

Association of Non-Syndromic Hypodontia with Skeletal Malocclusion in Orthodontic Patients

FAIZA RANA¹, FAIZA MALIK², ESHA RANA³, HANA PERVEZ⁴, RABIA TABASSUM⁵, MEHREEN ISHTIAQ LONE⁶

¹Demonstrator Orthodontics, Sharif Medical & Dental College, Lahore

²Assistant Professor, HOD Orthodontics, Sharif Medical & Dental College, Lahore

³Demonstrator Operative Dentistry, Sharif Medical & Dental College, Lahore

⁴Assistant Professor, HOD Orthodontics, Jinnah Medical & Dental College, Karachi

⁵Senior Lecturer, University Medical & Dental College, Faisalabad

⁶Demonstrator Periodontology, Sharif Medical & Dental College, Lahore

Correspondence to: Faiza Rana, Email: dr.faizarana03@gmail.com, Cell: 0333-4870621

ABSTRACT

Background: Hypodontia is one of the frequently observed dental anomalies in which dentofacial esthetics, phonetics, mastication, self-esteem and quality of life can be adversely affected. Awareness of disproportionate tooth number is important and must be considered by orthodontists while making treatment plans to achieve proper occlusion, overbite, and overjet, in order to restrain oral health deterioration. The aim of this study was to determine the frequency of non-syndromic hypodontia in orthodontic patients and its association with skeletal malocclusion.

Methods: This retrospective case-series was conducted at the department of Orthodontics, Sharif Medical & Dental College. It involved screening the records of orthodontic patients from last 5 years from October 2017 – October 2021, consisting of standardized good quality orthopantomograms and lateral cephalograms. Patient files with incomplete records, any craniofacial syndrome and/or previous history of tooth loss were excluded. Non-syndromic hypodontia and skeletal malocclusion was recorded along with demographic data, in predesigned proforma.

Results: Out of 244 orthodontic patients, 18 patients (7.37%) had non-syndromic hypodontia. Moreover, 63 teeth were missing in 18 patients of NSH. Maxillary arch (52.4%) and upper left quadrant (28.6%) were found to be more frequently affected. The difference of non-syndromic hypodontia among dental arches, quadrants and skeletal malocclusion was statistically significant while for genders it was insignificant.

Conclusion: Non-syndromic hypodontia was significantly associated with skeletal malocclusion, highlighting their genetic etiology. Most commonly absent tooth was maxillary lateral incisor followed by mandibular second premolar and lateral incisor.

Keywords: congenitally missing tooth, dental anomaly, dentofacial esthetics, genetic etiology, skeletal malocclusion

INTRODUCTION

Dental anomalies that occur during the development of tooth bud present as variations in the tooth morphology, shape, size, or color.¹ Multiple genetic and environmental factors are accountable for affecting the normal tooth development.² Any variation in the number of either deciduous or permanent dentition results in supernumerary teeth or missing teeth in either maxillary or mandibular arch, or both.³

By definition, congenitally missing teeth are those that do not erupt in the oral cavity and remain invisible on radiographs. A tooth is confirmed as congenitally absent when it cannot be identified or recognized on the basis of calcification radiographically and extraction is not evident.⁴ Orthodontists frequently come across patients with tooth agenesis that generally promotes oral health deterioration. Radiographic and clinical examinations are required to precisely differentiate and to make the diagnosis whether the tooth is congenitally absent, impacted or extracted.⁵

Hypodontia is one of the frequently observed dental anomalies in which dentofacial esthetics, phonetics, mastication, self-esteem, professional performance and quality of life can be adversely affected.⁵ Patients with hypodontia may experience anxiety and oral health impairment such as malocclusion, loss of alveolar bone and periodontium, inefficient mastication, inarticulate pronunciation, as well as changes in maxillomandibular skeletal relationships.⁶ In restoring congenitally missing teeth, consideration of the alveolar bone quality and volume is necessary, which is related to the mini or micro esthetics.^{5,6} Treatment of congenitally missing tooth can be done by either space opening or closing with orthodontic mechanics in order to correct dento-skeletal problems. Adjunctive restorative procedures can be done along with orthodontic treatment when veneering or re-contouring of the substituting teeth is required. Therefore, management of tooth agenesis involves multiple dental specialties.^{7,8}

