Orofacial, radiographic and salivary changes in thalassemia a major patients in Mosul

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Abstract:

Thalassaemia is considered one of the major health problem, which is widely distributed throughout the world.

Clinical orofacial, and radiographical examinations, in addition to the physical and biochemical analysis of the whole unstimulated saliva had been studied in Major thalassaemia patients (MTP) and the results compared with that of the normal subjects.

The study included (254) subjects. Thalassaemia patients (study group) composed of (201) patients and non-thalassaermic. patients (control group) composed of (53) subjects. Each group was divided into three subgroups according to their ages and sex distribution to study the chronological changes of the disease.

The first,second, and third groups were (6-11, 12-17,≥ 18) years old respectively.

The results of the study showed that, there was a significant difference in occlusal relation between thalassaemic and non-thalassaemic groups.

Thalassaemic patients had a significant degree of malocclusion and high significant degree of teeth discoloration than non-thalassaemic patients.

There were significant difference in oral hygein indices between thalassaemic and non-thalassaemic patients and even between male and female thalassaemic patients.

The intraoral radiographical assessment of the major thalassaemic patients showed that, there was thinning of the lamina dura and bone marrow hyperplasia which were significant when compaired with the non-thalassaemic patients.

Facial pigmentation and saddle nose were highly significant in major thalassaemic than non-thalassaemic patients.

Keywords:

Patients, tooth discolaration, maloclosion, facial pigmentation.

Introduction:

The thalassaemias are hetrogenous group of inhereted disorders characterized by deficient synthesis of specific globin chains normally present in human haemoglobin [1].

In 1925 and 1927 Cooley and associator's drew attention to an anaemia that had hetrofore been regarded as belonging to the hetrogenous group of Von Jaksch's anaemia but which possessed such well defined features as to constitute defined clinical entity and named as Cooley's anaemia. Outstareling features were its anaemia, ectreus,

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familial aspects, characteristic facies, skeletal changes, splenomegaly and the appearance of large number of circulating normoblast, in the circulating blood. Because of the late aspect the disease was initially termed erythroblastic anaemia [2].

The name thalassaemia, first applied by Whipple and Bradford in 1936, is derived from the Greek word thalassa, the sea, because the condition is particularly common in people originating from the Mediterranean basin [3].

The syndrom Mediterranean anaemia is still used although the distribution is now known to be much more extensive and lies in a belt including south Europe and north Africa through the Middle East to India, Indonesia and the far east [4].

Thalassaemia syndrom are named according to the type of chain defect so that there are α, β, γ and δ thalassaemias[5]. In some cases the synthesis of more than one chain is defective so that there are also α, β-and δβ-thalassaemias, moreover genes may be associated with those for other structurally abnormal haemoglobins so producing sickle cell/thalassaemia, haemoglobin C thalassaemia and so forth [6].

The terminology is sometime comfused by the use of clinical description such as major, intermedia, minor and minima. The usage is not uniform but major would imply the homozygous state and minor the hetrozygous state, intermedia could be either, while minima or "microcytemia" is a very common symptomless hetrozygous carrier state[7].

In homozygous beta-thalassaemia (thalassaemia-major), because both β globin genes are affected, there is marked deficiency in β globin chain synthesis but α glubin chain synthesis continues at an approximately normal rate [8].

Marked ineffective erythropoisis is the hallmark of thalassaemia because α globins highly insoluble and form large intracellular inclusions which interfere with erythroblast maturation, leading to intramedullary death of many red cell precursors[9].

The onset of thalassaemia major occurs with in the first two years of life, often in the first few months and run as short fulminating course. It may be less severe but terminating during childhood, or it may be relatively mild causing little disability and permitting survival into adult life. With vigorous and persistent treatment, patients who in the past would have died in childhood are now surviving into adult life [10].

The disease usually causes retardation of physical and mental development of the infant and children. There is palor, patchy skin pigmentation, abdominal distention due to enlargement of the spleen and liver, and various bony defects due at least partly to enlargement and extension of marrow cavities. Pathological fractures may occur[11].

The severely anaemic patient presents a pathognomonic facial appearance, including prominent frontal and parietal bosses, enlargement of the head, prominent molar eminence, depression of the bridge of the nose, puffy eyelids, a mongoloid slant of the eyes, often with an epicanthal fold[2]. Bimaxillary protrusion and malocclusions are frequent in thalassaemia major cases. As a result of these skeletal changes, the upper lip is retracted giving the child a "chipmunkfacies" [12].

The dentin and enamel are indicators of iron deposition, and deciduous and permanent teeth of thalassaemic patients contain up to five

times the iron concentration measured in normal patients. The high concentration of iron explains the discoloration of teeth in β-thalassaemic major patients [13].

