

## ORAL AND MAXILLOFACIAL MANIFESTATIONS IN 50 $\beta$ -THALASSEMIC PATIENTS — A CLINICAL STUDY

<sup>1</sup>SYED MUHAMMAD ALI

<sup>2</sup>SYED MAHMOOD HAIDER

<sup>3</sup>SUFYAN AHMED

<sup>4</sup>SYED GHAZANFAR HASSAN

<sup>5</sup>SARFARAZ HUSAIN JAFFRY

### ABSTRACT

*Thalassemia is a worldwide disease. 5-8% of Pakistani population (approx. 8-10 millions) are carrying thalassemia genes. It causes various abnormalities in different organs of patients. In Pakistan (to the best of our knowledge) no research work on oral and maxillofacial manifestations had been carried out, therefore present study was under taken. This study was carried out in Abbasi Shaheed Hospital, Karachi with collaboration of Husaini Institute of Blood Diseases, Karachi.*

*The aim of this study was to evaluate the frequency of oral maxillofacial manifestations in thalassemic patients from of Karachi groups. Fifty diagnosed  $\beta$ -thalassemia major patients were randomly selected from the patients who were registered for their treatment at the Husaini blood bank and Institute of Blood Diseases Karachi. Their clinical examination and percentage of recorded features were calculated and results were deduced. The most prominent features recorded were frontal bossing, seen in 54% cases, Parietal bossing in 88%; Depressed nasal bridge in 70%; Pallor of oral mucosa in 84%; Intra oral pigmentation in 88%; Proclination of teeth in 26%; Gingivitis in 82%; Mamelon in 22%.*

**Key Words:** *Thalassemia, Oral and Maxillofacial manifestations, Karachi.*

### INTRODUCTION

Thalassemia is an inherited single gene ( $\beta$ -thalassemia) or multiple genes ( $\alpha$ -thalassemia) recessive, autosomal blood disease, where hemoglobin is totally absent or partially produced.<sup>1,2,3</sup> It is very common in Mediterranean region.<sup>4</sup> Hemoglobin is composed of four protein chains, two  $\alpha$ -globin chains and two  $\beta$ -globin chains arranged in a hetro-tetramer.<sup>5</sup> Patient suffering from thalassemia defects occur either in  $\alpha$  or  $\beta$ -globin chain which produced abnormal red blood cells.<sup>2</sup>

In  $\beta$ -thalassemia mutations occur in the HB  $\beta$ -gene at chromosome No. 11, and severity of the disease depends on the nature of the mutation. According to severity it is classified in three sub classes. I) Thalassemia major; II) Thalassemia intermedia; III) Thalassemia minor (Severity of disease depends upon the amount of  $\alpha$ -globin. However in each sub class tetramer do not form and they bind to the red blood cell membranes, causing damage to membrane. Further more at high concentrations they form toxic compounds.<sup>6,7,8,9,10,11</sup>

In  $\alpha$ -thalassemia two genes HB  $\alpha_1$  and HB  $\alpha_2$  at chromosome No. 16 are involved and inherited, resulting excess of  $\beta$ -globin chains in adults and excess  $\gamma$ -globin chains in new born babies. The excess  $\beta$ -chains form unstable tetramers, which are characterized by abnormal oxygen dissociation curves.<sup>2,12,13</sup>

Generally hemoglobin is composed of  $\alpha$  and  $\beta$ -chains, however approximately 3% of adult hemoglobin is made of  $\alpha$  and  $\Delta$  chains. Mutations also effect the production of  $\Delta$ -chains.<sup>13</sup> The general manifestations in thalassemic patients are due to lack of total or partial production of  $\alpha$  or  $\beta$  globin chain, causes serious effects on their bodies, details of effects has been fully discussed by many worker.<sup>2,3,7,8,14,15</sup>

<sup>1</sup> **Corresponding Author:** Dr Syed Muhammad Ali, BDS, MS, Trainee Oral and Maxillofacial Surgery, Karachi Medical and Dental College, Karachi, Pakistan.

