

EFFECT OF HEMOGLOBIN AND FERRITIN OF SERUM CONCENTRATIONS ON THE DENSITY OF JAWBONE THAT INTENDED FOR DENTAL IMPLANT IN PATIENTS WITH MAJOR THALASSEMIA: A CLINICAL AND COMPUTED TOMOGRAPHY STUDY

George H. Salloum¹, Mounzer Assad², Ammar M. Ammoun³

1.MSc Department of Oral Medicine, Faculty of Dentistry, Tishreen University, Lattakia, Syria.

2.Ass.Prof., Department of Oral Surgery, Faculty of Dentistry, Tishreen University, Lattakia, Syria.

3.Prof., Department of Oral Medicine, Faculty of Dentistry, Tishreen University, Lattakia, Syria

ABSTRACT:

Aim : To assess the effect of hemoglobin and ferritin of serum concentrations on the density of jaws bones and subsequently to assess the possibility of dental implantation in patients with major thalassemia .

Materials and Methods: Hemoglobin and Ferritin of serum concentrations were measured in 30 patients with major thalassemia (older than 16 years old) transfusion dependent during 12 months, then the density was assessed by dental CT scan . The results were compared with the results of same procedures in 10 healthy people with normal hemoglobin and ferritin of serum concentrations.

Results: There was a statistically significant relation between the low concentrations of hemoglobin and low density of both jaws . There was a statistically significant relation between the high concentrations of Ferritin and low density of the maxillary bone.

Conclusion: In subjects with relatively high concentrations of Hemoglobin and low concentrations of Ferritin, the density of the jaws bone in patients with thalassemia major maybe appropriate to receive dental implants.

Key words: Hemoglobin, Ferritin, Bone density, Jawbone, Dental implantation, LBD: Low bone density, Computed tomography.

INTRODUCTION:

Thalassemia is a form of inherited autosomal recessive blood disorder characterized by abnormal formation of hemoglobin. ^[1] Normally, the majority of adult hemoglobin is composed of four protein chains, two α and two β globin chains . In thalassemia, patients have defects in either the α or β globin chain, causing production of abnormal red blood cells. The thalassemias are classified according to which chain of the

hemoglobin molecule is affected. In α -thalassemias, production of the α globin chain is affected, while in β -thalassemia, production of the β globin chain is affected. Two genes encode the β chain, and four genes encode the α chain. In major thalassemia the two genes that encode the β chain are affected. ^[2]

Patients with major thalassemia are susceptible to have low bone density with multi factorial mechanism. Transfusion

related iron overload in endocrine organs leads to impaired growth hormone secretion, the direct iron toxicity on osteoblasts , chronic anemia and tissue hypoxia, gonadal dysfunction, hypothyroidism, hypoparathyroidism, and vitamin D deficiency that contribute to impairment in achieving an adequate bone mass. [3]

The aim of this study was to assess the effect of hemoglobin and ferritin of serum concentrations on the density of jawbone and subsequently to assess the possibility of dental implantation in patients with major thalassemia.

MATERIALS AND METHODS:

In this clinical and computed tomography study, 30 patients with transfusion dependent thalassemia (major thalassemia) older than 17 years old attending to thalassemia department in pediatric hospital in Lattakia , Syria were included.

Hemoglobin and ferritin of serum concentrations were measured every time before and after blood transfusion during 12 months, then the density was assessed by dental CT scan, Hounsfield-Unit value (HU) was determined in 4 sequenced slices in sagittal plane and 4 sequenced slices in frontal plane for both jaws. The results were compared with the results of same procedures in 10 healthy people (control group) with normal concentration of hemoglobin and ferritin of serum.

RESULT:

This study population included 30 patients (16 female , 14 male; mean age: 22.33 , range 17-32 years) with major thalassemia, and 10 healthy people (5 female , 5 male; mean age: 23 , range: 17-33 years) as a control group. The clinical characteristics of patient group and control group are summarized in Table1. The mean of hemoglobin concentration in patient group was 7.75 gr/dl , the mean of ferritin was 2580.9 ng/ml.

