

1 **DOI: <https://doi.org/10.47391/JPMA.213>**

2
3 **Evaluation of the cervical vertebral anomalies in patients with**
4 **cleft lip and palate in Aegean region of Turkey**

5
6 **Ege Dogan¹, Gulen Ozses Ergican², Servet Dogan³**

7 **1** Ali Cetinkaya Bulvarı, Alsancak, Izmir, Turkey; **2,3** Department of Orthodontics, Ege
8 University, Bornova, Izmir, Turkey

9 **Correspondence:** Ege Dogan. **Email:** dtegedogan@hotmail.com

10
11 **Abstract**

12 **Objective:** To identify the cervical vertebral anomalies in patients with cleft lip
13 and palate, and to compare unilateral and bilateral cleft lip and palate.

14 **Methods:** The retrospective cohort study was conducted in 2018 at Department
15 of Orthodontics, Ege University, Izmir, Turkey, and comprised non-deteriorated
16 lateral cephalometric radiographs of non-syndromic patients which showed the
17 entire cervical spine. The radiographs were divided into two groups, with group
18 A having those of patients with cleft lip and palate exposure, and control group
19 B having those with non-exposure. Within group A, unilateral and bilateral
20 cleft lip and palate cases were compared. Data was analysed using SPSS 22.

21 **Results:** Of the 220 subjects, 110(50%) were in group A with a mean age of
22 15 ± 6.3 years, and 110(50%) were in group B with a mean age of 15 ± 2.1 years.
23 Within group A, 56(50.9%) subjects had unilateral and 54(49.1%) had bilateral
24 cleft lip and palate. Cervical vertebral anomalies were found in 71(64.5%)
25 patients and 45(40.9%) controls ($p<0.001$). Among those with bilateral
26 condition, it was found in 41(75.9%) and in unilateral 56(56.6%) ($p<0.05$).
27 Occipitalisation was 21(38.9%) in bilateral and 4(7.1%) in unilateral cases
28 ($p<0.001$). Fusion was higher in bilateral patients 16(63%) compared to

29 23(41.1%) unilateral ($p<0.05$). Posterior arch deficiencies were found in
30 30(27.3%) patients in group A and 18(16.4%) controls in group B ($p<0.05$).
31 Fusion was seen in 57(51.8%) group A patients and 33(30%) group B controls
32 ($p<0.001$).

33 **Conclusion:** Cervical vertebral anomalies were mostly found in patients with
34 cleft lip and palate. In patients with bilateral condition, more than one anomaly
35 was seen.

36 **Key Words:** Cervical vertebral anomalies, Unilateral cleft lip and palate,
37 Bilateral cleft lip and palate.

38

39 **Introduction**

40 Cleft lip and palate (CLP) are common congenital malformations of the lip and
41 palate caused by genetic and environmental factors. There is an association
42 between CLP and cervical vertebral anomalies (CVA) as aetiological factors can
43 be affected by each other¹⁻⁴. From lateral cephalometric radiographs, cervical
44 vertebra can be recorded and can be used to identify CVA. The radiological
45 images of CVA on standardised lateral cephalometric radiographs have been
46 described in literature according to which, identification of CVAs early is very
47 important for referral to relevant professionals for the correct treatment⁵.

48 The cervical vertebrae develops from sclerotomes and the sclerotomal paraxial
49 mesodermal sheath appears at about 4 weeks into intrauterine life. By the 8th
50 week of foetal life, ossification begins and is completed at about three years³⁻⁵.

51 A deficiency of mesenchyme in median palatal process causes cleft lip (CL)
52 anomalies while defective development of the lateral palatal processes causes
53 cleft palate (CP) anomalies. The congenital anomalies of the cervical vertebrae
54 are developed from the same paraxial mesoderm, which may be one of the
55 possible mechanisms for CP development⁶⁻⁸. CVAs are divided into posterior
56 arch deficiencies (PADs) and fusions (FUS). PADs are subdivided into spina

57 bifida and dehiscence, while FUS are subdivided into block fusion and
58 occipitalisation^{1,9-11}.

59 The current study was planned to identify CVAs in the Aegean Region of
60 Turkey in CLP patients, and to compare patients with unilateral (UCLP) and
61 bilateral (BCLP) conditions in this regard.