Multiple genetic, systemic and environmental factors, play significant part in pathogenesis of dental and skeletal abnormalities. Several genes like myosin 1H gene (MYO1H), paired box 9 (PAX9), and fibroblast growth factor receptor 2

(FGFR2) are associated with both tooth and bone development.⁹⁻¹¹ Multiple factors, such as wingless type integration site (WNT), hedgehog (Hh) families and bone morphogenic protein (BMP) take part in the signaling of epithelial-mesenchymal interactions in tooth development.^{12,13} A number of genes such as ectodysplasin-A (EDA), axis inhibitor 2 gene (AXIN2), and msh homeobox 1 (MSX1) have been identified to be involved in odontogenesis and encode the transcription factor, which has a regulatory part throughout the developmental stages of the tooth organ.¹⁴⁻¹⁷ Anomalies or mutations in these signaling pathways or genes, lead to various forms of tooth agenesis and malocclusion.¹⁵ Therefore, tooth agenesis and skeletal malocclusion have a definite genetic influence.

Hypodontia or congenitally missing teeth can be categorized into syndromic and non-syndromic. Syndromic hypodontia indicates complicated syndromes related with tooth agenesis, like cleft lip and palate and ectodermal dysplasia. Non-syndromic hypodontia (NSH) includes only congenitally absent teeth in secluded form without any involvement of other extensive birth abnormalities.¹⁶ In worldwide literature, the prevalence of hypodontia ranges from 0.3% to 36.5%.⁵

Disproportion of tooth number causes tooth size arch length discrepancy such as crowding or spacing in the affected arch. In these conditions, knowledge of dental aberrations like congenitally missing teeth is important and must be considered by orthodontists while making treatment plans to achieve proper occlusion, overbite, and overjet, in order to avoid oral health deterioration. The association between specific skeletal pattern and non-syndromic tooth agenesis has not been emphasized much in Pakistani population. Therefore, the purpose of this study was to determine the frequency of non-syndromic hypodontia in orthodontic patients and its association with skeletal malocclusions, since, this will be a valuable addition to the local data base as the clinical implications of dental anomalies like hypodontia are inevitable. Early detection of a dental anomaly seeks the attention of orthodontists to search for associated anomalies in the same patient or family, for timely orthodontic intervention.

MATERIALS AND METHODS

This retrospective case-series of last 5 years from October 2017 to October 2021 was conducted after approval from Sharif Medical Research Center and Ethics Committee, Sharif Medical & Dental College. A sample of 244 patients was taken via non-probability consecutive sampling. Inclusion criteria was patients with permanent dentition, having good quality orthopantomograms and lateral cephalograms, along with written signed informed consent forms for orthodontic treatment and research purpose. Patient files with incomplete records, patients with cleft lip or palate, or any other craniofacial syndrome, previous history of tooth loss due to any cause such as caries, trauma, periodontitis, or orthodontic treatment, and patients with primary or mixed dentition, were excluded. Data was collected from November 2021- January 2022, by the primary researcher and two postgraduate residents trained for the purpose, in Orthodontics Department, College of Dentistry, SMDC. Non-syndromic hypodontia and skeletal malocclusion were recorded along with demographic data, in a predesigned proforma.

