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Evaluation of upper cervical vertebrae anomalies in patients with cleft lip and palate with cone beam computed tomography

Dudak damak yarıklı hastalarda üst servikal vertebra anomalilerinin konik ışınlı bilgisayarlı tomografi ile değerlendirilmesi

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Abstract

Aim: The purpose of this study was to compare upper cervical vertebral anomalies (CVAs) between patients with cleft lip and palate (CLP) and healthy individuals using cone-beam computed tomography (CBCT).

Materials and Methods: CBCT images of 100 CLP patients and 100 controls were analyzed**.** CVAs including occipitalization, fusion, block fusion, cleft, os odontoideum, ossiculum terminale, and arcuate foramen, were evaluated.

Results: CVAs were detected in 23% of CLP patients and 14% of controls. The most frequent anomaly was arcuate foramen (17% in CLP, 11% in controls), followed by vertebral cleft and fusion (each 3% in CLP). No cases of occipitalisation, block fusion, os odontoideum, or ossiculum terminale were observed. There were no significant differences between CLP and control groups or between unilateral and bilateral CLP (p>0.05).

Conclusion: CVAs can be reliably evaluated using CBCT, and they may occur more frequently in patients with CLP.

Keywords: Anomalies; Cervical vertebrae; Cleft lip and palate; Cone-beam computed tomography.

Öz

Amaç: Bu çalışmanın amacı dudak damak yarığı (DDY) olan hastalar ile sağlıklı bireyler arasındaki üst servikal vertebra anomalilerini (SVA) konik ışınlı bilgisayarlı tomografi (KIBT) ile karşılaştırmaktır.

Gereç ve Yöntemler: 100 DDY'li hastanın ve 100 sağlıklı bireyin KIBT görüntüleri incelendi. SVA'lar oksipitalizasyon, füzyon, blok füzyon, yarık, os odontoideum, ossiculum terminale ve arkuat foramen olarak değerlendirildi.

Bulgular: CVA oranı CLP hastalarında %23, kontrollerde %14 olarak bulundu. En sık görülen anomali arcuate foramen olup CLP grubunda %17, kontrol grubunda %11 oranındaydı. Vertebral cleft ve fusion her iki grupta da %3 oranında gözlendi. Occipitalisation, block fusion, os odontoideum ve ossiculum terminale saptanmadı. CLP ve kontrol grupları arasında, ayrıca unilateral ve bilateral CLP arasında istatistiksel olarak anlamlı fark bulunmadı (p>0,05).

Sonuç: SVA CBCT ile güvenilir şekilde değerlendirilebilir ve CLP hastalarında daha sık görülebilir.

Anahtar Kelimeler: Anomaliler; Yarık dudak damak; Servikal vertebra; Konik ışınlı bilgisayarlı tomografi.

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Introduction

Cleft lip and palate (CLP) is one of the most common congenital craniofacial malformations, with an incidence of approximately 1 in 700 live births worldwide.[1] It may occur as an isolated deformity or in combination with other congenital anomalies, and it is associated with considerable functional, esthetic, and psychosocial implications, including difficulties in feeding, speech, hearing, and facial growth.[2]

Cervical vertebral anomalies (CVAs) include structural variations such as occipitalisation, fusion, block fusion, cleft, os odontoideum, ossiculum terminale, and arcuate foramen.[3,4] These anomalies may cause a wide spectrum of clinical manifestations, ranging from restricted cervical mobility to neurological complications such as headache, myelopathy, or vertebrobasilar insufficiency.[5] Therefore, their detection is of clinical importance in both pediatric and adult populations.