The mean HU value of the patients' group was 255.86 for the maxillary bone and 398.48 for the mandibular bone. While the mean HU value of the control group was 615.51 for the maxillary bone and 859.46 for the mandibular bone. Comparing with control group, all 30 patients (100%) had LBD in maxillary bone and 28 patients (93.33%) had LBD in mandibular bone. Results of the patients group are summarized in Table2.

DISCUSSION:

Patients with major thalassemia are transfusion blood and iron chelation therapy dependent, they are at risk to develop osteopenia and osteoporosis. [4,5,6,7,8] The aetiology of thalassemia major induced bone mineral loss is multifactorial and complicated [9,10], a patient's weight, age, duration of the disease and history of hypogonadism or concurrent hypothyroidism are significant contributory factors or predictors.[7] Predisposing factors of osteoporosis in patients with transfusion related thalassemia are: endocrine insufficiency due to iron overload (delay in sexual maturation, hypoparathyroidism,

hypothyroidism, diabetes mellitus and growth hormone insufficiency), direct iron toxicity on osteoblasts, progressive marrow expansion due to accelerated hematopoiesis and side effect of Deferoxamine which is used as an iron chelator.^[11,12] This study showed there's a significant relation between hemoglobin level and LBD in both jaws, The lowest levels of hemoglobin associated with lower bone density in both jaws. Also there was a significant relation between ferritin of serum level and LBD in maxillary bone, higher levels of ferritin associated with lower bone density in maxillary bone that suggest the maxillary bone is more affected than the mandibular bone by ferritin of serum level. Also this study showed that the maxillary bone is more severity affected by hemoglobin and ferritin of serum levels than the mandibular bone.

In accordance with Kyriakou et al.^[9], Doxiadis et al.^[13] and Jensen et al.^[14], this study showed there is a relation between LBD and gender, male patients are more

severity affected than female patients. However, some studies didn't find a significant relation between LBD and gender.^[15,16] Therefore, more studies with wider population are required.

Depending on Misch bone density classification, bone is divided for 5 types (D1,D2,D3,D4,D5), and the suitable types for dental implantation are D2 and D3.^[17] In this study we found that patients with major thalassemia are at risk to have jawbone from type D4 and sometimes D5. Therefore, these patients have special criteria to make a decision for dental implantation.

CONCLUSION:

Dental implantation may be possible with major-thalassemia patients in special conditions. It's important to assess the density of the jawbone before making a decision. Keeping a good level of hemoglobin and a low level of ferritin in serum may increase the opportunities to have successful dental implants.

mineral density. *J Pediatr Hematol Oncol* 2010; 32: 267–273.

REFERENCES:

1. Mayo Clinic. "Thalassemia". Mayo Clinic. Retrieved 17 October 2014
2. Robbins Basic Pathology, Page No:428
3. Hamed EA, Mohamed NA, El-Metwally TH, Kamal MM. Iron chelation therapy in Upper Egyptian transfusion-dependent pediatric homozygous beta-thalassemia major: impact on serum L-carnitine/free fatty acids, osteoprotegerin/the soluble receptor activator of nuclear factor-kappa beta ligand systems, and bone
4. Scacchi M, Danesi L, Cattaneo A et al. Bone demineralization in adult thalassaemic patients: contribution of GH and IGF-I at different skeletal sites. *Clin Endocrinol (Oxf)* 2008; 69: 202–207.
5. Vogiatzi MG, Macklin EA, Fung EB et al.; Thalassemia Clinical Research Network. Bone disease in thalassemia: a frequent and still unresolved problem. *J Bone Miner Res* 2009; 24: 543–557
6. Gaudio A, Morabito N, Xourafa A et al. Bisphosphonates in the treatment of

