World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Prevalence of cleft lip-alveolo-palate in pediatric patients at the Vicente Corral Moscoso hospital, period 2016-2020

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World Journal of Advanced Research and Reviews, 2023, 18(01), 1229–1240

Publication history: Received on 15 March 2023; revised on 23 April 2023; accepted on 27 April 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.1.0747

Abstract

Cleft lip-alveolar-palatal fissures (FLAP) are one of the most frequent congenital malformations nationwide. Its etiology is complex and both genetic and environmental factors are directly associated with a higher number of births with this anomaly. The aim of this work is to determine the prevalence of FLAP in pediatric patients of the Vicente Corral Moscoso Hospital in the city of Cuenca in the period 2016-2020. For this purpose, the collection of medical records of patients with FLAP under 17 years of age between the period of 2016 to 2020 was carried out. The data obtained from the 582 records, were subjected to statistical analysis using the computer program IBM SPSS Statistics version 20; gender, age range, type and location of the fissure were analyzed. The results showed that 69.6% of the study sample belonged to the male gender and 30.4% to the female gender. The highest prevalence in age corresponds to the year with a percentage of 24.7%. According to its location, the most common type of cleft corresponds to the mixed cleft with 43.13%; and finally, according to the type, cleft of the hard palate and soft palate with unilateral cleft lip was the one with the most reported cases with a percentage corresponding to 24.2%.

Keywords: Prevalence; Cleft lip; Cleft palate; FLAP; Harelip

1. Introduction

1.1. Problem statement and justification

Congenital malformations have been recorded since the beginning of mankind, as evidenced by engravings and figures of past civilizations. It is considered that lip-alveolar-palatal fissures (FLAP) date from 2400 to 1300 B.C. (1).

FLAPs correspond to congenital defects caused by a failure in the union of some embryonic tissues of the facial mass, especially the upper lip, the premaxilla, the hard palate and the floor of the nostrils during the sixth week of intrauterine life, while exclusive clefts of the palate occur in the eighth week of gestation. (2) (3) (4)

Its etiology is complex and both genetic and environmental factors such as vitamin deficiency (folic acid, vitamin B6 and B12), smoking (alteration of metabolic pathways by aromatic and heterocyclic amines), alcohol consumption (inhibition of retinoic acid synthesis), drug use (vasoactive, antiepileptic, acne, psoriasis, cancer) and exposure to chemicals (cleaning products, cosmetics) are directly associated with a higher incidence of newborns with this anomaly (5) (6) (7). (5) (6) (7) (8) (9) (10)

The condition is manifested by characteristic symptoms affecting respiratory, swallowing, articulatory and auditory mechanisms. (11) In addition, infants with FLAP are at increased risk for abnormalities such as: supernumerary teeth,

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dental agenesis, dental deformities (especially in alveolar fissures); caries and periodontal disease are also more common in children with this anomaly. (12)

Cleft lip and cleft palate occur together or separately. The former with or without palate occurs in 1 per 1000 births; while the latter occurs in only 1 per 2500 births. Of the patients who suffer from it, only 25% know its cause. And the remaining 75% correspond to multifactorial origins, being 20-25% due to a family history (3).

Its management requires interdisciplinary work that includes: plastic and maxillofacial surgery, orthodontics and orthopedics, speech therapy, otolaryngology, psychology, among others (8).

Therefore, the present study, seeks to know the prevalence of lip-alveolus-palatal fissures in the Vicente Corral Moscoso hospital during the period 2016-2020 in the city of Cuenca to update the statistical information in order to contribute in future research work.

General objective

To determine the prevalence of FLAP cases considering clinical histories of pediatric patients (0-17 years) who were attended at Vicente Corral Moscoso Hospital in the period 2016-2020 in the city of Cuenca, Azuay province, in order to characterize them to various demographic variables.

Specific objectives

- To analyze the medical records by using tables and filters to count the number of cases diagnosed with FLAP.
- To evaluate the data obtained using the computer program IBM SPSS Statistics version 20 (IBM Corporation, Armonk, NY, USA) to express in number and percentage the study sample in relation to different factors such as sex, age and type of FLAP.
- Interpret the results through graphs and tables to contrast the results obtained with previous studies.

1.2. Hypothesis

The prevalence of FLAP in the Vicente Corral Moscoso Hospital in the city of Cuenca in the period from 2016 to 2020 is in relation to the sex of the patient.

