

Congenital Missing Permanent Teeth in Korean Unilateral Cleft Lip and Alveolus and Unilateral Cleft Lip and Palate Patients

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ABSTRACT

Objective: To investigate the differences in the congenital missing teeth pattern in terms of tooth type (permanent maxillary lateral incisor [MLI] and maxillary second premolar [MSP]) and sidedness (cleft vs noncleft) between boys and girls in Korean unilateral cleft lip and alveolus (UCLA) and unilateral cleft lip and palate (UCLP) patients.

Materials and Methods: This study used the charts, models, radiographs, and intraoral photographs of 90 UCLA patients and 204 UCLP patients (ages 6 to 13 years). Binomial test, chi-square test, Fisher exact test, maximum likelihood analysis of variance, and the odds ratio were performed.

Results: According to the relationship between the congenital missing teeth pattern and the cleft type, the UCLP patients had 2.98 times more missing MLIs and 1.80 times more missing MSPs than did the UCLA patients. The MLI was congenitally missing more in boys than in girls, but the MSP showed the opposite tendency. Boys had a higher frequency of congenital missing MLIs and MSPs on the cleft side than did girls. However, on the noncleft side and both sides, girls had a higher frequency of congenital missing MLIs and MSPs than did boys. Results showed a gender-dominant pattern of congenital missing MLIs and MSPs.

Conclusion: These results suggest that gender and cleft type might affect the congenital missing teeth pattern in terms of tooth type and sidedness.

KEY WORDS: Congenital missing; Maxillary lateral incisor; Maxillary second premolar

INTRODUCTION

Tooth agenesis is an intriguing phenomenon because it is frequently associated with other dental anomalies such as structural variations and malformations of other teeth, late eruption, transposition, and crowding.¹⁻³ The prevalence of congenitally missing teeth in the general population has been reported within a range of 0.027%⁴ to 10.1%,⁵ which varies greatly according to geographic location and race.⁶⁻¹⁰ In the

general population, the mandibular second premolar is the most frequently missing tooth, followed by the permanent maxillary lateral incisor (MLI) and maxillary second premolar (MSP).¹¹ In addition, there is a higher frequency of congenital missing teeth in girls than in boys.^{11,12}

When compared with the normal population, cleft patients have a markedly higher frequency of congenitally missing permanent teeth.^{9,13-15} The most frequently missing teeth in cleft patients are the MLIs in the cleft region and the MSPs outside the cleft region.^{9,16-18} According to Olin,⁹ the incidence of congenitally missing premolars was 24% in cleft patients, and the most frequently missing tooth was the MSP, followed by the mandibular second premolar. This is the opposite result when compared with studies of noncleft normal children, where the mandibular second premolar is the most frequently missing tooth.^{6,7,11}

Even though there is no clear difference in frequency of congenital missing teeth between the cleft and noncleft sides of the mandible, congenital missing

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teeth occurred on the cleft side more than three times as often compared with the noncleft side of the maxilla.^{19,20} These findings could be related to the development of the alveolar process in the cleft region determining the number, size, and eruption of the teeth,^{21,22} and the degree and frequency of tooth anomalies seems to be related to the severity of the cleft or cleft type.²³

Although there have been numerous studies on dental anomalies in cleft patients, almost all have used different types of clefts in their study samples; therefore, knowledge about a specific pattern for each cleft type is difficult to ascertain.²⁴⁻²⁷ Because of small sample sizes in previous studies,²⁴⁻²⁷ statistically significant differences could not be obtained. Moreover, there has been no consideration of the developmental etiology of the cleft. The cause and time of formation of clefts vary; cleft lip and alveolus (CLA) develops during the 4th to the 7th week of gestation, whereas cleft palate (CP) develops during the 7th to the 12th week of gestation. Therefore, a developmental classification between CLA and CLP is needed for epidemiological studies on cleft patients.²³

Because there was a dominant male tendency in cleft lip and palate (CLP) patients,²³ it is necessary to compare the frequency of congenital missing teeth between male and female cleft patients.

Therefore, the purpose of this study was to investigate the differences in the congenital missing teeth pattern in terms of tooth type (MLI and MSP) and sidedness (cleft vs noncleft side) between boys and girls in Korean unilateral CLA (UCLA) and unilateral CLP (UCLP) patients.

MATERIALS AND METHODS

A total of 690 Korean children with clefts visited the Department of Orthodontics at Seoul National University Dental Hospital from January, 1999, to December, 2004. From this group, 90 patients with UCLA and 204 patients with UCLP were selected for this study.

The distribution of congenital missing teeth in the maxilla was investigated by using the patients' orthodontic and cleft charts, diagnostic models, orthopantomograms, maxillary occlusal films, periapical films, and intraoral photographs. None of the patients had other known syndromes.

