Evaluation of Orofacial Manifestations in 50 Thalassemic Patients: A Clinical Study

**ABSTRACT**

**Background and Objectives:** Thalassemia has been reported as a high prevalence genetic disorder with some oromaxillofacial complications. The aim of this study was to evaluate the prevalence of oromaxillofacial disorders in thalassemia patients and to detect the presence of any correlation between the orofacial manifestations and the hematological picture/systemic findings.

**Materials and Methods:** A total of 50 thalassemic, 36 with thalassemia major and 14 with thalassemia minor were selected from the hematology Department of Lokmanyta Tilak Medical College and Government (LTMG) Hospital, Sion, Mumbai.

**Results:** The most prominent features included, skull bossing seen in 74% of the patients, hypertelorism, depressed bridge of the nose, prominent malar bones, pallor of oral mucosa, gingival pigmentation and proclination of teeth. Splenomegaly, hepatomegaly and cardiovascular changes were also commonly seen. The blood picture showed for a low mean Hb value of 6.63 gm/dl. Microcytosis, anisocytosis, hypochromasia and poikilocytosis was seen in the blood smear. Hemoglobin electrophoresis patterns revealed raise HbF and HbA2 levels.

**Conclusions:** This study showed that about 84% (42 cases) of all patients under consideration showed changes in oral and maxillofacial complications including upper and lower jaw protrusion, saddle nose, space between anterior teeth, anterior teeth protrusion, and frontal bossing. It was noted that the frequency of orofacial manifestations increased with a decline in the systemic health and a deterioration in the blood picture. Also, it was revealed that the rate of prevalence for oral and maxillofacial complications decreases when patients receive blood at younger ages.

**Keywords:** Thalassemia, Maxillofacial abnormalities.

**INTRODUCTION**

Thalassemia is considered the most common genetic disorder world-wide. The condition was first described by Thomas B Coolley and Pearl Lee of Detroit in 1925 and appeared as a single page article titled “A series of cases of splenomegaly in children with anaemia and peculiar bony change”. The term “Thalassemia” was first used by Wipple and Bradford in 1932 in their article on the pathology of the condition. The word was derived from Greek *thalasse* meaning the sea. Thalassemia refers to a group of inherited hemolytic anemias involving defects in synthesis of either the α or the β polypeptide chains of hemoglobin (α-thalassemia, β-thalassemia). Based on genetic and clinical entities, thalassemias are classified as homozygous, heterozygous or compound heterozygous. The heterozygous form of the disease (thalassemia minor) is mild and usually asymptomatic; the only manifestation is hypochromic microcytic anemia. The homozygous form of β-thalassemia (thalassemia major) exhibits the most severe clinical symptoms with marked orofacial deformities.

Homozygous β-thalassemia, also known as Cooley’s anemia or Mediterranean anemia, is seen chiefly in Mediterranean populations, with a prevalence as high as 15-20% in Greece, Turkey, Cyprus and southern Italy. The onset of symptoms occurs early in infancy and the patients are severely anemic and have a short life expectancy. Patients with the most severe form of the disease rarely survive into adulthood because of cardiac failure, chronic anemia and hypoxia. However, with modern management, the prognosis has improved greatly. Patients suffering from this disease are at considerable anesthetic risk. The most common oral and facial manifestations are enlargement of the maxilla, bossing of the skull and prominent malar eminences due to the intense compensatory hyperplasia of the marrow. This leads to expansion of the maxillary sinus cavity and a facial appearance known as “chipmunk” face. The overdevelopment of the maxilla frequently results in an increased overjet and spacing of maxillary teeth and other degrees of malocclusion.

General dental practitioners, especially those working in multiracial communities, are required to be aware of the nature of the disease and its implication on dental care. Most references of the orofacial manifestations of this disease in the medical and dental literature are found to be case reports and very few large group studies have been undertaken. Therefore, the aim of this study was to:

1. Evaluate the orofacial manifestations of thalassemia.
2. To detect any correlation if present, between the orofacial manifestations and hematological picture and/or systemic findings.

To find out if the orofacial manifestations could aid in early diagnosis and whether it could provide an indication to the progress of the disease.
METHODS

A study of 50 cases of thalassemia was undertaken by the Department of Oral Medicine and Radiology, Dr. DY Patil Dental College and Hospital, Nerul, Navi Mumbai. The cases were selected from hematology Department of Lokmanya Tilak Medical College and Government (LTMG) Hospital, Sion, Mumbai.

In each case:

- A thorough medical history, past dental history and family history was taken.
- A thorough and complete intraoral and extraoral examination was done. Patients were examined on a dental chair using mouth mirror, tweezer and probe.
- Systemic evaluation of:
  1. Liver and spleen
  2. Cardiovascular system
  3. A complete hematological investigation was done which included:
     - Red blood cell count,
     - Hemoglobin estimation,
     - Mean corpuscular hemoglobin (MCH),
     - Mean corpuscular volume (MCV),
     - White blood cell count,
     - Differential count,
     - Platelet count,
     - Peripheral smear for RBC morphology,
     - Serum Iron studies
     - Hemoglobin electrophoresis.

