

# Dental and periodontal condition in patients affected by $\beta$ -thalassemia major and $\beta$ -thalassemia intermedia: a study among adults in Sicily, Italy

## Abstract

**Background:**  $\beta$ -Thalassemia is an inherited blood disorder ranging from severe forms ( $\beta$ -Thalassemia Major) milder forms ( $\beta$ -Thalassemia Intermedia), till asymptomatic ones ( $\beta$ -Thalassemia minor). Affected patients can exhibit a higher risk of decay or periodontal disorders. Because of an enhanced average age of  $\beta$ -thalassemia patients, this study recruited an older population of individuals than the ones of previous investigations which were conducted on young patients.

**Aim:** The aim understands if  $\beta$ -Thalassemia Major and  $\beta$ -Thalassemia Intermedia influence oral health in patients with different ranges of age.

**Methods:** 100 patients affected by  $\beta$ -Thalassemia Major and 98 patients with  $\beta$ -Thalassemia Intermedia were compared to the respective control groups enrolling the same number of healthy individuals. Every group was divided in young (22-40 years) and old subgroups (41-55 years). Patients were examined for plaque deposits, gingivitis, periodontitis and dental caries using Silness and Løe plaque index (PI), Løe and Silness gingival index (GI), probing pocket depth (PPD) and decayed-missing-filled teeth (DMFT).

**Results:** There were significant differences in GI and PPD scores when old patients with  $\beta$ -Thalassemia Major were compared with both patients with  $\beta$ -Thalassemia Intermedia and healthy controls. DMFT was significantly higher in patients with  $\beta$ -Thalassemia Major (both young and old subgroups) and in the old ones with  $\beta$ -Thalassemia Intermedia compared to the controls.

**Conclusion:**  $\beta$ -Thalassemia Major is associated to a higher prevalence of decays independently to the age and adversely affects periodontal status in adult patients.  $\beta$ -Thalassemia Intermedia doesn't exhibit any relation to periodontal health while is associated to an increased caries experience in the old patients. Preventive dental care is crucial for thalassemia patients. Oral wellness of thalassemia subjects seems to be related to the severity of  $\beta$ -Thalassemia. The level of oral compliance doesn't influence the final outcomes of the present study because PI is almost identical in subgroups with the same age.

**Keywords:**  $\beta$ -thalassemia major,  $\beta$ -thalassemia intermedia, periodontal health, dental caries, plaque index, gingival index

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**Abbreviations:** GI, gingival index; PPD, probing pocket depth; DMFT, decayed missing filled teeth;  $\beta$ TI,  $\beta$ -thalassemia intermedia;  $\beta$ TM,  $\beta$ -thalassemia major; C- $\beta$ TM, thalassemia major control; M, mean; SD, standard deviation; C- $\beta$ TI,  $\beta$ -thalassemia intermedia control

## Introduction

$\beta$ -Thalassemia is an inherited blood disorder characterized by a defect in the synthesis of the beta-globin chains, leading to alpha/beta imbalance, ineffective erythropoiesis, and chronic anemia.  $\beta$ -Thalassemia exhibits a wide clinical spectrum<sup>1</sup> ranging from severe forms ( $\beta$ -Thalassemia Major, also known as Cooley's anemia), milder forms ( $\beta$ -Thalassemia Intermedia), till clinically asymptomatic ones ( $\beta$ -Thalassemia minor).

Signs and symptoms of  $\beta$ -Thalassemia Major appear within the first 2 years of life. Affected individuals may have an enlarged spleen, liver, heart and their bones may be misshapen. They need life-long

blood transfusions to replenish their red blood cell supply. Over time, an influx of iron-containing hemoglobin from chronic blood transfusions can lead to an overload of iron in the body, resulting in liver, heart and hormone problems.<sup>2</sup>

$\beta$ -Thalassemia Intermedia is milder than  $\beta$ -Thalassemia Major. Signs and symptoms appear in early childhood or later in life. Affected individuals have mild to moderate hypochromic microcytic anemia with no obvious clinical manifestations. The crucial distinction is the need for chronic red blood cell transfusions for "Major" and no or intermittent transfusions for "Intermedia".<sup>3</sup>

Although many studies evaluate dental and periodontal health in patients with  $\beta$ -Thalassemia<sup>4-7</sup> none compares the oral condition among individuals affected by severe and moderate forms. Thus, the present investigation evaluates dental diseases in patients with  $\beta$ -Thalassemia Major and  $\beta$ -Thalassemia Intermedia.

