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Characterization of phenotypes and predominant skeletodental patterns in pre-adolescent patients with Pierre–Robin sequence

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Objective: To investigate the phenotypes and predominant skeletodental pattern in pre-adolescent patients with Pierre–Robin sequence (PRS). **Methods:** The samples consisted of 26 Korean pre-adolescent PRS patients (11 boys and 15 girls; mean age at the investigation, 9.20 years) treated at the Department of Orthodontics, Seoul National University Dental Hospital between 1998 and 2019. Dental phenotypes, oral manifestation, cephalometric variables, and associated anomalies were investigated and statistically analyzed. **Results:** Congenitally missing teeth (CMT) were found in 34.6% of the patients (n = 9/26, 20 teeth, 2.22 teeth per patient) with 55.5% (n = 5/9) exhibiting bilaterally symmetric missing pattern. The mandibular incisors were the most common CMT (n = 11/20). Predominant skeletodental patterns included Class II relationship (57.7%), posteriorly positioned maxilla (76.9%) and mandible (92.3%), hyper-divergent pattern (92.3%), high gonial angle (65.4%), small mandibular body length to anterior cranial base ratio (65.4%), linguoversion of the maxillary incisors (76.9%), and linguoversion of the mandibular incisors (80.8%). Incomplete cleft palate (CP) of hard palate with complete CP of soft palate (61.5%) was the most frequently observed, followed by complete CP of hard and soft palate (19.2%) and CP of soft palate (19.2%) ($p < 0.05$). However, CP severity did not show a significant correlation with any cephalometric variables except incisor mandibular plane angle ($p < 0.05$). Five craniofacial and 15 extra-craniofacial anomalies were observed (53.8% patients); this implicated the need of routine screening. **Conclusions:** The results might provide primary data for individualized diagnosis and treatment planning for pre-adolescent PRS patients despite a single institution-based data.
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Key words: Pierre–Robin sequence, Phenotype, Skeletodental pattern

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INTRODUCTION

The main features of Pierre–Robin sequence (PRS) are micrognathia, glossoptosis, respiratory difficulties, and/or cleft palate (CP).[1] Possible etiologies for a micrognathic mandible in these patients include intrauterine compression of the fetal mandible and *de-novo* mutations of GAD1, PVRL1, SOX9 or KCNJ2 gene.[2]

The incidence of PRS is known to be between 1/2,685 and 1/30,000;[3-5] this wide range can be attributed to differences in ethnic background and geographic regions as well as the absence of a consensus regarding uniform diagnostic criteria. Most clinical studies on PRS have usually focused on the management of respiratory probelms,[6-8] size and shape of the mandible,[9,10] and presence of mandibular catch-up growth.[11-15]

Since micrognathia is a key factor in occurrence of PRS, the skeletodental pattern including the position, shape, and size of the maxillomandibular complex and the inclination of the maxillary and mandibular incisors should be considered at the time of diagnosis by orthodontists.

With regard to dental anomalies in PRS patients, several studies have reported a high prevalence of congenitally missing tooth and taurodontism.[16-18] However, the prevalence of other dental anomalies including microdontia, short root, and supernumerary tooth in Korean PRS patients remains to be investigated. Furthermore, to the best of our knowledge, no clinical demographic studies have evaluated the oral manifestations, detailed skeletodental pattern of the maxillomandibular complex, and associated anomalies in Korean pre-adolescent patients with PRS. Therefore, the purpose of this retrospective study was to investigate the dental phenotypes, oral manifestations, predominant skeletodental pattern of the maxillomandibular complex, and associated anomalies in Korean pre-adolescent patients with PRS.

