

## Prevalence of Gingivitis in Beta Thalassemia Major Patients- A Study amongst Pakistani Adults

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### Authors' contributions

This work was carried out in collaboration among all authors. Author AH wrote the original draft and did literature searches. Author ZHC performed the study design and reviewed the manuscript. Author SA did formal analysis and literature searches. Author MYA did conceptualization and wrote the original draft of the manuscript. Author ZAK wrote the original draft, did formal analysis and helps in conceptualization. Author KA wrote the original draft and initial review of the manuscript. All authors read and approved the final manuscript.

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### ABSTRACT

**Aims:** This study aimed to determine the prevalence of gingivitis in patients suffering from Beta Thalassemia Major.

**Study Design:** Cross-sectional study.

**Place and Duration of Study: Sample:** Sundus Foundation, a voluntary blood transfusion center in Lahore, Pakistan, between March 2017 and September 2017.

**Methodology:** This descriptive cross-sectional study had a total of 110 cases of beta thalassemia major, 15-35 years of either gender were included. Patients with immunosuppressive therapy or anti-inflammatory therapy, smokers and partially erupted teeth, retained roots, teeth with periapical

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lesion were excluded. Demographic profile of all the patients was recorded and a thorough dental checkup will be carried out. A single clinician carried out the clinical examination for all the subjects using WHO probe. Frequency of gingivitis was recorded.

**Results:** The mean age of participants was  $22.10 \pm 5.37$  years. The majority of the patients 77 (70.0%) were between 15 to 25 years of age. Out of the 110 patients, 59 (53.64%) were male and 51 (46.36%) were females with male to female ratio of 1.1:1. Gingivitis was found in 102 (92.73%) cases, whereas there was gingivitis in 08 (7.27%) cases.

**Conclusion:** This study concluded that the prevalence of gingivitis in patients suffering from Beta Thalassemia Major is very high.

*Keywords: Thalassemia major; dental disease; gingivitis.*

## 1. INTRODUCTION

“Beta-thalassemia is a group of hereditary blood dyscrasias caused by anomalies in beta chains of hemoglobin, which result in variable phenotypes that range from severe anemia to clinically asymptomatic individuals” [1]. “Thalassemias are defined as quantitative defects in the synthesis of hemoglobin, where specifically in beta thalassemia, there is an inherited mutation of the beta-globin gene” [2]. “Three main forms have been described: thalassemia major, thalassemia intermedia, and thalassemia minor” [3]. “It is a severe form of anemia associated with splenomegaly and bone abnormalities. The total annual incidence of symptomatic beta thalassemia individuals is estimated at 1 in 100,000 throughout the world, with higher incidence reported in India, China, Mediterranean countries, and Southeast Asia” [4]. Individuals who suffer from beta thalassemia report symptoms such as tiredness, tachycardia, slow growth, pale skin, and shortness of breath [5]. Such patients require regular blood transfusions to overcome deficient hemoglobin and pharmacological support to overcome iron overload with newer treatments such as gene therapy offered to patients [6].

“Reports of oral complications from thalassemia are rare in the literature. Pain and swelling in the parotid glands of patients with thalassemia major have been reported, possibly as a result of iron deposits in the serous cells” [7]. A few oral clinical findings in patients suffering from beta thalassemia include enlargement of the maxilla that leads to protrusion of teeth, spacing between teeth, open bite, overbite, and varying malocclusion [8]. “However, it seems reasonable to believe that oral manifestations may be more common in thalassemia than the literature would indicate. Iron deficiency anemia and folic acid deficiency may produce symptoms of glossodynia and loss of papillae on the tongue

similar to those seen in the patient whose case is presented here” [9]. “The hematologic findings in thalassemia minor are very similar to those of iron-deficiency anemia, and folic acid deficiency is a common complication of thalassemia minor. Therefore, a form of thalassemia may be considered in a differential diagnosis of glossodynia and loss of papillae” [10].