- thalassemia associated osteoporosis. *J Endocrinol Invest* 2008;31: 181–18
7. . El-Edel RH, Ghonaim MM, Abo-Salem OM, El-Nemr FM. Bone mineral density and vitamin D receptor polymorphism in beta-thalassemia major. *Pak J Pharm Sci* 2010; 23: 89–96
 8. Leung TF, Chu Y, Lee V et al. Long-term effects of pamidronate in thalassaemic patients with severe bone mineral density deficits. *Hemoglobin*.2009; 33: 361–369.
 9. Kyriakou A, Savva SC, Savvides I et al. Gender differences in the prevalence and severity of bone disease in thalassaemia. *Pediatr Endocrinol Rev*. 2008; 6 (Suppl 1): 116–122.
 10. . D'Eufemia P, Finocchiaro R, Celli M et al. Taurine deficiency in thalassemia major-induced osteoporosis treated with neridronate. *Biomed Pharmacother* 2010; 64: 271–274.
 11. Voskaridou, E. & E. Terpos. New insights into the pathophysiology and management of osteoporosis in patients with beta thalassaemia. *Br J Haematol*.2004;127(2):127-39.
 12. Olivieri, N.F. The beta-thalassaemias. *N. Engl. J. Med*. 1999;341(2): 99–109
 13. Doxiadis S, Georgaki E, Papamichael D, Papadakou-Lagogianni S, Lapatsanis P. Bone density in thalassaemic children during the course of the disease. *Pediatr Res* 1978; 12: 811–815.
 14. Jensen CE, Tuck SM, Agnew JE et al. High prevalence of low bone mass in thalassaemia major. *Br J Haematol* 1998; 103: 911–915.
 15. Chapelon E, Garabedian M, Brousse V, Souberbielle JC, Bresson JL, de Montalembert M. Osteopenia and vitamin D deficiency in children with sickle cell disease. *Eur J Haematol* 2009; 83: 572–578.
 16. Shamshirsaz AA, Bekheirnia MR, Kamgar M et al. Metabolic and endocrinologic complications in beta-thalassemia major: a multicenter study in Tehran. *BMC Endocr Disord* 2003; 3: 4.
 17. Carl. E. Misch, "Contemporary Implant Dentistry", ed 2, St. Louis, 1999, Mosby Inc

TABLES:

Table1: clinical characteristics of patient group and control group

| Mean clinical characteristic | Patient group | Control group |
|------------------------------|---------------|---------------|
| Age | 22.33 | 23 |
| Hemoglobin | 8.1 | 14.36 |
| Ferritin | 2414.3 | 80.6 |

Table2: Demographic features of patients

| PATIENT | Age | Gender | Hemoglobin (gr/dl) | Ferritin (ng/ml) | HU of the maxillary bone | HU of the mandibular bone |
|---------|-----|--------|--------------------|------------------|--------------------------|---------------------------|
| 1 | 20 | Male | 9.7 | 4326 | 235.5 | 498.6 |
| 2 | 20 | Female | 10.1 | 2319 | 417.3 | 752.8 |
| 3 | 18 | Female | 6.2 | 1874 | 295.7 | 321.2 |
| 4 | 28 | Female | 8.9 | 5148 | 251.1 | 580 |
| 5 | 32 | Female | 8.5 | 2113 | 217.7 | 337 |
| 6 | 19 | Female | 7 | 1872 | 311.4 | 389.3 |
| 7 | 22 | Female | 7.6 | 4927 | 209.9 | 211,05 |
| 8 | 20 | Female | 9.5 | 2298 | 381.3 | 588.4 |
| 9 | 20 | Male | 6.9 | 4428 | 144.7 | 266.25 |
| 10 | 22 | Male | 5.5 | 2113 | 165.5 | 244.2 |
| 11 | 29 | Female | 7.4 | 1213 | 211.35 | 240.3 |
| 12 | 17 | Male | 6.6 | 2884 | 195.2 | 293.7 |
| 13 | 23 | Female | 8.7 | 1092 | 193.8 | 255.2 |
| 14 | 19 | Male | 8.5 | 2610 | 219.6 | 412.9 |
| 15 | 19 | Male | 7.3 | 4193 | 210.2 | 255.1 |
| 16 | 29 | Male | 6.8 | 1163 | 301.6 | 363.1 |
| 17 | 22 | Male | 7.1 | 2315 | 256.3 | 399.2 |
| 18 | 17 | Male | 8.4 | 2440 | 198.1 | 431.1 |
| 19 | 21 | Female | 9.3 | 1149 | 412.6 | 647.3 |
| 20 | 19 | Male | 9 | 2008 | 276.1 | 482.8 |
| 21 | 19 | Female | 6.6 | 1647 | 241.4 | 269.7 |
| 22 | 18 | Male | 7.8 | 3745 | 167.75 | 285.85 |
| 23 | 25 | Male | 5.8 | 1306 | 249.3 | 289.6 |
| 24 | 27 | Female | 10 | 1104 | 329 | 467.8 |
| 25 | 29 | Male | 9.3 | 1087 | 249.1 | 488.4 |
| 26 | 28 | Male | 7 | 800 | 209.85 | 358.15 |
| 27 | 19 | Male | 10.3 | 1826 | 339.4 | 728.1 |
| 28 | 27 | Female | 10.2 | 1499 | 359.23 | 548.32 |
| 29 | 17 | Female | 8.8 | 1493 | 299.7 | 413.6 |
| 30 | 25 | Male | 5.6 | 5437 | 126.1 | 147.6 |