Thalassemias are globally widespread. The highest frequencies are observed in the South-East Asia and sub-Saharan Africa.<sup>5</sup> In

this country, some of these inherited hemoglobin disorders, if left untreated, result in death in the first few years of life.<sup>8</sup>

In South European areas, it is also common for individuals to inherit alleles for  $\beta$ -Thalassemia.<sup>5</sup> In these high-income countries long-term follow-up of cohorts of patients treated has shown a progressive improvement in life expectancy. This is due to the adoption of neonatal screening programs and the effective management of inter current infections,<sup>9</sup> over that thanks to the administration of adequate pharmacological protocols<sup>10</sup> and the management of many life-threatening complication related to  $\beta$ -Thalassemia.<sup>11</sup>

As a consequence of an enhanced average age of  $\beta$  thalassemia patients, this study has been conducted by using an older population of individuals, than the ones of previous investigations.<sup>4-7</sup> Thus, the aim of this clinical research was investigate the influence of  $\beta$ -Thalassemia Major and  $\beta$ -Thalassemia Intermedia on oral health of patients with different ranges of age.

## Material and methods

A prospective study was carried out at Catania University (Italy) for two years (October 2012 to September 2014). 143 patients with  $\beta$ -Thalassemia Major ( $\beta$ TM) and 133 affected patients with  $\beta$ -Thalassemia Intermedia ( $\beta$ TI) were referred to Catania University at Ferrarotto and Vittorio Emanuele Hospitals for intra-oral examination. All of them were resident in the Eastern Sicily, in the south of Italy. They were steered to our clinics not for suspect of a dental disease but only for the study purpose.

Ethical committee of both hospitals approved this investigation and verbal and written consents were obtained from all enrolled patients.

The inclusion criteria included:

- a. Presence of a no thalassemia relative with same age, sex and dental care background.
- b. Verbal and written Consent, as established by ethical committee.

The exclusion criteria were:

- a. Suffering from other diseases known to influence dental caries or severity of periodontal disease as diabetes and Down's syndrome.
- b. Dental prophylaxis during previous 6 months.
- c. Antibiotic, immune-suppressive or anti-inflammatory therapy in the previous 6 months.
- d. Therapy with biphosphonate in osteoporotic individuals.
- e. Patients affected by life-threatening complications.

Among  $\beta$ TM patients, only 100 of them met inclusion criteria, while 98 subjects were enrolled between  $\beta$ TI patients.

As above mentioned, all 198 thalassemia patients, aged from 22 to 55, were affiliated to a control person. The healthy controls (198 subjects) were chosen from relatives of every thalassemia individual in the attempt to have matched sex, age, socio-economic status and oral condition. No control patient had undergone to dental prophylaxis or antibiotic and anti-inflammatory therapy during 6 months before.

This way, patients were divided in four different groups:

1.  $\beta$ -Thalassemia Major group ( $\beta$ TM group)

2.  $\beta$ -Thalassemia Major Control group (C- $\beta$ TM group)
3.  $\beta$ -Thalassemia Intermedia group ( $\beta$ TI group)
4.  $\beta$ -Thalassemia Intermedia Control group (C- $\beta$ TI group)

Life-threatening consequence of  $\beta$ -Thalassemia, like heart disease secondary to severe anemia and chronic renal failure [12], can adversely influence quality of life and the level of oral compliance. As a consequence, subjects who were deemed not to be able to maintain a regular grade of dental hygiene were discarded.

After having performed a thorough medical history and a general examination, including their demographic data, intra-oral examination was done by a single operator and a single recorder throughout the study period.

According to the previous scientific literature,<sup>4,5</sup> the following indexes were registered:

- A. Decayed-Missing-Filled Teeth (DMFT)<sup>13</sup>
- B. Plaque Index<sup>14</sup>
- C. Gingival Index<sup>15</sup>
- D. Probing Pocket Depth (PPD)

The presence of decayed and filled teeth was recorded by visual examination using an autoclaved mouth mirror (MIR3HD, Hu-Friedy, Chicago, U.S.A.) and an explorer (EX23/66, Hu-Friedy, Chicago, U.S.A.). In order to facilitate caries detection and make it more accurate a light induced fluorescence evaluation was conducted using the SoproLife Camera (Acteon-North America, Mount Laurel, U.S.A.).<sup>16</sup> Data were recorded adopting criteria recommended by World Health Organization<sup>17</sup> and documented using the tooth description code (DMFT index).