1.3. Theoretical framework

1.3.1. Epidemiology

The prevalence of FLAP is higher in continents such as Asia and America. A study led by the International Perinatal Database on Common Orofacial Clefts through the WHO human genetics program in 2003, showed that the incidence was highest in Japan and lowest in South Africa. (5)

The accepted worldwide incidence of FLAP is 1 per 1000 births. However, it depends on ethnicity, place of birth and race. The incidence of the anomaly is 0.3 per 1000 births in African populations; 0.7-1.3 per 1000 births in European populations; 1.4-2.1 per 1000 births in Asian populations; and, 3.6 per 1000 births in American populations. (13) At the family level, the risk of FLAP depends on several factors. If there is one child in the family with the anomaly, the risk of the next child being affected by it increases by 2-5%; if there is more than one child with a cleft, the risk increases by 10-12%. If, in addition, there is a coexisting syndrome in the family, the risk increases to 50%. Studies have shown that the prevalence of FLAP is significantly higher in maternal twins (40-60%) compared to paternal twins (3-5%). Regarding demographic studies, in Turkish populations, it was shown that the prevalence increased in the eastern regions, in relation to the use of pesticides and chemicals used in agriculture and animal husbandry (5).

1.3.2. Etiology

- Cleft lip and palate is considered a common birth defect, which results in medical, psychological and social problems that affect the life of the patient and his or her family. Its etiology is multifactorial and complex (5).
- Vitamin deficiency: Vitamins are essential organic components that catabolize metabolic reactions, and their deficiency results in multiple systemic complications. Several studies indicate that deficiency of Thiamine (B1), Pantothenic Acid (B5), Biotin (B8) and Folate (B9) are especially linked to the development of FLAP, as they directly affect the synthesis of specific proteins that are related to the formation of the palate (14).
- Smoking: Cigarette smoke is a complex aerosol comprising about 400 compounds that are detrimental to health. In the case of pregnant women, smoking was considered the main causative agent of FLAP in 2014 by

the U.S. Surgeon General's Report. While the exact mechanism is unknown, there are two theories. The first points to a direct interaction between tobacco products with neonatal tissues, inducing hypoxia due to altered nicotine-mediated angiogenesis and vasoconstriction, which disrupts palatal fusion in animal models. The second theory mentions that smoking affects DNA methylation in the fetus, which has a direct impact on gene expression, responsible for the formation of the lip and palate.(15)

- Alcohol consumption: Alcohol consumption during pregnancy and its possible complications have been a subject of long discussion. In the United States, about 10% of women have consumed alcohol while pregnant and about 2% are alcoholics during this stage. 1-3 of every 1000 births have fetal alcohol syndrome, and 9% to 18% of these have some form of FLAP.(16) Although the exact mechanism by which alcohol increases the risk of developing this anomaly is not defined, it is known that it reduces folate levels while inhibiting its metabolism; it also inhibits the synthesis of retinoic acid, which is necessary for the formation of the neural crest.(5)
- Drug use: The first trimester of gestation is linked to the development of oral abnormalities. Medications used in treatments for acne, psoriasis, arthritis and cancer increase the risk of the fetus developing FLAP, as do vasoactive drugs such as aspirin and ibuprofen. (5) In addition, antiepileptic drugs such as Primidone, Carbamazepine and Lamotrigine are teratogenic, as they contain folate antagonist properties, which also increase the risk of congenital heart disease. (17)
- Exposure to chemicals: if the mother ingests food with high doses of pesticides, is in contact with cleaning products or cosmetics, the possibility of developing congenital anomalies increases (5).
- Traumatic/emotional disturbances: The loss of amniotic fluid or any alteration of the intrauterine environment can result in congenital defects during the first trimester of pregnancy (embryogenesis/organogenesis), and this is mainly associated with situations of high levels of stress to which the mother is subjected. (5)
- Age of parents: In the case of cleft lip, the age of the parents does influence the development of cleft lip. The risk increases if the mother's age exceeds 29 years, as well as if both parents are older than this age. However, cleft palates are not directly associated with this factor (18).
- Other syndromes accompanying FLAP: Approximately 30% of patients with FLAP have syndromes such as Pierre Robin, Van der Woude, ectrodactyly and ectodermal dysplasia. In addition, patients with FLAP are exposed to functional limitations such as maxillofacial growth, language abnormalities, nutritional deficits and hearing loss. (5)

1.3.3. Embryology

The embryology of the head is composed of multiple interactions between cells and the coordination of multiple transduction signals. The development of the face is a coordinated process that includes the formation of the lip, palate, nose, and mouth; which occurs between the fourth and twelfth week of gestation. (13)

Specialized neural crest cells migrate to the fronto-nasal and visceral regions in the fourth week of gestation, resulting in the five facial structures of the primordium: these constitute the maxillofacial massif (mandibular processes, maxillary processes and the fronto-nasal process). And, although cleft lip and cleft palate occur simultaneously in most cases, they have a different embryonic origin (13).

