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RESEARCH ARTICLE

Determination and Comparison of the Types of Facial Asymmetry among the Sickle Cell Anaemic and Normal Children in Kano State Nigeria

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Abstract

Objective: To determine and compare the types of facial asymmetry of Sickle and non-Sickle Cell Anemic children in Kano State, Nigeria.

Materials and Method: Three hundred and sixty-five (365) subjects were used out of which 186 (96 males and 90 female) were children with Sickle Cell Anemia and 179 (108 males and 71 females) were not. Subjects were photographed based on standard method after consent was given by each of the guardian. Required dimensions were acquired from standard facial landmarks placed on the photos. The facial dimensions were recorded and the types of facial asymmetry were determined (using a standard formula) and compared between the Sickle Cell Anemic and normal subjects.

Results: Directional and Fluctuating facial asymmetry exist in all parts of the faces of the Sickle Cell or non-Sickle Cell Anemic children. However, some of the dimensions were only peculiar to Sickle or non-Sickle Cell Anemic children, while others were only peculiar to the male or female Sickle or non-Sickle Cell Anemic children.

Conclusion: This study concludes that Sickle cell Anemia determines the types of facial asymmetry and these types are also affected by sex factor.

Keywords: Sickle cell, Face, Asymmetry, Nigeria

Introduction

Sickle cell disease (SCD) is a hereditary blood disorder characterized by abnormally shaped red cells. The anaemia associated with SCD is caused by an abnormal haemoglobin mutation, haemoglobin (Hb) S, as a result of which glutamic acid is replaced by valine on the beta chain. This mutation causes chronic haemolytic anaemia and vaso-occlusive episodes with ischaemic injury of many tissues [1]. There are several forms of SCD. The principal genotypes include homozygous sickle cell anaemia, sickle cell haemoglobin C disease, and Sickle cell- β –thalassaemia. Kano State in northern Nigeria is an endemic area for Hb S and the prevalence of the trait is approximately 2 per cent. Although it is primarily a haematological disorder, SCD frequently exhibits multisystemic manifestations. Oral manifestations, while not common in SCD, include anaesthesia of the mandibular nerve [2, 3], pulpitic pain and pulpal necrosis [4,5]which can be ascribed to the microvascular occlusions that tend to affect organs with terminal circulation [6]. A review of the literature reveals histological changes in dental tissues [7], a greater incidence of caries in young African SCD patients, but no increase in periodontal disease [8].

Although craniofacial features, such as maxillary protrusion and more forward growth of the mandible with significantly returned maxillary and mandibular incisors, have been documented in black American children with SCD [9, 10] no craniofacial data have been reported for Caucasian individuals with SCD.

Asymmetry is defined in the Stedman's dictionary as "any deviation from normal or difference in size or relationship between two sides of the body". According to Smith, 2010, facial asymmetry is defined as the variation between sides in terms of size and shape or where one side is larger than the other.

Facial asymmetry results from congenital causes such as trauma, infection, tumour and functional factors such as habit or occulusal interference [11].

The purpose of this study is to quantify facial asymmetry in sickle cell disease patients attending Murtala Muhammed Specialist Hospital, Kano.

Materials and Methods

This study was a comparative cross-sectional study which was carried out in the department of pediatrics, Murtala

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Muhammad Specialist Hospital, Kano, Nigeria. It is a health facility considered as number one Kano state hospital which is located in Kano municipal, Kano State, Nigeria. The study population was divided into two groups, the first group (cases) were sickle cell disease patients attending sickle cell clinic of Murtala Mohammad Specialist Hospital, Kano, aged 5 to 18 years while the second group (controls) were non-sickle cell disease patients attending pediatric outpatient department of Murtala Mohammad Specialist hospital, Kano aged 5 to 18 years. A brief questionnaire was completed for all individuals that included sickle cell disease status, age, sex, tribe, birth order, identification number, level of education and parents' occupation. A total of 368 patients were used for this study out of which 188 were sickle cell disease patients and 180 were patients attending Pediatric outpatient department of the hospital without sickle cell disease.

Sample Size Determination

The sample size was calculated using formula; $N = Z^2PQ/D^2$, where Q = (1-P). (Naing, *et al.,* 2006)

Where N = sample size

Z= standard normal deviation 1.96 at 95% confidence level

P= prevalence of sickle cell disease = 0.28 (28%) from previous study (Fleming *et al*, 1979).

