Research Article

The Development of Causative Patterns of Cleft Lip and Palate in Eastern Indonesia

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Abstract

Cleft lip or cleft palate (CL/P) is a congenital disorder involving genetic and environmental factors. Eastern Indonesia is a region with the fourth-highest incidence of CL/P in Indonesia. Low socioeconomic conditions in this region are thought to contribute to the high prevalence of CL/P, both directly and through maternal health and environmental factors. This study aims to identify and analyze the evolving patterns of causative factors for cleft lip and/or palate (CL/P) in Eastern Indonesia. Conducted between February and October 2024, the research employs a cross-sectional design integrated with a path analysis approach to explore the complex interplay between environmental exposures and genetic predispositions contributing to CL/P in the region. Purposive sampling was used to interview families of CL/P patients to gather samples; the number of respondents was chosen based on the predetermined inclusion criteria. The data obtained were then analyzed using path analysis to examine the relationship between environmental and genetic factors, utilizing the SmartPLS 4.0 software. This study showed that social factors significantly affected CL/P with a t-statistic value of 0.043. Meanwhile, neither economic nor genetic factors had a significant effect. This result may be attributed to limited awareness among families regarding genetic influences, such as those identified through pedigree tracing in individuals with CL/P. Furthermore, as public knowledge has improved, the incidence of consanguineous marriages in Eastern Indonesia has declined, which is one factor that influences CL/P from a genetic perspective. This study highlights the importance of social and economic interventions in reducing the incidence of CL/P. It emphasizes the need for further research employing a genetic analysis approach to obtain more comprehensive results.
Keywords: *CL/P, Eastern Indonesia, economy, genetics, social.*

Perkembangan Pola Penyebab Kejadian Bibir Sumbing dan Langit-Langit di Wilayah Indonesia Timur

Abstrak

Bibir sumbing atau sumbing langit-langit (CL/P) merupakan kelainan kongenital yang melibatkan faktor genetik dan lingkungan. Wilayah Indonesia Timur merupakan wilayah dengan tingkat kemisikanan tertinggi ke empat di Indonesia. Kondisi sosio-ekonomi yang rendah di wilayah ini diduga berkontribusi terhadap tingginya prevalensi CL/P, baik secara langsung maupun melalui faktor kesehatan ibu dan lingkungan. Penelitian ini bertujuan untuk mengetahui perkembangan pola penyebab kejadian CL/P di wilayah Indonesia Timur. Penelitian ini dilaksanakan antara Februari hingga Oktober 2024 dengan menggunakan desain potong-lintang. Dilakukan pendekatan analisis jalur untuk menyelidiki hubungan antara faktor lingkungan dan genetik yang terkait dengan CL/P di wilayah tersebut. Sampel diperoleh melalui wawancara dengan keluarga penderita CL/P menggunakan metode purposive sampling dengan jumlah responden sesuai kriteria inklusi yang ditetapkan. Data yang didapatkan selanjutnya dianalisis jalur antara faktor lingkungan dan genetik menggunakan aplikasi SmartPLS 4.0. Hasil menunjukkan bahwa faktor sosial berpengaruh secara bermakna terhadap CL/P dengan nilai t-statistik 0,043. Sedangkan faktor ekonomi dan genetik tidak berpengaruh secara bermakna. Hasil ini mungkin disebabkan oleh kurangnya kesadaran di kalangan keluarga mengenai pengaruh genetik, seperti yang diidentifikasi melalui penelusuran silsilah pada individu dengan CL/P. Selain itu, seiring berkembangnya pengetahuan masyarakat, kasus kawing tungku di Indonesia Timur juga semakin menurun, yang merupakan salah satu faktor yang memengaruhi CL/P dari aspek genetik. Penelitian ini menggarisbawahi pentingnya intervensi sosial dan ekonomi untuk menekan angka kejadian CL/P serta perlunya penelitian lebih lanjut dengan pendekatan analisis genetik untuk hasil yang lebih komprehensif.
Kata kunci: *CL/P, Indonesia Timur, ekonomi, genetik, sosial.*