Regular transfusions are life-saving, prevent the development of bony deformities, but lead to increasing deposition of iron in the tissues. Haemosiderosis is the main cause of complications in survivors and leads to dysfunction of glands and other organs. Xerostomia can result from iron deposition in the salivary glands[14].

Radiographically, patients exhibit enlarged marrow spaces in the jaw and thinning of the cortical layers. Widening of the diploic spaces in the skull, the trabeculae are thickened and arranged vertically, giving the "hair-on-end" appearance [15].

The purpose of the present study was to evaluate the clinical,and radiographical changes in addition to the salivary analysis of major thalassaemic patients in mosul.

Materials and methods:

The study was carried out on (254) subjects who were attending to Ibn Al-Atheer Teaching Hospital in Mosul. .

The study group consisted of (201) MTP, (112) patients were males and (89) patients were females.

The control group consisted of (53) subjects, (26) subjects were males and (27) subjects were females. The control group was taken from the patients' relatives who were attending the dental clinic in Ibn Al-Atheer Hospital.

The thalassaemic patients attending mainly every one month for blood transfusions, medical examinations and dental treatment if necessary. Each of the study and control groups were divided into three groups according to their ages and sex distribution as shown in table (1).

First group (Childhood): It consisted of subjects with the age range between (6-11) years old.

Second group (Adulthood): It consisted of subjects with the age ranged between (12-17) years old.

Third group (Adult): it consisted of subjects with the age (≥18) years old.

All the subjects were informed for the purpose of examinations, and it would include clinical, radiographical examinations and salivary analysis. Permissions to examine the patients were obtained from the concerned authorities in the ministry of health, and thalassaemia center in Ibn Al-Atheer teaching hospital.

Table (1): The distribution of the study and control groups according to age.

	Group No.	Age range (year)	Male	Female	Total
	Group I	6-11	12	13	25
Control	Group II	12-17	9	9	18
	Group III	≥18	5	5	10
	Group I	6-11	54	53	107
Study	Group II	12-17	48	33	81
	Group III	≥18	8	5	13

Data source

Case sheet was performed especially for the purpose of examination. It was include the following informations:

I. Case history: name, age, sex, address and other informations were included in the case history.

II. Clinical examinations: it was including:

a. Extraoral examinations: it was include the examination of the face for the presence of facial pigmentations, and also the examination of the nose to determine whether it was normal or saddle which was one of characteristic feature of MTP. Any other facial abnormalities were recorded in the examination.

b. Intraoral examination (IOE): it was carried out after the subjects were seated on a straight dental chair with a portable head rest under quite standardized conditions.

Dental mouth mirror, dental probe, WHO probe and a artificial light source were used using the recommendation of the WHO (World Health Organization).[16]

The IOE was include the following criteria:

1. Occlusal relation: Occlusal relation (class I, class II, class III) was determined for every subject under the study after asking the subject to close in centric occlusion.

2. Teeth relations: teeth relations were carried out by the examiner using a dental mouth mirror and dental probe to determine either the alignment of the teeth were normal or had a varying degree of spacing, crowding, open-bite and protrusion.

3. Teeth discoloration: teeth discoloration which were concerned in the study were the internsic discoloration. Polishing of the teeth using a pomus and rubber cups by contra angle hand piece were performed prior to examination to remove all the extrinsic stain.

The colour of discoloration was determined, which was varied from yellowish to brownish passing by yellowish brown discoloration.

The location of discoloration also was determined, which might be located at the gingival third, gingival and the middle third, or all the crown may be discoloured.

4. Dental conditions: The prevalence of dental caries was recorded in all study and control groups using (DMFT) Index for permanent dentition.and dmft/DMFT index for mixed dentition.

Examination of permanent teeth were started from the upper right 2 nd molar crossing the mid line to the upper left 2nd molar ,then the lower left 2 nd molar to the lower right molar. The 3rd molars were excluded.[17]

Diagnosis of dental caries was based on criteria by Jackson,[18] a lesion considered as caries when the probe plugged in the fissure and show resistance to pull.

5. Oral hygiene condition: Oral hygiene conditions were determined by using the following indices.

a. Gingival index system according to Loe and Silness,[19] used to determine the occurrence of gingival inflammation at (4) surfaces of the teeth.

b. Plaque index: The presence of dental plaque were examined at (4) surfaces of the teeth, and scored according to the criteria of plaque index system of Loe and Silness.[19]

c. Calculus index: The calculus was determined on (4) surface of the teeth, and scored according to the criteria of calculus index of simplified oral hygiene index for Green and Vermillion.[20]

6. Radiographical examination (RE)

The RE was undertaken using X-ray unite (QD) operated at "60 KVP and 10 m.a."

