journal of Infectious Diseases. 2005;192(1):178-186.
7. May J, Evans J, Timmann C, Ehmen C, Busch W, Thye T et al. Hemoglobin Variants and Disease Manifestations in Severe Falciparum Malaria. JAMA. 2007; 297(20):2220.
8. Diggs, L. (1967). Bone and Joint Lesions in Sickle-Cell Disease. Clinical Orthopaedics and Related Research, &NA;(52),
9. CHARACHE, S. (1967). Infarction of Bone Marrow in the Sickle Cell Disorders. Annals of Internal Medicine, 67(6), p.1195.
10. Brown, C. (1972). Bone marrow necrosis. A study of seventy cases. Johns Hopkins Med J(1972 Sep;131(3), pp.189-203.
11. Chatel, B., Messonnier, L., Hourdé, C., Vilmen, C., Bernard, M. and Bendahan, D. (2017). Moderate and intense muscular exercises induce marked intramyocellular metabolic acidosis in sickle cell disease mice. Journal of Applied Physiology, 122(5), pp.1362-1369.
12. Chatel, B., Hourdé, C., Gondin, J., Fouré, A., Le Fur, Y., Vilmen, C., Bernard, M., Messonnier, L. and Bendahan, D. (2017). Impaired muscle force production and higher fatigability in a mouse model of sickle cell disease. Blood Cells, Molecules, and Diseases, 63, pp.37-44.
13. Ravelojaona, M., Féasson, L., Oyono-Enguéllé, S., Vincent, L., Djoubairou, B., Ewa'Sama Essoue, C. and Messonnier, L. (2015). Evidence for a Profound Remodeling of Skeletal Muscle and Its Microvasculature in Sickle Cell Anemia. The American Journal of Pathology, 185(5), pp.1448-1456.
14. Chaouch, L., Kalai, M., Jbara, M., Chaabene, A., Darragi, I., Chaouachi, D., Mallouli, F., Hafsia, R., Ghanem, A. and Abbes, S. (2013). Association between rs267196 and rs267201 of bmp6 gene and osteonecrosis among sickle cell aneamia patients. Biomedical Papers.
15. Sadat-Ali, M., Al-Elq, A., Sultan, O. and Al-Turki, H. (2008). Secondary osteoporosis due to sickle cell anemia: Do sex steroids play a role?. Indian Journal of Medical Sciences, 62(5), p.193.
16. Sarrai, M., Duroseau, H., D'Augustine, J., Moktan, S. and Bellevue, R. (2007). Bone mass density in adults with sickle cell disease. British Journal of Haematology, 136(4), pp.666-672.
17. Miller, R., Segal, J., Ashar, B., Leung, S., Ahmed, S., Siddique, S., Rice, T. and Lanzkron, S. (2006). High prevalence and correlates of low bone mineral density in young adults with sickle cell disease. American Journal of Haematology, 81(4), pp.236-241.
18. Buison, A. (2005). Bone Area and Bone Mineral Content Deficits in Children With Sickle Cell Disease. Pediatrics, 116(4), pp.943-949.
19. Serarslan, Y., Kalacı, A., Özkan, C., Doğramacı, Y., Çokluk, C. and Yanat, A. (2010). Morphometry of the thoracolumbar vertebrae in sickle cell disease. Journal of Clinical Neuroscience, 17(2), pp.182-186.
20. Vignerová J. Anthropometric Standards. An Interactive Nutritional Reference of Body

Size and Body Composition for Children and Adults. Economics & Human Biology. 2009 Mar 1;7(1):130-1.
21. Eveleth PB, Tanner JM. Worldwide variation in human growth. CUP Archive; 1976 Dec 30.
22. Eveleth, P. and Tanner, J. (1991). *Worldwide Variation in Human Growth*. Cambridge: Cambridge University Press.
23. David HG, Bridgman SA, Davies SC, Hine AL, Emery RJ. The shoulder in sickle-cell disease. Bone & Joint Journal. 1993 Jul 1;75(4):538-45.
24. Han TS, Hooper JP, Morrison CE, Lean ME. Skeletal proportions and metabolic disorders in adults. European journal of clinical nutrition. 1997 Dec 1;51(12):804-9.
25. Gunnell DJ, Smith GD, Frankel S, Nanchahal K, Braddon FE, Pemberton J, Peters TJ. Childhood leg length and adult mortality: follow up of the Carnegie (Boyd Orr) Survey of Diet and Health in Pre-war Britain. Journal of Epidemiology & Community Health. 1998 Mar 1;52(3):142-52.
26. Järvelin MR. Fetal and infant markers of adult heart diseases. Heart. 2000 Aug 1;84(2):219-26.
27. Smith GD, Greenwood R, Gunnell D, Sweetnam P, Yarnell J, Elwood P. Leg length, insulin resistance, and coronary heart disease risk: the Caerphilly Study. Journal of Epidemiology & Community Health. 2001 Dec 1;55(12):867-72.
28. Eveleth PB, Tanner JM. Worldwide variation in human growth. CUP Archive; 1976 Dec 30.
29. Eveleth, P. and Tanner, J. (1991). *Worldwide Variation in Human Growth*. Cambridge: Cambridge University Press.
30. Serrat MA, King D, Lovejoy CO. Temperature regulates limb length in homeotherms by directly modulating cartilage growth. Proceedings of the National Academy of Sciences. 2008 Dec 9;105(49):19348-53.
31. Andersen HE. The influence of hormones on human development. Human development. 1966:184-221.
32. Lasker GW. Human biological adaptability. Science. 1969 Dec 19;166(3912):1480-6.
33. Bogin B. Patterns of human growth. Cambridge University Press; 1999 May 6.
34. Leitch I. Growth and health. British Journal of Nutrition. 1951 Feb;5(1):142-51.
35. Crews DE. Human senescence: Evolutionary and biocultural perspectives. Cambridge University Press; 2003 Dec 11.
36. Larke A, Crews DE. Parental investment, late reproduction, and increased reserve capacity are associated with longevity in humans. Journal of physiological anthropology. 2006;25(1):119-31.
37. Bogin B. Childhood, adolescence, and longevity: a multilevel model of the evolution of reserve capacity in human life history. American Journal of Human Biology. 2009 Jul 1;21(4):567-77.
38. Zemel BS, Kawchak DA, Ohene-Frempong KW, Schall JI, Stallings VA. Effects of delayed pubertal development, nutritional status, and disease severity on longitudinal patterns of growth failure in children with sickle cell disease. Pediatric Research. 2007 May 1;61(5):607.
39. Goldstein A, Anderson M, Serjeant G. Parvovirus associated aplastic crisis in homozygous sickle cell disease. Archives of Disease in Childhood. 1987;62(6):585-588.
40. Almeida, A. and Roberts, I. (2005). Bone involvement in sickle cell disease. British Journal of Haematology, 129(4), pp.482-490.

How to cite this article: Bardhan M, Das I, Tiwari R et.al. Assessment of Cormic Index in sickle cell disease subjects and its association with clinical severity. International Journal of Science & Healthcare Research. 2019; 4(4): 70-78.

******