Plaque and gingivitis assessment were carried out using respectively the Plaque Index and gingival index .

Periodontal status was evaluated by registering the probing pocket depth (PPD) - that is the distance between the bottom of the pocket and the margin of the gingiva -using a periodontal probe (PCPUNC156, Hu-Friedy, Chicago, U.S.A.) and performing a full mouth periodontal probing for each patient.

Intra-examiner variability was estimated by randomly re-examining twenty patients. Kappa statistic value for DMFT was 0.69. Kappa for PI and GI was calculated at 0.80 and 0.90, respectively. Kappa for PPD was 0.87. Descriptive statistics including mean (M) and standard deviation (SD) of each clinical parameter were determined for all the groups examined. The Mann-Whitney test was used for comparison among groups. The level of significance was set at  $P < 0.05$ .

## Results

According to the age, every group was divided into two subgroups: young (22-40 years) and old (41-55 years) (Table 1). Average age of  $\beta$ TM and  $\beta$ TI subgroups was similar to the respective control ones. Furthermore, all subgroups contain an analogue number of male and female patients.

Table 2 shows that PI value is quite identical among subgroups of the same age but it exists a significant difference ( $P < 0.001$ ) between all young subgroups and the parallel old ones. The mean GI and PPD are respectively indicated in Table 3&4. Data reveals that there isn't a significant difference among thalassemia and control patients aged 22

to 40 years. On the other hand, we noticed a significant higher value of GI and PPD in  $\beta$ TM old subgroup compared to both C- $\beta$ TM and  $\beta$ TI old subgroups ( $P < 0.01$ ). Moreover, GI and PPD score indicate a significantly higher gingival inflammation and periodontal diseases when old subgroups are compared to the respective young ones ( $P < 0.05$ ).

**Table 1** Mean and SD of Sex and Age of the sample population in groups

Age groups variables	$\beta$ TM (n=100)	C- $\beta$ TM (n=100)	$\beta$ TI (n=98)	C- $\beta$ TI (n=98)
<b>22-40 (young)</b>				
Male	32	32	33	33
Female	20	20	17	17
Age (M $\pm$ SD)	30.88 $\pm$ 10.32	31.51 $\pm$ 7.21	31.16 $\pm$ 5.76	28.83 $\pm$ 4.62
(Range)	(22.43-35.98)	(23.45-39.93)	(22.62-39.39)	(23.01-39.09)
<b>41-55(old)</b>				
Male	29	29	27	27
Female	19	19	21	21
Age (M $\pm$ SD)	46.35 $\pm$ 4.70	47.55 $\pm$ 4.35	48.57 $\pm$ 4.99	45.03 $\pm$ 4.26
(Range)	(41.68-54.85)	(41.30-53.62)	(42.62-54.23)	(40.08-53.99)

**Table 2** Oral hygiene condition of the sample population (Plaque Index -PI)

Age groups (M $\pm$ SD)	$\beta$ TM	C- $\beta$ TM	$\beta$ TI	C- $\beta$ TI
22-40 (young)	1.53 $\pm$ 0.41a	1.27 $\pm$ 0.46a	1.37 $\pm$ 0.20a	1.45 $\pm$ 0.07a
41-55 (old)	2.70 $\pm$ 0.19b	2.40 $\pm$ 0.45b	2.64 $\pm$ 0.18b	2.38 $\pm$ 0.42b

**Table 3** Gingival condition of the sample population (Gingival Index -GI)

Age groups(M $\pm$ SD)	$\beta$ TM	C- $\beta$ TM	$\beta$ TI	C- $\beta$ TI
22-40 (young)	1.86 $\pm$ 0.21a	1.62 $\pm$ 0.32a	1.69 $\pm$ 0.20a	1.73 $\pm$ 0.21a
41-55 (old)	2.74 $\pm$ 0.40a	2.16 $\pm$ 0.39b	2.07 $\pm$ 0.35b	2.01 $\pm$ 0.38b

