Original Research Article

Salivary Iron And Ferritin Levels, Orofacial Complications of Patients With Thalassemia Major In Babylon Teaching Hospital For Maternity and Children

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Abstract
Different common known genetic disorders such as β-thalassemia major; cause the oral and dental problems. Elevated levels or overload of ferritin and iron need continuous chelation to eliminate toxic effects on the body tissues. The purpose of this study to detect the salivary ferritin and iron levels and association with oral and maxillofacial abnormalities or complications in β-thalassemia major. This study was done from January to march in 2017, thirty (30) patients with thalassemia type (β) major participated in pediatric and gynecology Babylon teaching hospital/department of hematology- hereditary blood disorders centers-sub branch (thalassemia), the examination procedures including (laboratory), intra and extra-orally views obtained foe each patients. Salivary analysis was highly significant (0.000) in salivary ferritin and iron levels in compared to controls. Different percentages of oral and perioral complications were appeared in those patients due to toxic effect of iron depositions.

Key Words: Thalassemia, blood disorders, iron deposition, organ failure.

Introduction

Emoglobinopathies is considering as other genetic disturbance[1]. Two alpha (α) and beta (β) chains are normally a tetramer of hemoglobin in adult persons; deficient synthesis of either the above α or β chains of globin in the molecules of hemoglobin lead to congenital disorder is called thalassemia in which the erythrocyte are an aberrant morphology with both microcytic and hypochromic [2]. The more severe congenital hemolytic anemia is β-thalassemia major. Hemolysis is huge and iron overload is precipitate in different types in human body, hematocrit level decrease below than 20% and hemoglobin level can reach 2 to 3 g/dl [3-6]. Iron over load remains high, that lead to prevalence of multiple complications. The
accumulations of iron in Beta thalassemia major patients is the sequel of defective erythropoiesis, elevated G.I.T absorption of iron, and loss of excreting mechanism of excess iron. About 250 mg of iron is the unit of transfused blood, while only about 1 mg of iron that the body excreted per day. If the iron binding capacity of transferrin present in the body plasma is consider highly toxic to the tissues as non-transferrin bound iron [7]. Dysfunction of heart, liver and endocrine glands are due to progressive accumulation of iron. Evaluation of iron loaded in Beta thalassemia major by measuring the serum ferritin level in the body [8, 9]. 1000 ng/l (usually after 10th to 12th transfusion) level of serum ferritin, generally used as a point to begin iron chelation therapy. Ashen-gray color of the face because the mixing pallor, hemosiderosis and jaundice. Cardiomegaly, hepatomegaly and splenomegaly are also notice in patients with thalassemia [10].

Oral and dental systems are affected, the main complications that appears in mouth, jaw and the face of thalassemia major. The preventing tooth structure from decay and therapeutic measures for control and reduce risk of infection whether dental or non-dental in origin, those seriously in these patients [11]. Level of ferritin in different body tissues is increases, due to lysis of red blood cells and lead to tissues and organs damage. Sedimentation of ferritin in salivary acini, will lead to salivary glands destructive and damage and dryness of the mouth, tooth decay as a consequences [12].

Dental and orofacial abnormalities include teeth spacing, saddle nose and protrusion of maxillary, molar bones, anterior open bite [13]. Expansion of marrow spaces are seen in radio graphical viewing, including the long bones as a cortical erosion rarefaction, nutrient foramina is enlarge and "raindrop" spaces in the cortex [14, 15].

As general taking in the jaws; the rarefaction in the alveolar bone, cortical bone is appear thin and a "chicken-wire" shape of the enlarge marrow spaces and lamina dura appear thin and premaxilla bone is thin and roots of the teeth are short in some cases [16]. Delayed pneumatization of the Para nasal sinuses. Because anemia and deposition of bilirubin pigment lead to lemon yellow or pale color of the oral mucosal surface [17].

Finally, defective globin chain structure, iron not related with hemoglobin inside the cells with increased iron in plasma lead to increase oxidative stress within thalassemia major patients. In these patients, periodontal diseases and chronic localized oral infections are appearing due to local and systemic immune with inflammatory response [18].

Materials and Methods
In this study was done for two months from January to march in 2017, thirty (30) patients with thalassemia type (β) major in pediatric and gynecology Babylon teaching hospital / department of hematology- hereditary blood disorders- sub branch (thalassemia), the examination procedures including (laboratory), intra and extra-orally with dental diagnostic disposable instruments( mirror, probe, flash light and sterilized gauze). Those patients were already diagnosed by hematology specialists in this center (pediatric and gynecology Babylon teaching hospital). The questionnaire was prepared and followed in each step of patient's examination. The patients with thalassemia majors were identical or matched in numbers and age ranges with control samples. Analysis of salivary iron by manual spectrophotometric method and salivary ferritin by Mini-vidus instrument. These patients that already compare with same numbers of controls persons with no signs and symptoms of any medical history.