Q= 1-p = 1- 0.28 = 0.72

D= degree of precision = 0.05

$(1.96)^2(0.28)\,(0.72)$

$$N = \frac{(1.96)^2(0.28)\,(0.72)}{0.05^2} = 309$$

The minimum sample size was calculated to be 309. However, to further minimize the level of error, three hundred and sixty-eight (368) subjects were used. Simple random sampling technique was used and Ethical approval was granted via a letter issued by ethics and research committee, Kano State Ministry of Health, and consent form was signed on behalf of each participant by his or her guardian, and questionnaires were also filled by the guardians. Subjects included were those diagnosed as having Sickle cell disease or not, through Hemoglobin electrophoresis.

Each of the subjects was photographed and the photographic set up consisted of a tripod stand (Manfrototripod, model FB 10) that held a 24 mm wide-angle lens camera (sony, model DSC-W380 made in India) and a primary flash light. The tripod stand controlled the stability and adjust the height of the camera according to the subject's height with a zooming power of 3.6 [12].

Record taking

The camera was used in its manual position, with a distance of approximately 120 cm from the subject, that was kept constant, and each of the subjects was asked to sit at rest on a chair, facing the camera with the head in anatomical position, and lips repose [12]. An identification number was placed behind and lateral to the subject so as to merge each subject with his/her questionnaire. The subject's forehead, neck, and ears were clearly visible during the recording (Plate1).

Plate I: Photographic set up

The photographic records, 24mm slide format, were analyzed using Facial landmark detection software for BUK Kano version 1.0.0.0 program for Windows operating system. The program was customized with the landmarks used in this study.

A software for facial landmark detection was used for this task, the required landmarks were manually adjusted, and once identified the software calculates the measurements. A correction factor of 0.59 was used to adjust the pictures to life size, and the software processed all the information and records inputted and lastly transferred to microsoft excel.

Facial asymmetry measurement

Facial dimensions were measured to the nearest millimeters (mm) from a 2D image using the facial detection software installed in a computer.

Data analysis

The data was analyzed using statistical package for social scientists (SPSS) statistical package (IBM 23 software). Histograms with a Gaussian curves were used to determine the type of facial asymmetry by using mean of the distribution as a reference (plates 2 and 3).

Results

Table 1 and 2 shows 28 facial dimensions that exhibit 2 categories of Facial Asymmetry, in which each category of the Asymmetry was found in the Sickle and non-Sickle Cell Anaemic male or female children. This indicates that these facial dimensions are not affected by sex or Sickle Cell Anaemia.

1. The first category consists of 9 dimensions (32.1%) that exhibit Directional Asymmetry. The dimensions include: tr-ex, prn-ex, prn-go, sn-go, sl-go, st-go, il-go. sm-go, m-go.
2. The second category consists of 19 dimensions (67.9%) that exhibit Fluctuating Asymmetry. The dimensions include: tr-ch, g-ch, sn-en, sn-ch, sl-ch, sl-en, st-en, st-al, st-ch, il-ex, il-en, il-al, sm-ex, sm-en. sm-al, sm-ch, m-en, m-al, m-ch.

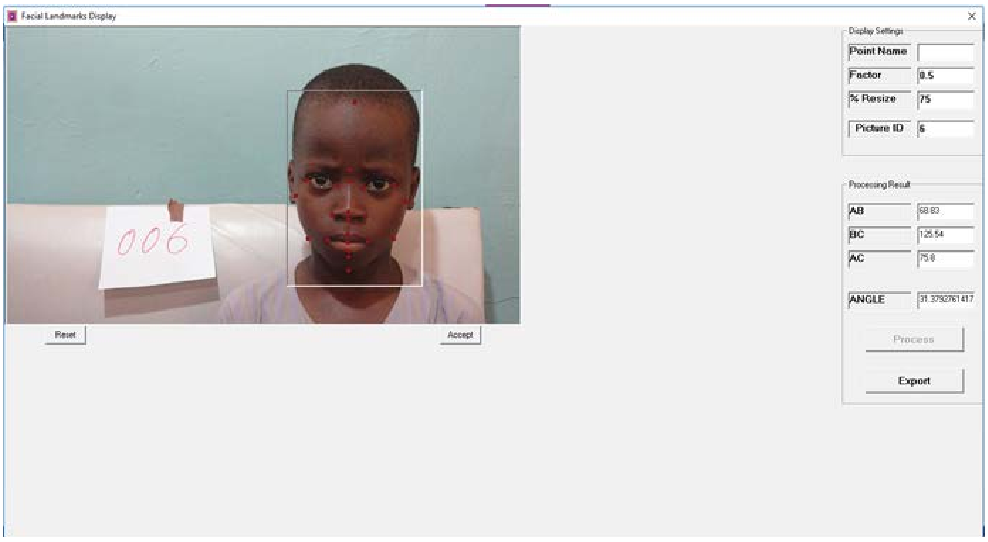

Plate II: Facial dimensions measurements.

