Original Article

Is Third-Molar Agenesis Related to the Incidence of Other Missing Teeth?

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ABSTRACT

Objective: The aim of this study was to investigate whether third-molar agenesis is related to agenesis of other missing teeth (incisor-premolar hypodontia [IPH]).

Materials and Method: A sample of 94 Turkish patients with agenesis of upper lateral incisors and/or second premolars was selected from 2357 records. Another sample of 94 patients without agenesis (excluding third molars) was drawn from the same set of records and used as a control group. An orthopantomograph of each patient was used to determine the presence or absence of teeth. Differences in the frequency of third-molar agenesis between sexes and between the groups were assessed by chi-square test.

Results: No difference in the prevalence of third-molar agenesis between the groups was shown (p=0.30). The incidence of IPH was found to be significantly different between genders (p=0.00), whereas no significant difference in the incidence of third-molar agenesis was found between sexes (p=0.07).

Conclusion: The subjects with IPH were not found to be more prone to third-molar agenesis than subjects without any tooth agenesis. Consequently, the results of this study did not reveal a relationship between IPH and third-molar agenesis. Moreover, in contrast to typical tooth agenesis, no difference was found in the prevalence of third-molar agenesis between the sexes. (*Turkish J Orthod*. 2014;27:143–147)

KEY WORDS: Incisor-premolar hypodontia, Third-molar agenesis

INTRODUCTION

Dental agenesis or hypodontia is the most common morphologic anomaly among all populations and has been increasing in recent decades.[1–3] The incidence of agenesis has been reported to vary from 2.6% to 11.3%, depending upon demographic and geographic profiles.[4] The prevalence rates of this situation in both dentitions are significantly higher in females than in males (3:2, respectively).[1,4,5]

Although the etiology of dental agenesis is not clearly understood,[1,2] studies show that the problem is multifactorial. Causes include environmental factors like infection,[6] trauma,[7] chemical substances or drugs,[8] radiation therapy,[9] and disturbances in jaw innervation,[10] though the cause is genetic in most cases.[11] The best supported theory suggests a polygenic mode of inheritance in which epistatic genes and environmental factors exert some influence on the phenotypic expression of the genes involved.[12]

In whites, approximately 80% of tooth agenesis cases involve only 1 or 2 teeth.[4] Because the second premolars and the upper lateral incisors are the teeth most often missing, this condition has been called *incisor-premolar hypodontia* (IPH).[13] *Third-molar agenesis*, another type of hypodontia, has a prevalence of 9%–30%[11] and was found in 23.8% of the East Anatolian population.[14]

Previous studies have shown that third-molar agenesis is associated with the incidence of other missing teeth; presumably, it is not an isolated anomaly.[15,16] It has also been claimed that 75% of agenesis of any tooth is related to agenesis of the third molar.[15]

The aim of this study was to investigate whether third-molar agenesis is related to agenesis of other missing teeth (IPH). To this end, the prevalence of

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To cite this article: Altan AB, Bicakci AA. Is third-molar agenesis related with the incidence of other missing teeth? *Turkish J Orthod*. 2014;27:143–147 (DOI: http://dx.doi.org/10. 13076/TJO-D-15-00005)

Date Submitted: January 2014. Date Accepted: March 2015.

Table 1. Missing third molars in the control group

	Upper Right (%)	Upper Left (%)	Lower Right (%)	Lower Left (%)	Frequency (%)
One third molar	7 (3.5)	4 (2.0)	6 (3.0)	11 (5.5)	28 (14.0)
Two third molar	16 (8.0)	17 (8.5)	12 (6.0)	13 (6.5)	29 (14.5)
Three third molar	1 (0.5)	2 (1.0)	2 (1.0)	1 (0.5)	2 (1.0)
All third molars	15 (7.5)	15 (7.5)	15 (7.5)	15 (7.5)	15 (7.5)
	39 (19.5)	38 (19.0)	35 (17.5)	40 (20)	

third-molar agenesis in subjects with IPH was compared with its prevalence in subjects without agenesis of any tooth. Secondly, the incidences of the anomalies in females and males were compared to determine the vulnerability of the sexes to the different types of tooth agenesis.

MATERIALS AND METHOD

A sample of 94 patients (23 male, 71 female) with agenesis of the upper lateral incisors (48) and/or the second premolars (46) was selected from 2357 records of Cumhuriyet University, Faculty of Dentistry, Department of Orthodontics. The samples were selected according to the following criteria: (1) agenesis of lateral incisors and/or premolars (4 teeth at most); (2) at least 14 years old, to exclude any case of late mineralization[15] (if the first panoramic radiograph was taken when the subject was under 14 years old and another radiograph was taken after age 14, then the subject was included); and (3) no history of tooth loss due to trauma, caries, periodontal disease, or orthodontic extraction.