A case history format was charted out and was used while examining the patients.

RESULTS

A total of 50 thalassemic subjects were selected from the Hematology Department of LTMG Hospital, Sion, Mumbai.

The study comprised of 36 patients with thalassemia major and 14 patients with thalassemia minor.

Extraoral examination revealed the findings as shown in Table 1.

Intraoral examination revealed the findings as shown in Table 2.

### Systemic Evaluation

An evaluation of liver, spleen and cardiovascular system was done for all 50 patients.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Total (%)</th>
<th>Thalassemia major (%)</th>
<th>Thalassemia minor (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color of skin</td>
<td></td>
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<tr>
<td>Muddy yellow (Fig. 1A)</td>
<td>38 (19/50)</td>
<td>36 (13/36)</td>
<td>43 (6/14)</td>
</tr>
<tr>
<td>Dark brown (Fig. 1B)</td>
<td>28 (14/50)</td>
<td>31 (11/36)</td>
<td>21 (3/14)</td>
</tr>
<tr>
<td>Frontal bossing (Fig. 2A)</td>
<td>74 (37/50)</td>
<td>81 (29/36)</td>
<td>57 (8/14)</td>
</tr>
<tr>
<td>Parietal bossing (Fig. 2B)</td>
<td>28 (14/50)</td>
<td>33 (12/36)</td>
<td>14 (2/14)</td>
</tr>
<tr>
<td>Hypertelorism (Fig. 1A)</td>
<td>74 (37/50)</td>
<td>72 (26/36)</td>
<td>79 (11/14)</td>
</tr>
<tr>
<td>Depressed nasal bridge (Fig. 2B)</td>
<td>70 (35/50)</td>
<td>70 (25/36)</td>
<td>71 (10/14)</td>
</tr>
<tr>
<td>Flaring of alae (Fig. 3)</td>
<td>36 (18/50)</td>
<td>39 (14/36)</td>
<td>29 (4/14)</td>
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<tr>
<td>Maxillary hyperplasia (Fig. 1B)</td>
<td>70 (35/50)</td>
<td>78 (28/36)</td>
<td>50 (7/14)</td>
</tr>
<tr>
<td>Incompetence of lips (Fig. 1B)</td>
<td>54 (27/50)</td>
<td>67 (24/36)</td>
<td>21 (3/14)</td>
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<table>
<thead>
<tr>
<th>Feature</th>
<th>Total (%)</th>
<th>Thalassemia major (%)</th>
<th>Thalassemia minor (%)</th>
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<tbody>
<tr>
<td>Gingiva</td>
<td></td>
<td></td>
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<tr>
<td>Pigmentation (Fig. 4)</td>
<td>60 (30/50)</td>
<td>69 (25/36)</td>
<td>36 (5/14)</td>
</tr>
<tr>
<td>Gingivitis and recession (Fig. 5)</td>
<td>26 (13/50)</td>
<td>28 (10/36)</td>
<td>21 (3/14)</td>
</tr>
<tr>
<td>Tongue</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pallor (Fig. 6)</td>
<td>68 (34/50)</td>
<td>81 (29/36)</td>
<td>36 (5/14)</td>
</tr>
<tr>
<td>Depapillation (Fig. 6)</td>
<td>24 (12/50)</td>
<td>31 (11/36)</td>
<td>7 (1/14)</td>
</tr>
<tr>
<td>Pigmentation (Fig. 7)</td>
<td>34 (17/50)</td>
<td>42 (15/36)</td>
<td>14 (2/14)</td>
</tr>
<tr>
<td>Pallor of oral mucosa (Fig. 8)</td>
<td>60 (30/50)</td>
<td>78 (28/36)</td>
<td>14 (2/14)</td>
</tr>
<tr>
<td>Proclination of teeth (Fig. 4)</td>
<td>40 (20/50)</td>
<td>47 (17/36)</td>
<td>21 (3/14)</td>
</tr>
<tr>
<td>Spacing (Fig. 4)</td>
<td>40 (20/50)</td>
<td>53 (19/36)</td>
<td>7 (1/14)</td>
</tr>
<tr>
<td>Persistence of mammelons (Fig. 9)</td>
<td>24 (12/50)</td>
<td>33 (12/36)</td>
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Evaluation revealed hepatomegaly in 88% of the patients and it ranged from 1.5-11 cm (mean 3.8 cm). Splenomegaly was noted in 82% of the patients and it ranged from 1-12 cm (mean 4.8 cm). One patient had undergone splenectomy.

