

## Cleft lip and palate. Review of the literature.

Fisuras labio palatinas. Revisión de la literatura

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### ABSTRACT

Cleft lip and palate are among the most frequent congenital malformations worldwide. In Latin America, their prevalence is approximately 1 in 1000 live births. The aim of this article is to provide specific information on the etiology, classification, complications, diagnosis and treatment of cleft lip and palate. An electronic search was performed in: PubMed, Lilacs, SciELO and Google Scholar, the following keywords were used for the search: "cleft palate", "cleft lip", "cleft lip and palate" "congenital anomalies" obtained from Decs, and related with Boolean operators AND and OR. The results show that the malformation develops within the first trimester of gestation, during craniofacial development and is produced by the lack of fusion between the facial prominences, its etiology is multifactorial and is related to genetic and environmental factors, and because this alteration affects several anatomical structures, its treatment should be multidisciplinary to avoid various complications that occur in these children during their first months of life. In conclusion, it is important that the health professional has previous knowledge and is able to make a timely diagnosis, in addition to educating pregnant mothers.

**Keywords:** Cleft palate, cleft lip, cleft lip and palate, congenital anomalies.

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## RESUMEN

Las fisuras labio palatinas se encuentran dentro de las malformaciones congénitas más frecuentes a nivel mundial. En Latinoamérica, su prevalencia es aproximadamente de 1 en 1000 nacidos vivos. El objetivo de este artículo es brindar información concreta sobre la etiología, clasificación, complicaciones, diagnóstico y tratamiento de las fisuras labio palatinas. Se realizó una búsqueda electrónica en: PubMed, Lilacs, SciELO y Google Scholar, se utilizaron para la pesquisa las palabras clave: “Fisura del paladar”, “Labio hendido”, “labio y paladar fisurado” “anomalías congénitas” obtenidas de los Decs, y relacionados con operadores booleanos AND y OR. Los resultados demuestran que la malformación se desarrolla dentro del primer trimestre de gestación, durante el desarrollo craneofacial y se produce por la falta de fusión entre las prominencias faciales, su etiología es multifactorial y está relacionada con factores genéticos y ambientales, y debido a que esta alteración afecta varias estructuras anatómicas, su tratamiento debe ser multidisciplinario para evitar diversas complicaciones que se presentan en estos niños durante sus primeros meses de vida. Concluyendo que es importante que el profesional de la salud tenga conocimientos previos y sea capaz de realizar un diagnóstico oportuno, además de educar a las madres gestantes.

**Palabras clave:** Fisura del paladar, Labio hendido, labio y paladar fisurado, anomalías congénitas.

## INTRODUCTION

Since the end of the 20th century, diseases with a genetic component have been a major cause of disease and death in the Western world.<sup>1</sup>

An adequate embryonic and fetal development is mandatory to avoid different pathologies that are associated with childhood, for example, congenital anomalies, which have a high mortality rate. For this reason, during this period it is necessary to maintain an adequate gestational control, since these disorders can be diagnosed during pregnancy.<sup>2</sup>

The World Health Organization (WHO) determined that orofacial clefts affect approximately 1 in every 1,000 live newborns in the world.

the world, showing a great predominance at world level<sup>3</sup>. In 2015, a systematic study was conducted about the global prevalence of oral cleft births, in which study it was determined that there are 0.99 to 1 cases of cleft lip and palate (FLP) in South America per 1,000 live births. It is important to mention that most underdeveloped countries do not have surveillance systems for congenital defects and orofacial clefts, which is why they do not obtain accurate data and may be subject to biases, which is why it is recommended to develop these systems to prevent congenital defects.<sup>4</sup>

Cleft lip and palate is a congenital malformation that affects the anatomical, morphological and functional structure of the fetus and is detected during gestation, at birth or later in life.<sup>5</sup>This malformation occurs most frequently in the craniofacial mass and constitutes alterations in the structure of the embryo as a result of the poor fusion that occurs between some craniofacial structures that form the primary and secondary palate from the sixth and eighth gestational week.<sup>6</sup>

This anomaly is of multifactorial etiology and produces several complications in the baby, such as feeding problems (breastfeeding, malnutrition), dental anomalies, nasal voice, hearing, etc.<sup>7</sup>. In addition to being a facial malformation, it will represent biological and psychological problems in the individual, which seriously affects the family nucleus, as well as the patient's relations with the social environment.<sup>8</sup>. Its treatment is multidisciplinary, due to the complexity of the maxillofacial deformity.<sup>9</sup>For the treatment of FLP, pre-surgical and surgical procedures are performed; and it is important to mention that there is a growing demand for surgical care to repair orofacial cleft defects.<sup>10</sup>

Therefore, it is essential for professionals to have basic knowledge on the subject, since there is a high prevalence of cleft lip and palate in South America. Therefore, the aim of the manuscript is to provide the professional with a broad overview of this malformation, its etiology, classification, complications, diagnosis and treatment.