“Gingivitis is dental plaque-induced inflammation of the gingiva without bone loss and clinical attachment loss. It is a frequently encountered disease in dental practice, affecting people of all ages” [11]. The role of the prevalence of gingivitis in patients suffering from beta thalassemia major has been unclear. There has been a hypothesis that the occurrence of iron overload in thalassemia patients changes the levels of matrix-metalloproteinases (MMP) in saliva, and gingival crevicular fluid (GCF), that causes detrimental effects on the periodontal health of such patients [12]. Since gingivitis is prevalent in patients suffering from beta thalassemia, older patients tend to experience more severe gingivitis, as compared to younger individuals when assessed on Loe and Sillness gingival index [13]. This could be due to increased accumulation of plaque and calculus in older individuals as teeth are subjected to more dental diseases as compared to young individuals. However, at times it has been concluded that younger patients who have been suffering from beta thalassemia major show a higher prevalence of gingivitis and periodontitis. [14]. “It has been well known that if gingivitis is not treated, it may lead to patients developing periodontitis which is an irreversible condition. Gingival conditions are associated with a wide variety of blood dyscrasias including beta thalassemia and sickle cell anemia. Although periodontal diseases have been associated with both beta thalassemia and sickle cell anemia, it has been found to be more significant in patients suffering from beta thalassemia” [8].

“In Pakistan, 5,000 children are diagnosed with thalassemia-major, every year. About 9.8 million carriers are estimated in the general population with a carrier rate of 5–7%” [15,16] [8,9]. “While in 2008 Modell and Darlinson calculated a national carrier frequency for  $\beta$ -thalassemia of 4.6%” [17]. Since few studies have been carried out to find out the prevalence of gingivitis amongst beta thalassemia patients, this study aimed to find out the prevalence of gingivitis in patients of  $\beta$ TM coming to a local blood transfusion center in Lahore, Pakistan. The study will help to find out the relationship between the two diseases and it can be used as a basis for incorporating dental care as routine healthcare service for Beta Thalassemic patients in the local population as no local literature is available.

## 2. MATERIALS AND METHODS

This descriptive cross-sectional study was carried out at Sundus Foundation, a voluntary blood transfusion center in Lahore, Pakistan. The duration of this study was from 3<sup>rd</sup> March 2017 to 2<sup>nd</sup> September 2017. In this study, the participants were recruited using a non-probability consecutive sampling method. To determine the sample size of this study, OpenEpi software was used keeping the confidence level at 95%, the margin of error at 9%, and taking the expected percentage of gingivitis in beta thalassemia major patients as 32.6% [14]. The sample size was calculated to be 110 patients.

### 2.1 Inclusion and Exclusion Criteria

The participants in this study were invited and included on the basis of the following criteria: Patients suffering from Beta Thalassemia Major with no h/o other systemic diseases that is known to affect the periodontium e.g., Diabetes, Leukemia, etc. on detailed history or as mentioned in the patient records, young adults between the ages of 15 and 35, and Both males and females. The participants were excluded on the basis of: Dental prophylaxis done in the last 6 months, Antibiotic, immunosuppressive therapy or anti-inflammatory therapy in the last 6 months, Patients affected by life-threatening conditions, Smokers, Patients with decayed, missing or filled Ramjford teeth, partially erupted teeth, retained roots, teeth with periapical lesion and third molars would be excluded without substitution.

### 2.2 Data Collection

Subjects who fulfilled the selection criteria were selected from the inpatient department at Sundus

foundation. On getting approval from the Institutional Review Board (IRB) of Fatima Memorial Hospital and Sundus Foundation, informed consent was taken from every selected patient. The demographic profile of all the patients was recorded and a thorough dental checkup will be carried out. A single clinician carried out the clinical examination for all the subjects using a WHO probe. According to Loe and Sillness Gingival Index, the gingivitis scores of the patients were categorized as follows: No bleeding (Healthy Gingiva), Erythematous Gingiva, Bleeding on Probing, and Spontaneous Bleeding, respectively [18]. The tooth brushing habits of the patients were noted and categorized as follows: Not at all, Once a day, Twice a day, and Thrice a day, respectively.

### 2.3 Statistical Analysis

Collected data were entered and analyzed in the computer program SPSS version 20. Qualitative data like gender and gingivitis were presented in the form of frequency and percentages. Quantitative data like age was presented in the form of mean standard deviation. Stratification was done with regard to age and gender and post-stratification chi-square was applied to see their effect on the outcome. P-value  $\leq 0.05$  was considered as significant.