Non-syndromic hypodontia was confirmed when there was no crypt formation visible on orthopantomogram. Skeletal malocclusion was assessed using the angular measurement of ANB (it is the difference between SNA & SNB) on lateral cephalogram, for each patient to be classified on the following criteria:¹⁸

- Skeletal Class I: ANB 0° - 4°
- Skeletal Class II: ANB > 4°
- Skeletal Class III: ANB < 0°

SPSS version 25 was used for data analysis. Qualitative data like gender and hypodontia were presented in the form of frequency and percentage. Baseline information on demographics were analyzed using descriptive statistics. Chi-square test was applied for the comparison of frequency of NSH between genders, maxillary and mandibular arches, right and left sides and skeletal malocclusions. $p < 0.05$ was considered statistically significant.

RESULTS

A total of 262 patient files were reviewed, out of which 8 incomplete files and 10 files of cleft lip and palate patients were not included. The remaining sample consisted of records of 244 orthodontic patients (155 females, 89 males) out of which 18 patients (7.37%) had non-syndromic hypodontia. Among these 18 patients, 5 (2.04%) patients had one tooth agenesis, 9 (3.75%) patients had two congenitally missing teeth and only 2 (0.81%) patients had more than 6 teeth missing (Table I). The mean age of the sample was 17.2 ± 7.9 years, ranging from 12 to 30 years. The most prevalent malocclusion was skeletal class II (53.7%), followed by skeletal class I (38.9%), and lastly skeletal class III (7.4%). Moreover, we found that 63 teeth were missing in 18 patients of NSH, and frequently affected tooth by hypodontia was maxillary lateral incisor followed by mandibular second premolar and lateral incisor (Figure 1).

With respect to dental arch and quadrant, maxillary arch (52.4%) and upper left quadrant (28.6%) were found to be more frequently affected respectively (Table II). Chi square test yielded a significant difference for both arches ($p = 0.001$) as well as for right and left quadrants ($p = 0.001$), as shown in Table III. Table IV shows the difference of non-syndromic hypodontia among genders which was statistically insignificant ($p = 0.215$), while for skeletal malocclusion, it was statistically significant ($p = 0.016$). Skeletal class I was most commonly affected by hypodontia.

Table 1: Frequency and percentage of Non-Syndromic Hypodontia with respect to the number of missing teeth

Number of missing teeth	1	2	3	4	5	>6	Total
Frequency	5	9	1	1	0	2	18
Percentage	2.04	3.75	0.40	0.40	0	0.81	7.37%

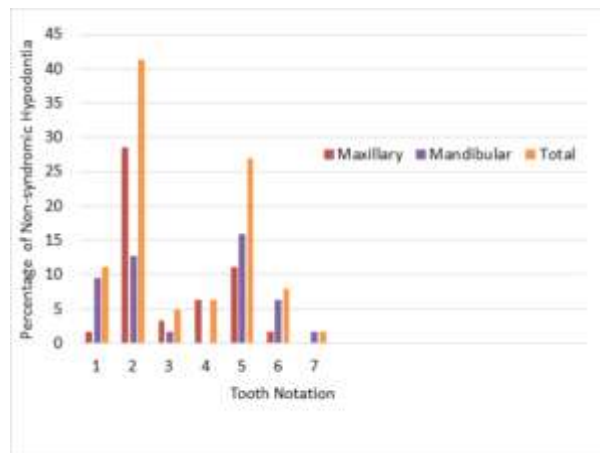


Figure 1: Maxillomandibular distribution of Non-Syndromic Hypodontia

Table 2: Number of missing teeth with respect to Dental Arch & Quadrant

		Number of missing teeth (n=63)	Percentage
Arch	Maxilla	33	52.4%
	Mandible	30	47.6%
Quadrant	Upper Right	15	23.8%
	Upper Left	18	28.6%
	Lower Right	15	23.8%
	Lower Left	15	23.8%

Table 3: Stratification of Non-Syndromic Hypodontia with respect to Affected Arch & Quadrant

Groups		Hypodontia		p-value
		Present	Absent	
Affected Arch	Maxilla	13(72.2%)	5(27.7%)	0.001*
	Mandible	10(55.5%)	8(44.4%)	
Affected Quadrant	Right	13(72.2%)	5(27.7%)	0.001*
	Left	17(94.4%)	1(5.5%)	