MATERIALS AND METHODS

The study design of this study was a retrospective one. The initial samples were PRS patients who visited the Department of Orthodontics, Seoul National University Dental Hospital (SNUDH), Seoul, Korea. The inclusion criteria were as follows: (1) Korean patients; (2) patients diagnosed with PRS, (3) patients treated by a single orthodontist (BSH); (4) patients treated and/or followed-up between 1998 and 2019, (5) patients whose charts, clinical photographs, cephalometric and panoramic radiographs were available; and (6) patients whose chronological age was between 5 and 12 years at the time of investigation of oral manifestations, dental phenotypes, and skeletodental pattern of the maxillomandibular complex. Patients who were receiving orthodontic or orthopedic treatment at the time of cephalometric analysis and dental phenotype investigation were excluded in order to avoid any influence on the skeletodental pattern of the maxillomandibular complex. This study was reviewed and approved by the Institutional Review Board of the SNUDH (ERI20010).

As a result, the final samples consisted of 26 unrelated Korean pre-adolescent patients with PRS (11 boys and 15 girls). The mean age at the first consultation at the Department of Orthodontics, SNUDH (T0 stage) was 7.63 ± 2.49 years, while that at the time of cephalometric analysis and dental phenotype investigation (T1 stage) was 9.20 ± 1.46 years.

The prevalence of dental phenotype (congenitally missing tooth, microdontia, tooth with short root, tooth with taurodontism, and supernumerary tooth), oral manifestations (severity of CP and degree of overbite), cephalometric variables (sella-nasion-A point angle [SNA], sella-nasion-B point angle [SNB], A point-nasion-B point angle [ANB], sella-nasion to mandibular plane angle [SN-MP], mandibular body length to anterior cranial base ratio {gonion-menton [Go-Me]/sella-nasion [S-N]}, gonial angle, upper incisor to sella-nasion angle [U1-SN], and incisor mandibular plane angle [IMPA]) at the T1 stage were investigated along with associated anomalies. Korean ethnic norms were used to determine the predominant skeletodental pattern of the maxillomandibular complex with reference to the cephalometric analysis chart used in the Department of Orthodontics, SNUDH and the findings of a previous study.[19]

Table 1. Prevalence of dental phenotypes in Korean pre-adolescent patients with Pierre–Robin sequence

Dental phenotype	Number of patients (%) (n = 26)	Number of tooth	Mean number of tooth per patient
Congenitally missing tooth	9 (34.6)	20	2.22
Microdontia	3 (11.5)	5	1.67
Tooth with short root	0 (0)	0	0
Tooth with taurodontism	0 (0)	0	0
Supernumerary tooth	1 (3.8)	1	1

The mean age of patients at the time of dental phenotype investigation (T1 stage) was 9.20 ± 1.46 years.

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Table 2. Summary of the patterns of congenitally missing tooth in Korean pre-adolescent patients with Pierre–Robin sequence

Patient number	Sex	Number of congenitally missing tooth	Location of the congenitally missing tooth			Presence of bilateral and symmetrical missing
			Mandibular incisor	Mandibular premolar	Maxillary premolar	
#4	Male	3	#32,42	#45		Yes
#6	Female	4	#31,32,41,42			Yes
#8	Female	2		#35	#15	
#15	Male	2		#45	#15	
#16	Female	2		#35,45		Yes
#18	Male	1			#15	
#24	Male	2	#32,42			Yes
#25	Male	1			#25	
#26	Male	3	#31,32,42			Yes
Sum	6 boys and 3 girls	20	11	5	4	5

The mean age of patients at the time of dental phenotype investigation (T1 stage) was 9.20 ± 1.46 years.

Descriptive statistics, Man–Whitney *U* test, chi-square goodness of fit test, chi-square independence test, Fisher's exact test, and Spearman's correlation analysis were used for statistical analysis with SPSS software version 12.0 (SPSS Inc., Chicago, IL, USA). A *p*-value of < 0.05 was considered statistically significant.

RESULTS

Dental phenotypes (Tables 1 and 2)

In total, 34.6% of PRS patients exhibited congenitally missing tooth (n = 9/26, 20 teeth, 2.22 teeth per patient). The most common congenitally missing tooth was the mandibular incisors (n = 11/20, 55.0%), followed by the mandibular premolars (n = 5/20, 25.0%), and the maxillary premolars (n = 4/20, 20.0%). However, none of the patient showed congenital missing of the maxillary incisors. In addition, among nine patients who exhibited congenitally missing tooth, seven patients (77.8%) had more than two missing teeth; while five patients (55.5%) showed a bilateral and symmetric missing pattern.