Periapical X-ray films size-2-speed-D-were used as intraoral films.

One radiographical X-ray film had been taken for the subject under

the study at the upper anterior region using standardized intraoral paralleling techniques. Lead appron were used for the child subjects for protection of their gonodal areas.

The X-ray films were examined for bone marrow hyperplasia (large marrow spaces and coarse trabiculae). The lamina dura of the bone was also examined.

7. Saliva

The examination of saliva should be started by preparing salivary samples.

The salivary samples obtained by:

A. Collection of saliva

The unstimulated whole mixed saliva was usually collected with the subject sitting quietly using spitting method. [21]

The samples were usually collected (2) hours after the breakfast. The subject was started by rinsing his mouth many times with water to remove all food debris retained in the mouth.

The subject asked to swallow the saliva collected in his mouth, the tip's tongue was placed against the upper lip; this will prevent the movement of the tongue which stimulates salivation and also prevents the swallowing of saliva.

Sterile graduated plane tube or sterile beaker was given to the subject for spitting the collected saliva. Stopwatch was started to collect the saliva of a given time. The saliva was collected for about (10) minutes, then the tops of the tube were closed to prevent the contamination of salivary samples.

B. Treatment of salivary samples: After getting the salivary samples; the salivary flow rate was calculated in (ml/minutes).

The samples were centrifuged at (2000 r.p.m.) for about 3 minutes to separate the foreign material.[22]

C- Physical analysis

Salivary flow rate (SFR):

The SFR was calculated by dividing the volume of collected saliva (ml) by the time required for the collection in minute.[22]

$$\text{Flow rate (ml/minute)} = \frac{\text{Volume(ml)}}{\text{Time(minute)}}$$

D- Biochemical analysis included salivary calcium, sodium,and potassium was determined by colormetric method.

Data was collected and analysed using SPSS 10 for windows software. Differences between observations wee considered significant at $P<0.05$.The following stastical method were used for the analysis of data.[24]

1-Standard stastical methods were used to determine the number , percentage, the mean and standard deviation(SD).

2-Fisher exact test was used to compare between frequencies of variables for males and females in the study groups; and between study groups and control for males, females ,and total.

3- Unpaired student t-test or z-test was used to compare between males and females in the study groups ; and between study groups and control for males, females and total for caries prevelance, oral hyagen conditions for saliva.

Results:

Occlusal Relation

In the study groups, (137) patients (68.2%) were class II occlusal relation. There is no significant difference between males and females in the study group. In comparison with the control group, the results are highly significant ($p<0.0001$), (Table 2).

Table (2): Occlusal relation in control and study groups.

Group	Sex	Male		Female		Total	
	Occlusal relation	No.	%	No.	%	No.	%
Control	Class I	22	84.6	24	88.9	46	86.8
	Class II	3	11.5	3	11.2	6	11.3
	Class III	1	3.9	0	0.0	1	1.9
Study	Class I	32	29.1	31	34.1	63	31.3
	Class II	77	70	60	65.9	137	68.2
	Class III	1	0.9	0	0.0	1	0.5
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

No significant difference between males and females in study group.

Teeth Relation

In the study group (59) patients (29.4%) had a varying degree of spacing in one arch and crowding in the other. There is a significant difference (p=0.001) between males and females in the study group. In comparison with the control group the results are highly significant (p<0.0001), (Table 3).

Table (3): Teeth relations in study and control groups.

Group	Sex	Male		Female		Total	
	Teeth relation	No.	%	No.	%	No.	%
Control	Normal	13	50	14	51.9	27	51.0
	Spacing	7	27	7	26.0	14	26.4
	Crowding	5	19.2	6	22.2	11	20.8
	S & C	1	3.8	2	7.4	3	5.7
	Open-bite	1	3.8	0	0.0	1	1.9
	Max pro.	1	3.8	0	0.0	1	0.0
	Bi-pro.	0	0.0	0	0.0	0	0.0
Study	Normal	16	14.5	16	17.6	32	15.9
	Spacing	29	26.4	27	29.7	56	27.9
	Crowding	22	20.0	27	29.7	49	24.4
	S & C	32	29.1	27	29.7	59	29.4
	Open-bite	17	15.5	10	11.0	27	13.4
	Max pro.	1	0.9	3	3.3	4	2.0
	Bi-pro.	2	1.8	1	1.1	3	1.5
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

Significant difference between males and females in study group (p=0.001).

Teeth Discoloration

In the study group, (186) patients (92.5%) had teeth discoloration. There is no significant difference between males and females in the study group. In comparison with the control group, the results are highly significant ($p<0.0001$), (Table 4).

Table (4): Teeth discoloration in control and study groups.