The embryogenesis of lip, palate, and cervical vertebrae occurs during the early weeks of intrauterine life. As these structures develop concurrently, disturbances in embryological processes may result in the simultaneous occurrence of CLP and CVAs. This developmental synchrony provides a plausible biological explanation for the coexistence of these two conditions.[6,7]

Several investigators have suggested that CVAs may act as potential risk factors for the development of CLP.[8,9] It has been proposed that vertebral synostosis or a shortened cervical spine may limit craniofacial growth, thereby restricting the anterior and inferior development of the glossomandibular complex. [9] During palate development, the lateral palatine processes move horizontally and converge at the midline. Anomalies of the vertebrae may impede the glossomandibular complex's development. Therefore, the space in the superior region of the tongue, which is necessary for the horizontal movement of the lateral palatine processes, may be insufficient, potentially leading to the development of CLP.[9,10]

In most previous studies, CVAs were evaluated using lateral cephalometric radiographs, which offer advantages such as low radiation exposure, ease of use, standardized head positioning, and suitability for longitudinal assessment.[5,11,12] Owing to these advantages, this technique has been widely preferred for examining cervical vertebral morphology. Reported rates of CVAs in CLP patients range from 13.3% to 38.7%, demonstrating a higher prevalence compared with healthy individuals.[13,14] However, cephalometric evaluation may yield inaccurate results due to the superimposition of anatomical structures. Therefore, three-dimensional imaging methods, such as cone beam computed tomography (CBCT) and computed tomography (CT), may provide more accurate and reliable results in the evaluation of cervical vertebral anomalies.[5,15]

CBCT is widely used for diagnostic assessment and treatment planning in CLP patients, as it provides three-dimensional visualization with minimal superimposition and substantially lower radiation exposure compared with CT.[16] Although CT offers superior soft-tissue contrast and a wider field of view, its higher radiation dose limits routine use in dental imaging. [17] Nevertheless, CT has been employed by some researchers to evaluate CVAs because it enables assessment of both osseous and soft-tissue structures.[15,18] Despite this, few studies have investigated CVAs in CLP patients using CBCT, which allows detailed analysis of bone morphology at a lower dose. Early detection and appropriate referral are important to prevent potential neurological complications.[5,19]

This study aimed to compare CVAs between healthy individuals and patients with CLP using CBCT, and to provide dentists with insights into upper cervical vertebral anomalies.

Materials and Methods

The type of the study

This study was designed as a retrospective cross-sectional study. The study was approved by the Ethics Committee of Marmara University Faculty of Medicine (Approval Date: March 5, 2024; Protocol No:

09.2024.1543). The study was conducted using anonymized patient records. In our institution, all patients provide written informed consent at the time of admission, permitting the use of their clinical and radiographic data for research purposes.

The samples of the research

The study group consisted of 100 patients diagnosed with CLP who underwent CBCT at the Department of Oral and Maxillofacial Radiology, Marmara University, between January 2021 and July 2024. CBCT scans in this group were obtained for clinically justified purposes, such as orthodontic treatment planning, preoperative evaluation prior to alveolar bone grafting or orthognathic surgery, assessment of impacted or supernumerary teeth, and detailed examination of craniofacial structures associated with the cleft condition. Both unilateral cleft lip and palate (UCLP) and bilateral cleft lip and palate (BCLP) patients were included.

The control group comprised 100 healthy individuals without craniofacial clefts, whose CBCT scans were taken during the same period for other clinical indications, including dental implant planning, localization of impacted or supernumerary teeth, orthognathic surgery planning, evaluation of pathological lesions, and complex endodontic assessments.

Patients were included if they were six years or older, had CBCT scans of diagnostic quality, and if both the palatal region and the upper cervical vertebrae (C1–C3) were clearly visible within the field of view (FOV). Exclusion criteria included a history of maxillofacial or cervical trauma, inadequate image quality, or the presence of syndromic conditions known to affect craniofacial or vertebral development (e.g., Klippel–Feil syndrome, Down syndrome, Turner syndrome, Marfan syndrome, achondroplasia, spina bifida, scoliosis).

CVAs were comparatively evaluated for their presence or absence in the CLP-control groups and UCLP-BCLP groups according to the following definitions: [3,20]

Occipitalization: Partial or complete union of the atlas with the occipital bone.

Fusion: The union of one vertebral segment with another can occur at the articular facets, transverse processes, or components of the neural arch.

Block fusion: Fusion of more than 2 vertebrae.

Cleft: Incomplete ossification of part of the anterior or posterior arch of the Cl vertebra, presence of a defect line.

Os odontoideum: Failure of fusion of the dens of odontoid process to the body of axis.

Ossiculum terminale: An incomplete fusion between the apex and base of the odontoid process.