The embryological development of the head and neck is given by the formation of the gill arches in the fourth and fifth week of gestation, from the mesenchymal tissue and are separated by brachial clefts.

1.3.4. Embryology of the lip

Normal lip development occurs between the fourth and eighth week of intrauterine life. The maxillary processes begin to grow medially at the lateral parts and fuse first with the lateral nasal process to give rise to the upper lip and cheeks. The lateral nasal processes give rise to the ala of the nose. The maxillary processes fuse with the medial nasal process on each side and give rise to the nostrils around the fifth week of gestation.

The fusion of the medial nasal process guides the formation of the intermaxillary segment. This then fissions with the maxillary process and leads to the formation of the philtrum and the middle third of the upper lip, primary palate, the central part of the nose and the nasal septum. If this process fails, cleft lip develops.

1.3.5. Embryology of the palate

The two maxillary prominences grow and due to this the medial nasal prominences fuse and form the intermaxillary segment, which develops from the labial component which in turn forms the philtrum of the upper lip, the maxillary component which carries the 4 incisor teeth and the palatine component.

The palatal prominences are positioned horizontally on the tongue and fuse to form the secondary palate; this occurs in the seventh week of intrauterine life. The incisor foramen is formed in the midline of the fusion of the palatal prominences on the other hand the fused palatal prominences join with the triangular primary palate and thus, the nasal septum joins with the cephalic face of the formed palate.

As for the facial fissures when there are deformities, they are divided into 2 groups, being the incisor foramen the reference point between the anterior and posterior fissures.

- The deformities of the anterior sector are the lateral labial fissure, fissured maxilla and fissure between the primary and secondary palate.
- Deformities of the posterior sector are secondary cleft palate and fissure of the uvula.

Oblique facial fissures are formed because the maxillary prominence does not fuse with the lateral nasal prominence. When there is no union between the middle nasal process and the maxillary process, the lateral labial fissure is formed.

When there is no union between the middle nasal processes, the medial labial fissure is formed. When there is no union between the lateral nasal process and the maxillary process, the oblique facial cleft is formed. (13)

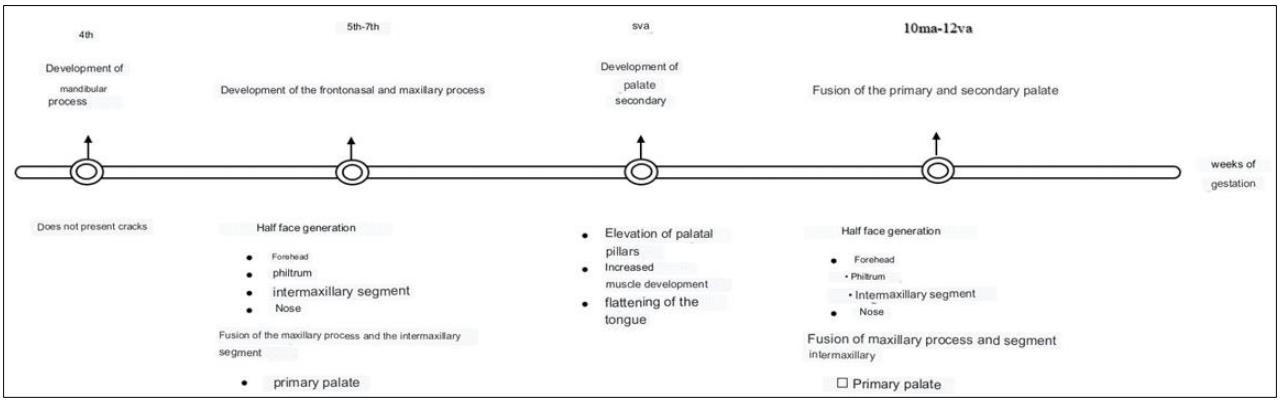

Figure 1 Embryogenesis of the lip and palate.

1.4. Classification

Within these anomalies, structures such as the lip, the alveolar process, the hard palate and the soft palate are altered. They can be isolated, combined, unilateral or bilateral. In other words, they have different characteristics in relation to their degree of severity, which leads to different prognosis and treatment. Therefore, their classification should allow a detailed description of the fissure (19).