## **MATERIALS AND METHODS**

A bibliographic, documentary study was carried out by searching for original scientific articles in meta-search engines such as: PubMed, Lilacs, SciELO and Google Scholar. For the research, the following DeCS in Spanish were used as search strategy: "cleft lip and palate", "cleft lip", "cleft palate", "orofacial cleft", "cleft lip", "cleft palate", "congenital anomalies", "cleft lip", and MeSH in English "Cleft lip", "Cleft lip and palate", "Cleft palate", "Congenital Abnormalities"; together with the Boolean operators AND and OR.

A total of 545 possible articles were identified, by keyword search, the search was limited to manuscripts published between 2012 to 2022, in English, Spanish and Portuguese, 133 articles were identified for reading titles and abstracts, finally 69 articles were selected for full text reading, open access and 23 articles were excluded among duplicates, non-relevant articles, theses, monographs, letters to the editor, clinical cases. After critical reading, 46 articles with relevance to the development of the topic were selected.

In addition, it is important to mention that for the development of this article it was necessary to consider information obtained from official web pages of governmental and world institutions that deal with the subject of study.

## RESULTS

### 3.1 Development of the lip and palate

The development of the face is established between the 4th and 10th week after conception.<sup>11</sup> From the fifth week of gestation, when the embryo is 3 mm long, the ectoderm near the neural plate folds in on itself to form the neural tube, then the special cells of the neural crest differentiate to form a special ectomesenchyme, then the ectomesenchyme migrates over and around the head and participates in the formation of the 5 facial prominences that will surround the stomodeum or primitive oral cavity.<sup>12</sup> These prominences that will form the face are: a frontonasal (central) prominence and paired maxillary and mandibular prominences.<sup>13</sup>

Later, within the fifth week, the nasal placodes will develop and as these widen until the sixth week, the center of the placode invaginates, thus dividing the frontonasal prominence into the medial and lateral nasal process.<sup>14</sup> These processes will continue to grow until the seventh week and then fuse to form the intermaxillary process; this will eventually give rise to the philtrum (forms the middle part of the upper lip), the premaxillary component of the maxilla (originating the upper incisors) and the primary palate; subsequently the lateral nasal process will give rise to the alar base and nasal wings.<sup>13,15</sup>

At this time, the palatal processes also extend medially from the paired maxillary prominences, hence the fusion of these palatal processes will give rise to the secondary palate as early as the 9th embryonic week.<sup>15</sup> However, the upper lip and primary palate must complete their formation before secondary pathogenesis begins.<sup>13</sup>

The formation of the palate involves the growth of the palatine processes, their elevation, their fusion and the elimination of the epithelial raphe at the fusion site. The lateral palatine processes, which are the precursors of the secondary palate, develop from the maxillary processes during the sixth week and at first these will grow medially and downward; on each side of the tongue<sup>14,16</sup>. As the mandible grows downward and forward, the position of the tongue will descend and the palatine processes will have to rotate to a position horizontal to the tongue and then undergo intramembranous ossification to form the palatine process of the maxilla and the palatine bone.<sup>11</sup>

After elevation, the palatine processes begin their fusion rapidly behind the incisive foramen and extend posteriorly to close the palate like a "zipper" and terminate at the uvula.<sup>13</sup>

It is important to mention that any error during fusion of these anatomical structures during the first trimester of pregnancy will result in a cleft lip or palate, morphological errors of formation leading to cleft palate include inadequate growth of the palatal processes, failure of elevation and fusion of the process, and secondary degradation after fusion.<sup>17</sup>

On the other hand, cleft lip occurs due to the lack of fusion of the frontonasal and maxillary processes, which results in a cleft of variable extension through the lip, alveolus and nasal floor. It should be noted that the common term for this condition is "cleft lip", however, this term has fallen into disuse due to its degrading connotation of inferiority, since it is related to the term hare, for this reason the most appropriate terms for the defect are cleft lip or cleft lip.<sup>18</sup>