Group	Sex	Male		Female		Total	
	Discoloration	No.	%	No.	%	No.	%
Control	Yes	2	7.7	5	18.5	7	13.2
	No	24	92.3	22	81.5	46	86.8
Study	Yes	105	25.5	81	89.0	186	92.5
	No	5	4.5	10	11.0	15	7.5
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

No significant difference between males and females in study group.

The colour of Discoloration

In the study group, (153) patients (82.3%) of all patients with teeth discoloration had yellowish discoloration. There is no significant difference between males and females in the study group (Table 5).

Table (5): The colour of discoloration in control and study groups.

Group	Sex	Male		Female		Total	
	Colour of discoloration	No.	%	No.	%	No.	%
	Yellowish	2	100	5	100	7	100
Control	Brownish	0	0.0	0	0.0	0	0.0
	Yellowish -Brown	0	0.0	0	0.0	0	0.0
	Yellowish	83	79.0	70	86.4	153	82.3
Study	Brownish	17	16.2	7	8.6	24	12.9
	Yellowish -Brown	5	4.8	4	5.0	9	4.8

No significant difference between males and females in study group.

The Location of Discoloration

Teeth discoloration were divided according to their location into:

1. Discoloration in the gingival area:

Twenty-two (11.8%) MTP had yellowish discoloration in the gingival area of the teeth. There is no significant difference between males and females in the study group (Table 6).

Table (6): The location of discoloration in control and study groups,
a. In gingival area

Group	Sex	Male		Female		Total	
	Colour	No.	%	No.	%	No.	%
Control	Yellowish	1	50	4	80	5	71.4
	Brownish	0	0.0	0	0.0	0	0.0
	Yellowish -Brown	0	0.0	0	0.0	0	0.0
Study	Yellowish	12	11.4	10	12.34	22	11.8
	Brownish	2	1.9	1	1.23	3	1.6
	Yellowish -Brown	1	1	0	0.0	1	0.54

No significant difference between males and females in study group.

2. Discoloration in the Gingival and Middle Areas of the Teeth

In the study group, (25) patients (13.4%) had yellowish discoloration in the gingival and middle areas of the teeth. There is no significant difference ($p>0.05$) between males and females in the study group (Table 7).

Table (7): The location of discoloration in control and study groups,
b. In Gingival and middle areas.

Group	Sex	Male		Female		Total	
	Colour	No.	%	No.	%	No.	%
Control	Yellowish	0	0.0	0	0.0	0	0.0
	Brownish	0	0.0	0	0.0	0	0.0
	Yellowish –Brown	0	0.0	0	0.0	0	0.0
Study	Yellowish	15	14.3	10	12.3	25	13.4
	Brownish	1	1	1	1.23	2	1.1
	Yellowish –Brown	1	1	0	0.0	1	0.54

No significant difference between males and females in study group.

3. Discoloration in All the Crown (Diffused)

In the study group, (106) patients (57%) had diffused yellowish discoloration. There is no significant difference between males and females in the study group (Table 8).

Table (8): The location of discoloration in control and study groups,

c. All the crown (Diffused).

Group	Sex	Male		Female		Total	
	Colour	No.	%	No.	%	No.	%
	Yellowish	1	50	1	20	2	28.6
Control	Brownish	0	0.0	0	0.0	0	0.0
	Yellowish -Brown	0	0.0	0	0.0	0	0.0
	Yellowish	56	53.3	50	61.73	106	57
Study	Brownish	14	13.3	5	6.2	19	10.22
	Yellowish -Brown	3	2.8	4	4.93	7	3.8

No significant difference between males and females in study group.

DMFT Index

The mean value of DMFT index in the study group was (9.81). There is no significant difference between males and females in the study group. The mean value of DMFT index in the control group was (7.42).

There is a high significant difference ($p<0.0001$) between study and control groups. In comparison between males and females in the study and control groups, the result is highly significant ($p<0.0001$) between males and significant ($p<0.01$) between females, as shown in table (9).

Table (9): DMFT index in the study and control groups.

Sex	Age (year)	Mean ± SD		Z	p-value
		Control	Study		
	6-11	7.33 ± 3.52	10.0 ± 4.14		<0.05
Male	12-17	7.78 ± 0.67	10.29 ± 2.92		<0.01
	≥18	8.80 ± 2.39	13.25 ± 3.41		<0.05
	6-11	6.69 ± 1.55	8.09 ± 3.71		<0.01
Fm	12-17	6.44 ± 2.40	9.94 ± 3.55		0.001
	≥18	9.20 ± 2.39	13.00 ± 4.12		>0.05
	6-11	6.72 ± 2.81	8.94 ± 3.70	2.10	<0.01
Total	12-17	7.11 ± 1.84	10.15 ± 3.18	2.48	<0.0001
	≥18	9.00 ± 2.26	13.15 ± 3.53	2.63	<0.01
Total males		7.77 ± 2.61	10.36 ± 3.66		<0.01
Total females		7.07 ± 2.20	9.12 ± 3.83		<0.01
Total sample		7.42 ± 2.41	9.81 ± 3.78		<0.0001