Most typifications refer to the anatomical segments involved in the fissure, but not how severely it is affected, with the exception of Kernahan, which has a wider scope since it graphs the type of fissure in a practical way. Unfortunately, neither does it specify the extent of tissue deficiency in the cleft, as is the case of Mortier's classification, which, in turn, does not include the diameter of the lip and palatal cleft. (19)

1.4.1. Veau's classification (1931)

Veau's classification is based on the degree of anatomical rupture of the primary and secondary palate, which generates speech problems. (20) It is one of the most used classifications, due to its simplicity and clinical relevance; it divides fissures according to morphological aspects in four large groups:

- Group I: soft palate fissures; it does not contemplate those that partially divide the uvula.
- Group II: hard and soft palate fissures, which can extend between the incisor foramen and the posterior border of the palate. It describes divisions of the roof of the mouth and soft palate, without involving the alveolar process or lip.
- Group III: soft and hard palate fissures extending unilaterally through the alveolar process (complete unilateral). The fissure feature is between the canine and lateral incisor, there is involvement of the uvula and the unaffected segment joins the nasal septum.

- Group IV: fissures of soft and hard palate extending bilaterally through the alveolar process (complete bilateral). There is uvula involvement and maxillary segments are not attached to the nasal septum (3).

1.5. Classification proposed by doctor Victor see

Table 1 Classification of Dr. Víctor Veau

Lip abnormalities _		**palate abnormalities _**	
Lip cleft complete	When there has not been fusion of the upper maxillary process with the labial philtrum and the floor of the nose has not been formed.	Type I	Cleft palate soft
Lip cleft incomplete	When there is partial fusion of the maxillary process with the labial philtrum , the floor of the nose is closed, but the orbicularis oris muscle is not properly oriented in a circular fashion.	Type II	Hard and soft palate cleft involving only the secondary palate.
Lip cleft cicatricial	When there is complete fusion of the maxillary process with the labial philtrum , but there is a small scar-like indentation in the labial red roll.	Type III	Unilateral complete cleft from the uvula through the incisive foramen and reaching one side of the premaxilla.
Lip bilateral crease	When there is no fusion of the labial philtrum with the two upper maxillary processes.	Type IV	Bilateral complete cleft from the uvula through the incisive foramen and reaching both sides of the premaxilla.

1.6. Stark and Kernahan embryogenic classification

In 1958 Kernahan and Stark designated the incisive foramen as the dividing point between the primary and secondary palate, which correctly describes the anomaly and leads to future classification schemes. (19)

Table 2 Stark and Kernahan embryogenic classification

cleft palate _ primary		**cleft palate _ secondary**	**Primary and secondary cleft palates**	
Unilateral	Total and subtotal	Total	Unilateral	Total and subtotal
Median	Total (absent premaxilla) and subtotal (rudimentary premaxilla)	Subtotal	Median	Total and subtotal
Bilateral	Total and subtotal	submucous	Bilateral	Total and subtotal

1.7. Treatment

The rehabilitation of FLAP patients comprises a complex problem where specialists in the medical and dental area are required; in addition, these patients have psychosocial difficulties. Therapy in infants takes place before the primary repair surgery, here, the orthodontist has the task of reducing the separation between the segments to stimulate the bony development of the palate. Surgical treatment is performed between the ages of 6 months to 2 years, when articulation of words begins. However, there are several treatment options, especially when it comes to replacing soft and hard tissue loss, including removable dental prostheses, fixed dental prostheses and prosthetic implants. (21)

- Cleft lip repair: To close the split in the lip, the surgeon makes incisions on both sides of the cleft and forms tissue flaps. The flaps are sewn together, and the lip muscles are included. The repair should create a more normal appearance, structure and function of the lip. If necessary, the initial nasal repair is performed at the same time.
- Cleft palate repair: Various procedures may be used to close the cleft and reconstruct the palate (hard and soft palate), depending on the child's situation. The surgeon makes incisions on both sides of the cleft and reattaches the tissue and muscles. The repair is then closed.

- Ear ventilation tube surgery. For children with cleft palate, ventilation tubes may be placed in the ears to reduce the risk of chronic fluid in the ears, which can lead to hearing loss. Ear ventilation tube surgery involves placing small coil-shaped tubes in the eardrum to create an opening to prevent fluid buildup.
- Surgery to reconstruct the appearance. Additional surgeries may be needed to improve the appearance of the mouth, lips and nose.