Microdontia was found in 11.5% of PRS patients (n = 3/26, 5 teeth, 1.67 teeth per patient), which was observed at the maxillary lateral incisors. A supernumerary tooth was found only in one PRS patient (n = 1/26, 1 tooth, 1 tooth per patient) at the maxillary incisor area. None of the patients exhibited a tooth with short root or with taurodontism.

Oral manifestations (Table 3)

In terms of CP severity, incomplete CP of hard palate with complete CP of soft palate (-hSh-, 61.5%, n = 16/26) was the most commonly observed, followed by CP of soft palate (-S-, 19.2%, n = 5/26) and complete CP of hard and soft palate (-HSH-, 19.2%, n = 5/26) ($p < 0.05$).

In terms of overbite, the frequency of open bite (3.8%, n = 1/26) was lower than that of normal overbite (61.5%, n = 16/26) and deep bite (34.6%, n = 9/26) ($p < 0.01$).

Table 3. Distribution of cleft palate severity and overbite in Korean pre-adolescent patients with Pierre–Robin sequence (PRS)

Oral manifestations		PRS (n = 26)	*p*-value
CP severity†	-S-	5 (19.2)	0.01*
	-hSh-	16 (61.5)	
	-HSH-	5 (19.2%)	
Overbite‡	Normal overbite	16 (61.5)	0.001**
	Deep bite	9 (34.6)	
	Open bite	1 (3.8)	

Values are presented as number (%).
Deep bite was defined as the full coverage of the maxillary incisor over the mandibular incisor. Open bite was defined as absence of vertical overlap between the maxillary and mandibular incisors.
The mean age of patients at the time of oral manifestation investigation (T1 stage) was 9.20 ± 1.46 years.
CP, cleft palate; -S-, complete CP of soft palate; -hSh-, incomplete CP of hard palate and complete CP of soft palate; -HSH-, complete CP of hard and soft palate.
*$p < 0.05$, **$p < 0.01$.
†Chi-square goodness of fit test was performed.
‡Fisher's exact test was performed.

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Table 4. Predominant type in the skeletodental patterns of the maxillomandibular complex in Korean pre-adolescent patients with Pierre–Robin sequence (PRS)

Skeletodental pattern			Korean norm		PRS (n = 26)		Type	Number (%)	*p*-value
			Mean	SD	Mean	SD			
Sagittal	Maxilla	SNA (°)	81.3	3.4	74.77	4.74	Protrusion (> 84.7)	1 (3.8)	< 0.001***
							Normal (77.9–84.7)	5 (19.2)	
							Retrusion (< 77.9)	20 (76.9)	
	Mandible	SNB (°)	78.9	3.0	69.77	4.53	Protrusion (> 81.9)	0 (0)	< 0.001***
							Normal (75.9–81.9)	2 (7.7)	
							Retrusion (< 75.9)	24 (92.3)	
	Intermaxillary relationship	ANB (°)	2.6	1.6	4.99	2.57	Class I relationship (1.0–4.2)	9 (34.6)	0.007**
							Class II relationship (> 4.2)	15 (57.7)	
							Class III relationship (< 1.0)	2 (7.7)	
Vertical		SN-MP (°)	33.8	4.9	46.89	7.42	Normo-divergent (28.9–38.7)	2 (7.7)	< 0.001***
							Hyper-divergent (> 38.7)	24 (92.3)	
							Hypo-divergent (< 28.9)	0 (0)	
Size and shape of the mandible		Mandibular body length to anterior cranial base ratio (Go-Me/S-N)	1.01	0.06	0.92	0.05	Small ratio (< 0.95)	17 (65.4)	< 0.001***
							Normal ratio (0.95–1.07)	9 (34.6)	
							Large ratio (> 1.07)	0 (0)	
		Gonial angle (°)	123.0	6.0	130.58	7.02	High (> 128.5)	17 (65.4)	0.001**
							Normal (117–128.5)	8 (30.8)	
							Low (< 117)	1 (3.8)	
Dental	Maxillary incisor inclination	U1-SN (°)	106.55	6.13	93.21	9.26	Labioversion (> 112.7)	0 (0)	< 0.001***
							Normal (100.4–112.7)	6 (23.1)	
							Linguoversion (< 100.4)	20 (76.9)	
	Mandibular incisor inclination	IMPA (°)	95.34	5.34	82.44	8.07	Labioversion (> 100.7)	0 (0)	< 0.001***
							Normal (90.0–100.7)	5 (19.2)	
							Linguoversion (< 90.0)	21 (80.8)	