### 3.2 Etiology

The etiology of cleft lip and palate is multifactorial and can be affected by both genetic and environmental factors.<sup>19</sup> The likelihood of recurrence of cleft lip or cleft palate in a family is high

and depends on the number of family members with one or more abnormalities, and the timing and magnitude of exposure to environmental risk factors.<sup>20</sup>

Several mutations and genetic diseases are the cause of facial defects, for this reason, it is important to mention that orofacial clefts can also present with different syndromes<sup>21</sup> such as Pierre Robin syndrome, Sticklers syndrome, Treacher Collins syndrome, Velocardiofacial syndrome, Patau syndrome, Edwards syndrome, Down syndrome, Van Der Woude syndrome, hemifacial microsomia, ectodermal dysplasia, among others.<sup>21,22</sup>

On the other hand, environmental factors such as tobacco, alcohol, drugs, deficiency of folic acid, zinc, vitamins and other microelements have a great effect on pregnancy during the first trimester of gestation.<sup>21</sup>. Some medications related to clefts are retinoids, steroids and anticonvulsants, such as phenobarbital and phenytoin, some anti-inflammatory drugs, antineoplastic drugs.<sup>13</sup>. maternal diseases such as: threatened miscarriage, bronchial asthma, diabetes Mellitus<sup>23</sup>diabetes mellitus<sup>24</sup>Exposure to chemicals, solvents and radiation may increase the risk of having a child with FLAP. Other factors related to the increase of orofacial clefts are low socioeconomic status and level of education.<sup>25</sup>.

### 3.3 Classification

Orofacial clefts involve several structures such as: the soft palate, the hard palate, the alveolar process and the lip; on the other hand, it must be taken into account that this congenital malformation can manifest unilaterally, bilaterally, combined or isolated.<sup>9</sup>. A proper classification is essential because the different types of oral clefts can be variably associated with additional anomalies and chromosomal disorders; thus, over the years, several different classification systems have been presented, based on the morphological, anatomical or pathological characteristics of the orofacial clefts.<sup>11</sup>. Thus, we have several classifications used in the past, such as the classification of Davis and Ritchie 1992<sup>26</sup>, Veau Victor 1931<sup>9</sup>, Kernahan and Stark 1958 and 1971<sup>17</sup>Otto Kriens 1989<sup>12</sup>among others.

There is also a current classification presented by the WHO and it is the Classification of International Classification of Diseases and Related Health Problems, 10th edition (ICD-10), which is presented below.

Lip, mouth and palate malformations<sup>27</sup>.

(Q35) Cleft palate.

- (Q35.0) Cleft hard palate, bilateral.
- (Q35.1) Cleft hard palate, unilateral.
- (Q35.2) Cleft soft palate, bilateral.
- (Q35.3) Cleft soft palate, unilateral.
- (Q35.4) Cleft hard palate and soft palate, bilateral.
- (Q35.5) Cleft hard palate and soft palate, unilateral.
- (Q35.6) Cleft palate, midline.
- (Q35.7) Fissure of the uvula.
- (Q35.8) Bilateral cleft palate, not otherwise specified.
- (Q35.9) Unilateral cleft palate, not otherwise specified.

(Q36) Cleft lip.

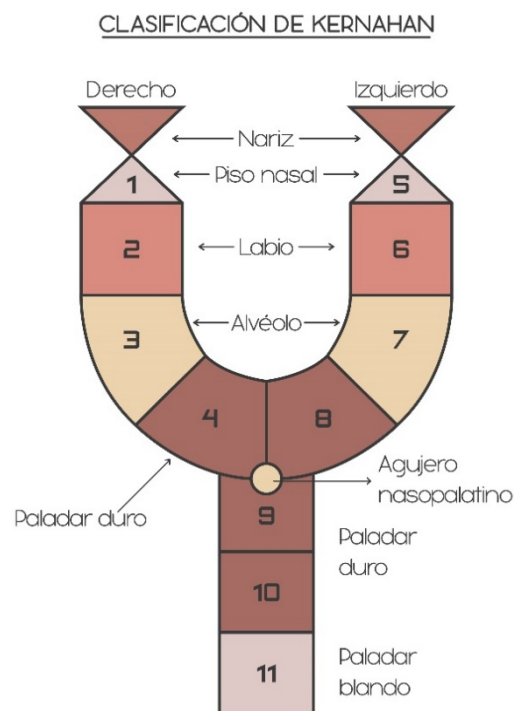
- (Q36.0) Cleft lip, bilateral.
- (Q36.1) Cleft lip, midline.
- (Q36.9) Cleft lip, unilateral.