The mean age of the patients was 10.05 years (range 6 to 13 years). The calcification of the MLI tooth germ is initiated at 10 to 12 months after birth, and completion of the crown calcification of the MLI occurs 4 to 5 years after birth. However, the mean age for initial crown calcification of the MSP is 3 years old, and the mean completion age is 6.2 years old. Therefore, at the age of 6 years (the age of the youngest

TABLE 1. Distribution of UCLA and UCLP Patients by Gender^a

Gender*	UCLA	UCLP**	Total
Boys ^b	53	146	199
Girls	37	58	95
Total	90	204	294

^a UCLA indicates unilateral cleft lip and alveolus; UCLP, unilateral cleft lip and palate.

^b Odds ratio of UCLP over UCLA in boys was 1.76 (95% confidence interval: 1.046 ~ 2.951).

* Chi-square test for analysis of UCLA and UCLP according to gender; $\chi^2 = 4.591$; $P = .032$ ($P < .05$).

** Binomial test for gender analysis ($P < .001$).

patient in our study), it is usually possible to determine the presence or absence of the MLI and MSP with radiographs. Our patients' population was racially and ethnically similar.

The following established criteria were used to determine the congenital missing MLIs.²⁸ This study considered the MLI as a single tooth in the vicinity of the cleft on the mesial or distal side. Any morphology was accepted. These criteria were chosen because it was assumed that the tooth bud of the MLI can develop either at the mesial or distal side of the cleft. Furthermore, the tooth on the cleft side is almost certain to be the MLI, not a supernumerary canine.²⁹ Therefore, if the tooth was present on the cleft side, it was regarded as an MLI.

A single observer analyzed the orthodontic records and then reassessed the data again after 2 weeks. The degree of agreement showed no difference between the two assessments; therefore, the latter assessment was used.

Chi-square and binomial tests were used for analysis of all the patients. Then the patients were defined according to the tooth type (MLI or MSP) missing in the maxilla regardless of the cleft side and according to the congenital missing tooth on the cleft side regardless of the missing tooth position. The association between congenital missing tooth and cleft type was analyzed by Fisher exact test, maximum likelihood analysis of variance, and the odds ratio. Boys and girls were analyzed separately.

RESULTS

UCLP patients showed a statistically significant male-dominant tendency ($P < .001$) (Table 1), but in UCLA patients there was no statistically significant difference between the genders in spite of a male-dominant tendency (Table 1). However, there was statistically significant higher prevalence of boys in the UCLP patients than in the UCLA patients ($P < .05$) (Table 1).

Although the UCLA patients did not show any difference in distribution of the cleft sidedness, the UCLP

TABLE 2. Distribution UCLA and UCLP Patients by Cleft Side^a

Side*	UCLA	UCLP**	Total
Right	38 (42.2%)	85 (41.7%)	123
Left	52 (57.8%)	119 (58.3%)	171
Total	90 (100%)	204 (100%)	294

^a UCLA indicates unilateral cleft lip and alveolus; UCLP, unilateral cleft lip and palate.

* Chi-square test for analysis of UCLA and UCLP according to side, $\chi^2 = 0.008, P = .929$.

** Binomial test for side analysis ($P < .01$).

TABLE 3. Relationship Between Congenital Missing Teeth Pattern and Cleft Type in Boys^a

	Type 1	Type 2	Type 3	Type 4	Total
UCLA	18 (33.96%)	2 (3.77%)	0 (0.00%)	33 (62.26%)	53
UCLP	70 (47.95%)	4 (2.74%)	22 (15.07%)	50 (34.25%)	146
Total	88	6	22	83	199

^a Type 1 indicates congenital missing of the maxillary lateral incisor (MLI); Type 2, congenital missing of the maxillary second premolar (MSP); Type 3, congenital missing of the MLI and MSP; Type 4, presence of the MLI and MSP; UCLA, unilateral cleft lip and alveolus; and UCLP, unilateral cleft lip and palate. Fisher exact test was used to analyze the difference between the congenital missing teeth and the pattern in boys, $P < .001$.

TABLE 4. Distribution of Congenitally Missing Teeth Position in UCLA and UCLP Patients in Girls^a

	Type 1	Type 2	Type 3	Type 4	Total
UCLA	9 (24.32%)	1 (2.70%)	0 (0%)	27 (72.97%)	37
UCLP	27 (46.55%)	3 (5.17%)	7 (12.07%)	21 (36.21%)	58
Total	36	4	7	48	95

^a UCLA indicates unilateral cleft lip and alveolus; UCLP, unilateral cleft lip and palate; Type 1, congenital missing of the maxillary lateral incisor (MLI); Type 2, congenital missing of the maxillary second premolar (MSP); Type 3, congenital missing of the MLI and MSP; and Type 4, presence of the MLI and MSP. Fisher exact test was used to analyze the difference between the congenital missing teeth and the pattern in girls ($P = .002$).

patients showed a significantly higher incidence on the left side than the right side ($P < .01$) (Table 2).