Surgery can significantly improve your child's appearance, quality of life, and ability to eat, breathe, and speak. Possible risks of surgery include bleeding, infection, poor healing, widening or elevation of scars, and temporary or permanent damage to nerves, blood vessels or other structures. (17)

2. Materials and methods

2.1. Population

The population consists of all those patients who attended the Vicente Corral Moscoso Hospital between 2016 to 2020.

2.2. Inclusion criteria.

All medical records of those patients with FLAP under 17 years of age between 2016 - 2020 were included in the sample.

2.3. Exclusion criteria.

Medical records without complete data.

2.4. Variables to be studied.

- Types of FLAP/Gender: Allows to determine the most frequent type of cleft by gender.
- Types of FLAP/Age Range: Allows to determine and classify the population by age attending Vicente Corral Moscoso Hospital.
- FLAP Type/Location: Allows analysis of the most frequent tissues in which FLAP occurs.

The analysis of the data will be carried out in percentages and proportions, with absolute and relative frequency, presented in frequency diagrams.

2.5. Data collection instrument

Data will be collected from the medical records of the Vicente Corral Moscoso Hospital to obtain clinical data on the child and diagnosis of the type of FLAP.

2.6. Procedure

2.6.1. Data collection procedure.

The clinical records will be analyzed to know the number of cases diagnosed with FLAP.

2.7. Statistical analysis

The data obtained, will be subjected to statistical analysis using the computer program IBM SPSS Statistics version 20 (IBM Corporation, Armonk, NY, USA). Qualitative variables will be expressed in number and percentage and the results will be presented in graphs and tables.

3. Results

The Vicente Corral Moscoso Hospital in a period from 2016 to 2020 treated 582 patients, in pediatric age, from 0 to 17 years, with cleft lip-alveolo-palatine, including

3.1. Index of patients according to sex

Table 1 Tabulation of patients according to sex

Sex					
		Frequency	**Percentage**	**Percentage valid**	**Percentage accumulated**
Valid	Man	405	69.6	69.6	69.6
	Women	177	30.4	30.4	100.0
	Total	582	100.0	100.0	

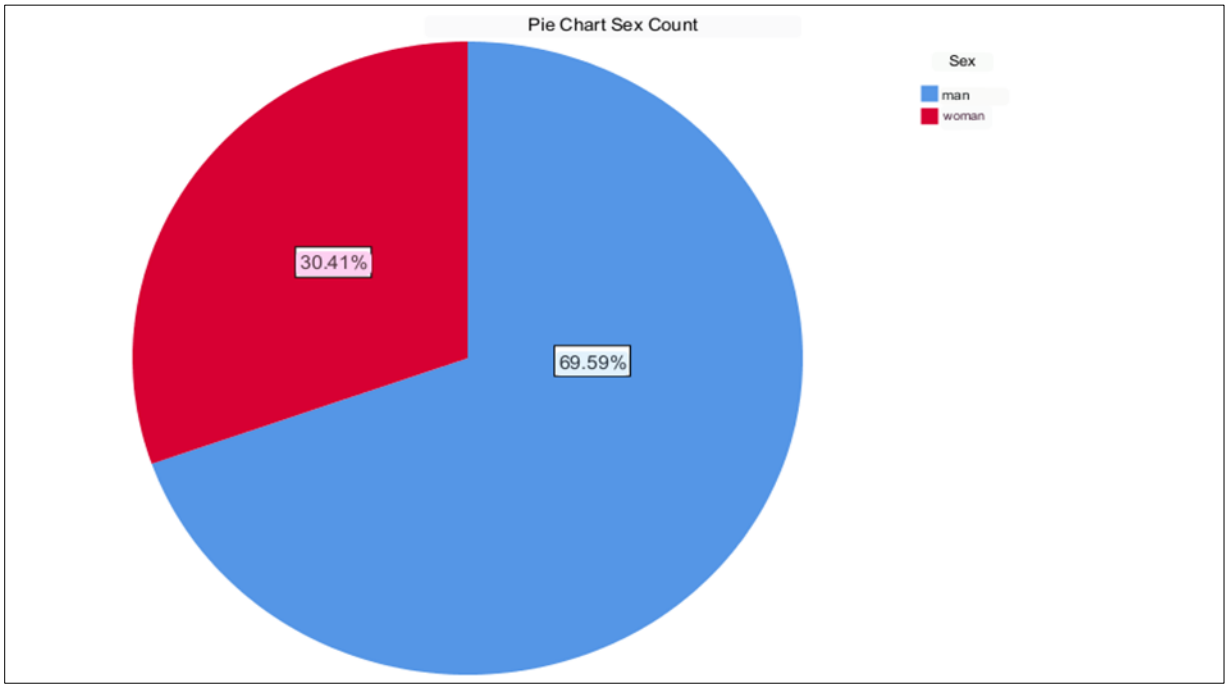

Figure 1 Percentage of patients with FLAP according to sex

It can be seen that, of the 582 infants cared for in the period 2016 to 2020, 69.6% corresponding to 405 patients belong to the male gender and 30.4% corresponding to 177 patients belong to the female gender, which It means that there is a higher prevalence in men than in women.