## 3. RESULTS

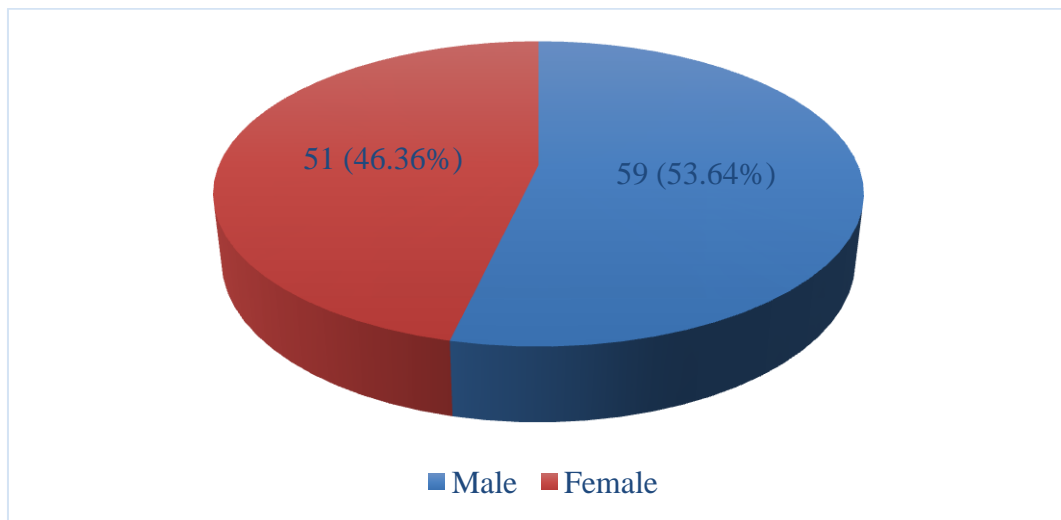
In this descriptive, cross-sectional study, we recruited a total of 110 patients who met the criteria of being included in the study. The age range in this study was from 15 to 35 years with a mean age of  $22.10 \pm 5.37$  years. The majority of the patients 77 (70.0%) were between 15 to 25 years of age as shown in Table 1.

**Table 1. Age distribution of patients (n=110)**

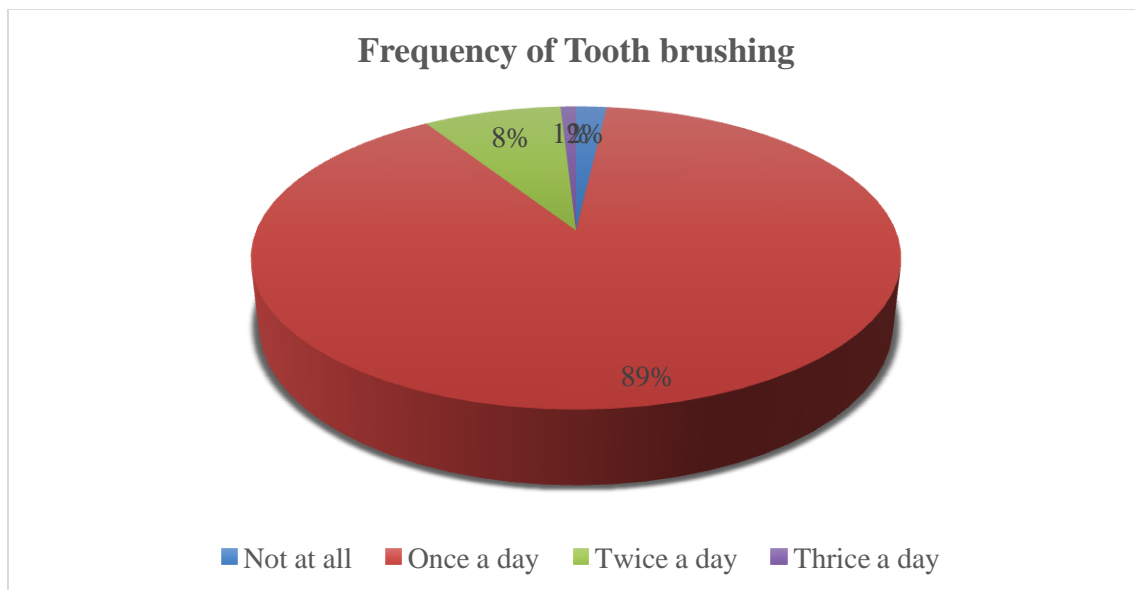
Age (in years)	No. of Patients	Percentage
15-25	77	70.0
26-35	33	30.0
Total	110	100.0

Out of the 110 patients, there were 59 (53.64%) males and 51 (46.36%) females, with a male-to-female ratio of 1.1:1, as presented in Fig. 1.

Regarding the frequency of tooth brushing among the 110 patients, the majority of the 98 (89.1%) patients brushed their teeth “Once a day”, as presented in Fig. 2.



**Fig. 1. Distribution of patients according to gender (n=110)**



**Fig. 2. Frequency of tooth brushing amongst the patients (n=110)**

Regarding the comparison of tooth brushing frequency with the prevalence of gingivitis, the majority of the patients who brushed their teeth

once a day had suffered from gingivitis (89.2%) as compared to few patients who brushed twice a day (8.8%), as presented in Table 2.