Table 1: Facial dimensions and Landmarks.

SN	DIMENSION	LANDMARK	SN	DIMENSION	LANDMARK
1	trichion	tr	12	Exocanthion (right)	exR
2	glabella	g	13	endocanthion (left)	enL
3	nasion	n	14	endocanthion (right)	enR
4	pronasale	prn	15	zygion (left)	zyL
5	subnasale	sn	16	zygion (right)	zyR
6	superior labrum	sl	17	alar (left)	alL
7	stomium	st	18	alar (right)	alR
8	inferior labrum	il	19	gonion (left)	goL
9	supramentale (right)	sm	20	gonion (right)	goR
10	menton	m	21	cheilion (left)	chL
11	Exocanthion (left)	exL	22	cheilion (right)	chR

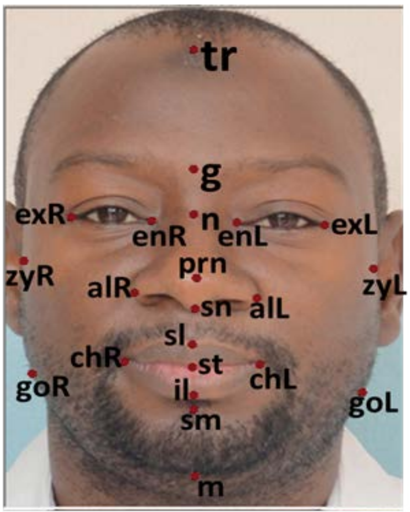

Plate III: Facial landmarks.

Table 3 shows 8 facial dimensions that exhibit 2 categories of Facial Asymmetry

1. The first category consists of 3 dimensions (37.5%) that exhibit Fluctuating Asymmetry in the male and female Sickle Cell Anaemic and male non-Sickle Cell Anaemic children. This indicates that these dimensions with this category of Fluctuating Facial Asymmetry is not seen in female non-Sickle Cell and thus affected by normal female sex factor. The dimensions include: n-ch, prn-en, prn-ch. In the table, it portrays that these dimensions show Fluctuating Asymmetry in male and female Sickle Cell and male non-Sickle Cell Anaemic children but show Directional Asymmetry in the female non-Sickle Cell Anaemic children.

2. The second category consists of 5 dimensions (62.5%) that exhibit either Directional or Fluctuating Asymmetry in the male and female Sickle Cell Anaemic and female non-Sickle Cell Anaemic children. This indicates that these dimensions in this category are thus affected by normal male sex factor.

a. Four (4) of the dimensions show Directional Asymmetry in the male and female Sickle Cell Anaemic and non-Sickle Cell Anaemic female children but show Fluctuating Asymmetry in the non-Sickle Cell Anaemic male children. These dimensions include: n-al, prn-al, sm-zy, m-zy.

b. One (1) of the dimensions shows Fluctuating Asymmetry in the male and female Sickle Cell Anaemic and female non-Sickle Cell Anaemic children but show Directional Asymmetry in the male non-Sickle Cell Anaemic Children. The dimension is: tr-zy.

* Dimensions affected by normal female factor

Table 2: Facial dimensions not affected by disease or sex factors

Variables	Male Cases	Male Controls	Female Cases	Female Control
tr-ex	Directional	Directional	Directional	Directional
prn-ex	Directional	Directional	Directional	Directional
prn-go	Directional	Directional	Directional	Directional
sn-go	Directional	Directional	Directional	Directional
sl-go	Directional	Directional	Directional	Directional
st-go	Directional	Directional	Directional	Directional
il-go	Directional	Directional	Directional	Directional
sm-go	Directional	Directional	Directional	Directional
m-go	Directional	Directional	Directional	Directional
tr-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
g-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sn-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sn-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sl-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sl-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
st-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
st-al	Fluctuating	Fluctuating	Fluctuating	Fluctuating
st-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
il-ex	Fluctuating	Fluctuating	Fluctuating	Fluctuating
il-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
il-al	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sm-ex	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sm-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sm-al	Fluctuating	Fluctuating	Fluctuating	Fluctuating
sm-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating
m-en	Fluctuating	Fluctuating	Fluctuating	Fluctuating
m-al	Fluctuating	Fluctuating	Fluctuating	Fluctuating
m-ch	Fluctuating	Fluctuating	Fluctuating	Fluctuating

