



## The Genogram Characteristic of Cleft Lip and/or Palate Cases in Aceh

**Andi Akbar Ibhaliswan<sup>1\*</sup>, Budiman<sup>2</sup>, Khairan<sup>3</sup>, Mirnasari Amirsyah<sup>4</sup>, Jufriady Ismy<sup>5</sup>**

<sup>1\*,4</sup>Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Universitas Syiah Kuala, dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia

<sup>2</sup>Departement of Plastic and Reconstructive Surgery, Gatot Subroto Army Hospital, Jakarta, Indonesia

<sup>3</sup>Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia

<sup>5</sup>Department of Urology, Faculty of Medicine, Universitas Syiah Kuala, dr. Zainoel Abidin General Hospital, Indonesia

### ABSTRACT

**Objective:** To describe the characteristic of genogram of CL/P cases in Aceh with sociodemographic features and maternal pregnancy history. **Methods:** cross sectional study with retrospective approach. Data of patients underwent CL/P surgery at the Yayasan Senyum Aceh from 2021-2023 were collected and family member interview was conducted via telephone. **Results:** 155 patients met our study criteria. Results showed that the majority of patients were male(56.1%), with left unilateral CLP type(43.2%), and live at an altitude of 0-500 meter-ASL(67.09%). Regarding family characteristics, data was obtained for each father and mother, the majority had a secondary education 47.1% and 49.7% respectively, Acehnese 78.7% and 80.6%, working 100% and 29%, with medium category household-income(32.9%), mothers were  $\geq 25$ -35 years old(57.4%) age group and fathers were  $< 40$  years old(52.2%). For the pregnancy history: 72.2% of mother aged 21-34 years old, 65.8% had  $\leq 2$  children, 96.8% had no comorbidities, 94.2% no history of trauma and folic acid consumption during pregnancy. A family history found in 20% of all cases, with 11% was from 2nd generation. Left unilateral CLP was diagnosed in 1st generation(6.06%), 2nd generation(21.22%), and 3rd generation(18.18%). **Conclusion:** The characteristics of CL/P patients in Aceh were mostly: male, with left unilateral CLP type, live at altitude of 0-500meter-ASL, from parents with secondary education, working fathers with medium category household-income, mothers aged  $\geq 25$ -35 while fathers were  $< 40$  years old. Pregnancy history : mothers were 21-34 years old, had  $\leq 2$  children, with no comorbidities, trauma, nor folic acid consumption during pregnancy. The majority of CL/P family history was found from the second generation.

**Keywords:** cleft lip and or palate, family history, genogram

---

Corresponding author: Andi Akbar Ibhaliswan

Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Universitas Syiah Kuala, dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia

Email: andiakbaribhaliswan@gmail.com

## INTRODUCTION

Cleft lip and palate are one of the most common craniofacial birth defects and have become quite complex social problems. Newborns with CL/P not only have feeding difficulties but will also experience speech problems, dental anomalies and may also be associated with social and psychological problems. The prevalence of cleft lip and palate varies in each country. Collectively, cleft lip with or without cleft palate or cleft palate alone (CL/P) has become the most common condition found among all congenital birth defects. (Setó-Salvia N, 2014)

The prevalence of cleft lip varies between 1.5 until 25/10,000 births. The results of several studies showed that the global prevalence of cleft lip and palate is 0.992/1,000 live births. The other studies stated that the incidence of cleft lip and palate was 1 in 700 births worldwide and 1 in 500 births in Asia and Native Americans. The highest incidence rate was in Asia and the lowest in Africa. Most cases of cleft lip are generally unilateral (80-85%) with 33% of them are bilateral. Badan Penelitian Dan Pengembangan Kesehatan. 2018. p. 674.

Riskesdas in 2018 published that the incidence of cleft lip contributed 0.12% to the category of birth defects. In 1989, Marzoeki reported that in Surabaya the incidence of cleft lip with/without cleft palate was 1:1983 live births, while cleft palate was 1:9000 live births. The Aceh province area contributed 7.8% of the total national cases or 1 in 140 births. (Marzoeki et al., 2002; Tim Riskesdas 2018. Laporan RISKESDAS Provinsi Aceh 2018. Lembaga Penerbit BALITBANGKES. 2018., n.d.) Jailani in 2018 conducted a study in Aceh and found that 232 children (0.2%) of 116,118 live births suffered from cleft lip and palate (labiopalatoschisis). (Jailani, 2021) Data obtained from the Yayasan Senyum Aceh showed that surgery of CL/P have been performed on 7000 patients from 2007 to 2023, with an average number of surgeries of 350-400 patients per year. In sequence, the highest number of patients came from North Aceh district, followed by East Aceh, Bireuen, Pidie, Central Aceh, Southeast Aceh and South Aceh.