3.2. FLAP index according to the age of the patients

The results of the age variable show us that most of the cases were found in records of one-year-old patients with a percentage of 24.7% corresponding to 144 individuals, followed by records of newborn patients with 12, 4% corresponding to 72 individuals, the percentages of the other ages being considerably lower in relation to the percentage of the group of pediatric patients in their first year of age.

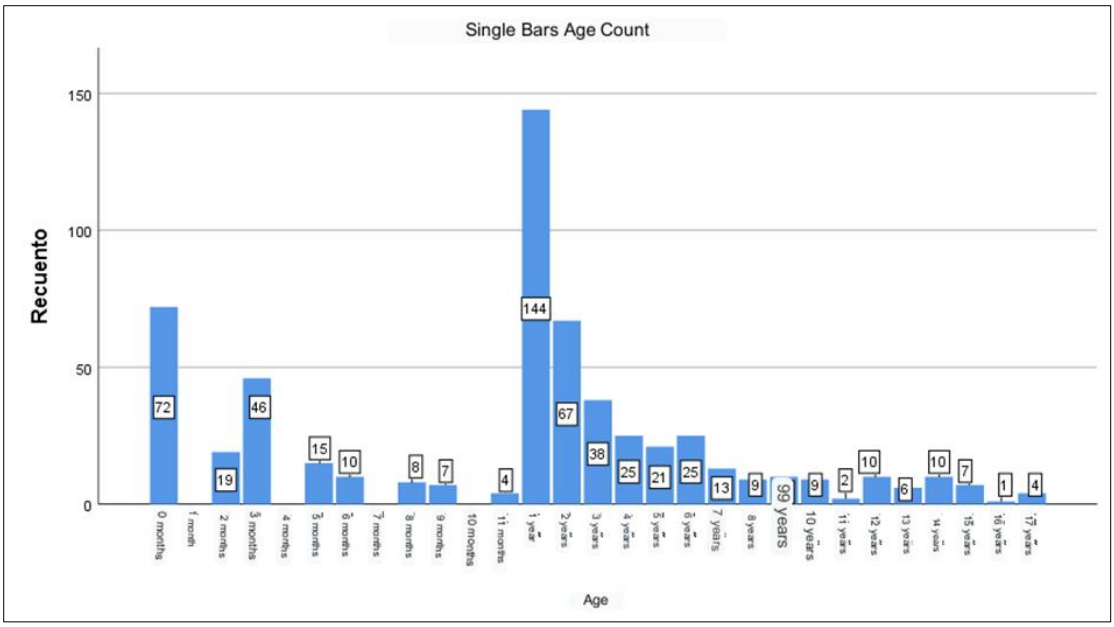

Figure 2 Percentage of FLAP according to age

3.3. FLAP index according to its location

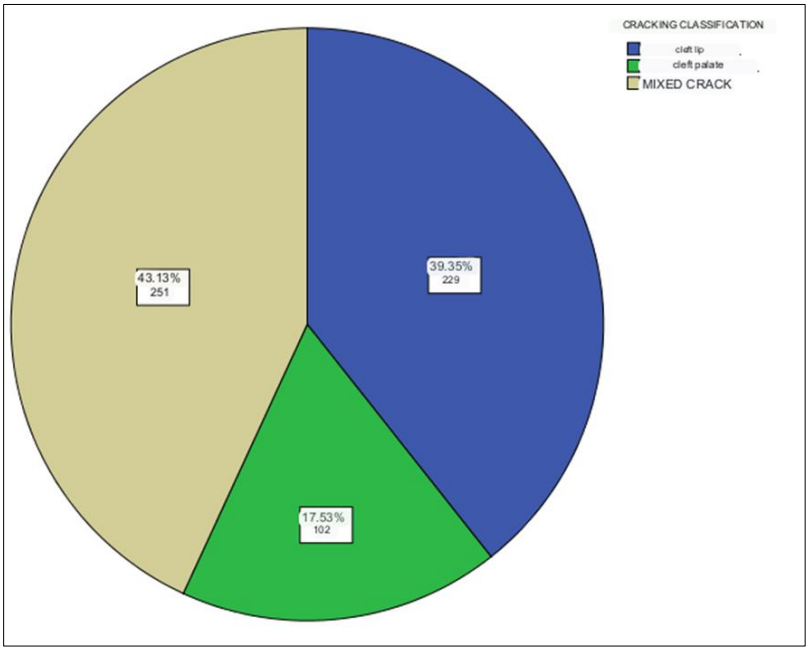

Figure 3FLAP percentages according to their location

According to the results, according to its location, the type of fissure that had the most prevalence in the period 2016 to 2020 corresponds with 43.13% to mixed fissure, that is, 251 patients attended the Vicente Corral Moscoso Hospital presenting this anomaly. Following