Another sample of 94 patients (23 male, 71 female) without IPH was selected from the same set of records and used as a control group. Additionally, 106 subjects (77 male, 29 female) were added to the control group in order to (1) enhance statistical reliability and (2) homogenize the gender make-up of the group to evaluate whether third-molar agenesis occurs more frequently in females, as is the case for IPH.

The absence of teeth was investigated on panoramic radiographs of each patient. The data were analyzed with a chi-square test at a significance level of 0.05 using SPSS software (version 16.0 for Windows).

RESULTS

Of the 2357 subjects in the archive, 94 met the inclusion criteria for the IPH group. Accordingly, the incidence of IPH was 4% in the orthodontic patient population that was referred to Cumhuriyet University.

The incidence of third-molar agenesis in the control group was found to be 37%. Table 1 represents the percentage distributions of third-molar agenesis for upper and lower jaws. In the control group, agenesis was found most frequently in 2 third molars, followed by 1, 4, and 3 third molars (Table 1). No difference was found in the prevalence of third-molar agenesis between the IPH and control groups (p=0.30, Table 2).

The intra-group comparisons of the prevalences of agenesis in regard to sex revealed that the prevalence of IPH was significantly different between sexes (p=0.00), whereas no significant difference was found in the prevalence of third-molar agenesis between the sexes (p=0.07, Table 3) in the control group.

DISCUSSION

This study compared the prevalence of third-molar agenesis in subjects with and in those without IPH to

Table 2. Incidence of third molar agenesis (TMA) in groups (chi-square test, $p \leq 0.05$)[a]

		Gender		TMA					
Groups		**Male**	**Female**	**UR**	**UL**	**LR**	**LL**	**TMA Incidence**	
Incisor-premolar hypodontia	Incisor	10	38	12	11	11	13	39	41.5%
	Premolar	11	32	14	12	8	8		
Control		23	71	25	22	23	24	46	48.9%
Significance	Chi-square			0.027	0.029	0.491	0.263	1.052	
	p			0.870 NS	0.864 NS	0.484 NS	0.608 NS	0.305 NS	

[a] UR indicates upper right; UL, upper left; LR, lower right; UR, upper right; and NS, not significant.

Table 3. Intragroup comparisons according to gender (chi-square test, $p<0.05$)

	Gender				Significance	
Groups	**Male (%)**		**Female (%)**		**Chi-square**	***p***
Incisor-premolar hypodontia	23	(24.5)	71	(75.5)	24.511	0.000***
Control	31	(31.0)	43	(43.0)	3.089	0.079 NS

*** $p=0.000$; NS indicates not significant.

determine whether third-molar agenesis is related to agenesis of any other tooth. Additionally, to determine whether a gender tendency exists in the groups, the incidences of the different types of hypodontia (IPH and third-molar) in females and males were compared.

The archive searched for this study consisted of 2357 patients of the Department of Orthodontics of Cumhuriyet University, and 94 of these met the inclusion criteria for the IPH group, revealing an incidence of 4%. Because the subjects in this study were orthodontic patients, this percentage might not be representative of the general population. In fact, the prevalence of hypodontia has been found different in several studies.[3,4] Racial differences and sampling variation (i.e., sample size, local factors, and preselection of the individuals) might contribute to these differences among studies.

To test the first hypothesis of this study, the first part of the control group was composed of 94 subjects without IPH. The subjects were chosen randomly regarding the gender distribution in the IPH group (71 female, 23 male). Afterwards, new subjects were added to the control group (29 female, 77 male) to homogenize it in order to test the second hypothesis regarding gender distribution. The incidence of third-molar agenesis in this group was found to be 37%, but this percentage might not be representative of the general population. In fact, the prevalence of this anomaly was previously reported as 9%–30%.[11] In the control group, no statistically significant difference was observed in the occurrence of third-molar agenesis between genders. This finding is compatible with the findings of Thomsen[17]; however, Garn and Lewis[15] observed this anomaly more in females.

Various patterns of third-molar agenesis have been reported in several studies.[18–20] In all of these studies, the least observed agenesis type was either 3 or 4 third molars. When we consider the increased number of missing teeth in severe hypodontia, the pattern of third-molar agenesis may gain importance in distinguishing types of hypodontia. In this study, the most observed type of third-molar agenesis was the agenesis of 2 teeth followed by 4 teeth.