**Cardiovascular System**

Evaluation of the cardiovascular system revealed that 6 patients had an S1S2 murmur and one patient showed initial signs of congestive cardiac failure. All these patients were thalassemia major.

**Hepatitis**

Two patients had tested positive for hepatitis B subsequent to multiple blood transfusions.

**Elisa Reactivity**

One patient was tested ELISA reactive.

**Hematological Investigation**

Hematological investigations revealed that the RBC counts were in the range of 1.1-6.6 \times 10^{12} /l, the mean value being 3.07 \times 10^{12} /l.

Hemoglobin levels were in the range of 2.6-15 gm/dl, the mean value being 6.63 gm/dl.

The MCV values were in the range of 43-84.2 fl, with the mean being 70.4 fl and the MCH values ranged from 14- 26.8 pg with the mean value being 21.2 pg.
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Fig. 4: Gingival pigmentation. Proclination of teeth and spacing

Fig. 5: Gingivitis and gingival recession

Fig. 6: Pallor and depapillation of tongue

Fig. 7: Pigmentation of tongue

Fig. 8: Pallor of oral mucosa

Fig. 9: Persistence of mammelons
Peripheral smear showed microcytosis (94%), anisocytosis (87%), poikilocytosis (63%) and hypochromia (85%), polychromasia (18%) and basophilic stippling was noted in 2% of the cases.

Hemoglobin electrophoretic patterns revealed HbF levels in the range of 20-90% and HbA2 levels in the range of 0.2-8.8%.

The relationship between orofacial manifestations and hemoglobin values was as shown in Figure 10.

**DISCUSSION**

Thalassemia is one of the commonest of the genetic disorders. It is a hereditary blood disease which is transmissible through an autosomal recessive gene. In our study, comprising of 36 thalassemia major and 14 thalassemia minor patients, it was observed that majority of the patients with thalassemia major presented the symptoms by 1 year of age and from then have undergone regular follow-ups for blood transfusion every month. Thalassemia minor patients presented at a much later age and required blood transfusions at 2 to 3 months interval. The patients’ parents were found to be having beta thalassemia trait and many children were born of consanguineous marriages. Majority of them had pallor in varying degrees, reported with recurrent fever and cough. Many patients reported with a progressive abdominal distention and failure to thrive. General examinations revealed that 90% of the patients had a retarded growth and development, which could be a cause of severe anemia. It can be prevented although not corrected by an aggressive blood transfusion program.

The observed change in color of the skin to dark brown and muddy yellow is due to the deposition of excessive iron in the subcutaneous tissue caused by excessive breakdown of abnormal erythrocytes, repeated transfusions, or excessive iron absorption from the gut induced by chronic hypoxia. The frontal bossing is due to bone marrow hyperplasia leading to enlargement of the outline of the flat bones of the skull including the frontal bone, in response to the underlying anemia. Flaring of the nose is due to the air hunger caused by the chronic anemic condition in these patients. The oxygen carrying capacity is reduced, which leads to excessive exertion of the accessory respiratory muscles to compensate for the required amount of oxygen. This forceful breathing gives rise to flaring of the alae of the nose, which is accentuated by the depression of the bridge of the nose. Prominence of malar bones was because of the hyperplasia of the bone marrow. Maxillary hyperplasia was due to overgrowth of its marrow in response to the underlying anemia. Incompetency of the lips is due to the maxillary hyperplasia and proclined maxillary anteriors which prevents the complete closure of the lips. This leads to mouth breathing habit which was observed in 41% of the patients.

Pallor of the mucous membrane was the most common finding, which was most evident on the buccal mucosa, tongue and palate. The pallor could be attributed to the chronic anemic status of these patients. Brownish to black pigmentation of the tongue was seen in 43% of the patients. At times, it was present on the entire dorsum or only on the tip and lateral borders, which could be attributed to the iron overload. Loss of papilla was observed in vitamin B complex deficiency. Each of these B vitamins form parts of coenzymes essential for metabolism of proteins, carbohydrates and fats. In thalassemic patients, hyperplastic bone marrow requires increased amount of vitamin B, to perform sufficient amount of erythropoietic function. Increased requirement of vitamin B leads to severe deficiency and ultimately leads to tongue changes.

Gingival pigmentation could be either racial pigmentation or may be due to iron deposition in the gingival which gave the characteristic brownish-black color to it. Marginal gingivitis and recession could be attributed to the maxillary hyperplasia which leads to incompetency of the lips along with the mouth breathing habit which aggravates the condition. Also many patients had poor oral hygiene. Proclination was also another striking feature found especially in patients who had maxillary hyperplasia. This is due to erythroid hyperplasia of the bone marrow of the maxilla.