this type, we find cleft lip with a percentage of 39.35%, which results in 229 patients with it; and, with a lower prevalence is cleft palate with 17.53% that obeys 102 patients with it.

3.4. FLAP index by type

Regarding the most frequent cleft lip-alveolo-palatine, 141 patients presented cleft hard palate and soft palate with unilateral cleft lip, which corresponds to 24.2% of all patients in the study sample. And, on the other hand, the anomaly with the lowest prevalence corresponds to the fissure of the uvula with a total of 3 patients, which corresponds to 0.5% of the total sample.

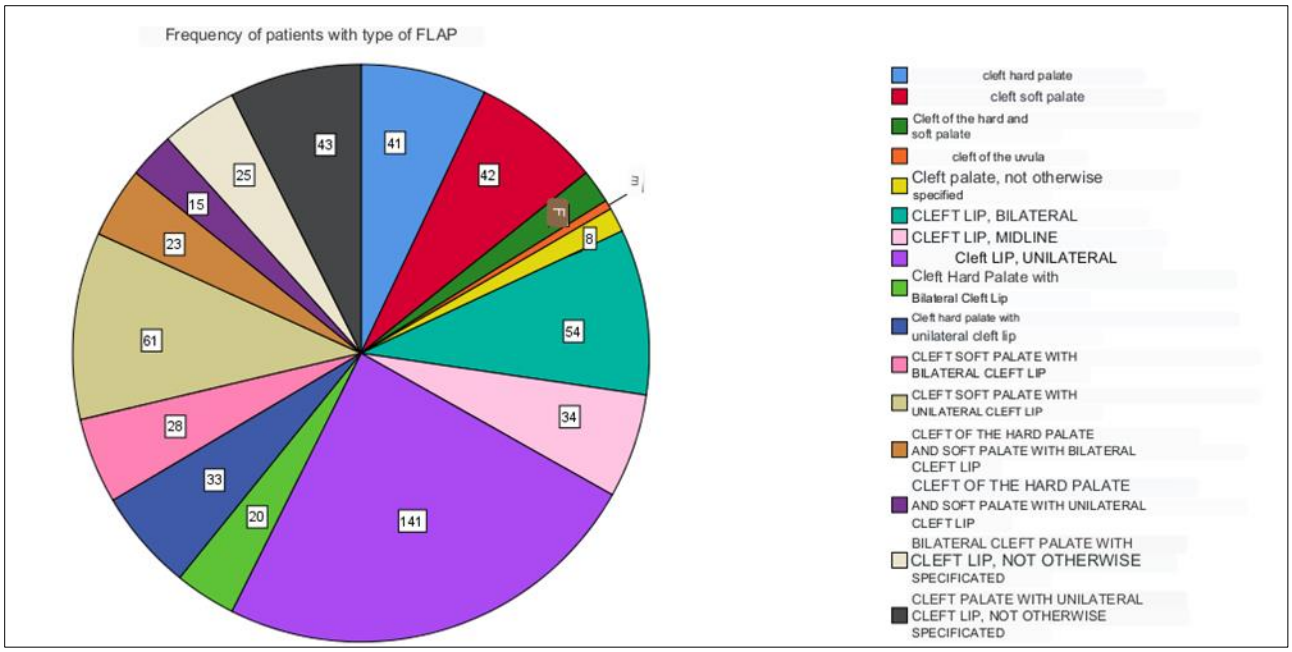

Figure 4 FLAP cases by type

3.5. Asymptotic chi- square test

To evaluate the impact of the FLAP in the study sample, the category of sex (independent) was related to the type of cleft lip-alveolo-palate (dependent), based on the following hypothesis: Ho: the variables are independent H1: the variables are dependent.