Cleft lip and/or palate (CL/P) is caused by various factors including heredity and environment. To understand the developmental mechanisms underlying CL/P, it is important to consider these various factors that may influence the embryological process. These factors include maternal age, use of drugs such as anti-epileptic drugs or corticosteroids, smoking and alcohol consumption during pregnancy. Low socioeconomic circumstances also has been reported can increase the risk of CL/P. Occupational status, lower household income, and lower parental education were also associated with higher incidence. (Kruppa et al., 2022; Setó-Salvia N, 2014; Silva et al., 2018; Yusuf et al., 2018)

A genogram is a family tree that depicts individual and family biopsychosocial factors over 3 generations. Genograms can also describe family life cycles, illnesses and relationships between family members, which are useful for finding out relationships between family members, family medical and psychological problems in a simple, easy and fast way. The information obtained from the genogram can be used by a healthcare worker to make decisions about patient and family problems. (Arisanti N, Gondodiputro S, Djuhaeni H. Penggunaan Genogram Dalam Deteksi Dini Faktor Risiko Penyakit Degeneratif Dan Keganasan Di Masyarakat. J MKB. 2016;48(38)., n.d.)

Research conducted by Bambang Pardjianto in East Nusa Tenggara showed that genetic has a greater influence than the environmental factors on the incidence of CL/P. This was traced using a genogram on three generations of the family to see the etiology of the incidence. The fairly high incidence of CL/P in this population was associated with low Zinc levels, a large number of consanguineous marriages (endogamy) so it was thought to influence deviations in fetal organogenesis in the 1st and 2nd trimesters which have an impact on increasing cases of CL/P.6

Based on the explanation above, we are interested in looking at the genogram characteristics of cleft lip and/or palate cases in the CL/P Surgery Center of Aceh using sociodemographic descriptions and maternal pregnancy history. The results of this study are expected can be used for education and information for patients and their families.

## RESEARCH METHOD

A population-based retrospective study was carried out on data drawn from the Yayasan Senyum Aceh that reported a surgery of cleft lip and/or palate patients from 2021-2023. Total of 444 data of CL/P patients who underwent surgery at the Yayasan Senyum Aceh were collected. Respondents from patient parents who were connected by telephone from the data population at the Aceh Smile Foundation were used as samples, after fulfilling the inclusion and exclusion criteria. Inclusion criteria included patients diagnosed with cleft lip and/or palate as a single or mixed disease based on data from the Yayasan Senyum Aceh and parents and/or guardians of patients who are willing to be respondents and know about the patient's history based on the desired variables.

## RESULTS AND DISCUSSION

After conducting structured interviews via telephone with the patient's family member, a sample size of 155 samples was obtained from a total population of 444 patients. The characteristics of the patient are presented in table 1. As displayed in Table 1, the total of male patients who have undergone cleft lip and/or palate surgery was more than female patients. Based on altitude, it was found that the majority of respondents came from an altitude of 0-500 meters above sea

level while there was no respondent from altitudes 2000-2700m and > 2700m. Most mothers and fathers had middle education as their last formal education level. The majority of fathers were in the age group of <40 years, while mothers were in the 25-35 years old. All fathers with children diagnosed with CL/P in this study were employed, but mothers were more likely to be unemployed. Most of the respondents had moderate family incomes, and their parents were Acehnese. Table 2 showed that the majority of respondent mothers had pregnant age of 21-34 years with parity  $\leq 2$  children, had no history of drug use, had no comorbidities, did not take folic acid supplements during pregnancy and had no history of trauma during pregnancy. Based on Table 3, it was found that the most common type of CL/P was left unilateral cleft lip and palate. Table 5 displayed that the majority of cases of cleft lip disorders in each generation are diagnosed with left unilateral cleft lip and/or palate; there were 2 cases from the 1<sup>st</sup> generation, 7 cases from 2<sup>nd</sup> generation and 6 cases from 3<sup>rd</sup> generation.