Arcuate foramen: A bony or calcified bridge formed by ossification of the posterior atlanto-occipital membrane, partially or completely enclosing the vertebral artery, suboccipital nerve, and accompanying veins as they pass over the posterior arch of the atlas (Figure 1).

Data collection tools

The CBCT images were obtained by an operator using a ProMax 3D Mid imaging device (PlanmecaOy, Helsinki, Finland) operated with avaible FOV, 90 kVp and 10 mA, with a scan time of 36 seconds. The CBCT scans were analyzed in multiplanar reconstructions (coronal, axial and sagittal), using Romexis 2.92 software (PlanmecaOy, Helsinki, Finland). Image evaluation was performed on a 23-inch Acer monitor (1920×1080 pixels) connected to an HP workstation.

All CBCT scans were evaluated by a single oral and maxillofacial radiologist with 4 years of experience. To assess intraobserver reliability, a random 20% subsample of scans was re-evaluated after a two-week washout, in a randomized order and blinded to the initial ratings, under identical viewing conditions. Agreement between the two sessions was quantified using Cohen's kappa(κ), which demonstrated excellent reliability (κ=1.00).

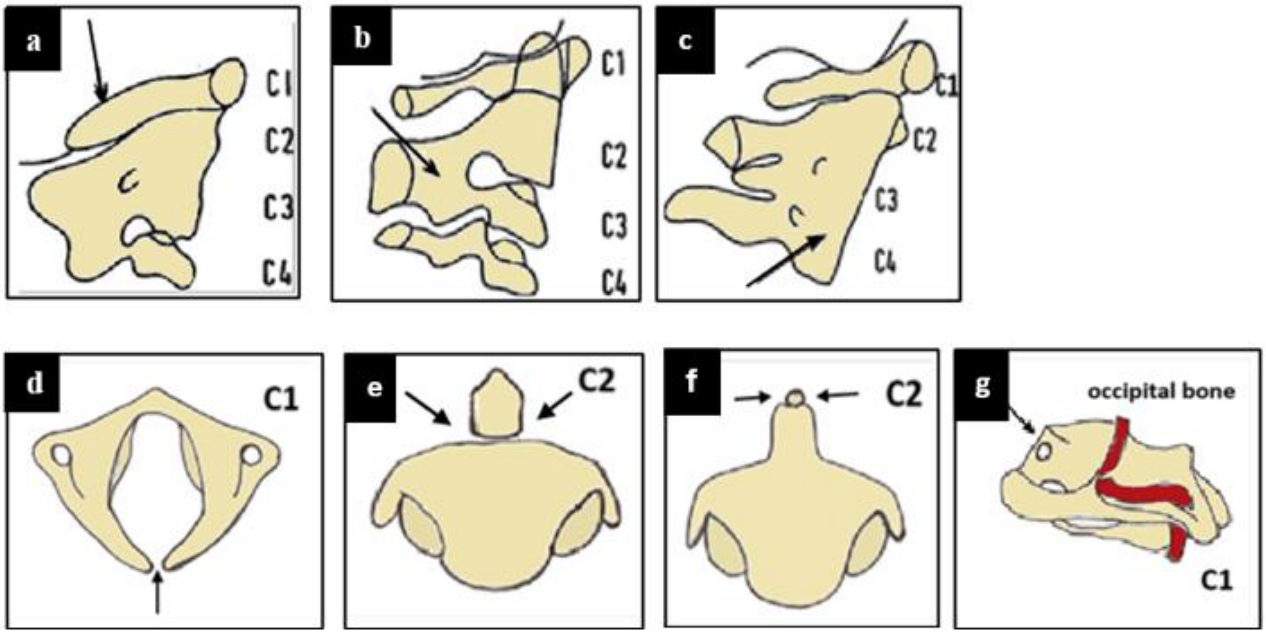

Figure 1. Illustrations of cervical vertebral anomalies **a.** occipitalization **b.**fusion **c.**block fusion **d.**cleft **e.**os odontoideum **f.**ossiculum terminale **g.**arcuate foramen (Modified and redrawn based on Dogan et al.[20] and images from Radiopaedia.org.)