Table 3: Facial dimensions affected by sex factor

Variable	Male Cases	Male Control	Female Cases	Female Control
n-ch*	Fluctuating	Fluctuating	Fluctuating	Directional
prn-en*	Fluctuating	Fluctuating	Fluctuating	Directional
prn-ch*	Fluctuating	Fluctuating	Fluctuating	Directional
tr-zy**	Fluctuating	Directional	Fluctuating	Fluctuating
n-al***	Directional	Fluctuating	Directional	Directional
prn-al***	Directional	Fluctuating	Directional	Directional
sm-zy***	Directional	Fluctuating	Directional	Directional
m-zy***	Directional	Fluctuating	Directional	Directional
Sl-ex*	Directional	Directional	Fluctuating	Directional
tr-go*	Directional	Directional	Fluctuating	Directional
g-go*	Directional	Directional	Fluctuating	Directional
n-zy*	Directional	Directional	Fluctuating	Directional
tr-en**	Fluctuating	Directional	Directional	Directional
n-go**	Fluctuating	Directional	Directional	Directional
g-zy***	Directional	Fluctuating	Fluctuating	Fluctuating
il-ch***	Directional	Fluctuating	Fluctuating	Fluctuating
m-ex***	Directional	Fluctuating	Fluctuating	Fluctuating

(Fluctuating in male & female Sickle Cell Anemic and non-Sickle Cell Anemic male children but turns to be Directional Asymmetry in non-Sickle Cell Anemic female children)

** Dimensions affected by normal male factor

Fluctuating Asymmetry in male & female Sickle Cell Anemic and non-Sickle Cell Anemic female children but turns to be Directional Asymmetry in non-Sickle Cell Anemic male children)

*** Directional Asymmetry in male & female Sickle Cell Anemic and non-Sickle Cell Anemic female children but turns to be Fluctuating Asymmetry in non-Sickle Cell Anemic male children)

Table 4 shows 9 facial dimensions that also exhibit 2 categories of Facial Asymmetry.

1. The first category consists of 5 dimensions (62.5%) that exhibit either Directional or Fluctuating Asymmetry in the male and female non-Sickle Cell Anaemic and Sickle Cell Anaemic female children. This indicates that these dimensions in this category are thus affected by female Sickle Cell Anaemic factor.

c. Four (4) of the dimensions show Directional Asymmetry in the male and female non-Sickle Cell Anaemic and Sickle Cell Anaemic male children but show Fluctuating Asymmetry in the Sickle Cell Anaemic Female children. These dimensions include: sl-ex, tr-go, g-go, n-zy.

d. Two (2) of the dimensions also show Directional Asymmetry in the male and female non-Sickle Cell Anaemic and female Sickle Cell Anaemic children but show Fluctuating Asymmetry in the Sickle Cell Anaemic Male Children**.** The dimensions are: tr-en, n-go

Thus, the dimensions in Table 3 are affected by Sickle Cell Anaemic factor.

2. The second category consists of 3 dimensions (37.5%) that exhibit Fluctuating Asymmetry in the male and female non-Sickle Cell Anaemic and female Sickle Cell Anaemic children but show Directional Asymmetry in the male Sickle Cell Anaemic children. This indicates that these dimensions with this category of Fluctuating Facial Asymmetry turns to be Directional in male Sickle Cell Anaemic children and thus affected by Sickle Cell Anaemic/male sex factor. The dimensions include: g-zy, il-ch, m-ex.

* Dimensions affected by female Sickle Cell Anemic factor

(Directional Asymmetry in male & female non-Sickle Cell Anemic and male Sickle Cell Anemic children but turns to be Fluctuating Asymmetry in female Sickle Cell Anemic children)
** Dimensions affected by male Sickle Cell Anemic factor

Fluctuating Asymmetry in male & female Sickle Cell Anemic and non-Sickle Cell Anemic female children but turns to be Directional Asymmetry in non-Sickle Cell Anemic male children)

*** Fluctuating Asymmetry in male & female non-Sickle Cell Anemic and Sickle Cell Anemic female children but turns to be Directional Asymmetry in Sickle Cell Anemic male children)
Table 5 shows 14 facial dimensions that also exhibit 2 categories of Facial Asymmetry with 3 sub-categories.