Relationship Between the Congenital Missing Teeth Pattern and the Cleft Type

There were significant differences in the congenital missing teeth pattern according to cleft type in boys ($P < .001$) (Table 3) and in girls ($P < .01$) (Table 4). The UCLP patients had 2.98 times more missing MLIs than did the UCLA patients (Table 5). Similarly, the UCLP patients had 1.80 times more missing MSPs than did the UCLA patients (Table 5). Boys appeared to have 1.26 times more missing MLIs than did girls. To the

TABLE 5. The Odds Ratio of Congenital Missing of the MLI and MSP in UCLP vs UCLA Patients and in Boys vs Girls^a

	Odds Ratio	
	MLI Missing/Present	MSP Missing/Present
UCLP vs UCLA	2.98	1.80
Boys vs girls	1.26	0.82

^a MLI indicates maxillary lateral incisor; MSP, maxillary second premolar; UCLP, unilateral cleft lip and palate; and UCLA, unilateral cleft lip and alveolus.

TABLE 6. Relationship Between Congenital Missing Side and Cleft Type in Boys^a

	Type 1	Type 2	Type 3	Type 4	Total
UCLP	84 (57.53%)	5 (3.42%)	7 (4.79%)	50 (34.25%)	146
UCLA	18 (33.96%)	1 (1.89%)	1 (1.89%)	33 (34.25%)	53
Total	102	6	8	83	199

^a Type 1 indicates missing on cleft side regardless of missing teeth position; Type 2, missing on noncleft side; Type 3, missing on both cleft and noncleft sides; Type 4, presence on both sides; UCLP, unilateral cleft lip and palate; and UCLA, unilateral cleft lip and alveolus. Fisher exact test was used to analyze the difference between the pattern in UCLA and UCLP patients in boys; $P < .005$ ($P = .0046$).

TABLE 7. Relationship Between Congenital Missing Side and Cleft Type in Girls^a

	Type 1	Type 2	Type 3	Type 4	Total
UCLP	25 (43.10%)	5 (8.62%)	7 (12.07%)	21 (36.21%)	58
UCLA	9 (24.32%)	1 (2.70%)	0 (0.00%)	27 (72.97%)	37
Total	34	6	7	48	95

^a Type 1 indicates missing on cleft side regardless of missing teeth position; Type 2, missing on noncleft side; Type 3, missing on both cleft and noncleft sides; Type 4, presence on both sides; UCLP, unilateral cleft lip and palate; and UCLA, unilateral cleft lip and alveolus. Fisher exact test was used to analyze the difference between the pattern in UCLA and UCLP patients in girls; $P = .002$.

contrary, boys had 0.82 times less missing MSPs than did girls (Table 5).

Relationship Between the Congenital Missing Teeth in the Cleft Side and the Cleft Type

There were significant differences in congenital missing teeth regarding sides according to cleft type in boys ($P < .01$) (Table 6) and girls ($P < .01$) (Table 7). The UCLP patients had 3.25 times more congenital missing teeth on the cleft side, 4.65 times more congenital missing teeth on the noncleft side, and 12.94 times more congenital missing teeth on both sides than did UCLA patients (Table 8). Boys appeared to have 1.51 times more missing teeth on the cleft side

TABLE 8. The Odds Ratio of Congenital Missing Teeth and Presence of Teeth on the Cleft Side, Noncleft Side, or Both Sides in UCLP vs UCLA Patients and in Boys vs Girls^a

	Odds Ratio		
	Missing/ Presence on Cleft Side	Missing/ Presence on Noncleft Side	Missing/ Presence on Both Sides
UCLP vs UCLA	3.25	4.65	12.94
Boys vs girls	1.51	0.49	0.53

^a UCLP indicates unilateral cleft lip and palate; UCLA, unilateral cleft lip and alveolus.

than did girls. To the contrary, boys had 0.49 times less missing teeth on the noncleft side and 0.53 times more missing teeth on both sides as compared with girls (Table 8).

DISCUSSION

Cleft lip (CL) and CLP are known to be more common in boys. Cooper et al³⁰ reported the ratio of boys to girls as 1.6:1 for CL and CLP and 1:1.3 for CP. In Korean cleft patients, the ratios of boys to girls is about 2.1:1 for UCLA and 2.75:1 for UCLP²³ or 1.88:1 for UCLA and 2.49:1 for UCLP.³¹ In the present study, the ratios of boys to girls were 1.43:1 for UCLA patients and 2.52:1 for UCLP patients. There was a statistically significant difference of gender distribution between UCLA and UCLP patients. The male-dominant tendency existed in UCLP patients but not in the UCLA patients (Table 1).

