Effect of Blood Groups and Complications on Orofacial Measurements of B Thalassemia Adult Patients

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Abstract

Background: β- thalassaemia is a common hereditary disorders in Iraq and worldwide .with different treatment schemes,, including blood transfusion, iron chelation and splenectomy, patients with B thalassemia may develop different skeletal changes. Limited studies link these complications with orofacial changes, This study aimed to evaluate the orofacial dimensions in β- thalassemia patients with age, gender, blood groups, splenectomy and cholecystectomy and to assist surgeons for planning their future intervention.

Method: This study was conducted on 130 ß-thalassemia patients of both gender,,and two age categories (20-30 yrs), & (21-40 yrs), five orofacial measurements (face,eyes,nose,mouth and ears) and sixteen parameters were measured and calculated for differences,P value is estimated,data analysis were done by using Chi square test and SPSS version 20

Results: Significant findings were found for mandibular width and mouth width at older age group (31-40 years), the nasal width and ear height are more in male, patients with splenectomy have significance for lower 1\3 face and ear width. Cholecystectomy increase eye length measurments and ear height but for blood groups the $P > 0.05$

Conclusions: Orofacial bone changes are pronounced in β- thalassaemia with distinct findings regarding sex dimorphism, older are more prone to have variations, earlier splenectomy is advisable,cholecystectomy is better choice for symptomatic patients, blood groups have no significance.

Keywords: *βThalassemia,,Blood groups, Orofacial measurments, Complications.*

Introduction

Thalassemia are group of single gene inherited hematological disorders caused by deficiencies in the synthesis of hemoglobin chains that cause haemolytic anemia· [1] · ß-thalassemia major is the most severe form leading to severe anemia in infancy or childhood and used to be life threatening in absence of regular red cell transfusions[2]. Various studies found that patients with blood group O are more risky to develop ß thalassemia[3,4]. The common symptoms of the disease include severe anemia, poor growth, delayed sexual maturation,splenomegaly and gall bladder bilirubin stones, if patients are symptomatic, they may require laproscopic cholecystectomy,could be at the same time as the splenectomy.[5-8]

Patients with ß thalassemia commonly have skeletal abnormalities including limbs,vertebral column,skull and bones of the face, commonly called squirrel –like face[9]. Theorofacial bone changes are the results of ineffective erythropoiesis, the bones become thinner with pathological fractures may occur due to overexpansion

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of the bone marrow and extra medullary region and this is frequently noticed in patients who receive insufficient or irregular blood transfusions[10,11]. Patient survival depends on regular blood transfusions and iron chelating therapy,In spite of being an effective cure but there are many serious associated long-term problems. Iron toxicity (hemosiderosis) will lead to hepato splenomegaly which end with organ damage,surgical intervention and impaired growth [12,13] .

Different orofacial dimensions include face, eyes, nose, mouth and ears of thalassemia patients have significant differences from normal individuals which is documented in many studies[14,15] Although B thalassemia is a leading health problem in Basrah, southern of Iraq but limited published data were available on orofacial measurements therefore the aim of the study is to evaluate the effect of age,gender, blood groups, splenectomy and cholecystectomy on orofacial bone changes and determine their clinical outcome in thalassemia patients .

Material and Method

The present study was conducted during the period from August 2019 to March 2020, data obtained from a total number of 130 adult B Thalassemia Major Iraqi patients from Basrah city (72 female and 58 male) who attended to the thalassemia center for Hereditary Blood diseases at Basrah Maternity and Child Hospital irrespective to their social or educational backgrounds .All patients were diagnosed previously based on hemoglobin electrophoresis or high-performance liquid chromatography and submitted to frequent blood transfusions. The age ranged between 20-40 years. Patients were divided according to age into two groups, 21-30 age group, and 31-40 age group. Patient's data including age, sex, weight (in kg), and height (in cm), were obtained and evaluated . All patients receive different treatments and blood transfusion.

Verbal consent obtained from each participantin this study and the approval of the Ethical Committee of Al Zahraa Medical College/University of Basrah and Centre for Human Development of Basrah Health Authority (Ref. No. 261 at 13/5/2019} was obtained . The standard instruments used in this study were calipers and measuring tape, Fig. 1 & 2

Surface landmarks were marked on the face before taking the standard anthropometric measurement according to Farkas method[16]. The head orientation was achieved by positioning the head in Frankfurt horizontal plane aligned parallel to the floor. Three anatomical landmarks determined the facial midline: the nasion, the subnasal, and the gnathion. "Fourteen linear and two angular measurement taken, these are:.