The mean age of patients at the time of cephalometric analysis (T1 stage) was 9.20 ± 1.46 years.
Korean ethnic norms were used to determine the skeletodental pattern of the maxillomandibular complex with reference to the cephalometric analysis chart used in the Department of Orthodontics, Seoul National University Dental Hospital and the findings of a previous study.[19]
Chi-square goodness of fit test was performed.
SD, standard deviation; SNA, sella-nasion-A point angle; SNB, sella-nasion-B point angle; ANB, A point-nasion-B point angle; SN-MP, sella-nasion to mandibular plane angle; Go-Me, gonion-menton; S-N, sella-nasion; U1-SN, upper incisor to sella-nasion angle; IMPA, incisor mandibular plane angle.
**$p < 0.01$, ***$p < 0.001$.

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Table 5. Correlations of skeletodental pattern with mandibular body length (Go-Me) and cleft palate severity in Korean pre-adolescent patients with Pierre–Robin sequence

Cephalometric variable	Mandibular body length		Severity of cleft palate	
	ρ-value†	*p*-value	ρ-value†	*p*-value
SNA	–0.014	0.947	–0.281	0.164
SNB	0.230	0.258	–0.265	0.191
ANB	–0.462	0.018*	–0.099	0.630
SN-MP	–0.504	0.009**	0.223	0.273
Gonial angle	–0.477	0.014*	0.256	0.206
Ramus height	0.612	0.001**	–0.306	0.128
Mandibular body length (Go-Me)	-	-	–0.161	0.431
Mandibular body length to anterior cranial base ratio (Go-Me/S-N)	0.567	0.003**	0.292	0.148
U1-SN	–0.066	0.750	0.074	0.718
IMPA	0.404	0.041*	–0.409	0.038*

The mean age of patients at the time of cephalometric analysis (T1 stage) was 9.20 ± 1.46 years.
Spearman correlation analysis was performed.
*$p < 0.05$, **$p < 0.01$.
†Pearson product-moment correlation coefficient.
See Table 4 for definitions of each landmark or measurement.

The mean values of cephalometric variables (Table 4)

PRS patients had Class II relationship (ANB, 5.0°), posteriorly positioned maxilla (SNA, 74.8°), posteriorly positioned mandible (SNB, 69.8°), hyper-divergent pattern (SN-MP, 46.9°), high gonial angle (130.6°), small mandibular body length to anterior cranial base length ratio (Go-Me/S-N, 0.92), linguoversion of the maxillary incisor (U1-SN, 93.2°), and linguoversion of the mandibular incisor (IMPA, 82.4°).

Predominant skeletodental pattern of the maxillomandibular complex (Table 4)

PRS patients exhibited a higher percentage of the posteriorly positioned maxilla and mandible than normally or forward positioned maxilla and mandible (SNA, 76.9% vs. 19.2%, 3.8%, $p < 0.001$; SNB, 92.3% vs. 7.7%, 0%, $p < 0.001$). Class II relationship was more frequently found than Class I and Class III relationships (ANB, 57.7% vs. 34.6%, 7.7%, $p < 0.01$). A hyperdivergent pattern was more common than normo-divergent and hypo-divergent patterns (SN-MP, 92.3% vs. 7.7%, 0%, $p < 0.001$).

In terms of the shape and size of the mandible, high gonial angle was more frequently found than normal and low gonial angles (65.4% vs. 30.8%, 3.8%, $p < 0.01$) due to clockwise-rotated morphology of the mandible. Small Go-Me/S-N ratio was more prevalent than normal and large Go-Me/S-N ratios (65.4% vs. 34.6%, 0%, $p < 0.001$).