Plaque Index

The mean value of PI in the study group was (2.39). There is a significant difference ($p<0.05$) between males and females in the study group. The mean value of PI in the control group was (1.87). There is a significant difference ($p=0.001$) between study and control groups. In comparison

between males and females in the study and control groups, the results are significant ($p<0.0001$) and ($p=0.001$) between males and females respectively (Table 10).

Gingival Index

The mean value of GI in the study group was (2.14). There is a significant difference ($p<0.05$) between males and females in the study group (Table 10). The mean value of GI in the control group was (1.65). In comparison with the control group, the results are highly significant ($p<0.0001$), (Table 10).

Calculus Index

The mean value of CI in the study group was (2.13). There is a significant difference ($p<0.05$) between males and females in the study group. The mean value of CI in the control group was (1.61). In comparison between study and control groups, the results are highly significant ($p<0.0001$) (Table 10).

Table (10): Oral hygiene conditions (plaque, gingival and calculus indices) in control and study groups.

Sex	Parameters	Mean ± SD		Z	p-value
		Control	Study		
	PI	1.87 ± 0.56	2.44 ± 0.47	4.68	<0.0001
Male	GI	1.76 ± 0.54	2.19 ± 0.39	4.41	<0.0001
	Cal	1.73 ± 0.54	2.17 ± 0.45	3.97	<0.0001
	PI	1.94 ± 0.52	2.27 ± 0.46	3.18	0.001
Fm	GI	1.56 ± 0.52	2.07 ± 0.46	4.31	<0.0001
	Cal	1.52 ± 0.46	2.09 ± 0.55	4.69	<0.0001
	PI	1.89 ± 0.45	2.39 ± 0.47	3.20	0.001
Total	GI	1.65 ± 0.54	2.14 ± 0.43	6.34	<0.0001
	Cal	1.61 ± 0.50	2.13 ± 0.50	6.38	<0.0001

Salivary Flow Rate

The mean value of salivary flow rate in unstimulated whole saliva was (0.22) ml/min. There is no significant difference between males and females in the study group (Table 10). The mean value in the control group was (0.37) m/min. In comparison between study and control groups, the results are highly significant ($p<0.0001$), (Table 11).

Salivary Ions

Salivary Calcium Concentration

The mean value of calcium concentration in unstimulated whole saliva was (5.16) mg/dl. There is no significant ($p>0.05$) between males and females in the study group (Table 11). The mean value in the control group was (5.20) mg/dl. In comparison between study and control groups, the results are not significant (Table 11).

Salivary Potassium Concentration

The mean value of potassium concentration in unstimulated whole serum saliva was (45.1) mmol/L. There is no significant difference between males and females in the study group. The mean value in the control group was (27.82) mmol/l. In comparison between study and control groups, the results are highly significant ($p<0.0001$), (Table 11).

Salivary Sodium Concentration

The mean value of sodium concentration in unstimulated whole saliva was (28.73) mmol/L. There is no significant difference between males and females in the study group (Table 4.12). The mean value in the control group was (14.98) mmol/l. In comparison between study and control groups, the results are highly significant ($p<0.0001$), (Table 11).

Table (11): Salivary conditions in control and study groups.

Sex	Parameters	Mean ± SD		Z	p-value
		Control	Study		
	Sal-Flow	0.39 ± 0.08	0.22 ± 0.09	6.47	<0.0001
Male	S. Ca	5.21 ± 1.05	5.25 ± 1.48	0.09	>0.05
	S. K	30.45 ± 8.54	48.58 ± 22.01	4.09	<0.0001
	S. Na	16.40 ± 3.39	29.89 ± 10.28	5.78	<0.0001
	Sal-Flow	0.35 ± 0.08	0.22 ± 0.08	5.64	<0.0001
Fm	S. Ca	5.19 ± 1.09	5.03 ± 1.21	0.34	>0.05
	S. K	25.38 ± 7.57	39.84 ± 23.54	3.47	<0.0001
	S. Na	13.72 ± 3.86	26.99 ± 9.56	5.60	<0.0001
	Sal-Flow	0.37 ± 0.08	0.22 ± 0.09	8.60	<0.0001
Total	S. Ca	5.20 ± 1.06	5.16 ± 1.38	0.29	>0.05
	S. K	27.82 ± 8.37	45.10 ± 22.91	5.60	<0.0001
	S. Na	14.98 ± 3.86	28.73 ± 10.04	8.18	<0.0001

Radiographic Interpretations

Thinning of the Lamina of dura

In the study group (53) patients (89.8%) out of (59) patients included in the intraoral radiographical examination had thinning of the lamina dura. There is no significant difference between males and females in the study group. In comparison with the control group, the results are highly significant ($p<0.0001$).