**Table 2. Crosstabulation of gingivitis with frequency of tooth brushing (n=110)**

			Tooth brushing				Total
			Not at all	Once/Day	BD	TD	
<b>Gingivitis</b>	No	Count	0	7	0	1	8
		% With Gingivitis	0.0%	87.5%	0.0%	12.5%	100.0%
	Yes	Count	2	91	9	0	102
		% With Gingivitis	2.0%	89.2%	8.8%	0.0%	100.0%

Out of the 110 beta thalassemia patients, Gingivitis was found in 102 (92.73%) cases, whereas there was no gingivitis in 08 (7.27%) cases, as presented in Fig. 3.

According to the gingival index, the distribution for the 110 patients was as follows: 8 patients with “No bleeding”, 25 patients with “Erythematous gingiva”, 37 patients with “Bleeding on probing”, and 40 patients with “Spontaneous bleeding”, as presented in Table 3.

When stratification analysis of gingivitis was performed with the age groups, it was found that there was no significant difference between different age groups (p-value= 0.054), as presented in Table 4.

Furthermore, when stratification analysis was performed of gingivitis with the gender of the

participants, a significant difference was noted (p-value=0.015), as presented in Table 5.

#### 4. DISCUSSION

“The oral health of children suffering from Thalassemia major is reported to be poor by most researchers” [19,20,21]. “As low priority is given to the oral health status by the masses in the country in general, this negligence might be compounded for children already suffering from a life-threatening systemic disease because the parents might focus on the medical procedures required to overcome this disease during early childhood. So, this poor oral health in turn leads to further deterioration of systemic health in these children” [21]. This study was conducted to determine the prevalence of gingivitis in patients suffering from Beta Thalassemia Major.

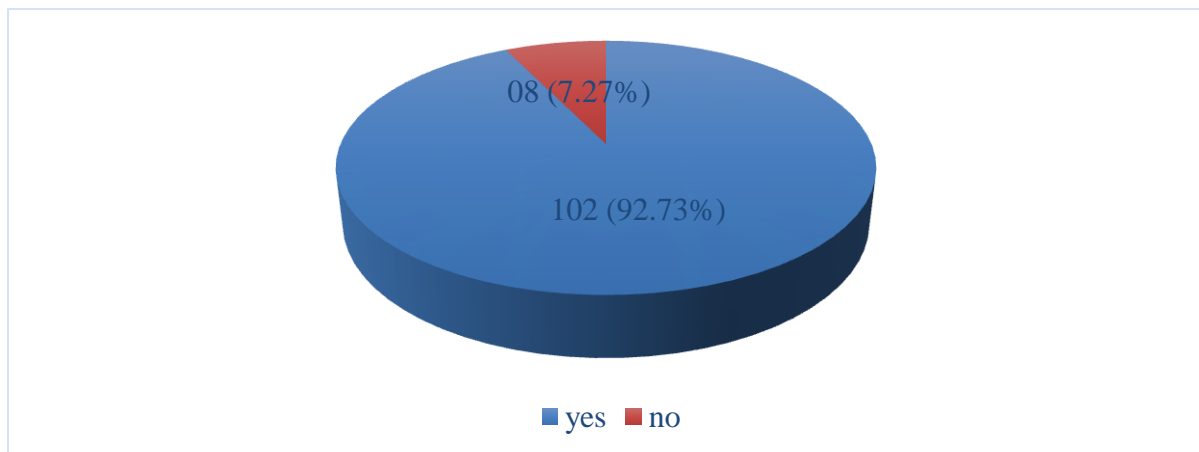


Fig. 3. Percentage of gingivitis in patients suffering from Beta Thalassemia Major (n=110)

Table 3. Categorization of gingival index amongst the patients (n=110)

Gingival Index		Count	Gender		Total
			Male	Female	
No Bleeding	Count	1	7	8	
	Percentage	12.5%	87.5%	100.0%	
Erythematous gingiva	Count	22	3	25	
	Percentage	88.0%	12.0%	100.0%	
Bleeding on Probing	Count	18	19	37	
	Percentage	48.6%	51.4%	100.0%	
Spontaneous bleeding	Count	18	22	40	
	Percentage	45.0%	55.0%	100.0%	

Table 4. Stratification of gingivitis with age of the patients (n=110)

Age (years)	Gingivitis		p-value
	Yes	No	
15-25	69 (89.61%)	08 (10.39%)	0.054
26-35	33 (100.0%)	00 (00.0%)	

**Table 5. Stratification of gingivitis with gender of the patients (n=110)**

Gender	Gingivitis		p-value
	Yes	No	
Male	58 (98.31%)	01 (1.69%)	<b>0.015</b>
Female	44 (86.27%)	07 (13.73%)	

In our study, gingivitis was found in 102 (92.73%) beta thalassemia patients, whereas there were no gingivitis in 08 (7.27%) patients. Similarly, a study by Mohadeseh Arabsolgher et al concluded that a higher prevalence of both gingivitis and periodontitis was found in patients as compared to the control group. [14].

