Original Article

UPDCJ OPEN ACCESS

The Comparative Analysis of Craniofacial Parameters in Thalassemic Patients and Non-Thalassemic Individuals across Both Sexes in Chattogram, Bangladesh

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ARTICLE INFO.

Received: 24 November, 2024
Accepted: 01 January, 2025

Volume: Vol-15, Issue-1, April 2025
DOI: https://doi.org/10.3329/updcj.v15i1.77925

Publisher: Update Dental College, Dhaka, Bangladesh
Web: www.updatedentalcollege.edu.bd
E-mail: updcj@hotmail.com

Scan to access article citation and full online link

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ABSTRACT

Introduction: Thalassemia is a hematologic disorder impairing craniofacial development in inadequately treated patients. Research on craniofacial parameters in the Bangladeshi thalassemic population compared to non-thalassemic is scarce. This study aimed to determine the differences in craniofacial parameters, if any, between thalassemic patients and non-thalassemic individuals in Chattogram, Bangladesh, across both sexes. **Materials and methods:** This cross-sectional analytical study was carried out among 100 respondents (50 transfusion-dependent thalassemia patients and 50 non-thalassemic healthy individuals) of 5-30 years during 2020 in Chittagong Medical College, Bangladesh. To measure 10 key craniofacial parameters (head circumference, 6 horizontal and 3 vertical) in cranial, facial, nasal, and orbital zones, a digital slide caliper and tape were used. To test statistical significance, Mann-Whitney U test and unpaired student's t-test were done as appropriate. **Results:** The face height of non-thalassemic males was higher than that of thalassemia patients, and this was significant ($p = 0.027$); the intercanthal distance in males with thalassemia showed a highly significant difference ($p = 0.024$). When compared to their non-thalassemic peers, thalassemic female patients were observed to have significantly larger head circumference ($p = 0.025$) and head width ($p = 0.031$). There were differences between the groups in other craniofacial parameters but statistically non-significant ($p > 0.05$). **Conclusion:** Distinct differences in craniofacial parameters between thalassemic and non-thalassemic individuals are highlighted, which emphasize the impact of thalassemia on craniofacial development, with potential implications for clinical management in thalassemic patients in Bangladesh. Further research is recommended to explore these differences' underlying mechanisms and broader inferences.

KEY WORDS: craniofacial measurements, morphometric study, sex, thalassemia**,** transfusion dependent

INTRODUCTION

Thalassemia is a diverse genetic hemoglobin disorder, affecting men and women equally, marked by an inability to synthesize hemoglobin due to abnormalities in the α, β, and δ globin genes, which ultimately leads to inefficient erythropoiesis and ultimately results in chronic anemia[1–3]. Owing to the high gene frequencies of HbE and β-thalassemia, this double heterozygosity for a structural hemoglobin variant in combination with reduced or absent synthesis may prove to be the most common type of thalassemic disorder around much of the world[4]. The Mediterranean, the Middle East, and Southeast Asia have the greatest rates of thalassemia prevalence, according to earlier research[2]. Every year, 320 thousand babies are considered to be born with a hemoglobin abnormality that is clinically significant, with about 80% of cases occur in developing nations. The most cautious estimates indicate that more than 100 million people with a global frequency of 1.5% for beta thalassemia and at least 5.2% of the world's population (over 360 million) carry a major hemoglobin variation[5,6]. It has been estimated that the largely prevalence of carriers of beta thalassemia is 2.78–4% in India, 5-7% in Pakistan, and roughly 3% in Bangladesh[7–9].

Its worldwide distribution has changed, although, as a result of migration. Consequently, previously non-endemic regions like as Western Europe and North America have seen an increase in the prevalence of β-thalassemia[2]. Usually the most prevalent types are α- and β-thalassemia[10]. In Southeast Asian descent both Alpha thalassemia and beta thalassemia are common[3]. Three groups for HbE beta thalassemia could be made based on clinical severity: mild, moderate, and severe[11]. Individuals suffering from severe Hb E/β

thalassemia, β thalassemia major, transfusion-dependent Hb H illness, and other thalassemias need to get lifelong blood transfusions, every three to four weeks for life sustenance[12].