**Table 1**  
*Characteristic of the samples*

Characteristic	n (%)	
<b>Sex</b>		
Male	87 (56,1)	
Female	68 (43,9)	
<b>Altitude</b>		
>2700 m	0 (0)	
2000-2700 m	0 (0)	
1500-2000 m	16 (10,3)	
500-1500 m	35 (22,6)	
0-500 m	104 (67,1)	
<b>Mother's Age</b>		
<25 tahun	10 (6,4)	
$\geq 25$ -35 tahun	89 (57,4)	
$\geq 35$ tahun	56 (36,2)	
<b>Father's Age</b>		
<40 tahun	81 (52,2)	
$\geq 40$ tahun	74 (47,8)	
<b>Education Level</b>	<b>Father</b>	<b>Mother</b>
Lower	40 (25,8)	33 (21,3)
Middle	73 (47,1)	77 (49,7)
Higher	42 (25,8)	45 (29)
<b>Occupational Status</b>		
Working	155 (100)	45 (29)
Not working	0	110 (71)
<b>Ethnicity</b>		
Aceh	122 (78,7)	125 (80,6)
Jawa	10 (6,5)	5 (3,2)
Gayo	11(7,1)	14 (9)
Batak	3 (1,9)	3 (1,9)
Melayu	3 (1,9)	4 (2,6)
Other	6 (3,8)	4 (2,6)
<b>Household-Income</b>		
Low	36 (23,2)	
Medium	51 (32,9)	
High	43 (27,7)	
Very high	25 (16,1)	
<b>Total</b>	155 (100%)	

**Table 2**  
**Pregnancy History of CL/P patient's mother**

<i>Characteristic</i>	<i>n</i>	<i>%</i>
<b><i>Pregnant mother's age</i></b>		
< 20	7	4,5
21-34	112	72,2
>36	36	23,3
<b><i>Parity</i></b>		
> 2 children	53	34,2
≤ 2 children	102	65,8
<b><i>Drugs consumption</i></b>		
Yes	25	16,1
No	130	83,9
<b><i>History of Comorbidity</i></b>		
Yes	5	3,2
No	150	96,8
<b><i>Folic Acid Consumption</i></b>		
Yes	9	5,8
No	146	94,2
<b><i>History of Trauma</i></b>		
Yes	9	5,8
No	146	94,2
<b>Total</b>	<b>155</b>	<b>100</b>

## DISCUSSION

Table 1 displayed respondents who went to the plastic surgery department with a diagnosis of CL/P at the Yayasan Senyum Aceh, the majority were male with total of 56.1% (87 respondents). An epidemiological study in Brazil also showed similar results from 1519 samples studied, male patients with CL/P were greater than women by 56%, and it was reported that men were at risk 2.7 times greater than women.(Daniella Reis Barbosa Martelli & da Cruz, 2010) This is in also in accordance with a study conducted in Indonesia, by Elfiah at the Rumah Sakit Paru Jember that showed the incidence of CL/P was 56% in men.(Elfiah, 2021) Other studies in Iran, Argentina and Pakistan also showed similar results.(Elahi MM, Jackson IT, Elahi O, Khan AH, Mubarak F, Tariq GB, 2004; Morteza Noorollahian, Mohsen Nematy, 2015; Rittler M, Lopez C, 2004).