To contrast these hypotheses, the Chi-square test of independence was used, the same part of the assumption that the variables (Category, sex and type of crack) are independent; that is, there is no relationship between them. The results of the Chi Square test corresponding to the verification of these hypotheses were obtained using the SPSS program.

Table 2 Chi square test

Chi- square tests			
	Worth	**gl**	**Asymptotic sign (bilateral)**
Pearson's chi- square	0.235 to	2	0,889
likelihood ratio _	0.238	2	0.888
linear by linear association	0.005	1	0.945
N°. of cases valid	582		
to. 0 cells (.0%) have an expected frequency less than 5. The frequency minimum expected is 31.02.			

Table number 2 presents the asymptotic Pearson Sig Chi square test with a value of p = 0.889, which is compared with the Alpha of significance (assumed as 5%), which is higher to reject Ho. This information denotes that there are no indications of a dependency relationship between both variables and, therefore, it can be concluded that the variables are not related.

4. Discussion

The prevalence of fissures obtained in this study, according to sex, corresponds to 69.6% in men and 30.4% in women, which means that the majority of cases are in male patients, similar to other studies. According to age, it follows the expected patterns, with a higher percentage corresponding to the year of life with 24.17% (144 patients) while in the other ages it does not exceed 13%. According to the location, 43.13% correspond to patients with mixed clefts, followed

by clefts of the labial type with a percentage of 39.35% and the remaining 17.53% are due to clefts of a palatal nature. According to the type of fissure, predictable results were also obtained, being the hard palate and soft palate fissure with unilateral cleft lip with 24.2%.

In a research similar to the present study, conducted by Norma Caraguay at the Hospital del Niño "Francisco Icaza Bustamante" in 2018, entitled "Prevalence and genetic predisposition of cleft lip and cleft palate in pediatric patients. Study to be conducted at the Francisco Icaza Bustamante Hospital during the period from January 2015 to January 2017." Of the 1365 patients 1% (100 patients) had a diagnosis of cleft lip and palate, and met the inclusion criteria. Of the total sample studied (100 patients), the highest percentage 74% (74 patients) were older than 1 year of age and 26% (26 people) were younger than 1 year. (22) The result reported by Caraguay in 2018 is in relation to that obtained in the present study, since of the 582 patients admitted and diagnosed with cleft lip-alveolo-palate at the Vicente Corral Moscoso Hospital, 181 (31.09%) correspond to infants under 1 year of age and 257 (44.15%) to those older than 1 year of age.

Similarly, a study conducted in Peru by Regalado Cabanillas and Cerquín Vargas called "Prevalence of cleft lip and palate in patients treated at the regional teaching hospital Cajamarca 2015 - 2018, obtained that of the 70 cases analyzed, 71% (50 cases) corresponded to the male gender and 29% (20 cases) referred to the female gender. (23) This is related to our results since of the study sample corresponding to 582 patients, 69.59% belong to the male gender and 30.41% to the female gender.

A study carried out in Mexico in 2015 by García Rojas and collaborators, called: ''Prevalence of cleft lip and palate in a Pediatric Hospital of Tabasco'' obtained as a result that, of the total of 327 medical records, 71.25% (233 patients) present cleft lip and palate, 18.34% (60 patients) correspond to cases of cleft palate and the remaining 10.39% to lip fissures (34 patients). (24).

This, in comparison with the present study, have close proximity since, of the study sample 41.13%, that is, 251 patients present mixed clefts (lip and palate), 39.35% (229 patients) correspond to lip clefts and 17.53% (102 patients) are due to palatal clefts.

5. Conclusion

Within the following study, the following points can be highlighted:

- The analysis of clinical records at the Vicente Corral Moscoso Hospital in the city of Cuenca presented a total of 582 patients diagnosed with FLAP in the period from 2016 to 2020.
- In Cuenca, in the outpatient area of the Vicente Corral Moscoso Hospital presents higher prevalence of FLAP in men and patients older than 1 year.
- Of the cases reported from the medical records, unilateral cleft lip was the most representative.
- The type of FLAP is not directly related to the sex of the patient and is subject to the factors mentioned above.

Compliance with ethical standards

Acknowledgments

We hereby express our gratitude and appreciation to the teaching department of Vicente Corral Moscoso Hospital and the Faculty of Dentistry of the University of Cuenca-Ecuador.

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

The present research work does not contain any studies that involve information about any individual e.g. case studies, survey, interview etc.

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