Facial and other skeletal bones deformities are particularly interesting among the countless problems associated with thalassemia as they affect both look and function, these anomalies emerge as a result of extramedullary expansion of hematopoiesis which the body compensates for long-term anemia[13,14].

Patients with thalassemia frequently have a Class II skeletal relationship, which is distinguished by prominent cheek bones, a mandible that is retrognathic and a clear vertical growth direction. A reduced jaw, midface projection, and a decreased posterior facial height as well as the collapsed nose bridge are typical characteristics. Research shows that there are no statistically significant variations in skeletal measurements of angle and linearity between males and females who are thalassemic. Similar patterns of craniofacial abnormalities, such as a smaller mandibular body and a more convex craniofacial shape, are seen in both male and female thalassemic individuals[15–17]. These craniofacial deformities and malocclusion due to bone marrow hyperplasia compensating for ineffective erythropoiesis[18]. Individuals who had blood transfusions on a monthly basis showed a non-significantly fewer instances of craniofacial deformities (CFD) compared to those who received transfusions less frequently (p = 0.495)[19]. However, there is debate because growth retardation is reported to be observed in children who receive thalassemic transfusions on a regular or irregular basis[20]. While the epidemiological, clinical and hematological aspects of thalassemia have been extensively studied, there is limited research focusing on the craniofacial parameters of thalassemic patients compared to non-thalassemic individuals in Bangladesh. Specifically, the differences in craniofacial dimensions between these two groups across both sexes remain underexplored, particularly in the Chattogram region, despite Bangladesh lying in the world's thalassemia belt[21,22]. Understanding these differences is crucial, as they can influence treatment planning, surgical interventions, and overall patient care. This knowledge will be valuable for healthcare providers in tailoring treatment plans for thalassemic patients, potentially improving patient outcomes. Furthermore, the study may lay the groundwork for future research in other regions, contributing to a broader understanding of how thalassemia affects craniofacial parameters globally. Present study aimed to determine the differences in craniofacial parameters if any between transfusion dependent thalassemic patients and non-thalassemic individuals in Chattogram, Bangladesh across both sexes.

MATERIALS AND METHODS

This cross sectional analytical study, carried out during 2020 in the department of Anatomy of Chittagong Medical College, Chattogram, Bangladesh, included conveniently selected 100 respondents of 5-30 years. Of them 50 were transfusion dependent thalassemia patients and rest were age-matched non-thalassemic healthy individuals. According to the result of Hb Electrophoresis the subjects were allotted in proper groups. After getting approval from Ethical Review Board of Chittagong Medical College data were collected from three centers of Chattogram- the Department of Pediatrics, Department of Hematology of Chittagong Medical College Hospital and Fatema Begum Red Crescent Blood Center. Individuals having no history of congenital craniofacial abnormality, orthodontic treatment, major craniofacial injury or reconstructive surgery in craniofacial region were included in non-thalassemic group.

Participants were informed of the steps of study. Ensuring safety study procedure all measurements were taken according to Farkas method by using measuring tape and digital slide caliper from the labeled faces of the respondents directly, applying negligible pressure to the soft tissues[23]. Head circumference[24],head width[25], face width, face height, nose height, nose width, nose tip protrusion, biorbital width, intercanthal width[21] and nose root width[26] were measured following validated techniques.

All data were analyzed with SPSS software (version 26). Data were presented as number, percentage, or mean ± standard deviation. For comparison, the Mann-Whitney U test and unpaired Student's t-test were performed as appropriate. Results were considered to be significant if p value was less than 0.05 at 95% level of significance.