In this study, we found that the majority of respondents came from an altitude of 0-500 m above sea level, with total of 104 respondents (67.09%). This was in line with study conducted by Yashoda that showed a significant relationship between zinc levels in soil and altitude. Areas with an altitude of > 2700 m above sea level have the highest zinc levels. Zinc levels at the soil surface ranged from 60-220 mg/kg and were found to decrease with lower altitude. The pathophysiology of impaired palatal fusion due to zinc deficiency resulting in CL/P has been described. Metalloproteinases (MMP-2 and MMP-3) are zinc-dependent enzymes that are required in the palatogenesis process. MMP plays a role in tissue remodeling, cell migration, and cell proliferation. Meanwhile, tissue inhibitor MMPs (TIMMPs) inhibit MMP activity and stimulate the cell apoptosis process. It has been reported that imbalance of regulation of these two enzymes are triggered by zinc deficiency conditions. Zinc cannot be stored in the body, so the physiological requirement for zinc must be obtained through food high in this micronutrient intake. WHO recommended a daily supplementation to pregnant women to prevent zinc deficiency conditions as this micronutrients is physiologically required since the first trimester of pregnancy and increases in the third trimester, estimated to be more (2-fold) and up to 3-fold in lactation. (Mahanani, Alanis Sakina Agniya, Eriska Riyanti, and Arlette Suzy Puspa Pertiwi. "Correlation between Maternal Zinc Deficiency and Nonsyndromic Cleft Lip with or without Cleft Palate: A Rapid Review." Journal of International Dental and Medical Research 15, n.d.; Samanich J, Adam HM. Pediatric in Review: Cleft Palate. Pediatr Rev. 2009;30(6):230–2, n.d.; World Health Organization. "WHO Antenatal Care Recommendations for a Positive Pregnancy Experience: Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy." 2020., n.d.; Nahas et al., 2021)

In this study, we found that last formal education of mothers and fathers were middle education level which was 47.1% for fathers and 49.7% for mothers. This was in line with a study by Silva et al on 173 parents of patients in Brazil showing that the majority of mothers and fathers were high school graduates, 39.9% and 27.7% respectively.(World Health Organization. "WHO Antenatal Care Recommendations for a Positive Pregnancy Experience: Nutritional Interventions Update: Multiple Micronutrient Supplements during Pregnancy." 2020., n.d.)

Based on the occupation status, all fathers of the CL/P patients are working while the majority of mothers are not (71%). It was stated that fathers play a very important role in children's health from pregnancy to adolescence, providing

psychological and financial support for children's growth and development primarily by fulfilling their finances.(Armi et al., 2018; Michael Yogman, 2022) Meanwhile, the majority of mothers do not work, this was in line with the unemployment rate in Aceh which was higher in women than men.(Badan Pusat Statistik Provinsi Aceh, 2018) This is also confirmed by Kim et al's study which found a high level of attrition among mothers with children who had congenital diseases. This condition caused the mother to leave work or be dismissed by the employer.(Kyung Jim, Dora Farkas, 2024) The average accumulated household income of both parents in this study categorized in medium category income of 32.9%, followed by higher then lower income. Lower income status including low education causes a lack of understanding of health during pregnancy which can increase the risk of incidents.(Purwitasari et al., 2020) The majority of respondents are Acehnese, fathers and mothers at 78.7% and 80.6%, followed by Gayo and Javanese.

This study found that the majority of parents were in the group age of mothers 25-35 years with 89 respondents and fathers <40 years with 81 respondents. Kadek's study reported that based on parental age, the incidence of cleft lip and cleft palate was in a higher proportion in mothers aged 21-35 years (60.0%)(Purwitasari et al., 2020) and study in Brazil also showed the highest age was <35 years group.(Carvalho Paulo, Machado Renato, 2016) However, other showed a different results, the 35-39 year age group is 20% higher than the 20-29 year age group while mothers over 40 years old are 40% higher and have a 1.56 times greater risk of having a CL/P child.(Conway JC, Taub PJ, Kling R, Oberoi K, Doucette J, 2015) Increase Maternal and paternal age are associated with an increased risk of various diseases, such as achondroplasia, Apert Syndrome and Neurofibromatosis, and an increased risk of CL/P.(Vieira AR, Orioli IM, 2002) The association of mutations in MSX1 (homeobox muscle segment) and CL/P strengthens the hypothesis of an association between paternal age and CL/ P, which has been observed in Apert syndrome.(Vieira AR., 2008) However, other studies have shown no association between parental age and the risk of CL/P.(Daniella Reis Barbosa Martelli, Renato Assis Machado, 2012).