Statistical analysis

Version 30.0 of the SPSS statistical software (IBM Corp., Armonk, NY, USA) was used for data analysis. Descriptive statistics were calculated, and the Chi-Square Test or Fisher's Exact Test was applied to compare categorical variables between groups where appropriate. A p value of less than 0.05 was considered statistically significant.

In addition, both a post hoc power analysis and a sensitivity (minimum detectable effect) analysis were performed using G*Power (version 3.1.9.7, Universität Düsseldorf, Germany). For the observed difference between the CLP and control groups (23% vs. 14%), the achieved post hoc power was approximately 38% at α= 0.05 (two-tailed). The sensitivity analysis indicated that, with 100 subjects in each group, the study had 80% power to detect an absolute difference of about 16 percentage points.

Ethics committee approval

Ethical approval for this retrospective study was obtained from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Approval Date: March 5, 2024; Approval No: 09.2024.1543).

This study was conducted in accordance with the principles of the Declaration of Helsinki. It was designed as a retrospective analysis based on anonymized patient data. At our institution, all patients provide routine informed consent upon admission, permitting the use of their clinical and radiographic records for research purposes.

Results

The demographic characteristics of the CLP and control groups are presented in Table 1. The mean age was 14.9 ± 5.4 years in the CLP group and 16.8 ± 5.3 years in the control group, and this difference was statistically significant (*p*=0.012, independent samples t-test). There was no significant difference in gender distribution between the groups (*p*=1.00, chi-square test).

Table 1. Demographic characteristics and statistical comparison between the cleft lip and palate and control groups.

Variables	Study samples		*p* values
	Cleft lip and palate group	Control group	
Age (years, mean ± SD)	14.9 ± 5.4	16.8 ± 5.3	0.012*
Gender	Male=53 (53%) Female=47 (47%)	Male=52 (52%) Female=48 (48%)	1

SD: Standard Deviation * Chi-square test

This research involved 100 individuals diagnosed with CLP (47 females and 53 males) aged between 7 and 33 years. CBCT images showed UCLP in 67 patients and BCLP in 33 patients. CVAs were observed in 23% of patients with CLP. Fusion and vertebral clefts were observed in 3%, while arcuate foramen was present in 17%. Occipitalisation, block vertebral fusion, os odontoideum, and ossiculum terminale were not detected in any of the patients.

The control group comprised 100 patients (48 females and 52 males) aged between 8 and 31 years. CVAs were observed in 14% of these patients. Cervical vertebral clefts were found in 3%, and arcuate foramen in 11%. Occipitalisation, fusion, block fusion, os odontoideum, and ossiculum terminale were not observed in this group (Figure 2).

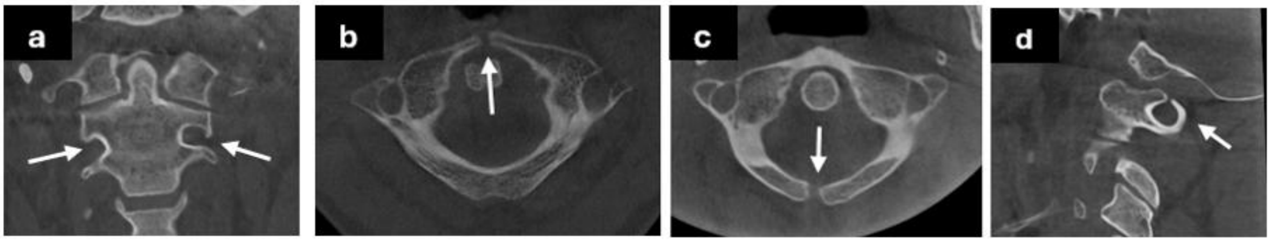

Figure 2. CBCT images of cervical vertebral anomalies **a**.fusion of C2-C3 vertebrae **b.** anterior cleft of C1 vertebrae **c.** posterior cleft of C1 vertebrae **d**.arcuate foramen

When CVAs were compared between patients with CLP and the control group, occipitalisation, block fusion, os odontoideum, and ossiculum terminale were not observed in either group. Fusion was observed only in the CLP group; however, this difference was not significant (*p*=0.246). Vertebral clefts were present at the same rate (3%) in both groups, with no significant difference (*p*=1.00). Although the prevalence of arcuate foramen was higher than that of other CVAs in both groups, no significant difference was found in this comparison (*p*=0.308) (Table 2). Moreover, no significant difference was observed between the UCLP and BCLP groups (Table 3).