**Table 4** Periodontal condition of the sample population (Probing Pocket Depth -PPD)

Age groups (M $\pm$ SD)	$\beta$ TM	C- $\beta$ TM	$\beta$ TI	C- $\beta$ TI
22-40 (young)	2.73 $\pm$ 0.42a	2.88 $\pm$ 0.42a	2.81 $\pm$ 0.33a	2.59 $\pm$ 0.23a
41-55 (old)	4.88 $\pm$ 0.37a	3.74 $\pm$ 0.40b	3.61 $\pm$ 0.22b	3.41 $\pm$ 0.42b

Different superscript letters in the same indicate statistic differences among groups ( $P < 0.001$ ).

Different superscript letters in the same line indicate statistic differences among subgroups ( $P < 0.05$ ).

Different superscript letters in the same indicate statistic differences among subgroups ( $P < 0.01$ ).

Table 5 enlists the DMFT score of sample population, demonstrating the increased prevalence of caries in people with  $\beta$ -Thalassemia Major, independently to the age ( $P < 0.01$ ). According to our results,  $\beta$ -Thalassemia Intermedia influences decay prevalence only for subjects aged from 41 to 55 years, as demonstrated by DMFT score ( $P < 0.01$ ).

Different superscript letters in the same indicate statistic differences among subgroups ( $P < 0.01$ ).

**Table 5** Caries prevalence of the sample population (Decayed-Missing-Filled Teeth -DMFT)

Age groups (M $\pm$ SD)	$\beta$ TM	C- $\beta$ TM	$\beta$ TI	C- $\beta$ TI
22-40 (young)	9.56 $\pm$ 0.41a	6.94 $\pm$ 0.66b	7.23 $\pm$ 0.62 b	6.71 $\pm$ 0.84b
41-55 (old)	13.86 $\pm$ 0.89a	7.26 $\pm$ 0.84b	9.57 $\pm$ 0.55c	7.23 $\pm$ 0.47b

## Discussion

$\beta$ -Thalassemia is a blood disorder that can influence oral health.<sup>4-6</sup> The present study is probably among first attempts to compare prevalence of dental caries and periodontal diseases among patients affected by  $\beta$ -Thalassemia Major and  $\beta$ -Thalassemia Intermedia in a systematic way.

A division according to the gender was done for any subgroup as performed in previous investigations.<sup>4,5</sup> The ratio among female and male subjects is steady in all subgroups, allowing us to exclude any kind of gender influence on the results.

The sample population was older than the ones of previous studies because survival has enhanced markedly over the past 3 to 4 decades due to improvements in transfusion and chelation practices. Thus, people born in the past 20 years are expected to have near-normal survival if treated appropriately.<sup>18</sup> Maximum age for young patients was arbitrary set to 40 years just to obtain homogeneous subgroups with a similar number of subjects. The distinction between young (22-40 years) old (41-55 years) subgroups enables to understand the influence of  $\beta$ -Thalassemia Major and Intermedia on oral health in different age subgroups.

Because of the difficulty in recruiting a numerically high number of patients aged from 22 to 55, the study's equipe of Vittorio Emanuele and Ferrarotto Hospitals took almost two years. The evaluation of oral hygiene level conducted by PI reveals a not significant difference among subgroups of the same age while there was a significant difference between all young subgroups and the respective old ones. These findings indicate that oral compliance and formation of plaque deposits depend on the age while they aren't influenced by the presence of any form of  $\beta$ -Thalassemia. This trend can be well explained by the similar dental care background among test and controls subjects.

GI and PPD scores reveal that  $\beta$ -Thalassemia Major negatively affects gingival and periodontal status only on the old sample population while its influence on young patients seems not to be relevant. On the contrary,  $\beta$ -Thalassemia Intermedia doesn't influence periodontal health neither in old nor in young subgroups. Old subgroups (both the thalassemia and the control ones) exhibits a moderate-to-severe gingivitis (2.01 till 2.74 GI scores) while all young subgroups were affected by mild-to-moderate gingivitis (1.62 till 1.86 GI scores). However, old patients affected by  $\beta$ -Thalassemia Major experienced a higher prevalence of severe gingivitis (GI = 2.74) and periodontal attachment loss (PPD=4.88) compared with both C- $\beta$ TM and  $\beta$ TI old subgroups.