Email: alischolar14@gmail.com Cell: 0335-0253011

<sup>2</sup> Prof Dr Syed Mahmood Haider, BDS, MSc, FDS RSC, FFD, RCSI, FCPS, Professor, Vice Principal, Head of Dentistry and Head of Oral and Maxillofacial Surgery

<sup>3</sup> Dr Sufyan Ahmed, BDS, FCPS, Assistant Professor Oral & Maxillofacial Surgery

<sup>4</sup> Dr Syed Ghazanfar Hassan, BDS, FDSRCS, Associate Professor, Head of Department of Oral and Maxillofacial Surgery, Liaquat University of Medical and Health Sciences, Hyderabad

<sup>5</sup> Dr Sarfaraz Husain Jaffry, MBBS, MBA, Administrator Husaini Institute of Hematological Diseases, Karachi, Pakistan

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$\beta$ -thalassemia is also responsible for causing various manifestations and complications of various degrees on different organs of patients.<sup>1,16,17,18,19,20,21,22,23,24,25</sup> In  $\beta$ -thalassemia, the oral and maxillofacial manifestation has been reported in several reports.<sup>14,16,17,18,22,24,26,27,28,29</sup> Changes in bones of face, resulting in severe disfigurement of face, high and bulging cheek bones, retraction of the upper lip. Protrusion of anterior teeth, and spacing of other teeth; Over-bite or Open-bite; Various degrees of malocclusion.

The skeletal changes are due to proliferation of the bone marrow in the facial skeleton.<sup>16</sup> This proliferated bone marrow is extensively used as an ancillary hematopoietic organ to compensate for the chronic hemolysis. Usually the mandible becomes less enlarged than the maxilla. The dense cortical plates of the mandible apparently prevent expansion and they may occur early in life and tend to persist particularly in skull.<sup>18,22,28,30</sup> In addition to a tint of lemon colour is also observed in oral mucosa due to existing bilirubin produced by the decomposition of red cells. Radiological changes are also occur but not evident up to first year of age. These include large bone marrow spaces, one of the most important and diagnostic radiographic features of thalassemia. This enlargement is due to damages to the membrane of RBC (red blood cells) by the excessive  $\alpha$  globin, resulting severe anemia and in response, body begin to increase the production of RBC, resulting expansion of the bone marrow up to 15-30 times the normal amount. Small maxillary sinuses are also due to bone marrow expansion, classical Chipmunk face with depressed cranial vault, maxillary expansion, frontal bossing, retracted upper lip and saddle nose, yellowish tinge at the junction of hard and soft palate, yellow tinged finger nails and spaces with widened trabeculae.<sup>24</sup>

The population of Pakistan was recorded 18.2490721 millions.<sup>31</sup> Thalassemia is very common in Pakistan and Azad Kashmir. It is a major health concern and is the most prevalent genetically transmitted blood disorder with 5-8% carrier rate. Every year 5000 children in Pakistan are diagnosed with thalassemia.<sup>31,32,33</sup> The total number of thalassemia major children in Pakistan are 60000-100,000.<sup>33</sup> It is prevalent in all provinces of Pakistan but total numbers of patients are more recorded in Punjab province than other provinces and may be due to its population which is 50% of all Pakistan population. Furthermore in South Punjab literacy rate is also low.<sup>29</sup>

The Pakistan Institute of Medical Sciences (PIMS) has diagnosed around 160 new cases of thalassemia major during four years (2008-2012). Furthermore 277 patients have been transfused for thalassemia by Pediatric department of the hospital during

(2011-2012). In Azad Kashmir the people suffering from thalassemia are 5%. There is only one blood bank in public sector which is insufficient for a large population.<sup>34</sup>

## METHODOLOGY

This study has been carried out in the Department of Oral and Maxillofacial Surgery Abbasi Shaheed Hospital, Karachi and Husaini Institute of Hematological Diseases Center Karachi, to evaluate the clinical oral and maxillofacial manifestations in thalassemia. This study consisted of 50 clinically proved cases of  $\beta$ -thalassemia attending for regular blood transfusions in the Husaini blood bank of Husaini Institute of Hematological Disease Center, Karachi, This study is a part of MS thesis in Oral Surgery, Faculty of Medicine University of Karachi (2012-2016).

Present study fulfilled the inclusion and exclusion criteria. In inclusion criteria, only  $\beta$ -thalassemia major patients were taken as study subject and consent from patients or their parents/guardians were taken for their participating in the study on voluntary basis. Where as in exclusion criteria patients suffering from any other systemic diseases, like diabetes mellitus or Down's Syndrome or any other systemic diseases known to influence oral and maxillofacial manifestations were excluded.