In terms of the inclination of the maxillary and mandibular incisor, linguoversion was more prevalent than normal inclination and labioversion (U1-SN, 76.9% vs. 23.1%, 0%; IMPA, 80.8% vs. 19.2%, 0%; all $p < 0.001$).

Interestingly, none of the patients showed a forward-positioned mandible, a hypo-divergent type, a large Go-Me/S-N ratio, and labioversion of the maxillary and mandibular incisors (Table 4).

Table 6. Number and percentage of Korean pre-adolescent Pierre–Robin sequence patients with and without craniofacial and extra-craniofacial anomalies

Variable	Number (%)	*p*-value
Patients who had craniofacial and extra-craniofacial anomalies	14 (53.8)	0.695
Patients who did not have craniofacial and extra-craniofacial anomalies	12 (46.2)	
Sum	26	

The chi-square goodness of fit test was performed.

Correlations between mandibular body length (Go-Me) and skeletodental pattern and between CP severity and skeletodental pattern (Table 5)

A short mandibular body length (Go-Me) was significantly correlated with Class II relationship (ANB, $p < 0.05$), high gonial angle ($p < 0.05$), linguoversion of the mandibular incisor (IMPA, $p < 0.05$), small Go-Me/S-N ratio ($p < 0.01$), and hyper-divergent pattern (SN-MP, $p < 0.01$) (Table 5). However, CP severity did not show a significant correlation with any cephalometric variables

Table 7. Summary of the craniofacial and extra-craniofacial anomalies observed in Korean pre-adolescent patients with Pierre–Robin sequence

Associated anomaly	Patient	Sex	Number of anomalies	Extra-craniofacial anomalies	Craniofacial anomalies
Absent	3	Female	0		
	5	Male	0		
	6	Female	0		
	7	Male	0		
	12	Male	0		
	13	Female	0		
	17	Female	0		
	19	Female	0		
	20	Female	0		
	21	Female	0		
	22	Female	0		
	23	Female	0		
Present	1	Female	1	Velocardiofacial syndrome	
	2	Female	1	Neurofibromatosis (upper trunk)	
	8	Female	1	Acampomelic campomelic dysplasia	
	9	Female	1		Tongue tie
	10	Male	1		Tongue tie
	15	Male	1	Gordon syndrome	
	16	Female	1	Pulmonary veno-occlusive disease	
	11	Female	2		Tongue-tie, HFM with Preauricular skin tag
	14	Male	2	Cataract	Strawberry hemangioma in the scalp
	18	Male	2	Retinal detachment	Subglottic stenosis
	24	Male	2	Coartation of aorta, clinodactyly	
	25	Male	2	Congenital clubfoot, congenital clasped thumb	
	4	Male	3	Congenital syndactyly, cryptorchidism,	Nager syndrome
	26	Male	3	Scoliosis, hemivertebrae	HFM with Preauricular skin tag
14 association and 12 no association	Sum	11 boys and 15 girls	7 one anomaly, 5 two anomalies and 2 three anomalies	11 patients with 15 kinds	6 patients with 5 kinds

HFM, hemifacial microsomia.

except IMPA ($p < 0.05$).

Associated anomalies (Tables 6 and 7)

Craniofacial and/or extra-craniofacial anomalies were observed in 53.8% of PRS patients. However, there was no difference between the percentages of patients with anomalies and that of patients without anomalies (53.8% vs. 46.2%, $p > 0.05$).

In terms of the number of associated anomalies, one anomaly was most common (n = 7/14, 50.0%), followed by two anomalies (n = 5/14, 35.7%) and three anomalies (n = 2/14, 14.3%). Five kinds of craniofacial anomalies were found in 42.9% of patients (n = 6/14; Nager syndrome, tongue tie, hemifacial microsomia, strawberry hemangioma, and subglottic stenosis). Meanwhile, 15 kinds of extra-craniofacial anomalies were found in

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78.6% of patients (n = 11/14; cardiovascular anomaly [n = 3], digit anomaly [n = 3], eye anomaly [n = 2], long bone anomaly [n = 1], skin anomaly [n = 1], genital anomaly [n = 1], kidney anomalies [n = 1], and vertebral anomaly [n = 1]). Three patients (21.4%) had both craniofacial and extra-craniofacial anomalies.