1. Face: Face width (zy- zy), Face height (n- gn), Upper face height (n- sto), Maxillary depth (t- sn), Mandibular depth (t- gn).
2. Nose: Nose width (al- al), Nose height (n- sn), Nasal tip protrusion (sn- prn)
3. Eyes: Biorbital width (ex-ex), Intercanthal distance (en- en), Palpebral fissure length (en- ex).
4. Mouth: Mouth width (ch- ch), Lower lip height (sto-ls), Upper lip height (sn- sto).
5. Ears: Ear width (par- pa), Ear length (sa- sba).

Facial measurments are taken in millimeters.

A comprehensive analysis of data was achieved by using SPSS version 20 and Chi square test

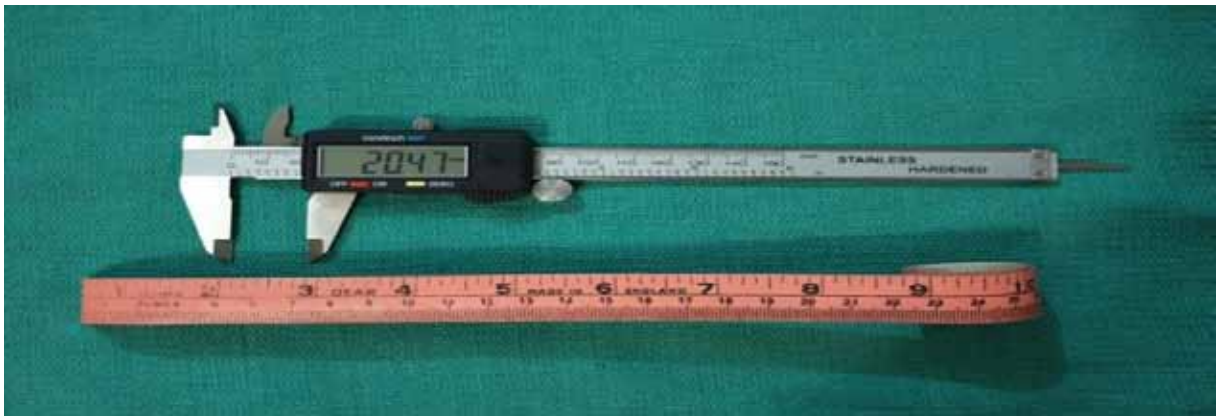

Fig. 1: The vernia and measuring tape

Fig. 2: Orofacial measurments

Results

A total number of 130 B - thalassemia adult patients of both gender (72 male/58 female; 1.2/1),age range from 20 to 40 years were enrolled in this study for estimating orofacial measurments (OFM).

Significant differences were found between different age groups regarding face, ear, eye, and nose, the mandibular depth (t-gn) show high results at age group 31-40 years ($p = 0.022$) and the mouth width (ch-ch) show significance at older age group also ($p = 0.041$). Table 1.

Table 1: Relation of age to OFM of B thalassemia patients

OFM		Age Group		
		20-30	31-40	
Face	Face width (zy-zy)	96.1	99.3087	0.129
	Facial height (n-gn)	107.1111	107.8261	0.801
	Upper facial Morphological height (n-sto)	68.7944	72.3957	0.099
	Maxillary depth (t-sn)	117.1278	118.9174	0.505
	Mandibular depth (t-gn)	128.0472	135.7652	0.022
Nose	Nasal width (al-al)	34.9139	35.4783	0.527
	Nasal height (n-sn)	48.0222	51.3783	0.083
	Nasal length (sn-pr n)	14.7778	17.2391	0.136
Mouth	Mouth width (ch-ch)	42.8556	45.6696	0.041
	Lower third face height (sn-gn)	59.0222	58.0826	0.616
Eye	Outer eye space (ex-ex)	90.8333	91.1261	0.94
	Inner corner eye space (en-en)	33.3306	34.0174	0.344
	Eye length (en-ex)	30.6806	31.5	0.373
Ear	Ear width (pra-pa)	36.6861	37.1261	0.785
	Ear Height (sa-sba)	54.9417	56.4917	0.367

$P<0.05$ is significant

No significant differences were detected between male and female in orofacial measurement, except for nasal width (al-al), and ear height (sa-sba) which show higher results in male patients (p = 0.019), (p = 0.011) respectively Table 2.