RESULT

Fifty thalassemia patients as case with similar number of age matched controls were enrolled in this study. The respondents' ages ranged from 5 to 30 years, with a mean age of 14.86±7.10 years in thalassemic patients and 14.70±1.04 years in non-thalassemic individuals. Out of 100 participants, male: female was 1:0.61. There were 56% male in thalassemia patient group and 68% male in the control group, 44% female were in thalassemia patient group and 32% female were in control group.

Table I- Craniofacial Dimensions

Elements	Male		p value	Female		p value
	Thalassemia (n=28)	Control (n=34)		Thalassemia (n=22)	Control (n=16)	
Head circumference (cm)	52.21±2.15	52.64±2.78	p=0.504	52.15±1.73	50.93±1.57	*p=0.025
Head width (cm)	14.54±0.89	15.19±1.62	p=0.119	14.39±1.01	13.86±0.80	*p=0.031
Face width (cm)	12.04±1.04	12.21±1.55	p=0.783	11.79±0.98	11.72±1.34	p=0.745
Face height (cm)	10.14±0.90	10.84±1.43	*p=0.027	10.30±0.96	10.05±1.28	p=0.488
Nose width (mm)	31.71±3.88	32.89±4.47	p=0.275	31.93±6.11	31.21±3.09	p=0.478
Nose height (mm)	39.45±3.55	37.85±6.44	p=0.276	39.63±6.38	37.96±5.91	p=0.535
Nasal root width (mm)	22.54±3.61	20.80±6.13	p=0.261	21.60±6.47	19.28±5.80	p=0.193
Nasal tip protrusion (mm)	20.90±3.73	19.52±6.99	p=0.323	21.34±6.85	18.32±7.82	p=0.124
Biorbital width (mm)	97.61±6.82	101.58±8.46	p=0.083	98.64±7.21	95.56±3.86	p=0.130
Intercanthal width (mm)	31.37±3.95	28.85±3.94	*p=0.024	31.29±6.05	29.63±4.10	p=0.261

* p<0.05= significant

In males, the mean head circumference, head width, face width, nose width, and biorbital width of non-thalassemic males were greater than those of thalassemic males, although these differences were not statistically significant ($p > 0.05$). The only exception was face height, which was significantly greater in non-thalassemic males ($p = 0.027$). Additionally, thalassemic males tended to have a wider intercanthal distance compared to non-thalassemic males, and this difference was statistically significant ($p = 0.024$). In female participants, thalassemic individuals were more likely to have a greater head circumference, wider face, nose, nasal root width, and a wider distance between the outer edges of their eye sockets (biorbital width), as well as a longer face and nose, compared to non-thalassemic females. However, these differences were not statistically significant except for head circumference, where thalassemic females had a significantly larger head size ($p = 0.025$), and head width, which was also significantly wider in thalassemic females ($p = 0.031$) (Table I).

DISCUSSION

During this study, the measurements were recorded from four craniofacial regions. During literature review, only a few studies were found where particularly the anthropometric measurements of the jaw and face in thalassemia patients were measured by direct approach. Different measurement methods were used in some other studies[27–29].

In a number of disciplines, including anthropology, orthodontics, prosthodontics, and forensic medicine, the assessment of facial measurements is crucial[30–33]. This is because precise facial anatomical data is essential to improving the validity of operations and therapies in these fields. In order to obtain both functional and aesthetically pleasing outcomes, orthodontics relies heavily on facial measurements for both diagnosis and treatment planning[32]. Dental prostheses are customized to fit each person's specific face anatomy. Therefore, precise facial measurements are essential in prosthodontics for the design and fitting of dental prosthesis. This is especially crucial when there are large skeletal disparities since accurate measurements are required to get the intended functional and aesthetic results[33]. Facial dimensions are crucial for facial reconstruction in forensic medicine, which combines science and art to restore recognizable faces from an unknown skull. This technique is highly reliant on the accurate measurement of the soft tissues thickness in the face, which fluctuates throughout populations and is influenced by age, sex and skeletal occlusions[31,34].