For clinical studies, in each case a thorough oral, maxillofacial and medical checkup were carried out and family history of the patient was taken and noted on a printed Proforma. A thorough intra oral and extra oral examination of patient was carried out on dental chair with the help of examination instruments. In extra oral examination; colour of skin; frontal bossing; parietal bossing; hypertelorism; depressed nasal bridge; flaring of alae and maxillary hyperplasia were recorded, while in, intra oral examination: pigmentation, gingivitis. Recession, pallor; intra oral pigmentation, pallor of oral mucosa, proclinations of teeth, spacing in teeth and persistence of mamelon were examined, observed and recorded.

The subjects were made to sit comfortably on the physiological dental chair with artificial illumination. During examination of subjects, sterilized hand gloves and mouth mask were used. Oral cavity was rinsed with diluted 0.2% Chlorohexidine gluconate. The clinical examination was carried out by adopting the methods of Kerr et al<sup>35</sup> and relevant data were recorded in the proforma. This study was also approved by the ethical and research committee Karachi Medical and Dental College, Karachi.

**RESULTS**

**EXTRA ORAL FINDINGS**

Features	No. of total patients studied	No. of patients in which features were present	%
Colour of skin	50	12	24
II) Pale yellow	50	22	44
III) Muddy black	50	16	32
Frontal bossing	50	27	54
Parietal bossing	50	44	88
Hypertelorism	50	32	64
Depressed nasal bridge	50	35	70
Flaring of alae Maxillary hyperplasia	50	38	76
Incompetence of lips	50	17	34
		27	54

**INTRA ORAL FINDINGS**

Features	No of total patients studied	No of patients in which features were present	%
Intra oral pigmentation	50	44	88
Gingivitis and recession	50	41	82
Pallor of oral mucosa	50	42	84
Proclination of teeth	50	13	26
Spacing of teeth	50	10	20
Persistence of Mamelon	50	11	22



Fig 2: Shows incompetent lips maxillary hyperplasia

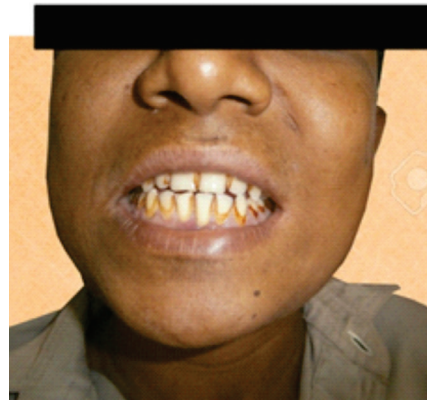


Fig 3: Shows muddy black colour of skin, gingivitis and staining of betel and nut



Fig 4: Shows frontal bossing



Fig 1: Lateral view shows parietal bossing

**DISCUSSION**

In the present study 45 patients (90%) showed changes in oral and maxillofacial manifestations and result of this study also confirm the result reported by the international studies.<sup>14,16,17,18,22,24,26,27,28,29,36</sup> In the current study normal skin colour was found in 24%, pale skin colour in 44% and muddy black skin colour in 32%, whereas Girinath et al<sup>36</sup> reported muddy pale skin colour in 38% and muddy brown skin colour in



28%, slightly less percentage than reported in the present study. Change of skin was due to excessive iron deposition in subcutaneous tissues by break down of abnormal erythrocytes, in the result of multiple blood transfusion, or absorption of excessive iron from the gut induced by chronic hypoxia. In the present study, frontal bossing was recorded in 58% and parietal bossing in 88% whereas Girinath et al<sup>36</sup> reported frontal bossing in 74% and parietal bossing in 28%. In the present study frontal bossing was low and parietal bossing was high in comparison to the study carried out by Girinath et al.<sup>36</sup> Anemia was also responsible for bone marrow hyperplasia resulting enlargement of outline of flat bones of skull including the frontal bone.<sup>17</sup> In the present study Hypertelorism was seen in 64% while Girinath et al<sup>36</sup> reported it 74%, higher than reported in the present study. Depressed nasal bridge was recorded in 70% cases in the present study, whereas Girinath et al<sup>36</sup> also reported it in 70% cases, same in both studies. Flaring of alae was recorded in 76% cases in the present study, while Girinath et al<sup>36</sup>, reported it in 36% cases, which is half of the present study. Anemic condition in patients reduced oxygen carrying capacity of RBC thus creating excessive pressure on respiratory muscles, causes force full pressure for breathing and thus nostrils of nose open widely causes flaring of alae and also responsible for depressed nasal bridge. Maxillary hyperplasia was recorded in 34% cases in the present study but Girinath et al<sup>36</sup> reported it in 70% cases which is more or less double from the present study. Maxillary hyperplasia of bone marrow was responsible for prominence of malar bones.<sup>27</sup> It is also related to incompetence of lips. Proclined maxillary anterior teeth prevents the complete closure of lips, this leads to mouth breathing habit.<sup>37,38</sup>