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Introduction

A cleft is a congenital abnormal space or gap in the upper lip, alveolus, or palate. Clefts are classified into three types: cleft lip (CL), in which only the lip structure is affected; cleft palate (CP), where only the palate structure is open; and cleft lip and palate (CLP), in which both structures are involved. A cleft lip is a failure of fusion of the frontonasal and maxillary processes, leading to clefts at different levels through the lip, alveolus, and nasal base. A cleft palate is a failure of the union of the palatal process with the maxillary process, leading to clefts in the hard or soft palate. Clefts appear in the fourth stage of development.[1] Clefts are common congenital disabilities worldwide, with a prevalence of 1.7 per 1,000 births.[2] According to Basic Health Research data, the prevalence of this condition in Indonesia increased from 0.08% in 2013 to 0.2% in 2018. Annually, there are approximately 7,500 cases in Indonesia.[3] According to Sjamsudin et al,[4] the prevalence was 1 in 1,596 births, with CL accounting for 24.42%, CP for 25.05%, and CLP for 50.53% of cases. This condition is more prevalent among low-income populations[4] and occurs more frequently in males than females, with a ratio of 2:1. Left-sided cleft lip is the most common, followed by right-sided and bilateral cases, with a ratio of 6:3:1. The Indonesian Association of Plastic Reconstructive and Aesthetic Surgeons (INAPRAS) reported 8,330 cases of CLP identified during social service activities in West Java from 1997 to 2019, during which they performed 6,320 labioplasties, 1,772 palatoplasties, and 238 other revision procedures.[3]

CL/P significantly affects individuals and their families, as it alters appearance and causes functional difficulties in speaking, eating, social interactions, and overall growth and development. Approximately 70% of children born with CL/P do not have an associated syndrome, and this anomaly is believed to result from a complex inheritance pattern influenced by both genetic and environmental factors.[5] One of the genetic factors linked to cleft conditions is the interferon regulatory factor 6 (IRF6) gene, whose expression increases the likelihood of cleft palate and/or cleft lip.[3] Several epidemiological studies have also highlighted the significant impact of socioeconomic factors on the risk of CL/P. Pregnant women who smoke, consume alcohol, take antiepileptic drugs or corticosteroids, have folic acid deficiencies, or experience infectious diseases during pregnancy are at a higher risk of giving birth to a child with CL/P. Additionally, conditions such as hyperthermia, diabetes mellitus, occupational factors, and obesity have recently been identified as risk factors for CL/P.[6] Several studies have proven that these behaviors contribute biologically to the occurrence of CL/P. Maternal behavioral and health-related factors—including cigarette smoking during the periconceptional period, alcohol consumption, use of antiepileptic or corticosteroid medications, folic acid deficiency, and infectious diseases—have been consistently associated with increased risk of non-syndromic cleft lip with or without cleft palate via biological mechanisms that disrupt normal craniofacial morphogenesis. Meta-analyses report modest but statistically significant associations—for example, the pooled odds ratio (OR) for maternal smoking is approximately 1.42 (95 % CI: 1.27–1.59),[5] and cohort-control data indicate elevated risks (OR ≈ 1.6–2.0) for both CL/P and CP depending on timing and phenotype. Folic acid deficiency impairs one-carbon metabolism, DNA methylation, and cell proliferation in the palate, thereby contributing to cleft formation; experimental supplementation improves palatal shelf adhesion and reduces severity in animal models.[5,7,8]

Eastern Indonesia is divided into several regions, including East Nusa Tenggara and West Nusa Tenggara. East Nusa Tenggara ranks fourth in poverty levels nationwide,[9] a condition closely linked to malnutrition, which affects embryonic development and contributes to the high prevalence of CL/P in the region. The prevalence of CL/P in East Nusa Tenggara Province is 8.6%, or 6–9 cases per 1,000 population,[10] making it an endemic area for CL/P. A study by Amri et al[11]

found that in East Nusa Tenggara, cleft palate in children aged 0–5 years occurs in both sexes at an equal ratio of 50:50. Another contributing factor to the high incidence of CL/P in East Nusa Tenggara is marriage between close relatives, which remains a local tradition.[13] Thus, this study aims to identify the patterns of causes of cleft lip and palate in the Eastern Indonesia region, specifically in Kupang, Borong, and Dompu, by examining social, economic, and genetic factors.

Methods

This study was conducted from February to October 2024 using a cross-sectional design with a path analysis approach. The sample in this study consisted of patients with CL/P in Eastern Indonesia (Kupang, Borong, Dompu), selected using a purposive random sampling technique. Data were obtained through interviews with the patients' families, specifically those familiar with the family history on both the paternal and maternal sides. The Saiful Anwar General Hospital Ethics Committee granted the study ethical approval No. 400/330/K.3/102.7/2024.