Hyperplasia of the Bone Marrow

In the study group (48) patients (81.4%) out of (59) patients included in the intraoral radiographical examination had hyperplasia of the bone marrow. There is no significant difference between males and females in the study group. In comparison with the control group, the results are highly significant ($p<0.0001$).

The Condition of the Nose

In the study group (174) patients (86.6%) had a saddle nose. There is no significant difference between males and females in the study group. (Table 12).

Table (12): The condition of the nose in control and study groups.

Group	Sex	Male		Female		Total	
	Condition	No.	%	No.	%	No.	%
Control	Normal	26	100	27	100	53	100
	Saddle	0	0.0	0	0.0	0	0.0
Study	Normal	13	11.8	14	15.4	27	13.4
	Saddle	97	88.2	77	84.6	174	86.6
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

No significant difference between males and females in study group.

Facial Pigmentation

In the study group (129) patients (64.2%) had a facial pigmentation. There is no significant difference between males and females in the study group (Table 13).

Table (13): Facial pigmentation in control and study groups.

Group	Sex	Male		Female		Total	
	Pigmentation	No.	%	No.	%	No.	%
Control	Present	0	0.0	0	0.0	0	0.0
	Absent	26	100	27	100	53	100
Study	Present	73	66.4	56	61.5	129	64.2
	Absent	37	33.6	35	38.5	72	35.8
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

No significant difference between males and females in study group.

Hepatitis

In the study group (53) patients (26.4%) had viral hepatitis (Table 14). Fourty three patients (81.13%) had HC. There is no significant difference between males and females in the study group (Table 15).

Table (14): Hepatitis in control and study groups.

Group	Sex	Male		Female		Total	
	Hepatitis	No.	%	No.	%	No.	%
Control	Yes	0	0.0	0	0.0	0	0.0
	No	26	100	27	100	53	100
Study	Yes	32	29.1	21	23.1	53	26.4
	No	78	70.9	70	76.9	148	73.6
Fisher Exact Test		p<0.01		p<0.01		p<0.0001	

No significant difference between males and females in study group.

Table (15): Types of hepatitis in control and study groups.

Group	Sex	Male		Female		Total	
	Hepatitis	No.	%	No.	%	No.	%
Control	HB	0	0.0	0	0.0	0	0.0
	HC	0	0.0	0	0.0	0	0.0
	HB + HC	0	0.0	0	0.0	0	0.0
Study	HB	1	3.1	3	14.3	4	7.55
	HC	27	84.4	16	76.2	43	81.13
	HB + HC	4	12.5	2	9.5	6	11.32

No significant difference between males and females in study group.

Splenoctomy

In the study group (87) patients (43.3%) were splenectomized. There is no significant difference between males and females in the study group (Table 16).

Table (16): Splenectomy in control and study groups.

Group	Sex	Male		Female		Total	
	Splenectomy	No.	%	No.	%	No.	%
Control	Yes	0	0.0	0	0.0	0	0.0
	No	26	100	27	100	53	100
Study	Yes	45	40.9	42	46.2	87	43.3
	No	65	59.1	49	53.8	114	56.7
Fisher Exact Test		p<0.0001		p<0.0001		p<0.0001	

No significant difference between males and females in study group.

Haemoglobin Concentration

The mean value of Hb concentration in the study group was (7.79) g/dl. There is no significant difference between males and females in the study group (Table 4.21). The mean value in the control group was (10.09) g/dl. In comparison between study and control groups, the results are highly significant ($p<0.0001$) in the total number. Between males and females, the results are significant ($p<0.05$) and ($p<0.01$) respectively, (Table 17).

Table (17): Haemoglobin concentration in control and study groups.

Sex	Parameters	Mean ± SD		Z	p-value
		Control	Study		
	Hb	10.53 ± 5.96	7.81 ± 1.67	2.41	<0.05
	Hb	9.73 ± 4.79	7.76 ± 1.93	2.92	<0.01
	Hb	10.09 ± 5.28	7.79 ± 1.75	3.92	<0.0001

Discussion:

To minimize the effect of individual variation, diurnal effect and other general factors, the method of subjects examination, the time of their examination and the posture had been standardized as possible to be the same for all subjects.

The control and study groups were divided into (3) groups according to their ages and sex distribution to study the chronological changes of the disease.