DISCUSSION

Dental phenotypes

In the present study, congenitally missing tooth was observed in 34.6% of PRS patients (Table 1), which was relatively lower than Antonarakis et al.[16] (42%) and de Smalen et al.[17] (47.8%) but higher than Mateo-Castillo et al.[18] (22.7%).

de Smalen et al.[17] reported that the most frequently missing teeth were the mandibular second premolars and maxillary lateral incisors. However, the present study showed different results. First, the most prevalent congenitally missing tooth was the mandibular incisor, followed by the mandibular premolar and maxillary premolar (55.0%, 25.0%, 20.0%; Table 2). Second, none of the patients showed congenital missing of the maxillary incisor (Table 2). Since the mean age at the time of dental phenotype investigation (T1 stage) was 9.20 years in the present study, congenital missing of the maxillary incisor and any other teeth could be properly determined. Therefore, different results might could be attributed to differences in the ethnic background and geographic regions as well as the age of patients between de Smalen et al.' study[17] and this study (more than 7 years vs. 9.20 years).

Antonarakis et al.,[16] in their systematic review and meta-analysis of nonsyndromic PRS, reported that the mandibular second premolars (#35 and #45, 26%) were the most common teeth to show a bilateral and symmetric pattern of congenital missing, followed by the maxillary second premolars (#15 and #25, 14%). However, in the present study, the mandibular incisor was the most common tooth showing a bilateral and symmetric pattern of congenitally missing, followed by the mandibular second premolar (80%, n = 4/5; 20%, n = 1/5; Table 2). The reason might be due to differences in the ethnic background and geographic regions.

Mateo-Castillo et al.,[18] in their retrospective study, reported that taurodontism was the most prevalent dental phenotype (92.7% in nonsyndromic PRS patients). However, in the present study, taurodontism was not found (Table 1).

Oral manifestations (Table 3)

In the present study, the distribution of CP severity significantly differed in PRS patients (complete CP of soft palate [-S-, 19.2%]; incomplete CP of hard palate with complete CP of soft palate [-hSh-, 61.5%], and complete CP of hard and soft palate [-HSH-, 19.2%], $p < 0.05$, Table 3). Since micrognathia leads to glossoptosis and/or failure of the palatal fusion process, the sagittal length and transverse width of CP might be indirectly related with the size of the mandible.[6,13] Further study is necessary to investigate this topic.

In the present study, PRS patients exhibited normal overbite and deep bite (61.5% and 34.6%, Table 3) despite hyper-divergent pattern and high gonial angle (mean SN-MP, 46.9°; mean gonial angle, 130.6°; Table 4). These might be related with linguoversion of the maxillary and mandibular incisors (mean U1-SN, 93.2°; mean IMPA, 82.4°; Table 4).

Cephalometric analysis of the skeletodental pattern (Table 4)

In the present study, PRS patients exhibited Class II relationship, posteriorly positioned maxilla and mandible, hyper-divergent pattern, high gonial angle, and linguoversion of the maxillary and mandibular incisors (mean values: ANB, 5.0°; SNA, 74.8°; SNB, 69.8°; SN-MP, 46.9°; gonial angle, 130.6°; U1-SN, 93.2°; IMPA, 82.4°; Table 4). These findings were similar to the results from previous studies.[9,12,14,20]

The finding that PRS patients had small mandibular body length to anterior cranial base length ratio (Go-Me/S-N, 0.92; Table 4) indicates that PRS patients have a short mandibular body length despite relatively normal length of the anterior cranial base.