Table 2: Relation of Sex and Orofacial measurements of B thalassemia patients

OFM		Sex		P-value
		Female	Male	
Face	Face width (zy-zy)	96.5364	98.3846	0.377
	Facial height (n-gn)	105.9182	109.2577	0.228
	Upper facial Morphological height (n-sto)	69.0091	71.7077	0.211
	Maxillary depth (t-sn)	115.2303	121.1192	0.022
	Mandibular depth (t-gn)	129.1515	133.4731	0.199
Nose	Nasal width (al-al)	34.2485	36.2577	0.019
	Nasal height (n-sn)	48.5212	50.3577	0.338
	Nasal length (sn-pr n)	16.3364	14.9769	0.405
Mouth	Mouth width (ch-ch)	43.5515	44.4615	0.509
	Lower third face height (sn-gn)	57.3091	60.3654	0.093
Eye	Outer eye space (ex-ex)	89.7	92.5308	0.455
	Inner corner eye space (en-en)	33.0182	34.3346	0.062
	Eye length (en-ex)	30.7303	31.3423	0.498
Ear	Ear width (pra-pa)	37.2667	36.3385	0.557
	Ear Height (sa-sba)	53.6942	57.8962	0.011

P < 0.05 is significant

Relation of different blood groups and orofacial parameters were insignificant for all parameters (face, nose, ear, eyes and ears) as shown in Table 3.

Table 3: Comparison between blood groups of B thalassemia patients and orofacial measurments

OFM		Blood group			P-value
		A	B	O	
Face	Face width (zy-zy)	97.4048	97.7941	96.9381	0.947
	Facial height (n-gn)	107.9714	108.3	106.0714	0.775
	Upper facial Morphological height (n-sto)	71	71.4059	68.419	0.464
	Maxillary depth (t-sn)	116.3905	118.4529	118.7524	0.716
	Mandibular depth (t-gn)	130.7143	130.6	131.7667	0.952
Nose	Nasal width (al-al)	34.1095	36.4353	35.1048	0.096
	Nasal height (n-sn)	49.2857	50.5059	48.4238	0.685
	Nasal length (sn-pr n)	16.9143	14.4353	15.6143	0.472
Mouth	Mouth width (ch-ch)	43.6952	43.9118	44.2429	0.945
	Lower third face height (sn-gn)	58.6524	57.7588	59.3857	0.778
Eye	Outer eye space (ex-ex)	89.5429	92.6412	90.981	0.808
	Inner corner eye space (en-en)	33.6762	33.2059	33.8381	0.768
	Eye length (en-ex)	31.3571	31.7588	30.0286	0.253
Ear	Ear width (pra-pa)	36.9762	36.3059	37.1857	0.9
	Ear Height (sa-sba)	55.9286	55.7118	55.029	0.897

p>0.05 NS

In evaluating the effect of splenectomy on OFM, significant difference was detected for the lower third face height (sn-gn) p=0.04 and ear width (pra-pa) p=0.053. Table 4.

Table 4: Relation of OFM of B thalassemia patient and splenectomy

OFM		Splenectomy		P-value
		-ve	+ve	
Face	Face width (zy-zy)	97.6	97.0	0.779
	Facial height (n-gn)	107.3	107.5	0.926
	Upper facial Morphological height (n-sto)	69.9	70.5	0.78
	Maxillary depth (t-sn)	118.8	116.8	0.442
	Mandibular depth (t-gn)	132.6	129.4	0.337
Nose	Nasal width (al-al)	35.6	34.6	0.226
	Nasal height (n-sn)	50.3	48.3	0.283
	Nasal length (sn-prn)	14.3	17.3	0.066
Mouth	Mouth width (ch-ch)	44.4	43.4	0.454
	Lower third face height (sn-gn)	56.9	60.6	0.04
Eye	Outer eye space (ex-ex)	93.0	88.6	0.244
	Inner corner eye space (en-en)	33.7	33.5	0.706
	Eye length (en-ex)	31.1	30.8	0.74
Ear	Ear width (pra-pa)	38.3	35.3	0.053
	Ear Height (sa-sba)	56.7	54.3	0.159

$p < 0.05$ = Significant

Table 5 show significant difference for cholecystectomy and orofacial measurements regarding eye length (en-ex) (p=0.000) and ear height (p= 0.019).