This study examined variables related to the social, economic, demographic, health status, and genetic conditions of patients with CL/P. Economic factors include family income, which encompasses the income of both parents, the number of dependents, and expenditures on nutrition, education, and health. Social factors include data on parental education, parental employment, marital status, lifestyle behaviors (such as smoking, alcohol consumption, or both), sanitation, and housing conditions, which are evaluated based on ventilation and lighting. The type of flooring, categorized as dirt, concrete, or ceramic, and staple food consumption were also recorded. Demographic factors include data on the mother's age during pregnancy and childbirth, the child's gender, the number of children, and marital history (exogamy or endogamy). To assess health status, direct patient examinations were conducted to determine the type of cleft, which included CL with or without alveolus (CL/A), CLP, isolated cleft palate (hard and soft) (CPO), and isolated cleft soft palate (CSO). The cleft's location, whether on the right or left side, its laterality as either unilateral or bilateral, and its severity as either complete or incomplete cleft were also assessed.[14] Maternal health status was evaluated based on BMI, medical history, vitamin intake, drug dependence, and pregnancy infections. For genetic conditions, the data included genealogical information on the father's and mother's family history, traced from F1 to F3 generations. All data collected were organized using Microsoft Excel. Path analysis was conducted to examine the relationship between environmental factors and genetic data using SmartPLS 4.0.

Results

The results obtained in this study were interpreted using a path model that describes the relationship between the research variables (Figure 1). The analysis results of the direct effects between variables on CL/P incidence are presented in Table 1, while the indirect effects between variables on CL/P incidence are presented in Table 2.

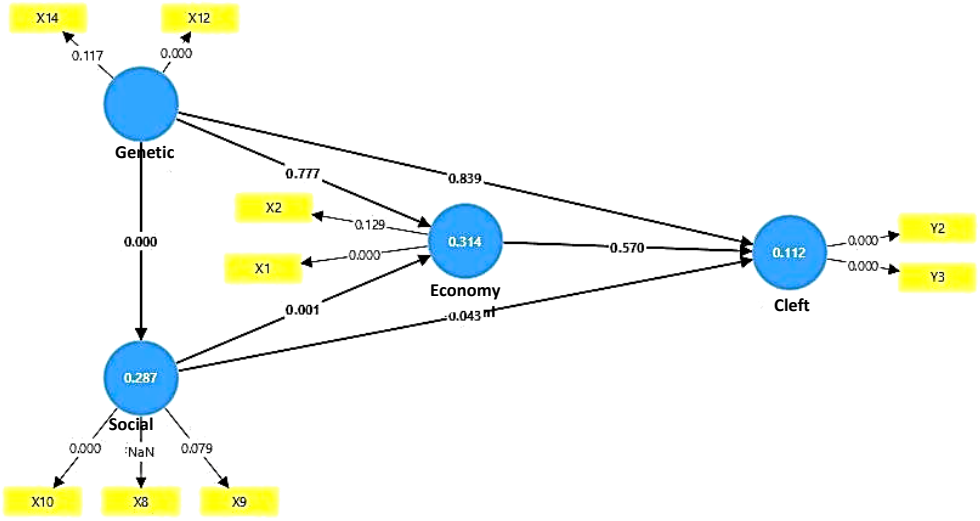

Figure 1. Analysis Results Using SMART-PLS

Table 1. Direct Effect Path Analysis

Variable	Sample Mean (M)	Standard deviation (STDEV)	T Statistics	p-value
Economy -> Cleft	-0.132	0.254	0.568	0.570
Genetic -> Economy	0.024	0.163	0.283	0.777
Genetic -> Social	0.530	0.124	4.326	0.000
Genetic -> Cleft	-0.034	0.211	0.204	0.839
Social -> Economy	0.562	0.155	3.449	0.001
Social -> Cleft	0.420	0.204	2.025	0.043

Table 1 presents the results of path coefficient analysis examining the relationship between genetic, social, and economic variables and the occurrence of CL/P. The relationship between economic factors and CL/P occurrence shows a coefficient value of -0.132 with a p-value of 0.570 (p>0.05). This indicates that economic factors do not directly affect the incidence of CL/P in respondents. The relationship between genetic and economic factors has a coefficient of 0.024 with a p-value of 0.777 (>0.05), which suggests that genetic factors do not significantly impact the economic conditions of families with CL/P. The relationship between genetic and social factors yields a positive coefficient value of 0.530 with a p-value of <0.001, indicating that genetic factors influence social conditions, for example, through a family history of CL/P, which can impact social stigma and interactions within the patient's family.