Surely, periodontal inflammation depends on the fact that, according to inclusion criteria, no dental prophylaxis was administered during previous 6 months or more. The incidence of gingivitis in people with  $\beta$ -Thalassemia Major seems likely related to local factors such as malocclusion and drying of the gums through the patient's inability to close his mouth over the protruding teeth. The chronic anorexia may in some cases predispose to gingival disorders.<sup>19</sup>

Additionally, old subgroups reveal a significantly higher prevalence of periodontal diseases when they are compared to the same young ones, confirming that periodontal diseases are more frequent with increasing age.<sup>20</sup>

It can be inferred that, in young population, periodontal structures of both thalassemia and healthy subjects express the same grade of inflammation and periodontal resorption (expressed by GI and PPD)

when they are exposed to the identical chronic irritative stimulus provided by plaque deposits (expressed by PI). Our data regarding young samples confirm results of Al-Wahali et al.,<sup>4</sup> who, on a population aged from 6 to 18 years, didn't notice any relation between periodontitis and  $\beta$ -Thalassemia. Kaur et al.,<sup>6</sup> and Veena R<sup>7</sup> got the same conclusions, stating that patients with  $\beta$ -Thalassemia Major had not significant increased levels of gingivitis or plaque accumulation than in controls. On the other hand, a higher GI and PPD scores were found in old  $\beta$ TM subgroup than the young one. Such finding may be related to the fact that periodontitis is encountered frequently in the adult population.<sup>21</sup>

On basis of our DMFT scores,  $\beta$ TM-group had higher caries experience than both C- $\beta$ TM and  $\beta$ TI groups. Level of dental caries may be explained on the basis of the chronic nature of thalassemia. Oral hygiene seems not to be influent on the prevalence of caries, because, according to PI score, all subgroups had almost identical dental hygiene. However, Kaplan et al.,<sup>19</sup> explained that dental caries in these patients appears to be associated primarily with dental neglect. Difference in terms of DMFT between  $\beta$ TM-group and  $\beta$ TI-group can be caused by the fact that  $\beta$ -Thalassemia Major appears early in life while Intermedia forms often occurs in teenage.<sup>1</sup> Furthermore subjects with  $\beta$ -Thalassemia Major usually present dental malposition and malocclusion<sup>22</sup> that can represent a risk factor for caries. In patients affected by  $\beta$ -Thalassemia Intermedia, caries experience is higher only for old patients, suggesting that the more severe is  $\beta$ -Thalassemia, the more frequent is the prevalence of caries on these patients.

A similar finding was documented in previous studies as Al-Wahadni et al.,<sup>4</sup> and Leonardi et al.,<sup>23</sup> who reported higher caries prevalence in  $\beta$ -Thalassemia patients with similar dmf/DMF-values for both sexes. De Mattia et al.,<sup>24</sup> reported that caries index (DMF) for permanent teeth calculated in all the 60-thalassemia major patients examined were 5.12 as well.

The results of the present study are in disagreement with Scutellori et al.,<sup>25</sup> who found similar incidence of dental caries in  $\beta$ -Thalassemia subjects and their controls. Literature reported that the higher dental caries experience observed in thalassemia subjects was associated with the lower concentrations of immunoglobulin A (IgA) in saliva which could allow increased microbial proliferation that could be involved in their higher caries experience.<sup>26</sup> An early study theorized that the endocrine dysfunction caused by Thalassemia is responsible for the increase in caries prevalence.<sup>27</sup>

## Conclusion

In conclusion, significant increased level of periodontal attachment loss was observed in old patients with  $\beta$ -Thalassemia Major than in their controls. Prevalence of caries is significantly higher in  $\beta$ TM-group compared with both C- $\beta$ TM group and  $\beta$ TI-group, suggesting that only severe variants of  $\beta$ -Thalassemia enhance remarkably risk of decay. Consequently, local and general modifications of thalassemia patients should be examined in order to explain prevent and treat the impact of this illness on dental and periodontal health. This means that dental care has a strong positive influence on oral health of patients with severe form of  $\beta$ -Thalassemia. Therefore, emphasis to educate such groups in the prevention of dental caries and periodontal disease should be considered.

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## Conflicts of interest

The authors declare that they have no competing interests.

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