“GI and PPD scores reveal that  $\beta$ -Thalassemia Major negatively affects gingival and periodontal status only in 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 either in old or young subgroups. Old subgroups (both the thalassemia and the control ones) exhibit 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”. Kaur et al [20] and Veena R [22] got “the same conclusions, stating that patients with  $\beta$ -Thalassemia Major had not significantly increased levels of gingivitis or plaque accumulation than in controls. On the other hand, higher GI and PPD scores were found in the old  $\beta$ TM subgroup than in the young one. Such findings may be related to the fact that periodontitis is encountered frequently in the adult population” [23].

“Another study concluded that  $\beta$ -Thalassemia Major is associated with a higher prevalence of decays independently to age and adversely affects periodontal status in adult patients.  $\beta$ -Thalassemia Intermedia doesn't exhibit any relation to periodontal health while is associated with an increased caries experience in 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” [24]. Caliskan et al. reported that gingivitis was observed in 100% of 22 thalassemia patients” [25]. “The small number of the patients in Caliskan et al. study may be the reason for the difference in the results of these

studies” [25]. “Al-Wahadni et al. reported no difference in gingival index, plaque index, and pocket depth between the case (61 patients) and control (healthy) group and concluded that there is no relationship between gingivitis and periodontitis with thalassemia” [19]. “Siamopoulou-Mavridou et al. evaluated gingivitis and caries in 22 thalassemia patients and suggested that the lower level of the salivary antibodies set the higher prevalence of gingivitis and caries in patients with thalassemia. The percentage of gingivitis prevalence was not reported in this study. Periodontitis was not assessed in this study either” [26].

A recent study conducted in Italy [13], assessed “the prevalence of periodontal disease, orofacial changes, and craniofacial abnormalities in patients with thalassemia major. Clinical and radiographic examinations were carried out. The sample consisted of 100 patients affected by beta thalassaemia major and 98 patients with beta thalassaemia intermedia; each sample was compared to the respective control groups of healthy individuals. Patients were examined for plaque deposits, gingivitis, and periodontitis using Löe and Silness plaque and gingival indices. The results showed a significantly increased level of periodontal attachment loss in older patients with beta thalassaemia”. Another study [27], was conducted “to assess the prevalence of periodontal disease, orofacial changes, and craniofacial abnormalities in patients with thalassaemia major. The sample consisted of 54 patients, and a similar number of unaffected individuals matched by age and sex served as a control. The results conclude that poor oral hygiene and gingivitis were observed in thalassaemic patients compared to control group. Subsequently, a study was conducted to know of any association between increased severities of periodontal disease in thalassaemic patients. The study concluded that thalassaemia major was not associated with increased prevalence of gingivitis or periodontitis” [19].

Ajami et al studied “oral and dental health in thalassemia patients and reported healthy periodontium, gingivitis, and periodontitis in 64.8, 33.0, and 1.8 percent of the patients,

respectively” [28]. Gingivitis was recorded in 82% of cases in a study [29] but Girinath et al reported in 26% [30]. In conclusion, this study indicated that those patients suffer from an increased prevalence of gingivitis and delayed eruption of their teeth with poor oral hygiene, dental knowledge and behaviors should be encouraged and their abnormalities should be corrected and preventive dental health programs should be applied to prevent these problems in addition to treat their medical abnormalities. In Pakistani population, it has been found that periodontitis and gingivitis existed in beta thalassemia patients and offering proper treatment improves their oral health [31].

About the gender difference in occurrence of gingivitis in thalassemia, our study concludes that male patients were effected to a greater degree as compared to the female counterparts. Similar difference of gender-wise has been found in a study by Gumus et al [32]. This difference could be due to females taking better care of their oral hygiene as compared to males.

## 5. CONCLUSION

This study concluded that the prevalence of gingivitis in patients suffering from Beta Thalassemia Major is very high.

## CONSENT

"All authors declare that 'written informed consent was obtained from the patient preserved.

## ETHICAL APPROVAL

This study was approved by ethical review committee of FMH College of Medicine and Dentistry

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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