Table 2. Indirect Effect Path Analysis

Variable	Sample Mean (M)	Standard deviation (STDEV)	T Statistics	p-value
Genetic -> Social -> Cleft	0.227	0.131	1.687	0.092
Genetic -> Economy -> Cleft	-0.002	0.050	0.134	0.894
Social -> Economy -> Cleft	-0.076	0.152	0.508	0.611
Genetic -> Social -> Economy -> Cleft	-0.043	0.083	0.499	0.618
Genetic -> Social -> Economy	0.300	0.113	2.534	0.011

As shown in Table 2, the path coefficient analysis reveals the relationships between genetic, social, and economic conditions and their influence on CL/P incidence. The pathway from genetic to social conditions shows a positive but statistically insignificant effect (β = 0.227, p = 0.092). Similarly, the paths from genetic to economic conditions (β = –0.002, p = 0.894) and

from social to economic conditions (β = –0.076, p = 0.611) were insignificant. However, a significant association was found in the pathway from genetic to social to economic conditions (β = 0.300, p = 0.011), indicating that social conditions play a mediating role.

Discussion

The results of this study indicate that social factors are the main determinants of CL/P incidence, as well as mediators between genetic and economic factors. Statistically, social factors have a direct effect on CL/P incidence. These findings are in accordance with the research by Mossey & Modell,[15] which suggested that although genetic predisposition is important, social factors, such as access to health services, maternal behavior during pregnancy, and family support, are crucial determinants of CL/P incidence. This study also shows a significant correlation between genetic and social factors. This indicates that genetic conditions can lead to specific social vulnerabilities. These results are in accordance with research conducted by Dixon et al,[16] which found that the genetic risk of CL/P can increase when combined with unsupportive social factors, such as low maternal education or smoking and alcohol consumption during pregnancy. In other terms, social factors can trigger genetic expression. Furthermore, social pathways that influence the economy also support these findings.

From a mediation perspective, social factors act as intermediaries between genetic predisposition and economic outcomes. Families with a genetic history of CL/P often face social stigma, lack of community support, and limited employment opportunities. These social challenges can exacerbate economic factors, which in turn lead to poor prenatal care during pregnancy. These findings highlight the complex interaction between biological and social determinants in shaping CL/P risk. This is in accordance with the concept of gene-environment interaction reported by Jugessur & Murray,[17] which stated that genetic factors will only contribute significantly when influenced by particular environmental or social conditions.

An interesting finding of this study is that genetic factors, identified through pedigree tracing, do not appear to affect the incidence of CL/P, either directly or indirectly, as respondents have limited knowledge of their predecessors' health history. This history can only be confirmed through genetic testing. Of the 42 respondents, 70% (29 respondents) stated that none of their predecessors had a history of CL. These results align with the findings from the path analysis above. According to Leslie,[18] the risk of CL/P in first-degree relatives with a family history of cleft lip is 32 times higher than in individuals without such a history. The concordance rate of 40–60% in monozygotic twins is significantly higher than the 3–5% rate in dizygotic twins, indicating a strong genetic etiology.[18]

Maternal education and knowledge are the most important social components. Limited knowledge about nutritional needs, pregnancy care, and the dangers of consuming harmful substances such as cigarettes and alcohol is closely correlated with low levels of education. As stated by Dardani et al,[19] there is a relationship between the mother's level of education and the incidence of CL/P in her offspring. This aligns with the situation in Eastern Indonesia, where educational disparities persist and can impact health behaviors and community awareness.

Based on data from the National Socioeconomic Survey (Susenas) in March 2024, most of the population of East Nusa Tenggara (NTT) aged 15 years and above have basic literacy skills, namely the ability to read and write using Latin, Arabic, and other types of scripts. This achievement represents an improvement over the previous period. However, the level of formal education among the people of NTT is still relatively low. Based on the data obtained, it is recorded that around 17.91% of the population aged 15 years and above do not have a diploma because they did not complete their formal education. The most significant proportion of the population only completed elementary school or equivalent, while the number of people who have completed higher education remains limited, at around 10.19%.[20]

Culture and behavior during pregnancy are also important social factors that need to be considered. Exposure to cigarette smoke during pregnancy can interfere with fetal development, causing growth retardation and congenital disabilities (Public Health Services, 2006). This study found that less than 5% of mothers were active smokers, while more than 40% were passive smokers. According to Martelli et al,[21] cigarette smoke contains harmful substances such as nicotine, polycyclic aromatic hydrocarbons, tar, carbon particles, and carbon monoxide. The degree of exposure of the embryo to these substances depends on the number of cigarettes smoked, smoking frequency, depth of inhalation, and metabolic transfer between the mother and the embryo.[21] These substances can affect fetal DNA methylation, potentially altering the expression of genes responsible for the formation of the lips and palate.[22]