* $p < 0.05$ is significant

Table 4: Stratification of Non-Syndromic Hypodontia with respect to gender & skeletal malocclusion

		Hypodontia				p-value
		Present		Absent		
Gender	Male	9	10.11%	80	89.88%	0.215
	Female	9	5.80%	146	94.19%	
Skeletal Malocclusion	Class I	11	11.57%	84	88.42%	0.016*
	Class II	4	3.05%	127	96.9%	
	Class III	3	16.6%	15	83.3%	

* $p < 0.05$ is significant

DISCUSSION

Dental anomalies occur due to genetic and epigenetic factors.¹⁹ If these factors impact unfavorably at the time of tooth bud initiation and formation, there is increased possibility of adverse consequences like congenitally missing tooth. If they impact after initial stages of tooth formation, the results are limited to aberrations in morphology of tooth only, like cusp shape and tooth size.²⁰ Juuri et al suggested that gradual decrease in odontogenic potential of dental lamina elaborates why last developing tooth in a family is most commonly affected by tooth agenesis.²¹

Prevalence of non syndromic hypodontia was found to be 7.37 % in this study on orthodontic patients. The prevalence of hypodontia varies from 0.03% to 10.1% among general populations of different regions of the world.⁴ It is reported to be 4.5–6.3% in Scandinavians, 2.2–2.7% in Arabs, 3.9% in North American population, 6.3% in Australian population and 5.5% in European population.^{22,23} Among orthodontic patients, the prevalence of NSH is relatively higher. Costa et al¹⁶ reported 8.04%, Kim⁵ reported 11.3%, Dastjerdi et al²⁴ reported 9.1% and Endo et al²⁵ found 8.5% prevalence of hypodontia in Brazilian, Korean, Iranian and Japanese orthodontic population respectively.

These statistics display greater figures for non-syndromic hypodontia in comparison to the current study on a sample of Pakistani orthodontic patients.

In this study, 5 (2.04%) patients had single tooth agenesis, 9 (3.75%) patients had two congenitally missing teeth and only 2 (0.81%) patients had more than 6 teeth missing. Moreover, we found that 63 teeth were absent in 18 patients, out of 244 patients, and most commonly tooth affected was maxillary lateral incisors (28.6%) followed by mandibular second premolar (15.9%) and lateral incisor (12.7%). This result is coinciding with Dastjerdi who reported that out of 197 missing teeth in 160 patients, the most common were upper lateral incisors (35.6%), second premolars (13.0%), and lower lateral incisors (9.6%), followed by lower second premolars (8.2%).²⁴ Endo et al. concluded that most commonly absent teeth were maxillary and mandibular lateral incisors.²⁶

Results of this study are contrary to Kim who reported that frequently absent teeth were lower second premolar (44.2%), lateral incisor (36.6%) and upper second premolar (34%).⁵ Costa et al reported in their study that 45 teeth were congenitally missing in 28 subjects. Thirteen (3.75%) subjects had missing premolar, while 13 subjects (3.75%) had missing maxillary lateral incisor.¹⁶ Higashihori et al. reported that mandibular second premolar was commonly affected by hypodontia (25.9%), followed by mandibular lateral incisor (19.4%) and maxillary lateral incisor (17.1%).²⁰

In this study, maxillary arch (52.4%) was more frequently affected by non-syndromic hypodontia and the difference between both jaws was found to be statistically significant. This result is coincident with Dastjerdi et al who also found hypodontia to be more prevalent in upper arch (71%) than in lower arch (29%).²⁴ On the contrary, Kim found that prevalence of hypodontia in lower arch (57.54%) to be higher than in the upper (42.45%).⁵ Shin et al found no significant differences in the prevalence of agenesis of teeth between both jaws.²⁷ Costa et al also found no significant association according to the dental arch.¹⁶ Firas et al noticed that all missing teeth in their sample were maxillary teeth, equally distributed on the right and left sides.²⁸