62

63 **Material and Method**

64 The retrospective cohort study was conducted from the lateral cephalometric
65 radiographs taken between the years of 2015-2018, in 2018 at the
66 Department of Orthodontics, Ege University, Izmir, Turkey. It was
67 comprised non-deteriorated lateral cephalometric radiographs of non-
68 syndromic patients with skeletal Class I anomaly in which the mesiobuccal
69 cusp of the maxillary first molar occludes in the buccal groove of the
70 mandibular first molar which showed the entire cervical spine.

71 After approval from the institutional ethics review committee, the sample size
72 was calculated using G Power software with a significance level of 0.05 and
73 power 80%. Additional archival material was used to increase the power of
74 study to >95%¹².

75 Written informed consent for participation in and publication of research had
76 been taken from parents of each patient.

77 Lateral cephalometric radiographs were outlined on an acetate paper with 0.7
78 graphite pencil and CVAs were noted by a single examiner. All the radiographs
79 were classified as mentioned in literature¹ (Figure).

80 Various CVAs were defined for the purpose of the study. Spina bifida:
81 Insufficient ossification in the spinous process, breakdown of posterior part of
82 the neural arch; Dehiscence: Spinous process indicating insufficient
83 development of the structures, breakdown of part of a vertebral unit; Fusion:
84 Bony union of one unit with another at the articulation facets, neural arch or

85 transverse processes of vertebrae; Block fusion: Fusion between two cervical
86 vertebrae, and Occipitalization: Assimilation of the atlas with occipital bone
87 either partially or completely.

88 The radiographs were divided into two groups, with group A having those of
89 patients with CLP exposure, and control group B having those of controls with
90 non-exposure. Within group A, UCLP and BCLP cases were compared.

91 Data was analysed using SPSS 22. Chi square test was used where applicable.
92 Intra-observer reliability was also evaluated using intra-class correlation
93 coefficients (ICC). The measurements were analysed again after two weeks in
94 randomly selected lateral cephalometric films. $P < 0.05$ was taken as statistically
95 significant.

96

97 **Results**

98 Of the 220 subjects, 110(50%) were in group A with a mean age of 15 ± 6.3
99 years, and 110(50%) were in group B with a mean age of 15 ± 2.1 years. Within
100 group A, 56(50.9%) subjects had UCLP and 54(49.1%) had BCLP. CVAs were
101 found in 71(64.5%) patients and 45(40.9%) controls ($p < 0.001$). Among those
102 with BCLP, it was found in 41(75.9%) and in UCLP 56(56.6%) ($p < 0.05$).
103 Occipitalisation was found in 21(38.9%) BCLP and 4(7.1%) UCLP cases
104 ($p < 0.001$) (Table 1). FUS was higher in BCLP patients 16(63%) compared to
105 23(41.1%) UCLP ($p < 0.05$). PADs were found in 30(27.3%) patients in group A
106 and 18(16.4%) controls in group B ($p < 0.05$). FUS was seen in 57(51.8%) group
107 A patients and in 33(30%) group B controls ($p < 0.001$) (Table 2). In UCLP sub-
108 group, there was one anomaly in 22(39.3%) cases and two anomalies in
109 8(14.3%) patients. In the BCLP sub-group, there was one anomaly in 23(41.8%)
110 cases, two in 14(25.9%) cases, and 3 in 1(1.9%) patient.

111 During the two-week analysis of the lateral cephalometric films, 55(25%) were
112 selected and ICC values were highly acceptable with a mean of 0.995 (± 2.4)
113 (range: 0.94-0.99).

114 **Discussion**

115 To the best of our knowledge, the current study is the first in Turkey to have
116 identified and compared CVAs in CLP and non-CLP patients, while also
117 comparing the UCLP and BCLP cases.

118 The study focussed on patients in the Aegean region of Turkey with minimum 9
119 years of age. Batwa et al.¹⁰ stated that the onset of the pubertal growth increase
120 was significantly earlier in the non-CLP participants in comparison with UCLP
121 participants. It was suggested that the lower age limit of the patients were 6
122 years of age because the malformations of the upper cervical vertebrae cannot
123 be confirmed at an earlier age^{3,9}. Upper cervical vertebrae malformations cannot
124 be assessed using conventional radiography until complete development has
125 occurred¹. Some studies^{1,9} excluded CLP patients aged <6 years for this reason.
126 Similar was the case with the current study.