As thalassaemia major is a sever disease and have many serious complications, it is most unusual for the child who had required regular blood transfusions to survive to the third decade. [1,2] This explained the declination in the number of subjects in the study group 3.

In the study group 3 there were only (13) patients examined and this small number of patients extremely affect the statistical and chrinological studies of the disease.

Occlusal relations:

Unusual prominence of the maxilla had been described in cases of cooley's anaemia. This may be attributed to the enlarged marrow spaces in response to a stimulus for increased production of red cells (Shefer et al., 1996; George and Stephen, 1978).

In the present study occlusal relation was accessed, (68.2%) of the MTP had class II occlusal relation. In the study group one (63.6%) had class II occlusal relation, in the study groups two and three, (75.3%) and (61.5%) of the MTP had class II occlusal relation respectively. There are no statistical differences between males and females in the study groups.

This finding is in agreement with Asbell (1964), who found a midfacial overgrowth in the major thalassaemia accompanied by incisal prominence and shortness of the mandibular corpus.

Teeth relations:

Expansion of the medullary cavities of the facial bones in thalassaemia major produce bossing and prominence of the maxilla, which leads to an overbite of the mandible and ectopia of the teeth, especially the incisors (Mengel *et al.*, 1973).

The degree of malocclusion corresponded with the deterioration of patient general condition (Cannel, 1988).

In the present study (29.4%) of the patients had a varying degree of spacing and crowding. In the study group one (33.6%) had spacing and crowding while, in the study group two (32.1%) had spacing and crowding. This decrease in the percentage due to the period of mixed dentition in the study group one.

In the study group three (30.8%) of the patients had spacing and crowding and the same percentage of the patients had only spacing. This increased percentage of spacing in this group due to increased rate of teeth exfolation in addition to bony changes.

There are significant differences in dental relations between males and females in the study groups, this can be attributed to the Taz and Tizar (1976) study, who found that the thalassaemic males showed more variation in dental size and morphology than thalassaemic females.

The result of this study is in agreement with Novak (1944), who conclude that the bony changes in MTP contribute to malocclusion.

Teeth discoloration:

Internsic teeth discoloration was reported in patient with blood dyscrasia such as sickle cell anaemia,

thalassaemia and hemolytic disease of the new born (HDN).

In the present study most of the patients (92.5%) had teeth discoloration. Discolorations were divided according to their locations and colours. In the group one (60.4%) had diffused yellowish discoloration and (6.3%) had diffused brownish discoloration. In the study group two (55.1%) of the patients had diffused yellowish discoloration and (10.25%) had diffused brownish discoloration. In the study group three (41.7%) had diffused yellowish discoloration and the same percentage had diffused brownish discoloration. These finding indicate that, there is a shifting from yellowish to the brownish discoloration of the teeth with the age and this is agree with Cullen (1990) who found that the haemolytic disease have the potential to cause hyperbilirubinemia and subsequent dose-dependant in corporation of the biliverdin into the developing teeth.

DMFT:

Thalassaemic patients have several factors which may affect the dental caries prevalence such as malocclusion and drying of the gingiva through the patient inability to close his mouth (Parkin, 1968), in addition to decrease salivary flow rate due to iron deposition in serous cells of salivary glands (Goldfrad, 1983).

In the present study the main DMFT index in the study group was (9.81) which is significantly higher than that of control group (7.42). This can be attributed to the role of iron ions which are incorporated or exchange with hydroxyapitite crystals or hard dental tissue of the newly erupted teeth (Narender, 1966; Benjamin, 1957).

The result of this study disagree with the result reported by Al-Yoshfani (2002), who found that, there is no significant difference in dental caries prevalence between thalassaemic and non-thalassaemic groups.

Also, the result disagree with the result reported by Kaplan and associates (1964), who found that the DMFT index in MTP were not unusual.

Oral hygiene condition:

Few studies deal with oral hygiene condition in thalassaemic patients. As those patients have a major health problem, their oral hygiene programs are neglected in comparison with saving their life.

In this study plaque, gingival and calculus indices were assessed to evaluate the oral hygiene condition.

The results shown that, these oral hygiene indices were relatively higher in MTP when compared with normal subjects. This can be attributed to the malocclusion in MTP and decreased salivary flow rate in addition to the limited oral hygiene programs for such medically compromised patients.

These results agreed with Al-Mashadany (1994), who studied the gingival and periodontal health of the MTP, he found an increase prevalence of periodantitis in MTP. But, these results disagree with Kaplen and associates (1964), who found that the gingival inflammation in thalassaemic patients were not unusual.

In the thalassaemic patients, there were significant differences in such oral hygein indices between males and females. This can be attributed to the differences in the size and morphology between males and females thalassaemic teeth (Taz and Tizar, 1976). In the study groups one and three, there are no significant difference between males and females, this can be attributed to the period of mixed dentition in the study group one

and large exfoliation of the teeth in the study group three. The significant differences are in the study group two when the permanent dentition are completed.