In this study, the non-thalassemic males (52.64±2.78 cm) had a slightly larger head compared to the thalassemic males (52.21±2.15 cm) but it was statistically not significant (p=0.504). The thalassemic females (52.15±1.73 cm) had a larger head compared to the non-thalassemic females (50.93±1.57 cm) and it was statistically significant (p=0.025). Regarding the head width of present respondents, non-thalassemic male and thalassemic female had wider head than their counterparts. The difference was statistically not significant in male (p= 0.119) but was significant in female (p= 0.031). In Turkey[13] the non-thalassemic males (55.2±2.6 cm) had a larger head compared to the thalassemic males (53.6±2.3 cm). In female, it was 53.5 cm in thalassemia group and 54 cm in control group. In both sexes the values were not statistically significant (p value was 0.071 and 0.635 respectively). The values and trend of the male group are nearly similar to the present study but in female group the observation is dissimilar. Head width in the thalassemic male was 14.8 ± 0.7 cm and in non-thalassemic group was 14.7±2.6 cm being statistically not significant (p=0.111). In thalassemic female head width was 14.97± 0.8 cm and in non-thalassemic group it was 14.9±0.8 cm being statistically not significant (p=0.692). The values of the female group are nearly similar to the present study but in male group the observation is dissimilar. Study from Jodhpur, India revealed, in comparison to normal individuals of similar sex and age, thalassemic male and female patients (in the 10–17-year age group) were found to have statistically significant reduced head circumferences. When comparing the anthropometric parameters for thalassemic males and healthy males, a highly significant difference emerged; however, there was no significant difference between the thalassemic females and the healthy females in the control group[35]. Findings of Cuttack, India revealed that the head circumference of β-thalassemia patients (age range for boys and girls being 11.05 ± 0.18 years and 10.7 ± 0.17 years respectively) illustrated a moderate decrease, with significant variation in the healthy population, β-thalassemia (minor), and β-thalassemia (major), with the exception of patients with β-thalassemia (intermedia). Due to marrow hyperplasia, people with sickle-β thalassemia have decreased head circumference growth than non-thalassemic people[36]. The trend of the male groups of our study is consistent to Indian studies but for female groups the trend is dissimilar. This dissimilarity is may be due to ethnic and racial variations and different sample size.

In present study, the non-thalassemic males had a slightly wider face (12.21±1.55 cm vs. 12.04±1.04 cm) with no statistical significance (p=0.783) and longer face (10.84±1.43 cm vs. 10.14±0.90 cm) compared to the thalassemic males with statistical significance (p=0.027). The thalassemic females tend to have a slightly wider face (11.79±0.98 cm vs. 11.72±1.34 cm) and longer face (10.30±0.96 cm vs. 10.05±1.28 cm) compared to the non-thalassemic females, both with no statistical significance (p=0.745 and p=0.488). A Turkish study[13] discovered that in male, face width in thalassemia patient group was 10.60 cm and 10.89 cm in control group. In female, the mean was 10.73 cm in thalassemia group and 10.31 cm in control group. In both sexes the values were not statistically significant (p value was 0.763 and 0.074 respectively). The findings of the study coincide with the present study. Regarding face height, non-thalassemic male and female had longer face height compared to the thalassemic males (10.66 cm vs. 12.05 cm; p=0.016) and female (10.97±0.98 cm vs. 10.49± 1.48 cm; p=0.329) respectively. For male, the findings regarding face height in the study are similar to the present study, but are slight dissimilar in case of female. The trend from the Iraqi[37] male population is dissimilar with the present study (face width in thalassemic male patients was 98.4±6 mm and 96±12.9 mm in control group). But the findings from the Iraqi female are similar to the present study where the mean face width in thalassemia patient group and in the non-thalassemic group was 96.6±9 cm and 95.1±6 cm respectively. No statistically significant difference was observed in both male and female (p=0.377 and p=0.413 respectively). Regarding face height, the mean face height was 10.93 ± 1.21 cm in the male thalassemia patients and 11.11 ± 1.45 cm in the counter group, with no statistically significant difference (p = 0.566); face height was 10.61 ± 1.21 cm in the female thalassemia patients and 10.77 ± 0.68 cm in the counter group, with no statistically significant difference (p = 0.412). These findings are comparable to the present study in case of male but it was slight dissimilar in case of female. In the current study, among males, the non-thalassemic