**Table 3. Classification of CL/P**

Type of CL/P	Male N (%)	Female N (%)	Total N	Persentase (%)
<i>Cleft lip unilateral</i>				
- Dextra	9 (5,8)	6 (3,9)	15	9,7
- Sinistra	6 (3,9)	7 (4,5)	13	8,3
<i>Cleft lip bilateral</i>	4 (2,6)	1 (0,6)	5	3,2
<i>Cleft lip and palate unilateral</i>				
- Dextra	12 (7,8)	9 (5,8)	21	13,6
- Sinistra	37 (23,9)	30 (19,3)	67	43,2
<i>Cleft lip and palate bilateral</i>	14 (9,0)	5 (3,3)	19	12,3
<i>Cleft palate</i>	7 (4,5)	8 (5,2)	15	9,7
<b>Total</b>	<b>89 (57,4)</b>	<b>66 (42,6)</b>	<b>155</b>	<b>100</b>

**Table 4. Family history of CL/P patients**

Family History of CL/P	n	%
Yes	31	20
1 <sup>st</sup> Generation	3	1,9
2 <sup>nd</sup> Generation	17	11
3 <sup>rd</sup> Generation	13	8,4
No	124	80

**Table 5. Classification of CL/P by generation from family history**

Type of CL/P	1 <sup>st</sup> Generation (%)	2 <sup>nd</sup> Generation N (%)	3 <sup>rd</sup> Generation N (%)	Total N (%)
<i>Cleft lip unilateral</i>				
- Dextra	0 (0)	4 (12,12)	2 (6,06)	6 (18,18)
- Sinistra	0 (0)	1 (3,03)	2 (6,06)	3 (9,09)
<i>Cleft lip bilateral</i>	0 (0)	0 (0)	1 (3,03)	1 (3,03)
<i>Cleft lip and palate unilateral</i>				
- Dextra	0 (0)	4 (12,12)	1 (3,03)	5 (15,15)
- Sinistra	2 (6,06)	7 (21,22)	6 (18,18)	15 (45,46)
<i>Cleft lip and palate bilateral</i>	1 (3,03)	1 (3,03)	1 (3,03)	3 (9,09)
<i>Cleft palate</i>	0 (0)	0 (0)	0 (0)	0 (0)
<b>Total</b>	<b>3</b>	<b>17</b>	<b>13</b>	<b>100</b>

Respondents who had a history of drugs consumption during pregnancy were 16.1% (25 respondents), the Drugs most frequently prescribed included antibiotics, pain relievers, and drugs for chronic diseases such as hypertension and diabetes. The relationship between antibiotics and cleft lip is still a controversial issue. Respondents who received folic acid supplementation during pregnancy were 5.8% (9 respondents), which less than those who did not receive folic acid supplements 94.2% (146 respondents). According to most studies, daily folic acid supplementation containing 400 mc folate g per day could reduce the risk of neural tube defects and the incidence of CL/P. In other words, lack of vitamin supplementation increases the risk of CL/P which was also found in this study.

We also found that the most of respondents categorized as unilateral cleft lip and palate left with number of 67 respondents (43.2%). This was in line with Resqiyah's study which found that the majority of patients were male (58.1%), the most diagnosis of CL/P types were left unilateral cleft lip and/or palate (18.4%). This was also similar to the study of Yilmaz et al. at the Department of Orthodontics at Marmara University School of Dentistry in Turkey which stated that the most common CL/P classification diagnosed was the left unilateral cleft lip and/or palate. There was no study in human showed aetiology and the mechanism explaining why this CL/P left side is more common yet. However, the results of studies on animals found that during the embryological development, the left palatine shelf took longer than the right to rotate until it reached a horizontal position, and the pressure in the left carotid artery was lower than the pressure in the internal carotid artery on the right side, and the development of the left carotid artery also took longer than the right so that blood perfusion to the left was lower (Fitrie et al., 2022). Our study showed that female dominated the cleft palate type in a non-significant manner. Previous research found that women showed risk factors for the occurrence of cleft palate type CL/P, while other types were dominated by men. (C. Ferrari-piloni, L. A. N. Barros, F. A. S. Jesuino, and J. Valladares-neto, 2021) However, this was not in line with Lei's study in Taiwan which showed the highest prevalence was cleft palate among other CL/P classification. It was thought to be influenced by various external factors. Studies suggested that CL/P classification result from differences in etiology, although the molecular dynamics behind these variations remain unclear. This difference lies in the DNA methylation pattern which is influenced by genetics during embryonic development. (Lei RL, Chen HS, Huang BY, Chen YC, Chen PK, Lee HY, 2013; M. Kuriyama et al., 2008).