1. The first sub-category consists of 4 (28.6%) dimensions (tr-al, g-al, sl-al, sn-al) that exhibit Fluctuating Asymmetry in the male and female non-Sickle Cell Anaemic children but turns to be Directional Asymmetry in both male and female Sickle Cell Anaemic children.
2. The second sub-category consists of 3 (21.4%) dimensions (n-en, g-ex, n-ex) that exhibit Directional Asymmetry in the male and female non-Sickle Cell Anaemic children but turns to be Fluctuating Asymmetry in both male and female Sickle Cell Anaemic children. This indicates that these dimensions are thus affected by Sickle Cell Anaemia.

Table 4: Facial dimensions affected by Sickle Cell Anemia factor

Variable	Male Cases	Male Control	Female Cases	Female Control
Sl-ex*	Directional	Directional	Fluctuating	Directional
tr-go*	Directional	Directional	Fluctuating	Directional
g-go*	Directional	Directional	Fluctuating	Directional
n-zy*	Directional	Directional	Fluctuating	Directional
tr-en**	Fluctuating	Directional	Directional	Directional
n-go**	Fluctuating	Directional	Directional	Directional
g-zy***	Directional	Fluctuating	Fluctuating	Fluctuating
il-ch***	Directional	Fluctuating	Fluctuating	Fluctuating
m-ex***	Directional	Fluctuating	Fluctuating	Fluctuating

Table 5: Facial dimensions affected by disease or sex factors

VARIABLES	MALE CASES	MALE CONTROL	FEMALE CASES	FEMALE CONTROL
tr-al*	Directional	Fluctuating	Directional	Fluctuating
g-al*	Directional	Fluctuating	Directional	Fluctuating
sl-al*	Directional	Fluctuating	Directional	Fluctuating
sn-al*	Directional	Fluctuating	Directional	Fluctuating
n-en**	Fluctuating	Directional	Fluctuating	Directional
g-ex**	Fluctuating	Directional	Fluctuating	Directional
n-ex**	Fluctuating	Directional	Fluctuating	Directional
prn-zy***	Fluctuating	Fluctuating	Directional	Directional
sn-ex***	Fluctuating	Fluctuating	Directional	Directional
sn-zy***	Fluctuating	Fluctuating	Directional	Directional
sl-zy***	Fluctuating	Fluctuating	Directional	Directional
st-ex***	Fluctuating	Fluctuating	Directional	Directional
st-zy***	Fluctuating	Fluctuating	Directional	Directional
il-zy***	Fluctuating	Fluctuating	Directional	Directional

3. The third sub-category consists of 7 (50%) dimensions (prn-zy, sn-ex, sn-zy, sl-zy, sl-ex, st-zy, il-zy) that exhibit Fluctuating Asymmetry in the Sickle and non-Sickle Cell Anaemic male children but turn to be Directional Asymmetry in the Sickle and non-Sickle Cell Anaemic female children. This indicates that these dimensions with this category are thus affected by sex factor. The dimensions include: g-zy, il-ch, m-ex.

Table 5: Facial dimensions affected by disease or sex factors

*Dimensions that exhibit Directional Asymmetry in Sickle Cell Anemic children but Fluctuating Asymmetry in non-Sickle Cell Anemic children.
** Dimensions that exhibit Fluctuating Asymmetry in Sickle Cell Anemic children but Directional Asymmetry in non-Sickle Cell Anemic children.

*** Dimensions that exhibit Fluctuating Asymmetry in Sickle Cell and non-Sickle Cell Anemic male children but Directional Asymmetry in Sickle Cell and non-Sickle Cell Anemic female children.

Discussion

Literature in the past has been scanty about the specific types of asymmetry among the sickle cell patients. In the present study, the types of facial asymmetry were determined and compared with non-sickle cell subjects. There were two types of facial asymmetry in both the sickle and non-sickle cell subjects, which were directional and fluctuating for both male and female sexes. However, Antisymmetry was not seen in this study because it is a less common condition [13] characterized by a bimodal distribution of deviation from bilateral symmetry [14].