This retrospective case-series found that the difference of non-syndromic hypodontia among both genders was statistically insignificant, however, it was more prevalent in males. Similarly Kim⁵ and Dastjerdi et al²⁴ also found no statistically significant difference between genders. Endo et al found hypodontia in 286 children with no statistically significant gender difference.²⁵ Shin et al also found no significant differences in the prevalence of congenitally missing tooth among males and females.²⁷

Current study showed that the upper left quadrant (28.6%) was more frequently affected, with statistically significant difference for right and left quadrants. Furthermore, this study concluded that the difference of hypodontia among skeletal malocclusion patterns was statistically significant and more prevalent in Class III malocclusion. However, due to its smaller sample size, the results of Class III malocclusion are less reliable, as compared to a larger group of Class I malocclusion (11.57%). Dermaut et al observed that skeletal class I was affected mostly among hypodontia group, as compared to the unaffected group.²² According to Shin et al there was no significant differences in the prevalence of unilateral, bilateral, or overall congenitally missing teeth between the skeletal malocclusion groups.²⁷ Chan et al found that there was no significant difference in hypodontia among the sagittal skeletal types of ethnic Chinese orthodontic patients.²⁹

The present study showed that hypodontia was significantly associated with skeletal malocclusion, emphasizing their parallel genetic origin. Therefore, it is essential to highlight the need for genetic studies to be carried out in patients with non-syndromic hypodontia and skeletal malocclusion, to further probe the association between them. This retrospective case-series was the first of its kind to address a very pertinent question regarding the association between non-syndromic hypodontia and skeletal malocclusion in a sample of Pakistani population. This study had a

limitation of small sample size, however, it emphasizes a very important domain in orthodontics.

CONCLUSION

This study concluded that the most commonly affected tooth by hypodontia was maxillary lateral incisor followed by mandibular second premolar and lateral incisor. Maxillary arch was more commonly affected by hypodontia, specifically the upper left quadrant. Skeletal class I & III presented with non-syndromic hypodontia most frequently. The difference of non-syndromic hypodontia among genders was statistically insignificant, while it was statistically significant for arches, quadrants and skeletal malocclusion. Further prospective studies on wider samples of Pakistani population from different regions of the country would yield more meaningful results.