group (32.89±4.47 mm) had a wider nose compared to the thalassemia patient group (31.71±3.88 mm) but it was statistically not significant (p value =0.275); the thalassemia patient group had a longer nose (39.45±3.55 mm) compared to the non-thalassemic group (37.85±6.44 mm) with no statistically significant difference (p=0.276); wider nasal root (22.54±3.61 mm) compared to the non-thalassemic group (20.80±6.13 mm) with no statistically significant difference (p= 0.261); thalassemia patients (20.90±3.73 mm) had a longer nasal tip protrusion compared to the non-thalassemic group (19.52±6.99 mm) with no statistically significant difference (p = 0.323). Among females, the thalassemia patient group had a wider and longer nose, wider nasal root and longer nasal tip protrusion compared to the non-thalassemic group with no statistically significant difference (p>0.05 for all four nasal measurements); and the mean nose width and nose height of thalassemic female patients were nearly similar as thalassemic male patients.

Data from Iraq[37] showed, in male, nose width, nose height and nasal tip protrusion in thalassemia patient group were 36.3±3.7 mm, 50.4±5.3 mm and 15±1.6 mm respectively, and in control group were 37±4.2 mm, 51±7.3 mm and 17.1±2.9 mm respectively. In female, nose width, nose height and nasal tip protrusion in thalassemia patient group were 38.7±22.7mm, 48.5±8.3 mm and 16.3±8 mm respectively, and in control group were 35.5±3.9 mm, 50.4±8 mm and 17.2±2.8 mm respectively . In both male and female, the values were not statistically significant for nose width (p >0.05) and nose height (p >0.05). The variation in nasal tip protrusion was statistically significant in male (p<0.001), but in female it was statistically not significant (p=0.523). The findings of Iraqi study regarding nose width are similar to the present study in both male and female. The dissimilarity of its findings to our study, in both male and female regarding nose height and nasal tip protrusion, are trivial. Turkish study[13] revealed that, in male, nose width, nose height, nasal root width and nasal tip protrusion in thalassemia patient group were 26.7±4.2 mm, 52.8 mm, 20.90±2.50 mm, 19.2 mm and 19.88±1.69 mm respectively, and in control group were 25.6±3.6 mm, 64.7 mm, 19.88±1.69 mm and 21.55 mm respectively. In female, nose width, nose height, nasal root width and nasal tip protrusion in thalassemia patient group were 25.6±3.6 mm, 52.08±8.76 mm, 20.92±2.20 mm and 18.9 mm respectively, and in control group were 22.37±1.74 mm, 58.1±8.38 mm, 18.82±2.09 mm and 20.6 mm respectively. The statistically significant variations were: nose width in female (p =0.006), nose height in male (p=0.003), nasal root width in female (p=0.011) and nasal tip protrusion in both male and female (p=0.002 and 0.007 respectively). The findings of this Turkish study regarding nose width are similar to the present study only for female. The dissimilarity of its findings to our study, in both male and female regarding nose height are huge.