(Q37) Cleft palate with cleft lip

- (Q37.0) Cleft hard palate with cleft lip, bilateral.
- (Q37.1) Cleft hard palate with cleft lip, unilateral.
- (Q37.2) Cleft soft palate with cleft lip, bilateral.
- (Q37.3) Cleft soft palate with cleft lip, unilateral.
- (Q37.4) Cleft hard palate and soft palate with cleft lip, bilateral.
- (Q37.5) Cleft hard palate and cleft soft palate with cleft lip, unilateral
- (Q37.8) Cleft palate with bilateral cleft lip, not otherwise specified.
- (Q37.9) Cleft palate with unilateral cleft lip, no other specification<sup>27</sup>.

However, it is important to mention that the most widely used classification, due to its simplicity, is that of Kernahan and Stark 1958 and 1971 (fig. 1).<sup>17</sup>.

**Figure 1** Kernahan and Stark classification of clefts.



## 1.4 Complications associated with cleft lip and palate

### 1.4.1 Feeding and nutrition problems.

They arise because babies are unable to suck their mother's nipple or bottle, this complication can cause dysphagia because there is no proper sealing of the oral cavity.<sup>9</sup> Consequently, the amount of milk or food ingested will not be sufficient and will affect the baby's growth and nutrition.<sup>22,28</sup> It should be noted that bronchoaspiration is another complication due to the communication between the palate and the nares; due to poor handling of nasopharyngeal secretions, milk or both.<sup>28</sup>

There are several methods for feeding infants with LPH problems, for example the positions of the infant at the time of feeding such as: "modified soccer method" or "Dancer's hand position", the baby should be kept in an upright position, so that the milk flows downwards and helps to prevent choking.<sup>29</sup> In fact, it is advisable to feed for 10 minutes and no more than 30 minutes, eight to ten times a day, and breastfeeding should be done at least every two to three hours. It

is also necessary for the baby to burp frequently due to the amount of air swallowed during feeding.<sup>30</sup>

On the other hand, there are different feeding devices on the market such as Mead Johnson, Haberman and Mini-Haberman bottles, Pigeon and the Playtex Feeder bottle, as well as special teats such as: MAM ventilated teat, NUK cleft palate teat and conical teat.<sup>30</sup> and special teats such as: MAM Ventilated Teat, NUK Cleft Palate Teat and Conical Teat. Other existing feeding methods are feeding plates and cup devices.<sup>31</sup>

#### **3.4.2 Hearing problems**

Hearing loss or otitis is caused by a dysfunction and horizontalization of the Eustachian tubes, which link the middle ear to the pharynx.<sup>28</sup> Consequently, recurrent otitis media is a complication in which fluid accumulates in the middle ear; this is due to the abnormal action of the Eustachian tube opening.<sup>22</sup>

#### **3.4.3 Speech problems**

Due to velopharyngeal dysfunction, the soft palate has the inability to move upward and generate a contact with the nasal cavity.<sup>22</sup> This velopharyngeal insufficiency is characterized by hypernasal speech or nasal voice and nasal air emission. If there is no closure of the velopharyngeal sphincter, the child lacks the aerodynamic conditions necessary for the adoption of normal articulation during speech development and will lead to pathological and incomprehensible articulation, it should be noted that the most notable articulatory errors during speech occur when articulating consonants that require high pressure in the oral cavity.<sup>7</sup>

#### **3.4.4 Airway and sleep-disordered breathing problems**

Patients with cleft palate experience higher rates of obstructive sleep apnea. The cause of obstructive sleep apnea is multifactorial, however, in these patients it may be caused by abnormal skeletal and soft tissue anatomy, which may include maxillary hypoplasia, palatal and pharyngeal muscle dysfunction or inferior hyoid bone position.<sup>16</sup>

#### **3.4.5 Dental problems**

Dental problems involve abnormalities in the size and shape of the teeth, as well as anomalies in the position of the teeth, delayed formation and eruption of the permanent teeth.<sup>22</sup> Crowding, overcrowding, supernumerary teeth.<sup>28</sup> High prevalence of dental caries, periodontal disease and malocclusions.<sup>32</sup>

#### **3.4.6 Aesthetic problems**

The facial region is the most affected and visible part of this malformation, so the treatment should also be focused on improving the aesthetics and function of the patient.<sup>33</sup>