According to Table 4, it was found that 20% of respondents had a family history of CL/P, with families at the second generation level at 11% (17 Respondents). Several previous studies also showed similar results, including research in Taiwan where CL/P patients had a family history of CL/P was 27% of the 194 respondents studied. (Morteza Noorollahian, Mohsen Nematy, 2015) Data from a population in China showed a lower incidence of CL/P, which was surprising because Asian ethnicity is the ethnicity with the highest epidemic of this congenital anomalies, this made it possible to suspect that there were other external factors that influence the incidence of cleft lip, such as the environment or teratogenicity. (Silva, C. M., Pereira, M. C. de M., Queiroz, T. B. de, & Neves, 2021) However, study conducted by Maranhao found a different results, where the most prevalent CL/P family member came from the first generation level. (Maranhão, S. C., Sá, J., Cangussú, M. C. T., Colleta, R. D., Reis, S. R. A. & Medrado, 2021) Other study have stated that the cleft lip and palate type was the most common type inherited through family history patterns. (Silva, C. M., Pereira, M. C. de M., Queiroz, T. B. de, & Neves, 2021) From the results of this study, we found a strong relationship between CL/P with family history, and the literature have stated that family history is a strong component for predicting the potential risk of new cases of orofacial clefts in the family, (Figueiredo, J. C., Ly, S., Magee, K. S., Ihenacho, U., Baurley & Sanchez-Lara, P. A., & Magee, 2015) even 4-8 times the risk of being inherited. (Salihu, S., Krasniqi, B., Sejfiija, O., Heta, N., Salihaj, N., Geci, A., Sejdini & Arifi, H., Isufi, R., & Ueek, 2014)

The most common classification of CL/P in patients by generations was left unilateral cleft lip and/or palate of all CL/P cases in Aceh. As a result of a literature search, no similar research was found showing CL/P classification with levels of family generational history. However, epidemiological research over 30 years in Iran showed that 3 groups in the time period 1982-1991 were dominant in the cleft lip type, 1992-2001 were dominant in the cleft palate type, and 2002-2011 were dominant in the cleft lip and/or palate type. These findings showed differences in time periods, which can represent variations in the type of CL/P by the generations found to vary from each time period. (Hamidreza Kianifar, Nadia Hasanzadeh, 2015)

We choose some patient's genogram to be displayed. Figure 1(a) showed the first generation can be seen from the genogram that NF's brother also experienced the same disease as the respondent. Figure 2 (b) in the second generation showed that IT's brother's uncle experienced labiogtoschiziz and in the third generation displayed on Figure 3 (c) showed that NB's grandmother experienced CL/P.

## CONCLUSION

Our study found that 31 respondents (20%) had a family history of cleft lip and palate and the majority came from the second generation. The characteristics of CL/P patients in Aceh are mostly found in male patients, left unilateral CLP type, came from residence with a height of 0-500 meters above sea level, from middle-educated parents, working father and non-working mother, with medium household income, middle-aged mother  $\geq 25$ -35 years old and father  $< 40$  years old, and both parents are Acehnese. Characteristics of pregnancy history showed that the mother was 21-34 years old at the time of pregnancy, with parity of  $\leq 2$  children, no history of comorbidities or trauma, or consuming folic acid supplements.