Table3: Misch Bone Density Classification

Carl. E. Misch, "Contemporary Implant Dentistry", ed 2, St. Louis, 1999, Mosby Inc

| Bone | HU value | Density |
|------|----------|--|
| D1 | >1250 | Dense cortical bone |
| D2 | 850-1250 | Thick dense to porous cortical bone on crest and coarse trabecular bone within |
| D3 | 350-850 | Thin porous cortical bone on crest and fine trabecular bone within |
| D4 | 150-350 | Fine trabecular bone |
| D5 | <150 | Immature, non-mineralized bone |

Figure1: Deference in HU value between patients group and control groupFI

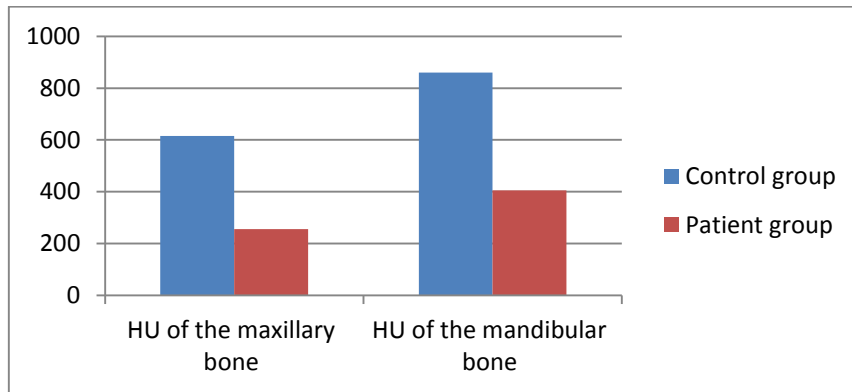


Figure2: Relation between Ferritin of serum level and HU value of the maxillarybone(x10)

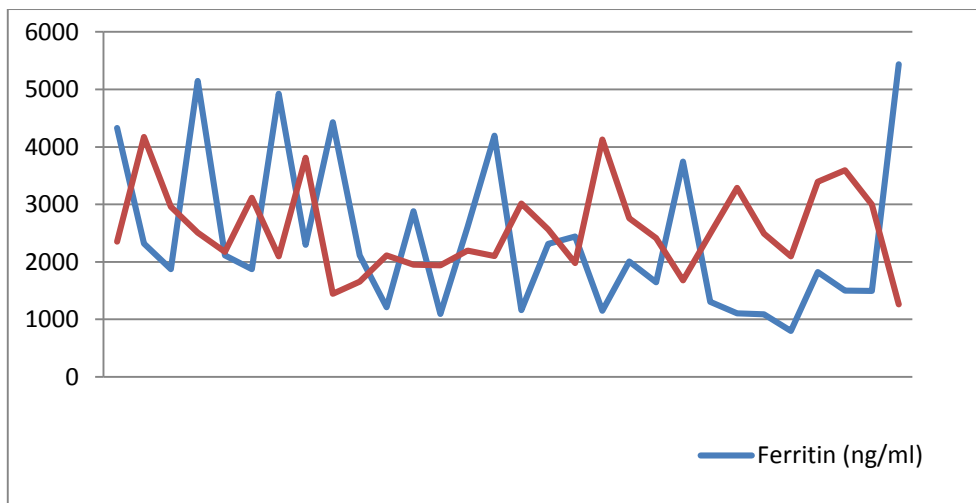


Figure3: A 3D computed tomography view shows the deference in bone density between a healthy person(a) and a patient with major thalassemia(b).