Predominant skeletodental pattern of the maxillomandibular complex

In terms of the position of the maxilla and mandible, the posteriorly positioned maxilla and mandible was a predominant phenotype in the present study (SNA, 76.9%; SNB, 92.3%; all $p < 0.001$, Table 4). This might be due to the combined effects of post-surgical scar tissue in the palate on maxillary growth and micrognathia of the mandible itself. Furthermore, Class II relationship was predominant (ANB, 57.7%, $p < 0.01$; Table 4) because the mandible is more posteriorly positioned than the maxilla. Hyperdivergent pattern was predominant (SN-MP, 92.3%, $p < 0.001$; Table 4) due to the vertical growth pattern of the maxillomandibular complex.

In terms of the shape and size of the mandible, high gonial angle and small Go-Me/S-N ratio were predominant (gonial angle, 65.4%, $p < 0.01$; Go-Me/S-N ratio, 65.4%, $p < 0.001$; Table 4) due to clockwise-rotated morphology of the mandible and relatively short mandibular body length.

In terms of incisor inclination, linguoversion of the maxillary and mandibular incisors was predominant (U1-SN, 76.9%; IMPA, 80.8%; all $p < 0.001$; Table 4). Lin-

guoversion of the maxillary incisors might occur due to dental compensation in Class II relationship, while linguoversion of the mandibular incisors might occur due to the pressure from the lower lip or the high prevalence of congenital missing of the mandibular incisors (Table 2).

Correlations of skeletodental pattern with mandibular body length (Go-Me) and CP severity

In the present study, with a decrease in the mandibular body length (Go-Me), the gonial angle, hyperdivergent pattern, and Class II relationship increased in Korean adolescent patients with PRS (gonial angle, $p < 0.05$; SN-GoMe, $p < 0.01$; ANB, $p < 0.05$; Table 5). These findings indicate that PRS patients had a typical size, shape and growth pattern of the mandible (micrognathia, high gonial angle, and clockwise-rotated morphology of the mandible), which can worsen the Class II relationship.

Do et al.[10] reported that a large CP at the time of primary palatorraphy was associated with an increase in the degree of mandibular retrusion (small value of SNB, rs = −0.5, $p < 0.05$). However, the present study exhibited that CP severity did not have a significant correlation with cephalometric variables, including SNB and mandibular body length (Go-Me) (Table 5). The size and shape of the mandible might directly affect the tongue position during development process, and this could influence the palatal fusion process and size of CP.[6,13] Therefore, it is necessary to investigate the relationships among the degree of micrognathia, position of the tongue, and severity of CP in patients with PRS in future studies.

Associated anomalies

The finding that more than half of PRS patients (53.8%) had craniofacial and/or extra-craniofacial anomalies including velocardiofacial syndrome, acampomelic campomelic dysplasia, pulmonary veno-occlusive disease, Nager syndrome, and Gordon syndrome (Tables 6 and 7) was similar to the results of previous studies.[2,21-23] Therefore, routine screening should be performed to determine the presence of any associated anomalies or syndromes in neonates with PRS.

Although this study was limited by the retrospective, single-center design and the small sample size, we were able to obtain some meaningful clinical data for Korean preadolescent patients with PRS. Since airway problems in neonates with PRS are an important issue for survival and growth, it is necessary to investigate the type and timing of airway treatment modalities for PRS patients in Korea. In addition, a nationwide multi-center study with a large sample size and systematic statistical analyses should be performed to determine the appropriate orthodontic diagnosis and treatment plan for PRS patients.

CONCLUSION

- One third of Korean pre-adolescent patients with PRS showed congenitally missing tooth, and half of them exhibited a bilateral and symmetric missing pattern.
- The CP severity was not significantly correlated with any cephalometric variables except IMPA.
- The predominant skeletodental patterns included Class II relationship, posteriorly positioned maxilla and mandible, hyper-divergent pattern, high gonial angle, small mandibular body length to anterior cranial base ratio, and linguoversion of the maxillary and mandibular incisors.
- Nearly half of PRS patients had craniofacial and/or extra-craniofacial anomalies, which implicated the need of routine screening.
- Although this study was based on data from a single university hospital, the results from this study might provide primary data for individualized diagnosis and treatment planning for Korean pre-adolescent patients with PRS.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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