In studies on Koreans, prevalence of the left-sided cleft was found to be between 65% and 70%.^{23,32,33} In studies of other races, Fraser³⁴ reported the prevalence of a left-sided cleft to be 66.6%, whereas Wilson³⁵ and Shapira et al³⁶ reported the prevalence to be 60%. The results of the present study showed the prevalence of a left-sided cleft in UCLP patients as 58.3% (Table 2), which was similar to the other Korean studies. However, in the UCLA patients of this study, there was no statistically significant difference in the distribution of the cleft side (Table 2). Baek et al²³ suggested that the incidence of the left-sided cleft increased from CL and CLA to CLP in ascending order, which was similar to the tendency found in this study.

In the normal population, except for third molars, the MLI is the most frequently missing tooth when only one or two teeth are absent, whereas the second premolar is the most frequently missing tooth when more than two teeth are absent.³⁷ In the cleft patients, the MLI is the most frequently missing, the MSP is the second, and the mandibular second premolar follows. The frequency of the congenital missing teeth outside the cleft site, in descending order of magnitude, was

7.5% to 32.3% for the MSP, 3.1% to 10.4% for the MLI on the nonaffected side, and 0.4% to 10.8% for the mandibular second premolar.³⁸ However, frequency of the congenital missing of both teeth is higher than in the normal population: 2.2% for the missing of the MLI and 3.4% to 6.6% for the missing of the second premolar were reported.³⁹

In this study, three UCLA patients and five UCLP patients had unilaterally congenital missing mandibular second premolars, and one UCLP patient showed bilateral absence of the mandibular second premolar. The total percentage of congenital missing mandibular second premolars was 3.9%, which was not higher than that in the normal population (about 4.1% to 7.1%).^{40,41} Therefore, we did not consider the congenital missing teeth in the mandible.

According to the relationship between the congenital missing teeth pattern and the cleft type, there were significant differences in both boys and girls (Tables 3 and 4). The UCLP patients had 2.98 times more missing MLIs and 1.80 times more missing MSPs than did the UCLA patients (Table 5). The patients with severe clefts might have a higher probability of congenital missing teeth, especially in the MLI region because of the proximity of the cleft itself.

The increased incidence of congenital missing MLIs and MSPs in children with severe clefts might suggest that the cleft itself does not cause hypodontia. The absence of an MSP, its remote location from the cleft area, or its delayed development probably has different etiological factors.

Epidemiological studies have proposed single gene models,⁴² multifactorial threshold models, and mixed major gene or multifactorial models to explain cleft inheritance.^{43,44} MSX1 and TGFA have been associated with a related developmental craniofacial defect, CLP,⁴⁵ and tooth agenesis.⁴⁶ Interaction between MSX1 and PAX 9 appears to play a role in tooth agenesis in humans. This suggests that the same etiological factors may be responsible for both the formation of the clefts and the congenital missing teeth in the affected children.⁴⁷

Regardless of the involved position of the teeth, there was a higher frequency of congenital missing teeth on the cleft side than on the noncleft side (Tables 6 and 7). There was a 3.25 times higher incidence of missing teeth on the cleft side, a 4.65 times higher incidence of missing on the noncleft side, and a 12.94 times higher incidence of missing teeth on both sides in UCLP patients than in UCLA patients (Table 8). Congenital missing teeth in UCLA patients were usually localized to the MLI on the cleft side. Also, these results show that the frequency of missing MLIs increases with the severity of the cleft.

In boys, the MLI was congenitally missing more of-

ten than in girls, but the MSP showed an opposite tendency (Table 5). The higher frequency of congenital missing MLIs was similar to that reported by Kim and Baek,³¹ but it was different from previous reports. Ranta³⁸ reported that the congenital missing MLI was more frequent in girls than in boys, but the differences were not statistically significant. However, in the current study, the gender-dominant patterns of the congenital missing MLIs and MSPs were present.

On the cleft side, boys had a higher frequency of congenital missing teeth than did girls. However, on the noncleft side and on both sides, girls had a higher probability of congenital missing teeth than did boys (Table 8). These results show that the etiology of the congenital absence of the MLI and MSP might be different.

These results show that boys had more congenital missing MLIs on the cleft side than did girls, but on the noncleft side, the congenital absence of the MSP was more frequent in girls than in boys. This might be related to gender-specific characteristics. Future studies should focus on genetic studies of UCLA and UCLP boys and girls.

CONCLUSION

- These results suggest that gender might affect congenital missing teeth pattern in terms of tooth type and sidedness in Korean UCLA and UCLP patients.

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