REFERENCES

- Batool A, Syed H, Association between hypodontia and angles malocclusion. *J Pak Med Assoc* October 2016;66(10):27-29.
- Gupta SP, Rauniyar S. Prevalence and Distribution of Dental Anomalies among Orthodontic Patients of Kathmandu, Nepal. *J Orthod Nepal*, Vol. 9 No. 2, July-December 2019;9(2):23-28.
- Chaturvedi, M, Thakkar J, Thaddanee R. Nonsyndromic oligodontia: A rare case report. *J Med Patil Uni* May-June 2015;8(3):337.
- Soni HK, Joshi M, Desai H, Vasavada M. An orthopantomographic study of prevalence of hypodontia and hyperdontia in permanent dentition in Vadodara, Gujarat. *Indian J Dent Res* 2018;29:529-33.
- Kim Young Ho. Investigation of Hypodontia as Clinically Related Dental Anomaly: Prevalence and Characteristics, ISRN Dent 2011;1-6.
- Rakhsan V. Congenitally missing teeth (hypodontia): A review of the literature concerning the etiology, prevalence, risk factors, patterns and treatment. *Dent Res J* 2015;12(1):1-13.
- Crossan E, Connell A. Parental perception on oral health-related quality of life and dental features of ectodermal dysplasia and isolated hypodontia in children *BMC Oral Health* 2021;21:510.
- Bilgin N, Kaya B. Etiology and treatment alternatives in tooth agenesis: a comprehensive review. *Stomatological Dis Sci* 2018;2:1-9.
- Fontoura CSG, Miller SF, Wehby GJ, Amend BA. Candidate gene analysis of skeletal variation in malocclusion. *J Dent Res* 2015;94(7):913-920.
- Mokhtar KI, BakarNA, tahir AH. Genetics of malocclusion: A Review. *Int. J Orofacial Health Sci.* 2020;1(1):10.
- Gershater E, Li C, Ha P, Chung C. Genes and pathways associated with skeletal sagittal malocclusion: A systematic review. *Int J Mol Sci* 2021;22:1-17.
- Al-Ani AH, Antoun JS, Thomson WM, Merriman T. Hypodontia: An Update on Its Etiology, Classification, and Clinical Management. *BioMed Res Int.* 2017;1-9.
- Fournier BP, Bruneau MH, Toupenay S. Patterns of Dental Agenesis Highlight the Nature of the Causative Mutated Genes. *J Dent Res.* 2018;97(12):1306-1316.
- Aslam K, Jabeen S, Jafri S, Saeed A, Anjum I. The Molecular Genetics of selective tooth agenesis. *J Pak Med Assoc.* 2020;70(11):1-5.
- Ritwik P, Patterson K. Diagnosis of Tooth Agenesis in Childhood and Risk for Neoplasms in Adulthood. *J Ochsner* 2018;18:345-350.
- Costa AMG, Trevisan M, Matsumoto MA. Association between Tooth Agenesis and Skeletal Malocclusions. *J Oral Maxillofac Res* 2017;8(2):1-7.
- Fauzi NH, Ardini YD, Zainuddin Z, Lestari W. A review on non-syndromic tooth agenesis associated with PAX9 mutations. *Jpn Dent Sci Rev.* Feb 2018;54(1):30-36.
- Al-Jabaa AH and Aldrees AM. ANB, Wits and Molar Relationship, Do they correlate in Orthodontic Patients? *Dentistry* 2014;4(6):1-5.
- Mohamed NF, Jayaraj G, Babu Y. Tooth agenesis- A Review. *J Eurp Mol Clin Med* 2020;7(1):3224-3238.
- Higashihori N, Takada Ji, Katayanagi M, et al. Frequency of missing teeth and reduction of mesiodistal tooth width in Japanese patients with tooth agenesis. *Prog Orthod* 2018;19:30.
- Juuri E, Balic A. The biology underlying abnormalities of tooth number in humans. *J Dent Res.* 2017;96(11):1248-56.
- Taju W, Sherriff M, Bister D. Association between severity of hypodontia and cephalometric skeletal patterns: a retrospective study *Europ J Orthod*, 2018; 200-205.
- Tangade SP, Ravishankar TL, Batra M, Shah AF. Familial Hypodontia: A Case Series. *Kathmandu Univ Med J* 2015;50(2):167-9.
- Dastjerdi EV, Farahani AB, Mahdian M. Non-syndromic hypodontia in an Iranian orthodontic population. *J Oral Sci* 2010;52(3):455-461.
- Endo T, Ozoe R, Kubota M, Akiyama M, Shimoooka S. A survey of hypodontia in Japanese orthodontic patients. *Am J Orthod Dentofac Orthop.* 2006;129(1):29-35.
- Endo T, Yoshino S, Ozoe R, Kojima K, Shimoooka S. Association of advanced hypodontia and craniofacial morphology in Japanese orthodontic patients. *Odontology.* 2004;92(1):48-53.
- Shin O, Hirakata C, Endo T. Prevalence and patterns of tooth agenesis among malocclusion classes in a Japanese orthodontic population. *J Oral Sci* 2019;1-4.
- Firas A, Khraisat A. Hypodontia: prevalence and pattern amongst the living Druze population - a Near Eastern genetic isolate. *Homo.* Jun 2014;65(3):201-13.
- Chan GX, Tan EL, Chew MT, Wong HC. Prevalence of Class I, II and III skeletal relationships and its association with dental anomalies in an ethnic Chinese orthodontic population. *Proceedings of Singapore healthcare.* 2021;1-5.