Table 2. Prevalence of cervical vertebral anomalies in patients with cleft lip and palate and in the control group

Cervical vertebrae anomalies	**Study samples**		**Total number**	***p* values**
	Cleft lip and palate group	**Control group**		
Occipitalisation	0	0	0	-
Fusion	3 (3%)	0	3(1.5%)	0.246**
Block fusion	0	0	0	-
Cleft	3(3%)	3(3%)	6(3%)	1**
Os odontoideum	0	0	0	-
Ossiculum terminale	0	0	0	-
Arcuate foramen	17(17%)	11(11%)	28(14%)	0.308*
Total	23(23%)	14(14%)	35(17.5%)	0.145*

* Chi-Square Test, **Fisher's Exact Test

Table 3. Comparison of cervical vertebral anomalies between unilateral and bilateral cleft lip and palate groups

Cervical vertebrae anomalies	**Cleft Lip and Palate**		***p* values**
	Unilateral	**Bilateral**	
Occipitalisation	0	0	-
Fusion	2(3%)	1(3%)	1**
Block fusion	0	0	-
Cleft	2(3%)	1(3%)	1**
Os odontoideum	0	0	-
Ossiculum terminale	0	0	-
Arcuate foramen	9(13.4%)	8(24.2%)	0.285*

* Chi-Square Test, **Fisher's Exact Test

The post hoc power analysis revealed that the observed difference between the CLP and control groups (23% vs. 14%) corresponded to an achieved power of approximately 38% at $\alpha = 0.05$ (two-tailed). The sensitivity analysis further indicated that with 100 subjects per group, the minimum detectable absolute difference at 80% power was about 16%, whereas the observed difference (9%) was below this threshold.

Discussion

The cervical vertebrae and the lip-palate structures develop concurrently during embryogenesis, and anomalies in these regions may be associated. It has been suggested that CLP and CVAs may develop at the same time as a result of early exposure to teratogenic compounds or other developmental disorders.[6] Supporting this hypothesis, previous research has highlighted a higher rate of CVAs among patients with CLP.[9,10,14,15,21-26]

Most previous studies, assessed CVAs using lateral cephalometric radiographs, a two-dimensional imaging technique. Although this method offers advantages such as low radiation exposure, easy accessibility, standardized head positioning, and suitability for craniofacial growth assessment,[11] it also presents notable limitations, including magnification, distortion, and superimposition of anatomical structures, which may obscure small anomalies or lead to misinterpretation.[27] The most critical limitation of cephalometric evaluation is the superimposition of structures at the craniovertebral junction, which may conceal minor variations.[25]

In contrast, CBCT provides three-dimensional visualization without superimposition, enabling accurate assessment of vertebral morphology in multiple planes. Compared with CT, CBCT offers shorter scanning times, lower radiation doses, and higher spatial resolution for osseous structures.[16] Nevertheless, its limited soft-tissue contrast and smaller field of view may restrict its use in cases requiring broader anatomical evaluation.[17] Despite these differences, only a few studies have analyzed the association between CVAs and CLP using CBCT.[3,15] The present study aimed to contribute to the literature by providing a detailed analysis based on three-dimensional imaging.

No significant difference in gender distribution was observed between the CLP and control groups, confirming demographic balance. Similar male-to-female ratios between groups have also been reported in previous studies, supporting the representativeness of the current sample.[13,20,28] The CLP group was significantly younger, which may be attributed to earlier clinical indications for CBCT imaging in orthodontic and surgical planning. The mean age in the present study (approximately 15 years) is consistent with that reported in earlier investigations.[28,29] The inclusion of a large number of nonsyndromic CLP patients and an equal number of age and gender matched controls minimized the likelihood of selection bias and strengthened the reliability of the findings.