127 Compared to the current study's findings, studies evaluating CVAs have
128 presented different scores for CLP and control groups. Our results are higher
129 than some of those studies^{1,4,9,13}.

130 Compared to some studies in literature^{1,7}, the current study evaluated lateral
131 cephalometric radiographs of patients having complete clefts to identify CVA
132 differences between UCLP and BCLP.

133 The number of male and female subjects in the current study was nearly equal
134 to detect any relationship of gender with CLP. Literature has studies with mixed
135 findings on this association, with some reporting in the affirmative¹⁴, while
136 others reporting in the negative¹⁵.

137 The current study showed that the prevalence of FUS in BCLP was higher than
138 UCLP. The finding is different from some reported earlier^{1,5,16}, but is similar to
139 the findings of one study.¹⁷

140 More detailed diagnostic methods are needed for evaluating BCLP patients.
141 Further studies are required to establish any association between oral clefts and
142 upper CVA at the genetic level.

143

144 **Conclusion**

145 CVAs were mostly found in CLP patients. In BCLP patients, more than one
146 anomaly was seen.

147

148 **Disclaimer:** None.

149 **Conflict of Interest:** None.

150 **Source of Funding:** None.

151

152 **References**

153 1-Sandham A. Cervical vertebral anomalies in cleft lip and palate. *Cleft Palate*
154 *J.* 1986;23(3):206-2014.

155 2-Smahel Z, Skvarilova B. Length of the cervical spine as a factor in the
156 etiology of cleft palate. *Cleft Palate Craniofac J* 1993;(30): 274–278.

157 3-Murray JC. Gene/environment causes of cleft lip and palate. *Clin Genet*
158 2002;(61):248–256.

159 4- Hoenig JF, Schoener WF. Radiological survey of the cervical spine in cleft
160 lip and palate. *Dentomaxillofac Radiol* 1992;(21):36-39.

161 5-Farman AG, Escobar V. Radiographic appearance of the cervical vertebrae in
162 normal and abnormal development. *Br J Oral Surg* 1982;(20):264-274.

163 6-Helmi C, Pruzansky S. Craniofacial and extracranial malformations in the
164 Klippel-Feil syndrome. *Cleft Palate Craniofac J* 1980;(17):65–88.

165 7-Horswell BB. The incidence and relationship of cervical spine anomalies in
166 patients with cleft lip and/or palate. *J Oral Maxillofac Surg* 1991;(49):693-695.

167 8-Yoshihara T, Suzukib J, Yasutaka Y. Anomaly of cervical vertebrae found on

- 168 orthodontic examination: 8-year-old boy with cleft lip and palate diagnosed
169 with Klippel-Feil syndrome. *Angle Orthod* 2010;(80):975-980.
- 170 9-Ugar DA, Semb G. The prevalence of anomalies of the upper cervical
171 vertebrae in subjects with cleft lip, cleft palate, or both. *Cleft Palate Craniofac J*
172 2001;(38):498-503.
- 173 10-Batwa W, Almoammar K, Aljohar A, Alhussein A, Almujel S, Zawawi KH.
174 The Difference in Cervical Vertebral Skeletal Maturation between Cleft
175 Lip/Palate and Non-Cleft Lip/Palate Orthodontic Patients. *BioMed Research*
176 International Volume 2018, Article ID 5405376,
177 <https://doi.org/10.1155/2018/5405376>
- 178 11-Rajion ZA, Townsend GC, Netherway DJ, Anderson PJ, Yusof A, Hughes
179 T, et al. A three-dimensional computed tomographic analysis of the cervical
180 spine in unoperated infants with cleft lip and palate. *Cleft Palate Craniofac J*
181 2006;(43): 513-518.
- 182 12- Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. Statistical power
183 analyses using G*Power 3.1: Tests for correlation and regression
184 analyses. *Behavior Research Methods*, 2009; (41):1149-1160.
- 185 13-Datana S, Bhalla A, Kumar P, Kumar Roy S, Londhe S. Comparative
186 Evaluation of Prevalence of Upper Cervical Vertebrae Anomalies in Cleft
187 Lip/Palate Patients: A Retrospective Study . *Int J of Clinical Pediatric Dentistry*,
188 2014; 7(3): 168-171 .
- 189 14-Ashwini C, David MP, Markande A, Swamy AA, Joseph S, Muthaiah M.
190 The association of cleft lip and palate with cervical vertebral anomalies- a
191 lateral cephalographic study. *Int. J of Dental Research* 2017;5(2):167-171.
- 192 15-Lima MC, Franco EJ, Janson G, Carvalho IM, Santos CF, Capelozza AL.
193 Prevalence of upper cervical vertebrae anomalies in patients with cleft lip and/or
194 palate and noncleft patients. *Cleft Palate Craniofac J* 2009;(46): 481-86.
- 195 16-Srivastava M, Aggarwal A, Batra P, Datana S, Kumar P, Macrcusson KA.