In the literature, a number of causal factors have been highlighted in the development of facial asymmetries. It is generally divided into clinical and non-clinical facial asymmetry. Chia et al., [15] suggested that facial asymmetries in general, could have pathological, traumatic, functional or developmental causal factors. Haraguchi et al., [16] claimed that the etiology of facial asymmetry can be grouped into hereditary factors of prenatal origin and acquired factors of postnatal origin. Conversely, Cheong and Lo [17] reported that the causes of facial asymmetry can be grouped into three main categories: (a) congenital, of prenatal origin; (b) acquired, resulting from injury or disease; and (c) developmental, arising during development and of unknown etiology.

Clinical asymmetry, which is the subject of this research is usually caused by many disease conditions that requires clinical intervention [18] because it exist as a nuisance to the individual [17]. It may occur due to craniofacial alterations in sickle cell anaemia patients as a result of hyperplasia and compensatory expansion of the bone marrow, resulting in exaggerated growth/protrusion of the mid face, maxillary expansion, predominant vertical growth, mandibular retrusion, a convex profile and maxillary protrusion [19]. Some of the causes of the non-clinical asymmetry includes poor health [20], from parasite and non-microbial infections [21], extreme temperature [22], poor living conditions [23], poor or inadequate nutrition [24], looking at the social and educational background of the patients attending Murtala Muhammad Specialist Hospital.

The present study examined 64 facial dimensions from the twenty-two (22) standard landmarks and these dimensions exhibited 2 categories of Facial Asymmetry and were found in both the Sickle and non-Sickle Cell Anaemic male or female children. Twenty-eight (28) of these dimensions exhibited same Asymmetry type (Directional or Fluctuating) in both Sickle and non-Sickle Cell Anaemic male or female children. It means therefore, these types of dimensions were not affected by sex or Sickle Cell Anaemia and it is therefore possible that they genetically stereotyped.

However, some dimensions exhibited one of the two types of Asymmetry in the normal female and the Sickle Cell Anaemic children (male & female), but the same dimensions exhibited the other type in the normal male children. This may mean that the actual Asymmetry exhibited by those dimensions is the one seen in the normal male children and thus Sickle Cell Anaemia and the normal female Oestrogen may have played a role in changing the direction of the Asymmetry shown by those dimensions in the Sickle Cell and the normal female subjects. Similarly, some dimensions exhibited one type of Asymmetry in the normal male and the Sickle Cell Anaemic (male & female) children but another type in the normal female children and therefore very much likely that Sickle Cell Anaemia and the normal male testosterone may have played a role in changing the type of Asymmetry shown by those dimensions in the Sickle Cell and the normal male subjects.

Interestingly, some of the dimensions exhibited a specific Asymmetry in Sickle Cell Anaemic females. The present study therefore, hypothesized that the actual Asymmetry type shown by those dimensions was the one seen in the normal male & female children and the Sickle Cell Anaemic males. It is thus possible that those dimensions are affected by a combination of Oestrogen and Sickle Cell Anaemia. Similarly, if such dimensions exhibited a specific Asymmetry in the Sickle Cell Anaemic males, those dimensions are possibly affected by a *combination of* testosterone and Sickle Cell Anaemia.

In the current study, some dimensions exhibited Fluctuating Asymmetry in the Sickle Cell Anaemic (male & female) subjects but Directional Asymmetry in the normal (male & female) subjects or exhibited Directional Asymmetr*y* in Sickle Cell Anaemic (male & female) subjects but Fluctuating Asymmetry in the normal (male & female) subjects. This has clearly indicated that those dimensions are purely affected by Sickle Cell Anaemia. Similarly, some dimensions exhibited Directional Asymmetry in the normal (male & female) subjects but Fluctuating Asymmetry in the Sickle Cell Anaemic (male & female) subjects. It means therefore, those dimensions were stereotyped genetically to be exhibit Directional Asymmetry, but the Sickle Cell Anaemia affected the stereotype and therefore Sickle Cell Anaemic subjects exhibit Fluctuating Asymmetry from those dimensions.

Conclusion

Fluctuating and Directional asymmetries were the only Asymmetries found in the face and Fluctuating Asymmetry is the common Asymmetry found in sickle cell disease patients, whereas Directional Asymmetry is common in the normal subjects and no Antisymmetry recorded. The study was able to showcase the effect of Sickle Cell and sex hormones on the type of Asymmetry on the normal or Sickle Cell Anemic children.

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Disclosure of Conflict of Interest

The authors declare that there is conflict of interest in this study because the subjects were the patients of one of the authors, although no subject included without his or consent.

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