Intra oral pigmentation was recorded in 88% cases in the present study, however Girinath et al<sup>36</sup> reported it in 60%, it is 28% higher in the present study. Gingivitis was recorded in 82% cases in the present study but Girinath et al<sup>36</sup> reported in 26%, three time higher in the present study, probably it was due to betel and betel nut (Pan, Chalia) chewing habit. Pallor of oral mucosa recorded in present study was 84% but Girinath et al<sup>36</sup> reported it 60%, it is 24% more in the present study. Pallor of mucosa, tongue and palate are also due to iron over load which is the result of multiple blood transfusion for treatment of severe anemia.<sup>39</sup> Proclination of teeth recorded in present study was 26%, but Girinath et al<sup>36</sup> reported it 40%, 14% less in the present study. It is generally found in patients who had maxillary hyperplasia. It is due to erythroid hyperplasia of bone marrow of maxilla.<sup>17,37,40</sup> Teeth spaces recorded in present study was 20%, but Girinath et al.<sup>36</sup> reported it 40%, 20% less found in the present study. Persistence of Mamelons recorded in the present study was 22% but Girinath et al<sup>36</sup> reported 24%, more or less the same in both studies. Persistence of Mamelon on permanent maxillary central anterior are due to increased over jet because the maxillary anterior are proclined or in labio version which prevents the normal wear.<sup>40</sup> Loss of papilla was due to deficiencies of Vitamin B-complex. In hyperplastic, bone marrow required high amount

of Vitamin. B-complex to perform erythropoietic function and Vitamin. B-complex also work as coenzyme in enzymes which synthesis proteins, carbohydrates and fats, therefore its deficiencies makes the patients under weight and low built. Increased over jet and over bite was due to maxillary hyperplasia, preventing anterior teeth for coming in contact and this lead to super eruption of mandibular anterior teeth resulting in overbite, in turn attrition and gingival recession. The increased over bite thus contribute incompetency of lips and leading to mouth breathing.<sup>27,37,40</sup>

In the present study manifestation intensity in oral and maxillofacial organs were comparatively low and this seems to be due to starting of blood transfusion in early age and control of iron over loading and thus the abnormalities were not so prominent in thalassemic patients. In the ceurent study patients with minimum abnormalities and gaining the age up to 36 years was an achievement with the hope that if patients will continue their blood transfusion regularly and continuing, treatment of over loading of iron, then, they will have a long span of life.

## CONCLUSION

From the present study authors concluded the followings;

- 1 94% of thalassemia patients showed oral and maxillofacial manifestations which confirmed the results of other workers.
- 2 Gingivitis (82%) was very high in the study group.
- 3 Most of the children were habitual betel, betel nut and gutkta chewer from the early age.
- 4 Severity of disease was directly proportional to the increase in age.
- 5 Regular and early treatment reduces the severity of the disease.

For disease control following recommendations are made;

- 1 Consanguineous and inter community marriages should be discouraged or banned (This is very difficult job in Pakistan since population of Pakistan is mostly based on closed family and community system. However, it can be done by public awareness programs by all means (electronic, social, print media, or by lectures and seminars).
- 2 Thalassemia test before marriages must be compulsory National Assembly of Pakistan and Sindh assembly have already passed bills in this connection. Law should be strictly implemented.
- 3 More thalassemia and bone transplantation centers should be established by government and private sectors with the help of international donor agencies or by public donations where free treatment of patients or on nominal charges is carried out.
- 4 Government of Pakistan should take proper action for the arrangement of free regular dental checkups and dental treatment for thalassemia patients in government and private hospitals.

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CONTRIBUTIONS BY AUTHORS

- |   |                                |  |
|---|--------------------------------|--|
| 1 | <b>Syed Muhammad Ali:</b>      | Main researcher and main writer.   |
| 2 | <b>Syed Mahmood Haider:</b>    | Supervisor, main guide and support .                                     |
| 3 | <b>Sufyan Ahmed:</b>           | Helped in literature providing   |
| 4 | <b>Ghanzanfar Hassan:</b>      | Help in literature providing   |
| 5 | <b>Sarfraz Husain Jaffery:</b> | Facilitator for working in Husaini Institute of Blood Diseases, Karachi. |