Children with FLP generally have a concave profile, inadequate support for the projection of both the tip of the nose and the anterior part of the upper lip, visually diminished upper incisors, and often have a crossbite and inverted bite, all due to maxillary hypoplasia, which contributes to facial deformity.<sup>34</sup>

#### **3.4.7 Psychological problems**

They may suffer from depression, anxiety and lack of esteem and are unable to communicate at school.<sup>22</sup> likewise the impact on the parents causes guilt or rejection; which implies a delay both psychoemotional and in the therapeutic management.<sup>28</sup> Multidisciplinary approaches with long-term treatment are very important to improve health and life.<sup>21, 35</sup>

#### **3.4.8 Fistulas Oronasal**

The cleft of the primary or secondary palate allows a link between the nasal and oral cavities. Persistent or recurrent oronasal fistulas may occur within days or years after palatal repair.<sup>16</sup>

#### **3.4.9 Jaw growth problems**

The restriction of maxillary growth could be related to the effects of healing from cleft palate surgeries, and the earlier timing of palatal repair, resulting in severe maxillary hypoplasia.<sup>16</sup>

**3.5 Diagnosis**

**3.5.1 Prenatal Diagnosis**

A prenatal diagnosis of cleft lip and palate is critical to establish long-term treatment planning, prognosis, and appropriate parental counseling. Although not a routine procedure, according to the American Institute of Ultrasound in Medicine, accurate evaluation of craniofacial malformations is generally possible with ultrasound performed during pregnancy.<sup>36</sup>

For prenatal diagnosis of oral clefts we have conventional ultrasound, three-dimensional ultrasound and magnetic resonance imaging (MRI).

**3.5.1.1 Conventional and three-dimensional ultrasound**

This test is performed through the emission of sound waves that are capable of producing an image of the fetus, achieving a precise diagnosis of this malformation from the 13th week of gestation (second trimester of pregnancy), and the closer you are to the delivery date, the more evident the diagnosis will be through this study.<sup>9, 37</sup>

The accuracy of ultrasound for prenatal diagnosis of cleft lip and/or palate also depends on many factors, including the experience of the ultrasonographer, fetal position, maternal body type, cleft type, amount of amniotic fluid, gestational age, gestational age, and the type of cleft.<sup>36</sup>gestational age<sup>37</sup>.

Compared to 2D studies, three-dimensional ultrasound has a higher diagnostic accuracy in these malformations.<sup>16</sup>and has demonstrated the ability to detect a cleft palate when a cleft lip has been previously detected on 2D ultrasound.<sup>15</sup>

**3.5.1.2 Magnetic Resonance Imaging**

MRI is the gold standard for the evaluation of possible associated intracranial abnormalities in the setting of cleft lip or cleft palate. Prenatal MRI can help characterize and confirm the cleft, as well as associated intracranial and extracranial findings.<sup>16</sup>

**3.5.2 Clinical Diagnosis**

It is performed at birth, because its morphological defect is evident. Although, among the most evident findings at the time of diagnosis, are the deviation of the philtrum with respect to the vertical axis of the patient's face, which is directed to the altered nostril, the tip of the nose approaches towards the unaffected side....<sup>9</sup>.

**3.6 Treatment**

The American Cleft Palate-Craniofacial Association stresses the importance of multidisciplinary management of these patients within the first few days of life. Often, patients with LPH require the care of multiple medical specialties (Table I) and should be monitored in a multidisciplinary clinic into early adulthood<sup>15</sup>.

**3.6.1 Cleft lip and/or palate team**

Due to the complexity of maxillofacial deformity, it requires a multidisciplinary management involving different areas:

- 1) Surgical areas: maxillofacial surgery, plastic surgery and anesthesia.
- 2) Non-surgical: Orthodontics/orthopedics, odontopediatrics<sup>38</sup>Otolaryngology, audiology, phoniatics, genetics, pediatrics, psychology, nursing, dentistry and a managing coordinator.<sup>9,22,39</sup>.