The various types of agenesis differ in clinical manifestation and genetic basis. The mild form of agenesis, nonsyndromic hypodontia, exhibits a wide phenotypic heterogeneity and is classified as a sporadic or familial form,[21] whereas the severe form is known as a syndromic condition. The nonsyndromic form of agenesis primarily affects the lateral incisors and the second premolars (IPH), whereas the syndromic form can affect the entire dentition, including the third molars. When more than 6 teeth are missing, excluding third molars, the condition is called severe hypodontia or oligodontia; it has an estimated prevalence of 0.25% in the general population.[22] In previous studies, a positive correlation was found between third-molar agenesis and that of any other tooth.[15,23] It has been claimed that subjects with agenesis of 1 or 3 third molars are 13 times more likely to have agenesis of other teeth than subjects without third-molar agenesis. It has also been found that 75% of agenesis of any tooth is related to third-molar agenesis. Conversely, the present study revealed no relationship between third-molar agenesis and that of any other tooth. Similarly, in a study by Thomsen[17], the population of Tristan da Cunha was investigated for missing teeth, and it was concluded that 1 group of teeth could be missing irrespective of the presence or absence of any other group of teeth. Moreover, the authors reported that in 13 of the 18 individuals in whom third molars were missing (74%), no other class of teeth was missing. These incompatible results may be due to differences in the methodologies of the studies. Sample selection and grouping may reveal different results, and these techniques were in fact undefined in the aforementioned studies.[15,23]

As demonstrated by Horowitz[24] and Silverman and Ackerman,[25] the prevalence of any type of hypodontia and the number of missing teeth per child are higher in orthodontic patients than in the general population.[26] Consequently, even though severe hypodontia is a rare condition, there is a

greater probability of choosing a subject with this condition from an orthodontic archive. Considering the increased possibility of missing third molars in severe hypodontia, researchers should exclude such patients from study groups. To ensure that the present study assessed only nonsyndromic cases, we included only subjects with lateral incisor or second premolar agenesis, at most 4 teeth. However, the subjects in the studies described above[15,23] were not classified according to the severity of agenesis. The incompatibility between the results of those studies and the present study may be attributed to this difference.

The literature reveals significantly higher prevalence rates of IPH (nonsyndromic agenesis) in females than in males (3:2, respectively),[1,4,5] whereas gender-specific vulnerability to third-molar agenesis is debatable. Thomsen[17] reported no statistically significant difference in the occurrence of missing teeth between genders, whereas Garn and Lewis[15] observed this anomaly more in females. In the present study, a significant gender tendency was observed for IPH (75.5% female, 24.5% male), whereas third-molar agenesis was found to be unrelated to gender (43% female, 31% male). This prompts the question: if these two types of agenesis are related, should they not be interosculated?

In literature, nonsyndromic tooth agenesis has been associated with mutations in MSX1 and PAX9.[27–30] MSX1 mutations were found to predominantly affect agenesis of the second premolars and the third molars,[27,28] whereas PAX9 mutations were found to be responsible for agenesis of maxillary molars and mandibular third molars.[31] Conversely, Scarel *et al*.[32] and Frazier-Bowers *et al*.[33] reported that mutations in MSX1 and PAX9 were detected only in some affected individuals, even though these are the strongest candidate genes for specific forms of tooth agenesis. According to the authors, the observed variations in the type of tooth agenesis may depend on the fact that other mutated gene products, acting in the same signalling pathways as MSX1 and PAX9, may influence the pattern of agenesis.[21] Similarly, Lidral and Reising[28] showed that MSX1 mutations result in a specific pattern of inherited tooth agenesis and that these mutations do not cause the more common cases of tooth agenesis, in which only 1 or 2 teeth are missing. Furthermore, Abe *et al*.[31] reported that no statistically significant association existed between agenesis of the third molars and agenesis of the other teeth, including the second premolars. Being in line with the genetic studies above, the results of the present study contrast with the literature showing a significant association of third-molar agenesis with agenesis of second premolars and lateral incisors. In the present study, the subjects with IPH were not found to be more susceptible to third-molar agenesis than the subjects without hypodontia.

Recently, a considerable amount of research has examined the genetic basis of dental agenesis; however, human studies and the success of genetic identification attempts have been limited. Moreover, controversy over the genetic epidemiology of dental agenesis remains. In view of recent research, it would be incorrect to assume that IPH and third-molar agenesis depend on the same, definite gene defect. It is conceivable that human dental agenesis is caused by several independent gene defects or mutations in molecules involving different interacting molecular pathways, acting alone or with other factors, leading to a specific phenotypic pattern.[11] In the absence of clear evidence from genetic studies, it cannot be assumed that third-molar agenesis is associated with the incidence of other missing teeth; that is, it also possible that third-molar agenesis is an isolated anomaly. Further studies examining genes and the possible effects of their mutations may contribute to a better understanding of the molecular pathogenesis of this disorder and complex clinical phenotypes.

CONCLUSION

Taking into account the limitations of this study, 2 conclusions can be drawn:

(1) The subjects with IPH were not more prone to third-molar agenesis than subjects without any tooth agenesis. Consequently, the results of this study did not reveal a relationship between IPH and third-molar agenesis.
(2) In contrast to IPH, third-molar agenesis did not represent a gender tendency.

ACKNOWLEDGEMENT

The authors would like to thank to Dr Tolga Topcuoglu for his contribution.

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