In the literature, CVAs in patients with CLP were reported with variable rates between 4.1% and 64.5%.[10,13-15,20-23,25,26,30,31] Among these studies, only de Rezende Barbosa et al.[3] used CBCT and evaluated 151 patients with CLP, reporting CVA prevalence of 27.8%. Rajion et al.[15] examined unoperated infants with CLP using CT and reported cervical vertebral anomalies in 10% of cases, while none were observed in the control group. They described variations such as underdeveloped posterior arch of C1, bifid anterior tubercle, and C2–C3 fusion, suggesting delayed upper spinal development in CLP infants. Although their work provided valuable early evidence, it was limited to infants and used CT with higher radiation exposure. In contrast, the present CBCT-based study evaluated older CLP patients and healthy controls, allowing clearer visualization of vertebral morphology with a lower radiation dose. Therefore, the higher anomaly rate found in the current study may reflect developmental changes that become more apparent with age

In the present study, CVAs were detected in 23% of CLP patients. Many other researchers used lateral cephalometric radiography due to its ease of access and low radiation exposure. However, anomalies can be evaluated insufficiently in this method due to superpositions. Therefore, CBCT and CT studies may provide more accurate and reliable results.[16]

When CVAs were evaluated separately, the presence of occipitalization, block fusion, os odontoideum, and ossiculum terminale were not observed in either the CLP or control groups. In earlier studies, the reported prevalence of occipitalization varied widely, ranging from 0.7% to 38.9%.[3,13,14,20,23,26] Similarly, block fusion was reported with varying prevalence ranging from 0% to 33.6% in the studies.[3,13,14,20,23,26] Consistent with the findings of the current study, de Rezende Barbosa et al.[3] also found no block fusion in the CBCT evaluation.

Os odontoideum and ossiculum terminale-both anatomical variations of the axis-have been investigated in only a limited number of studies.[3,28] One such study, conducted by Karsten et al.[28] using cephalometric radiography, evaluated os odontoideum in patients with CLP and reported a rate of 5.7%. On the other hand, de Rezende Barbosa et al.[3] used CBCT to assess both variations, reporting no cases of os odontoideum and a very low prevalence of ossiculum terminale (0.6%). Evaluating these anatomical structures using lateral cephalometric radiography is more challenging than other cervical anomalies due to their small size and the potential for superposition. In this study, these structures were assessed in diffe rent sections on CBCT and none of these anomalies were found.

Fusion, defined as the ossification of the intervertebral space, was observed in 3% of cases, consistent with the findings of de Rezende Barbosa et al.[3] In contrast, other studies have found a higher prevalence of fusion anomalies, ranging from 10% to 51%.[13,14,20,23,26,28] However, as these studies were performed with lateral cephalometric radiographs, it has been suggested that narrowing of the intervertebral space may have been misinterpreted as fusion, potentially leading to false-positive findings.

Failure of complete fusion in the anterior or posterior vertebral arches of the vertebrae may lead to vertebral clefts, such as dehiscence or spina bifida.[23,32] Cervical vertebral clefts have been documented in previous studies to range between 8.5% and 27%.[3,13,14,20,23,28] In contrast, the present study observed a substantially lower prevalence (3%), which could be attributed to the enhanced spatial resolution of CBCT in the axial plane, facilitating more accurate detection of vertebral clefts and reducing the potential for false-positive findings.

The arcuate foramen represents an anatomical variant resulting from bone formation in the posterior atlanto-occipital membrane, with its prevalence reported to range from 5% to 68%.[12,33,34] This variation is clinically significant due to its association with symptoms such as cranial discomfort, vascular complications like vertebral artery dissection, and musculoskeletal pain affecting the cervical region, shoulders, and upper limbs.[35] In this study, arcuate foramen was identified in 17% of CLP patients and 11% of controls, making it the most frequent anomaly observed. Notably, the arcuate foramen was the most frequently observed cervical vertebral anomaly. Consistent with these findings, Hoenig and Schoener[26] also reported the arcuate foramen as the most common anomaly (37%) in patients with CLP, whereas de Rezende Barbosa et al.[3] reported a considerably lower prevalence of 7%.