REFERENCES

- Arisanti N, Gondodiputro S, Djuhaeni H. Penggunaan Genogram dalam Deteksi Dini Faktor Risiko Penyakit Degeneratif dan Keganasan di Masyarakat. *J MKB*. 2016;48(38). (n.d.).
- Armi, N., Prodi, M. K., & Drg, I. M. (2018). *Yang Dirawat di Rumah Sakit Sentra Medika Cikarang Tahun 2017 Factors That are Related to Prevention of Labiopalatoschisis in Babies Cared in Sentra Medika Center of Cikarang 2017*. 7(1).
- Badan Pusat Statistik Provinsi Aceh. (2018). *Indikator Tenaga Kerja Provinsi Aceh Februari 2018*.
- C. Ferrari-piloni, L. A. N. Barros, F. A. S. Jesuino, and J. Valladares-neto. (2021). Prevalence of cleft lip and palate and associated factors in Brazil's Midwest: a single-center study *Braz. Oral Res.*, 35, 1–9. <https://doi.org/10.1590/1807-3107BOR-2021.VOL35.0039>.
- Carvalho Paulo, Machado Renato, R. S. (2016). Parental age is related to the occurrence of cleft lip and palate in Brazilian populations. *Brazil Journal Oral Science*, 15(2).
- Conway JC, Taub PJ, Kling R, Oberoi K, Doucette J, J. E. (2015). Ten-year experience of more than 35,000 orofacial clefts in Africa. *BMC Pediatr.*, 14(15), 8.
- Daniella Reis Barbosa Martelli, Renato Assis Machado, M. S. O. S. (2012). Non sindromic cleft lip and palate: relationship between sex and clinical extension. *Brazil Journal Otorhinolaryngology*, 78(5), 116–120.
- Daniella Reis Barbosa Martelli, K. W., & da Cruz, L. M. de B. (2010). Maternal and paternal age, birth order and interpregnancy interval evaluation for cleft lip-palate. *Braz J Otorhinolaryngol.*, 76(1), 107–112.
- Elahi MM, Jackson IT, Elahi O, Khan AH, Mubarak F, Tariq GB, et al. (2004). Epidemiology of cleft lip and cleft palate in Pakistan. *Plastic Reconstruction Surgery*, 113, 1548-55.
- Elfiah, ulfa. K. (2021). Analisis kejadian sumbing bibir dan langit: studi deskriptif berdasarkan tinjauan geografis. *Jurnal Rekonstruksi Dan Estetik*, 6(1).
- Figueiredo, J. C., Ly, S., Magee, K. S., Ihenacho, U., Baurley, J. W., & Sanchez-Lara, P. A., & Magee, W. (2015). Parental risk factors for oral clefts among Central African, Southeast Asians, and Central Americans. *Birth Defects Res A Clin Mol Teratol*, 103(10), 863– 879. <https://doi.org/https://doi.org/10.1002/bdra.23417>
- Fitrie, R. N. I., Hidayat, M., & Dahliana, L. (2022). Incidence of Cleft Lip with or without Cleft Palate at Yayasan Pembina Penderita Celah Bibir dan Langit-Langit (YPPCBL) in 2016-2019. *Journal of Medicine and Health*, 4(1), 12. <https://doi.org/10.28932/jmh.v4i1.3396>
- Hamidreza Kianifar, Nadia Hasanazadeh, A. J. (2015). Cleft lip and Palate: A 30-year Epidemiologic Study in North-East of Iran. *Iranian Journal of Otorhinolaryngology*, 27(1), 78.
- Jailani, M. (2021). *Modifikasi Prosedur Millard Tanpa Flap C Pada Celah Bibir Unilateral*. Universitas Syiah Kuala. *Kesehatan RK. Laporan Nasional RISKESDAS 2018 [Internet]*. Badan Penelitian dan Pengembangan Kesehatan. 2018. p. 674. Available from: [http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan\\_Nasional\\_RKD2018\\_FINAL.pdf](http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf). (n.d.).
- Kruppa, K., Krüger, E., Vorster, C., & der Linde, J. van. (2022). Cleft Lip and/or Palate and Associated Risks in Lower-Middle-Income Countries: A Systematic Review. *Cleft Palate-Craniofacial Journal*, 59(5), 568–576. <https://doi.org/10.1177/10556656211018952>
- Kyung Jim, Dora Farkas, V. W. (2024). Association between maternal employment status and presence of children with major congenital anomalies in Denmark. *Public Health*, 24, 715. <https://doi.org/https://doi.org/10.1186/s12889-024-18190-w>
- Lei RL, Chen HS, Huang BY, Chen YC, Chen PK, Lee HY, et al. (2013). Population-based study of birth prevalence and factors associated with cleft lip and/or palate in Taiwan 2002-2009. *PLoS One*, 8.
- M. Kuriyama et al. (2008). DNA methylation changes during cleft palate formation induced by retinoic acid in mice. *Cleft Palate-Craniofacial J.*, 45(5), 545–551. <https://doi.org/10.1597/07-134.1>
- Mahanani, Alanis Sakina Agniya, Eriska Riyanti, and Arlette Suzy Puspa Pertiwi. “Correlation between Maternal Zinc Deficiency and Nonsyndromic Cleft Lip with or without Cleft Palate: A Rapid Review.” *Journal of International Dental and Medical Research* 15. (n.d.).
- Maranhão, S. C., Sá, J., Cangussú, M. C. T., Colleta, R. D., Reis, S. R. A., & Medrado, A. R. A. P. (2021). Nonsyndromic oral clefts and associated risk factors in the state of Bahia, Brazil. *European Archives of Paediatric Dentistry*, 22(2), 121–127. <https://doi.org/https://doi.org/10.1007/s40368-020-00522-0>
- Marzoeki, D., Jailani, M., & Perdanakusuma, D. S. (2002). *Teknik Pembedahan Celah Bibir dan Langit-Langit*. Sagung Seto.
- Michael Yogman, A. E. (2022). *The Role of Fathers in Child and Family Health in Book Engaged Fatherhood for Men, Families and Gender Equality*.