In addition to smoking, other risk factors for CL/P include maternal malnutrition, viral infections, teratogenic drug consumption, maternal body mass during pregnancy, and maternal age.[23] A study from the Atlanta Congenital Defects Program revealed that pregnancy at a very young age (14–19 years) increases the risk of fetal abnormalities, particularly cleft lip and palate. Malnutrition during pregnancy often results from a lack of maternal knowledge regarding nutritional needs. This leads to deficiencies in essential supplements such as vitamin C, vitamin E, retinol, vitamin D, thiamine, folic acid, vitamin B12, zinc, and calcium.[24]

Social factors also include access to and utilization of health services. The uneven distribution of health facilities in Eastern Indonesia can create barriers for pregnant women in obtaining quality health services. This is in accordance with the findings of Beaty et al,[25] who stated that a lack of access to healthcare is one of the environmental factors that lead to the risk of cleft lip, especially in developing countries. Although economic factors are not directly related to cleft lip incidence in this study, social pathways link economic conditions and health outcomes. In other words, the availability of economic resources is only meaningful if it is accompanied by social behaviors that support the health of pregnant women.

These findings imply the need for public health interventions that emphasize social change rather than solely economic improvement. Efforts to educate mothers about health, raise awareness of the importance of healthy behavior during pregnancy, strengthen the role of families and communities, and improve access to antenatal care are priority strategies for reducing the incidence of cleft lip in Eastern Indonesia.

Conclusion

The results of this study indicate that social factors significantly affect the incidence of CL/P in Eastern Indonesia. Additionally, social factors serve as mediators between genetic and economic factors. These findings have important implications for health policy in eastern Indonesia, particularly the need to strengthen maternal and child health programs that focus on education, early antenatal care, and community-based health promotion to address the social determinants of CL/P. Preventive interventions should prioritize awareness raising, access to health services, and educational campaigns. However, because genetic data in this study were limited to pedigree analysis, further laboratory-based genetic studies are recommended to identify specific genes associated with CL/P in this region.

Conflict of Interest

The author declares no conflict of interest.

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References

1. Vyas T, Gupta P, Kumar S, Gupta R, Gupta T, Singh HP. Cleft of lip and palate: a review. J Family Med Prim Care. 2020;9:2621-5. doi: 10.4103/jfmpc.jfmpc_472_20
2. Mossey PA, Shaw WC, Munger RG, Murray JC, Murthy J, Little J. Global oral health inequalities: challenges in the prevention and management of orofacial clefts and potential solutions. Adv Dent