Increased overjet and overbite was present in the thalassemic patients which was due to the maxillary hyperplasia preventing the anterior teeth for coming in contact. This leads to supraeruption of mandibular anterior teeth resulting in increased overbite, in turn accentuating the gingival recession. The increased overjet thus contributes to the incompetency of lip and therefore leads to mouth breathing habit. Persistence of mammelons on permanent maxillary central incisors was due to the increased overjet because the maxillary anteriors are proclined or in labio version which prevents its normal wear.

Liver enlargement in early life is related to the extramedullary hematopoiesis, but later results from extensive cirrhosis with nodular aggregates of regenerating hepatocytes. Splenomegaly is a predictable problem for patients with thalassemia major and intermedia forms of the disease. Progressive splenomegaly: (1) expands the blood volume, (2) shortens red cells survival, (3) Increases the transfusion requirement and (4) accelerates iron loading. Myocardial hemosiderosis is the leading cause of death in transfused patients. Congestive heart failure and arrhythmias may
be noted as early as 6 years of age but usually these conditions do not have their onset till the mid portion of the second decade. A state of chronic anemia was noted. Low levels of hemoglobin were also reported. A slightly subnormal MCV and MCH values were noted, indicative of microcytosis. The WBC counts were slightly raised to normal. Leucocytosis results from an increase in the neutrophils and to a lesser extent from the myelocytes. In the peripheral smear, microcytosis, poikilocytosis, hypochromia, polychromasia and basophilic stippling were noted. Ficcare G et al (1980) and JasHes et al (1990) also reported similar findings. Hemoglobin electrophoretic patterns reveal that the percentage of HbF levels ranged from 20-97% (normal being less than 10%); HbA2 levels were in the range of 0.2 to 8.8% (normal 1.5-3.2%).

**Dental Considerations in Thalassemia**

Thalassemia is a relatively common condition seen in India and dental clinicians may come across many thalassemic patients in their routine dental practice. Hence they should be aware of the possible oral manifestations of the condition and complications that could arise either as a result of the disease or due to treatment.

A number of factors need to be taken into consideration in the management of thalassemic patients and they are:

1. Patients who have undergone splenectomy are at a massive risk of infection followed by bacteremia. General anesthesia should be avoided if possible because of the difficulty caused by low hemoglobin levels and cardiac insufficiency.

2. Hemoglobin levels of these patients are low.

3. Thalassemic patients are at an increased risk of viral hepatitis and AIDS due to repeated repeated blood transfusions and therefore screening tests for the same should be carried out at regular intervals. All members of the dental team should be aware of this, so as to ensure proper precautions being take.

4. Some patients have cardiomegaly, and hence all surgical procedures should be conducted with due precautions.

**Dental Treatment Planning**

The dental treatment for thalassemic patients should be carried out with the following points taken into account:

- Appointments should be as short as possible to avoid tiring the patient.
- These children are often listless and forget to brush their teeth and hence the importance of maintenance of good oral hygiene needs to be stressed to these patients and their parents.
- Regular prophylaxis and fluoride application is recommended in these children.
- The diagnosis of pain in the teeth and jaws may be made more difficult because of the attacks of bone pain caused by marrow changes. Conservative treatment should be of the highest standard possible. Because of the danger of intercurrent infection, deciduous teeth with infected pulp should be extracted without attempts at pulp therapy.
- Extractions should be carried out at the time of admission for blood transfusion, i.e. when the hemoglobin level is at its highest, with the administration of antibiotics.
- General anesthesia should be avoided if possible because of the difficulty caused by low hemoglobin levels and cardiac insufficiency.

Orthodontists, pedodontists and other dental practitioners should try to use whatever clinical approach available, to reduce the trauma that these children may sustain during childhood and adolescence due to their unesthetic appearance.

**SUMMARY AND CONCLUSION**

Every year almost one lakh children are born in the world with thalassemia, of those 5000-6000 are born in India alone. As of today, there is no cure for the disease and hence prevention seems to be the only cure. It was noted that many of the patients in our study were results of consanginous marriages between carriers. The incidence of thalassemia can certainly be reduced if carriers are counseled not to marry and the best approach for preventing the disease would be that of prospective genetic counseling.

The orofacial manifestations could be used as an aid to diagnosis in thalassemia minor, because these children present with problems at a much later stage, unlike thalassemia major, where patients present with problems at a very early age of 1-2 years, the changes are not clearly seen as development of face is not yet complete. Also the orofacial manifestations can be used to determine the progress of the disease because in children who are adequately transfused and whose hemoglobin levels are maintained at 9-10 gm/dl show less orofacial manifestations, compared to those who are inadequately transfused.

Thus, the study gives an insight to the various orofacial manifestations of thalassemia and also reveals a relationship that exists between the orofacial manifestations and systemic health in thalassemic patients, thus stressing the importance of the knowledge of this condition in the dental fraternity to help in the possible diagnosis of the disease.

**REFERENCES**