- Morteza Noorollahian, Mohsen Nematy, A. D. (2015). Cleft lip and palate and related factors: A 10 years study in university hospitalised patients at Mashhad — Iran. *African Journal of Paediatric Surgery*, 12(4), 286290. <https://doi.org/10.4103/0189-6725.172576>
- Nahas, L. D., Alzamel, O., Dali, M. Y., Alsawah, R., Hamsho, A., Sulman, R., Alzamel, M., & Omar, A. (2021). Distribution And Risk Factors of Cleft Lip And Palate On Patients From A Sample Of Damascus Hospitals A Case Control Study. *Heliyon*, 7(9). <https://doi.org/10.1016/j.heliyon.2021.e07957>
- Purwitasari, K. T. I., Sanjaya, I. G. P. H., & Hamid, A. R. R. H. (2020). Gambaran faktor risiko penyebab terjadinya celah bibir dan celah langit di Denpasar tahun 2019. *Intisari Sains Medis*, 11(2), 697–701. <https://doi.org/10.15562/ism.v11i2.656>
- Rittler M, Lopez C, C. E. (2004). Sex ratio and associated risk factors for 50 congenital anomaly types, clues for causal heterogeneity. *Clinical Molecular Teratology*, 70, 13–19.
- Salihu, S., Krasniqi, B., Sejfiija, O., Heta, N., Salihaj, N., Geci, A., Sejdini, M., & Arifi, H., Isufi, R., & Ueeck, B. A. (2014). Analysis of potencial oral cleft risk factors in the Kosovo population. . *International Surgery*, 99(2), 161–165.
- Samanich J, Adam HM. *Pediatric in Review: Cleft palate. Pediatr Rev.* 2009;30(6):230–2. (n.d.).
- Setó-Salvia N, S. P. (2014). Genetics of Cleft Lip and/or Cleft Palate : Association with Other Common Anomalies. *Eur J Med Genet [Internet]*, 57(8):381. <https://doi.org/10.1016/j.ejmg.2014.04.003>
- Silva, C. M., Pereira, M. C. de M., Queiroz, T. B. de, & Neves, L. T. das. (2021). Family history in non-syndromic orofacial clefts: Is there a pattern? *Oral Diseases*, 1–10. <https://doi.org/10.1111/odi.13942>
- Silva, H. P. V., Arruda, T. T. S., de Souza, K. S. C., Bezerra, J. F., Leite, G. C. P., de Brito, M. E. F., Lima, V. M. G. D. M., Luchessi, A. D., Bortolin, R. H., Ururahy, M. A. G., & de Rezende, A. A. (2018). Risk factors and comorbidities in Brazilian patients with orofacial clefts. *Brazilian Oral Research*, 32, 1–12. <https://doi.org/10.1590/1807-3107bor-2018.vol32.0024>
- Tim Riskesdas 2018. *Laporan RISKESDAS Provinsi Aceh 2018. Lembaga Penerbit BALITBANGKES.* 2018. (n.d.).
- Vieira AR, Orioli IM, M. J. (2002). Maternal age and oral clefts: A reappraisal. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.*, 94(5), 530–535.
- Vieira AR. (2008). Unraveling human cleft lip and palate research. *J Dent Res.*, 87(2), 119–125.
- World Health Organization. “WHO antenatal care recommendations for a positive pregnancy experience: nutritional interventions update: multiple micronutrient supplements during pregnancy.” 2020. (n.d.).
- Yusuf, H. Y., Frick, H., & Riawan, L. (2018). Characteristic Overview of Sociodemographic Patient with Cleft Lip and Palate in the Cleft Centre of Dental Hospital Universitas Padjadjaran, West Java Province Indonesia. *International Journal of Science and Research (IJSR)*, 7(10), 397–400. <https://doi.org/10.21275/ART20191803>