Results
In the beginning, the normal iron level = 50-180 mg/ dl for male and for female is 60-175 mg/dl, while the normal values for ferritin levels are: 10-160 mg/dl for male < 45 years and 68-430 mg/dl for female, with age range (4-20) years old and these
normal values are used as stranded in body secretion. Thirty (30) patients with thalassemia type (β) major were taken without signs and symptoms of any other systemic diseases. Age of patients in this group is very important; because too low age ranges is less significant according to many previous researches such as Mohammed Shooriabi et al., March, 2016. All the saliva samples (about 2 ml of unstimulated state) were deep freezing at -20°C and store in clean sterile collections and analysis ways.

Different orofacial complications were appeared in those samples clinically, as Xerotomia (dry mouth) and Halitosis, change in oral mucosa, enlargements of salivary glands, candidial infections. The percentages of orofacial complications as follow:

Table 1: The group statistics; By (T- test) depend on two samples

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of samples</th>
<th>Mean</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary iron</td>
<td>30</td>
<td>306.0333</td>
<td>0.000</td>
</tr>
<tr>
<td>Salivary ferritin</td>
<td>30</td>
<td>482.7000</td>
<td>0.000</td>
</tr>
<tr>
<td>Salivary iron (control)</td>
<td>30</td>
<td>90.044</td>
<td>Non sig.</td>
</tr>
<tr>
<td>Salivary ferritin (control)</td>
<td>30</td>
<td>101.034</td>
<td>Non sig.</td>
</tr>
</tbody>
</table>

1. Xerostomia and Halitosis (66.6%), 20 out of 30 cases.
2. Changes in oral mucosa (26.6%), 8 out of 30 cases.
3. Candidial infection (20%), 6 out of 30 cases.
4. Enlargements of salivary glands (76.6%), 23 out of 30 cases.

Figure 1: Distribution of Orofacial complications in β-thalassemia major in oral cavity
Discussion
The thalassemia is one of the most health trouble that result from genetically distributed disease, β-thalassemia major, is life-limited event lead to chronic severe anemia, growth and development reduction, hypertrophy skeletal changes, endocrine disorders, erythroid expansion, infections tendencies and myocardium iron deposition lead as a consequences to heart failure [19, 20].

Thirty patients were included in this study; salivary analysis was appearing highly significant (0.000) in salivary ferritin and iron levels. Iron deposition and overload requires removal from the body; lead to the clinical manifestations and consequences, this idea is very important to explanations how this overload lead to different complications.

Almost those patients were visiting the thalassemic centers to give all parameters for treatment; monitoring laboratory investigations and follow up. One of these parameters to prevent iron overload, the chelators (Deferoxamine) in the form of intravenous bolus at the time of transfusion. Large numbers of thalassemia patients have elevated levels of salivary ferritin and irons due to tissues and organs deposition, contaminated transfusion with infection, improper chelation [10].

Goals of transfusions to suppression increased gut iron absorption, correct state of anemia and inhibition of erythropoiesis. Because; improper chelation and progressive load of irons, results in dysfunction of heart with cardiac hypertrophy and dilation, myocardial degeneration but in rare cases fibrosis will occur, liver (cirrhosis and fibrosis) and endocrine glands (as anterior pituitary defect will cause sexual maturation dysfunction and secondary amenorrhea) [21].

Most common noticed oral and perioral manifestations; Xerostomia and Halitosis (66.6%), Changes in oral mucosa (26.6%), Candidial infection (20%), and Enlarged of salivary glands (76.6%). Different forms of oral mucosal changes were appeared in oral cavity of patients with thalassemia major that significantly higher in those patients when compared to controls, these oral changes due to nutritional deficiencies such as; vitamin-B 12, folate and iron levels defects, also angular stomatitis was noticed; all above clinical and dental manifestations were associated with opportunistic infection as Candida albicans, because immunological abnormalities occurred [21].

Low socioeconomically levels, difficulties in transplantations, and improper managements in rural areas unfortunately; all above factors causes clinical findings and abnormalities in thalassemia patients were higher in rural areas than urban [23-25].

Increasing age and severity with worsening of disease as a accumulative factor and heavily depositions of irons and ferritin in serum and saliva leading to infiltration of serous cells, acinar parotid and mixing cells in submandibular and other salivary glands will show xerostomia (dry mouth), enlargements or swellings of salivary glands, and halitosis as a sequel of dry mouth and due to improper oral hygiene [25].

Conclusion
Multiple signs and symptoms, with variety of complications in those patients that were suffered from thalassemia hemoglobinopathies.

Blood transfusion and chelation of iron are better option for managing β-thalassemia major but not curative, these options have efficacy to reducing the risk of toxicity.

Criteria for successful treatment of patients with thalassemia depend on proper diagnosis and managing plan including oral and systemic health. Regular blood and repeated infusion preserving hemoglobin levels at 10 mg/d with removal of iron load to prevent systemic, oral and perioral symptoms (including bones ,soft tissues). Degree of anemia and time of treatment beginning will reflect these abnormalities such as bone expansion and deformity, hyperactivity of marrow will compensate anemia. Early diagnosis and treatment leads to fewer complications.
References