Res. 2011;23:247-58. doi: 10.1177/0022034511402083
3. Sundoro A, Hilmanto D, Soedjana H, Lesmana R, Suryadinata KL. Cleft lip and palate surgery during COVID-19 pandemic in Indonesia: a 36-month experience at the Bandung Cleft Lip and Palate Center. Arch Craniofac Surg. 2023;24:111-6. doi: 10.7181/acfs.2023.00213
4. Sjamsudin E, Maifara D. Epidemiology and characteristics of cleft lip and palate and the influence of consanguinity and socioeconomic in West Java, Indonesia: a five-year retrospective study. Int J Oral Maxillofac Surg. 2017;46:69. doi: 10.1016/j.ijom.2017.02.251
5. Fell M, Dack K, Chummun S, Sandy J, Wren Y, Lewis S. Maternal cigarette smoking and cleft lip and palate: a systematic review and meta-analysis. Cleft Palate Craniofac J. 2022;59:1185-200. doi: 10.1177/10556656211040015
6. Khan AM, Prashanth CS, Srinath N. Genetic etiology of cleft lip and cleft palate. AIMS Mol Sci. 2020;7:328-48. doi: 10.3934/molsci.2020016
7. Khoury MJ, Gomez-Farias M, Mulinare J. Does maternal cigarette smoking during pregnancy cause cleft lip and palate in offspring? Am J Dis Child. 1989;143:333-7. doi: 10.1001/archpedi.1989.02150150091023
8. Maldonado E, Martínez-Sanz E, Partearroyo T, Varela-Moreiras G, Pérez-Miguelsanz J. Maternal folic acid deficiency is associated to developing nasal and palate malformations in mice. Nutrients. 2021;13:251. doi: 10.3390/nu13010251
9. Salesman F, Juraman SR, Paun R, Setiawan LW. Poverty and society health status in East Nusa Tenggara-Indonesia. IRJPEH. 2018;5:125-30. doi: 10.15739/irjpeh.18.017
10. Chandra D, Wihastyoko HYL, Agustin D. Hubungan antara protein EGFR (epidermal growth factor receptor) dan ERK-1 (extracellular signal-regulated protein kinase-1) pada kejadian bibir sumbing ras protomalayid di provinsi Nusa Tenggara Timur. Majalah Kesehatan. 2014;1:69-73.
11. Amri S, Putra RP, Wahyuni E, Pramono C. Characteristics of patients with cleft lip and palate during the community services in East Nusa Tenggara, Indonesia, 2017-2018. WJARR. 2024;21:1344-9. doi: 10.30574/wjarr.2024.21.1.0057
12. Patunru AA, Kusumaningrum S. Inequality and child wellbeing: the case of Indonesia. In: Child Poverty and Social Protection Conference. Jakarta: SMERU Research Institute; 2013.
13. Mahardika, RK, Suarsana IN, Arjani NL. Perkawinan sedarah di Desa Ruteng Pu'u Kecamatan Langke Rembong Kabupaten Manggarai Tengah Provinsi Nusa Tenggara Timur. Sunari Penjor Journal of Anhropology. 2021;5:87-94. doi: 10.24843/SP.2021.v5.i02.p05.
14. Bartzela T, Theuerkauf B, Reichardt E, Spielmann M, Opitz C. Clinical characterization of 266 patients and family members with cleft lip and/or palate with associated malformations and syndromes. Clin Oral Investig. 2021;25:5531-40. doi: 10.1007/s00784-021-03863-2
15. Mossey PA, Modell B. Epidemiology of oral clefts 2012: an international perspective. Front Oral Biol. 2012;16:1-8. doi: 10.1159/000337464
16. Dixon MJ, Marazita ML, Beaty TH, Murray JC. Cleft lip and palate: understanding genetic and environmental influences. Nat Rev Genet. 2011;12:167-78. doi: 10.1038/nrg2933
17. Jugessur A, Murray JC. Orofacial clefting: recent insights into a complex trait. Curr Opin Genet Dev. 2005;15:270-8. doi: 10.1016/j.gde.2005.03.003
18. Leslie EJ, Marazita ML. Genetics of cleft lip and cleft palate. Am J Med Genet C Semin Med Genet. 2013;163:246-58. doi: 10.1002/ajmg.c.31381
19. Dardani C, Howe LJ, Mukhopadhyay N, Stergiakouli E, Wren Y, Humphries K, et al. Cleft lip/palate and educational attainment: cause, consequence or correlation? a Mendelian randomization study. Int J Epidemiol. 2020;49:1282-93. doi: 10.1093/ije/dyaa047
20. Badan Pusat Statistik Provinsi Nusa Tenggara Timur. Statistik Sosial dan Kependudukan Provinsi Nusa Tenggara Timur 2024 [Internet]. BPS Provinsi Nusa Tenggara Timur. 2025. Available from https://ntt.bps.go.id
21. Martelli DR, Coletta RD, Oliveira EA, Swerts MS, Rodrigues LA, Oliveira MC, et al. Association between maternal smoking, gender, and cleft lip and palate. Braz J Otorhinolaryngol. 2015;81:514-9. doi: 10.1016/j.bjorl.2015.07.011
22. Lebby KD, Tan F, Brown CP. Maternal factors and disparities associated with oral clefts. Ethn Dis. 2010;20:S1–146-9.
23. Kulesa-Mrowiecka M, Lipowicz A, Marszałek-Kruk BA, Kania D, Wolański W, Myśliwiec A, et al. Characteristics of factors influencing the occurrence of cleft lip and/or palate: a case analysis and literature review. Children. 2024;11:399. doi: 10.3390/children11040399
24. Widayanti N, Sudjatmiko G, Putri NM. Parental age as a risk factor of children with cleft lip in Jakarta population: does paternal age play a role? Jurnal Plastik Rekonstruksi. 2017;4:88-94. doi: 10.14228/jpr.v4i1.220
25. Beaty TH, Murray JC, Marazita ML, Munger RG, Ruczinski I, Hetmanski JB, et al. A genome-wide association study of cleft lip with and without cleft palate identifies risk variants near MAFB and ABCA4. Nat Genet. 2010;42:525-9. doi: 10.1038/ng.580