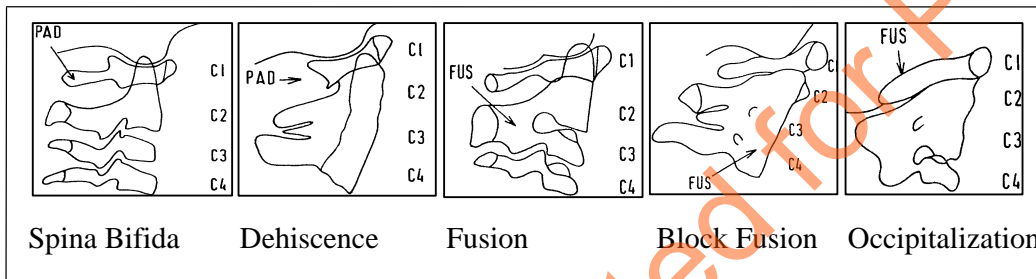
196 Association of cervical vertebra anomalies with cleft lip and palate. Cleft Palate
197 Craniofac J 2014;(1): 43-47.

198 17-Karsten A, Sideri M, Spyropoulos M. Morphologic Anomalies of Upper
199 Cervical Vertebrae in Swedish Children Born with Nonsyndromic Cleft Lip
200 and/or Palate Compared to Swedish Children without Cleft. Cleft Palate
201 Craniofac J 2018;11. <https://doi.org/10.1177%2F1055665618808621>.

202

203 -----

204



205

206

207

208 **Figure: Cervical vertebral anomalies¹**

209

210 -----

211

212 **Table 1: Distribution of cervical vertebrae anomalies**

213

	N	Spina Bifida		P value	Dehiscence		P value	Fusion		P value	Block Fusion		P value	Occipitalization		P value	Total		P value
		N	%		N	%		N	%		N	%		N	%		N	%	
CLASS I	110	18	16.4	0,05 *	0	0	-	24	21.8	0,069	1	0.9	0,175	10	9.1	0,00 6 **	45	40.9	0,000 ***
CLP	110	30	27.3		0	0		36	32.7		4	3.6		25	22.7		71	64.5	
UCLP	56	14	25	0,586	0	0	-	18	26.8	0,894	2	3.6	0,970	4	7.1	0,00 0 ***	30	56.6	0,014 *
BCLP	54	16	29.6		0	0		18	33.3		2	3.7		21	38.9		41	75.9	

214 (p<0.05) * (p<0.01) ** (p<0.001) ***

215 CLP: Cleft lip and palate; UCLP: Unilateral cleft lip and palate; BCLP: Bilateral
216 cleft lip and palate.

217

218 -----

219

220

221

222

223 **Table 2: Distribution of PAD and FUS anomalies**

224

	N	PAD		P value	FUS		P value
		N	%		N	%	
CLASS I	110	18	16.4	0,050 *	33	30	0,001 ***
CLP	110	30	27.3		57	51.8	
UCLP	56	14	25	0,586	23	41.1	0,022 *
BCLP	54	16	29.6		34	63	

225 (p<0.05) *(p <0.01) **(p <0.001) ***

226 PAD: Posterior arch deficiency; FUS: Fusion; CLP: Cleft lip and palate; UCLP:

227 Unilateral cleft lip and palate; BCLP: Bilateral cleft lip and palate.

228

Provisionally Accepted for Publication