Table 5: Relation of cholecystectomy to OFM of B thalassemia patients

OFM		Cholecystectomy		P-value
		-ve	+ve	
Face	Face width (zy-zy)	97.8	92.1	0.118
	Facial height (n-gn)	107.8	102.8	0.31
	Upper facial Morphological height (n-sto)	70.6	65.8	0.215
	Maxillary depth (t-sn)	118.0	116.0	0.665
	Mandibular depth (t-gn)	131.3	129.0	0.704
Nose	Nasal width (al-al)	35.1	36.0	0.545
	Nasal height (n-sn)	49.6	46.3	0.333
	Nasal length (sn-pr n)	15.9	13.6	0.422
Mouth	Mouth width (ch-ch)	44.1	42.5	0.53
	Lower third face height (sn-gn)	58.9	56.4	0.452
Eye	Outer eye space (ex-ex)	91.8	81.9	0.142
	Inner corner eye space (en-en)	33.7	32.6	0.372
	Eye length (en-ex)	31.5	26.1	0.000
Ear	Ear width (pra-pa)	37.4	31.1	0.021
	Ear Height (sa-sba)	56.1	49.2	0.019

$p > 0.05$ NS

Discussion

The ultimate cure of transfusion dependent thalassemia is bone marrow transplantation, but this is very costly procedure for the majority of patients, their survival, therefore, depends on regular blood transfusions and iron chelating drugs It was found that severe anemia, frequent blood transfusion,,iron over load and chelation drug toxicities and bone changes are common complications of this hereditary disease [17,18]. The pathogenesis of skeletal changes is still unclear in spite of the enhanced treatment,, patients used to have derange in bone mineral turnover with raised resorption rates and inhibition of osteoblast action which result in diminished bone mineral density (BMD) clearly evident asosteoporosis in the vertebrae,skull and face[13,19].

The results of the current study showed that the number of male affected by thalassemia are higher than females (M :1.3\ F :1). However the differences were not significant. Our study is consistent with a study of Baghianimoghadam *et al*. 2011, and Hannan et al,2018[20.21], bone changes are more common in older age group,(31-40 years old) for mandibular depth (135.76mm) and mouth width (45.66mm) as in Table 1 Furthermore the study found that the relation of sex and orofacial measurments were significant in patients with B thalassemia, the facial variations of nasal width (36.25) and ear height (57.89) are higher in male than female Table 2.

Bone changes in adult thalassemia patients can be explained on the bases that chronic anemia increases erythropoietin secretion, lead to bone marrow expansion and thinning of bony cortices beside overloaded iron interferes with growth of osteoid and deposited in hydroxyapatite crystals thus effecting the normal bone mineralization furthermore desferoxamine (iron chelator) prevents DNA synthesis, proliferation, and maturing of fibroblasts and osteoblasts which enhance the skeletal deformities in thalassemia[22,23]. Different blood groups have no significant effect in changing craniofacial parameters as shown in table 3.

Splenectomy result in minor changes on orofacial parameters in thalassemia patients,differences were seen for lower third face (60mm) and ear width (35.3mmL) when compared with those without splenectomy as in Table 4 . Spleen is most commonly affected organ in B thalassemia due to excessive destruction of abnormal red blood cells, extra medullary hematopoiesis, and transfusion overload. The splenectomy definitely reduce blood need therefore improve hemoglobin level but seems to have prolonged orofacial changes[24,25]. In severe cases bone changes could be minimized when splenectomy is done as early as possible.

Cholelithiasis (gallstones) is well known complication in patients with thalassemia major: (TM) .Several possible explanations for this observation, including older age, high degree of ineffective erythropoiesis, whenever symptoms found, cholecystectomy must be done with follow up to prevent complications like obstructive jaundice and cholangitis[26]. Table 5 showed significant effect of cholecystectomy on orofacial measurements regarding eye length (p=0.00) and ear height. (p=0.019).

Further studies may assist in better understanding of the pathogenetic mechanism underlying bone anomalies in B thalassemia patients and it is needed to develop useful treatment therapy like use of bisphosphonate in early osteoporosis which is an effective regime to minimize the severity of skeletal complications, new-generation of iron chelators may reduce the negative effects of deferoxamine on bone metabolism. and to improve the nutritional,hormonal deficits with the help of physical training programs.

Conclusion

The screening for carriers, premarital regulatory rules and counseling programs, can help in decreasing the incidence rate and complications although a high prevalence of thalassemia in Basrahsouthern Iraq was observed,Results had shown sex dimorphism,older age groups are prone to have obvious bony changes,earlier splenectomy is advisable in severe cases, cholecystectomy is done whenever symptoms are found, ABO blood groups have no remarkable changes on OFM.

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