Salivary flow rate:

Blood transfusion is a life saving in thalassaemia major, but unfortunately massive accumulation of iron from red blood hemolysis is the main complication in survivors and leads to the dysfunction of glands and other organs (Thompson, 1977).

The present study shown that, the salivary flow rate in the thalassaemic patients was (0.22) ml/min which is significantly lower than that of normal subjects (0.37) ml/min. This result is in agreement with the result reported by Cawson (1994), who found that xerostomia can results from iron deposition in the salivary gland.

Also, the result is in agreement with the result reported by Weatheral (1997), who found that the excess of iron derived from distructed red blood cells deposit in the vital organs like spleen, liver, heart and glands and interfere with their functions.

Salivary ions concentration:

In the present study salivary calcium, sodium and potassium ions concentration were measured. This is the first study concerned with the concentration of these salivary ions in MTP.

The present study showed that, the salivary calcium ions concentration in the study group was (5.16) mg/dl which is not significantly lower than control group (5.20) mg/dl. In the study group one, patients had mixed dentition and the eruption of the most permanent dentition completed, the salivary calcium ions concentration was (5.12) mg/dl which is slightly higher than control group (5.03) mg/dl. This finding can be attributed to the suggestion of Misra and Bowen (1998), who suggest that the cupric ions in beta-thalassaemic patients would probably exchange with labile tooth surface calcium of newly erupted teeth. Also the present study showed that, the salivary sodium and potassium ions concentration in the study group are significantly higher than control group.

These salivary ions alteration can be attributed the role of hemosiderosis on the salivary glands in the iron storage diseases (Benjamin, 1957).

Radiographical Changes :

Thalassaemia major is basically one of abnormal haemoglobin production and marked red blood cells haemolysis. To overcome this problem, the bones increase their activity (Poyton, 1982).

It is evident from the present study, that (81.4%) of the patients had bone marrow hyperplasia. In the study group one (68.2%) of the patients had bone marrow hyperplasia, in the study group two and three, the percentage increased to be (88.5%) and (90.9%) respectively.

This finding is in agreement with George and Stephen (1978), who found that the bony changes in major thalassaemia are related to the enlarged marrow spaces in response to a stimulus for increased production of red cells.

Also this finding is in agreement with Saap et al. (1997), who found that the maxilla and mandible have very large marrow spaces and a paucity of trabiculae, sometimes the trabicular are large and course.

The present study also showed that (89.8%) of the patients had thinning of the lamina dura. This finding agreed with Gorlin and

Goldman (1970) who describe the intraoral roentgenograms of the MTP as showing irregular osteoporosis and enlarged marrow spaces, and the lamina dura is less dense than normal.

Also this finding is in agreement with Poyten and Davey (1963) who found that the lamina dura about the roots and the opaque lamina around the crypts of the developing teeth of MTP may be thin.

Condition of the nose:

Hemolysis and compensatory bone marrow hyperplasia are generally considered responsible for skeletal changes in major thalassaemia (Poyten and Darey, 1968).

In the present study (86.6%) of the patients had a saddle nose. In the study group one (82.2%) had a saddle nose, in the study group two and three (91.4%) and (92.3%) of the patients had saddle nose respectively.

This finding is in agreement with Gupte (1986) who found that the facial appearance in major thalassaemia gradually assume what has been termed a "mongoloid appearance" with frontal bossing, hyperatrophy of the maxilla with depression of the nasal bridge.

Also this finding is in agreement with Kaeplen et al. (1991), who found that there is a midfacial overgrowth with flattening of the bridge of the nose in the major thalassaemia patient.

Facial pigmentation:

The human cells have a very limited ability to excrete iron, regular blood transfusions inevitably leads to a vast accumulation. Excess iron deposition occurs in virtually all organs. Most cells have a considerable ability to cope with this extra iron by marking ferritin and its partial degeneration product hemosiderin (Wyngarden and Smith, 1985).

The skin color in major thalassaemia become ashen-gray due to the combination of pallor, Jaundice and Hemosiderosis (Burkets, 1994).

In the present study (64.2%) of the patients had a facial pigmentation. In the study group one (52.3%) had facial pigmentation, while in the study group two and study group three (77.8%) and (77%) of the patients had facial pigmentation. This indicates that the facial pigmentation is gradually increased with age and directly related the amount of blood transfusion as the blood transfusion is the life saving in the major thalassemic patients.

This finding is in agreement with Behnman et al. 2000 who found that the haemosidcrosis is an inevitable consequence of prolonged transfusion therapy.

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