Table I. Basic cleft care		
Basic cleft care		
Age	Medical treatment	Surgery
Prenatal	• Genetic counseling	



	<ul style="list-style-type: none"> <li>• PHL consultation for feeding</li> </ul>	----
0-5 months	<ul style="list-style-type: none"> <li>• PHL for feeding and growth</li> <li>• Hearing control</li> <li>• NAM (if indicated)</li> </ul>	<ul style="list-style-type: none"> <li>• Cheiloplasty</li> <li>• Ear tubes (if they have OMC)</li> </ul>
9-12 months	----	<ul style="list-style-type: none"> <li>• Palatoplasty</li> <li>• Ear tubes (if they have OMC)</li> </ul>
1-4 years	<ul style="list-style-type: none"> <li>• Introduction to pediatric dentistry</li> <li>• Assess language development.</li> </ul>	----
4-6 years	<ul style="list-style-type: none"> <li>• Evaluate for DVF</li> </ul>	<ul style="list-style-type: none"> <li>• Corrective speech surgery</li> <li>• Lip revision if necessary</li> <li>• Minor nasal surgery if necessary</li> </ul>
6-12 years	<ul style="list-style-type: none"> <li>• Orthodontics</li> <li>• Assessing school/psychosocial adjustment</li> </ul>	<ul style="list-style-type: none"> <li>• Alveolar bone graft</li> </ul>
12-21 years	<ul style="list-style-type: none"> <li>• Orthodontics</li> </ul>	<ul style="list-style-type: none"> <li>• Orthognathic Surgery</li> <li>• Definitive rhinoplasty</li> </ul>

CMO, chronic otitis media; NAM, nasopalveolar molding; SLP, speech-language pathology; VPD, velopharyngeal dysfunction.

**Source:** Taken from Worley ML, Patel KG, Kilpatrick LA. Cleft Lip and Palate. Clinics in Perinatology. 2018;45(4):661-78.

### 3.6.2 Pre-surgical Orthopedics

The general term presurgical orthopedics (PSO) refers to any manipulation of the infant's alveolar segments prior to repair of the lips and nose.<sup>40</sup> Management of cleft lip and palate includes presurgical orthopedics with alveolar molding (NAM), lip tape, and lip bonding initiated in the first month of life.<sup>41</sup> In this way we seek to align and approximate the maxillary segments, lift and model the cartilage of the maxillary cartilage.<sup>35</sup>and model the affected alar cartilage and in bilateral cases, to elongate the columella.<sup>39, 42</sup>

### 3.6.3 Surgical treatment of cleft lip and palate

Prior to surgery, the "over ten" rule must be considered, i.e. the child must be: 10 weeks of age, 10 pounds and 10 g/dL hemoglobin.<sup>15,42</sup> The surgical approach is performed in three stages. During the first 3 to 6 months of life the reconstruction of the affected lip (cheiloplasty) is approached to avoid airway problems associated with forced nasal breathing in early childhood and post anesthetic apnea, then between 9 and 12 months the reconstruction of the palate (palatoplasty) is approached.<sup>15</sup>

### 3.6.4 Secondary Surgeries

After cheiloplasty and palatoplasty, patients will need other surgeries that serve to complement details of the lip and nose, also to improve the voice, as well as bone grafts for alveolar fissure, rhinoseptoplasty and possibly orthognathic surgery.<sup>39</sup>

## DISCUSSION

Cleft lip and palate are the most common craniofacial malformations.<sup>21,43</sup> When it occurs at a very early embryonic stage, a greater number of facial structures are usually affected.<sup>25,44</sup> The treatment of this type of malformation will require a multidisciplinary team formed by several professional specialists.<sup>21,45</sup> Because children with these fissures will need various multidisciplinary surgical procedures to reconstruct the affected structures and should be monitored frequently during their first months of life and into early adulthood.<sup>15</sup> It is also important to mention that there is a growing demand for surgical care to repair orofacial cleft defects, which is why it is important that children with cleft lip and palate be monitored frequently during their first months of life and into early adulthood.<sup>10</sup> For this reason it is important for dental professionals to know how this malformation develops and what are the complications if not treated early.

Most of the authors in their articles report that the etiology is multifactorial.<sup>20,23,25,44,46,47</sup> However, factors such as genetics, tobacco, alcohol, ethnicity, maternal malnutrition and maternal age, among others, have been found to be related.<sup>48,49</sup> Prenatal control is of great importance, not only for the prevention of this pathology but also to avoid maternal and perinatal morbidity.<sup>45,50</sup> In addition, it would be of great help that professionals provide advice about these risk factors to reduce the incidence of malformations.

On the other hand it is important to mention that the best technique to diagnose this facial deformity is the three-dimensional ultrasound and magnetic resonance imaging as they improve the accuracy of prenatal diagnosis of orofacial clefts.<sup>36</sup> There are different classifications and the most used by surgeons is the Kernahan and Stark classification, in the shape of a horseshoe, for its ease of application.<sup>17</sup> because of its ease of application.

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