In current study, the non-thalassemic male group (101.58±8.46 mm) had a greater biorbital width compared to the thalassemia patient group (97.61±6.82 mm) with no statistically significant difference (p value =0.083); the thalassemia male patient group had a greater intercanthal width (31.37±3.95 mm) compared to the non-thalassemic group (28.85±3.94 mm) with statistically significant difference (p=0.024). The thalassemic female patient group (98.64±7.21 mm) had a greater biorbital width compared to the non-thalassemia group (95.56±3.86 mm) with no statistically significant difference (p value =0.130); the thalassemia female patient group had a greater intercanthal width (31.29±6.05 mm) compared to the non-thalassemic group (29.63±4.10 mm) with no statistically significant difference (p=0.261).Values and trend regarding biorbital width and intercanthal width of Turkish people[13] (both male and female) are almost alike present study. In Iraq[37], among male, the thalassemia patient group had a narrower biorbital width compared to the non-thalassemic group (92.5±5.6 mm vs. 93.5±10.1 mm), and this difference was statistically not significant (p=0.655); the thalassemia patient group had a greater intercanthal width compared to the non-thalassemic group (34.3±2.4 mm vs. 31.9±2.9 mm), and this difference was statistically significant (p=0.000). Among female, the non-thalassemia group had a greater biorbital width compared to the thalassemic group (93.2±12.3 mm vs. 89.9±18.3 mm), but this difference was not statistically significant (p=0.387); the thalassemic group had greater intercanthal width compared to the non-thalassemia group (34±10 mm vs. 31.4±2.7 mm), and this difference was not statistically significant (p=0.139). The current study's findings differ from this one's.

All the observed differences may be the combined effect of methodological, environmental, systemic and biological factors.

Technological developments have brought up new instruments for facial digitalization, such as 3D facial scanners that are compatible with mobile devices. Studies have revealed that, although these scanners are more accessible and convenient, their accuracy is typically lower than that of professional 3D facial scanners[38]. But the variations are frequently within ranges that are clinically acceptable, so they can be a good choice in some situations. Precise facial anatomy data facilitates efficient treatment planning and implementation, which eventually improves patient outcomes in these domains. The capabilities of specialists in these fields are further enhanced by the integration of cutting-edge technology and creative measuring tools, which improves the accuracy and consistency of facial measures.

LIMITATIONS

The study was restricted to mono-center with relatively small sample size and lacked sex-matching. So, generalizability of the data may not be applicable for entire Bangladeshi population.

RECOMMENDATIONS

For more reliable results from this kind of research, a larger, more varied, age and sex matched sample obtained by multistage sampling is necessary. Confounding variables including thalassemia severity, nutritional state, socioeconomic condition, and genetic predispositions that may affect craniofacial dimensions could be taken into account to obtain more reliable results.

CONCLUSION

The study offers discerning information about the differences in craniums between the thalassemic and non-thalassemic individuals. The substantial variations in male face height and intercanthal width highlighted the impact of thalassemia on the development of the craniofacial structure. The head circumference and head width did, however, show a statistically significant difference, indicating that thalassemic female patients generally have bigger and wider head. Although there were changes in other craniofacial dimensions across the groups, these differences were not statistically significant. These results add to the regional data on thalassemia in Bangladesh and have important implications for tailored treatment plans, especially in surgical and orthodontic procedures. The study emphasizes the

value of public health campaigns and genetic counseling in the management of the illness.

ACKNOWLEDGEMENT

I would like to extend my deepest gratitude to Professor Dr. Mohd. Golam Rabbani, Head of the Department of Hematology, and Professor Dr. A. K. M. Rezaul Karim, Head of the Department of Pediatrics at Chittagong Medical College Hospital, for their invaluable guidance, encouragement, and insightful suggestions throughout this study. I am also sincerely thankful to Dr. Minhaz Uddin Taher, In-charge of Fatema Begum Red Crescent Blood Center, Chattogram, for her unwavering support and expert advice, which were instrumental in the successful completion of this research.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

FUNDING: This research received no external funding.

DATA AVAILABILITY STATEMENT: The data presented in this study are available on reasonable request from the corresponding author

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How to Cite
Tasnim S, Zahur T, Sumaiya SF, Reza R, Lina RS, Fatema S, et al. Comparative Analysis of Craniofacial Parameters in Thalassemic Patients and Non-Thalassemic Individuals across Both Sexes in Chattogram, Bangladesh. Update Dent. Coll. j [Internet]. [cited 2025 Apr. 27];15(1):9-14. Available from: https://www.banglajol.info/index.php/UpDCJ/article/view/77925