Several studies have evaluated the relationship between CVAs and CLP according to the type of cleft (unilateral or bilateral). In a study conducted by Datana et al.[14] fusion anomalies were found to occur at similar rates in patients with UCLP and BCLP, while block fusion and occipitalization were not observed both in two groups. Similarly, Uğar and Semb[23] reported that posterior arch deficiencies were twice as common in patients with UCLP compared to those with BCLP, whereas fusion anomalies were detected at comparable rates (8%) in both groups. Additionally, no cases of block fusion or occipitalization were reported in patients with CLP. Similar to the present study, de Rezende Barbosa et al.[3], using CBCT, the comparison between UCLP and BCLP groups revealed no statistically significant differences. However, the prevalence of spina bifida, occipitalization, and arcuate foramen was higher among patients with bilateral clefts, whereas vertebral cleft, fusion, and ossiculum terminale were more frequently observed in the UCLP group. In the current study, no significant differences were found between the two groups; fusion and vertebral cleft were observed at similar rates, while the arcuate foramen was more common in the UCLP group.

Although de Rezende Barbosa et al.[3] also used CBCT, to the best of our knowledge, the present study is the only one that comparatively evaluates the cervical vertebrae of patients with CLP and a control group. In this study, the CVA rate was 23% in patients with CLP, whereas it was 14% in the control group. However, comparison between the two groups revealed no statistically significant difference (p=0.145). Previous comparative studies using cephalometric radiographs generally reported higher CVA rates in CLP patients [9,14,15,22-26,30] and in some cases, statistically significant differences.[13,14,20,23]

These findings highlight the clinical importance of detecting CVAs in both CLP patients and healthy individuals. CBCT-based identification of these anomalies may enhance orthodontic planning, reduce surgical risks, and aid in recognizing potential neurological or vascular complications, thereby supporting multidisciplinary management.

Limitation of the study

This study examined CLP as a single group. The sample could have been further subdivided into cleft lip, cleft palate, and cleft lip and palate; however, because the study was retrospective and based solely on CBCT images, soft-tissue evaluation was not possible. Such differentiation would require additional clinical assessment. Furthermore, some types of CVAs were not observed in either group.

As this study relied solely on radiological evaluation without accompanying clinical assessment, the findings should be interpreted with caution, as they may not fully capture clinically meaningful differences.

As this study relied exclusively on radiological evaluation without accompanying clinical data, the findings should be interpreted with caution, as they may not fully capture clinically relevant variations. Although a large number of CBCT scans were initially reviewed, only a limited proportion simultaneously included both the palatal region and the upper cervical vertebrae within the FOV, which restricted the final sample size. Consequently, the study may be underpowered to detect small differences, as also indicated by the power analysis.

Despite these limitations, the findings hold important clinical relevance. CVAs may influence craniofacial growth and head posture, which are key considerations for orthodontic diagnosis and treatment planning in CLP patients. In surgical practice, awareness of vertebral fusion or occipitalisation is essential to prevent complications during orthognathic or reconstructive procedures. Moreover, anomalies such as arcuate foramen may be associated with vertebral artery variations and neurological symptoms, highlighting the need for a multidisciplinary approach involving orthodontists, surgeons, and neurologists.

Conclusion

The prevalence of CVAs was higher in patients with CLP; however, the analysis revealed no statistically significant association between these conditions. CBCT enables three-dimensional visualization and eliminates superimposition, thereby reducing the likelihood of false-positive findings compared with lateral cephalometric radiography. Consequently, the reported prevalence of CVAs may appear lower in CBCT-based studies.

Awareness of CVAs identifiable on CBCT images is essential for dental professionals, as timely recognition and appropriate referral can facilitate early diagnosis, prompt treatment, and effective multidisciplinary management. These practical implications underscore the importance of collaboration among orthodontists, surgeons, and neurologists to ensure accurate diagnosis and safe, comprehensive care for patients with CLP.

Ethics Committee Approval

This retrospective study was approved ethically by the Marmara University Faculty of Medicine (Protocol No: 09.2024.1543). This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent form were obtained from all patients.

Informed Consent

Signed informed consent form was obtained from all participants.

Author Contributions

Y.G. contributed to the conception, design, data collection, literature review, and writing. M.O.B. supervised, analyzed data, and critically revised the manuscript.

Conflict of Interest

The authors declare that there is no conflict of interest for this article.

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Statements

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Peer-review

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