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Research Article

Residential Environment and Parental Lifestyle as Risk Factors of The Co-Occurrence of Cleft Lip and Palate Birth Defect Cases in Indonesia

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Abstract
Cleft lip and palate (CLP) are multifactorial birth defects, and the etiology behind their occurrence remains insufficiently understood. This case-control study aimed to investigate the association between residential environmental factors, parental lifestyle, and the risk of CLP in Indonesia. A total of 213 participants from 14 provinces were selected using stratified random sampling. Multivariable logistic regression was employed to determine the odds ratios (ORs) with 95% confidence intervals (CIs) for each risk factor. The study identified significant associations between several residential environmental factors and CLP. Proper kitchen ventilation was found to be protective (OR = 0.245, 95% CI: 0.096–0.624, p = 0.003), while proximity to industrial sites significantly increased the risk (OR = 3.595, 95% CI: 1.029–12.558, p = 0.045). Additionally, using treated drinking water showed a protective effect (OR = 0.39, 95% CI: 0.16–0.95, p = 0.038), whereas concerns about water sources displayed a marginally significant risk increase (OR = 2.841, 95% CI: 0.876–9.211, p = 0.082). Regarding parental lifestyle factors, maternal active smoking exhibited a marginal protective association (OR = 0.052, 95% CI: 0.002–1.09, p = 0.057), while paternal passive smoking presented a marginally significant risk (OR = 2.309, 95% CI: 0.897–5.942, p = 0.083). Furthermore, paternal radiation exposure was associated with an elevated risk of CLP (OR = 3.489, 95% CI: 0.828–14.703, p = 0.089). These findings highlight the need for targeted public health interventions to mitigate environmental exposures and promote safer parental lifestyle behaviors in Indonesia.

Keywords: cleft lip, cleft palate, residential environment, parental lifestyle, epidemiology, child health

1. INTRODUCTION

Cleft lip and palate (CLP) occur due to the imperfect merging and integration of the rectal swellings, resulting in the formation of the soft and robust tissue that forms the roof of the mouth. Cleft lip occurs due to the failure of merging between the 4th and 6th month of pregnancy, while the palate cleft occurs between the 6th and 12th month of pregnancy [1]. As CLP develop, it will have an unpleasant impact on the affected individuals, affecting their facial appearance, mental function, physical abilities (speech, hearing, eating function), and even family psychological effects [2]. Cleft lip and cleft palate are congenital malformations that can occur individually or together, with the co-occurrence of both presenting a more severe clinical challenge. A cleft lip involves an opening or split in the upper lip that occurs when the developing facial structures in a fetus do not close completely. A cleft palate, on the other hand, is an opening or split in the roof of the mouth. When both conditions occur simultaneously, it is often referred to CLP, which requires more complex medical and surgical interventions compared to isolated cases of cleft lip or cleft palate alone [3][4].

CLP are among the most common congenital anomalies worldwide, with significant variability in prevalence across regions. According to a meta-analysis [5], the global prevalence of cleft lip is approximately 0.3 per 1,000 live births (95% CI: 0.26–0.34), while cleft palate alone has a prevalence of 0.33 per 1,000 live births (95% CI: 0.28–0.38). For combined CLP, the prevalence rises to 0.45 per 1,000 live births (95% CI: 0.38–0.52). The prevalence of CLP varies considerably across different regions, with notably higher rates observed in Indonesia. The national prevalence of CLP rose from 0.08% in 2013 to 0.12% in 2018 [6], which corresponds to an estimated 0.8 to 1.2 cases per 1,000 live births. These birth defects pose

Table 1. Characteristics of Children with cleft.

Factors	Classifications	Frequency	Percentage
Gender	Male	122	57%
	Female	91	43%
	Total	213	100%
Cleft Type/ Diagnosis	Cleft Lip only (CL)	47	22%
	Cleft Palate only (CP)	37	17%
	Cleft Lip and Palate (CLP)	129	61%
	Total	213	100%

substantial public health challenges due to their impact on feeding, speech development, and psychosocial well-being. Understanding the specific risk factors that contribute to CLP, especially within the context of Indonesia, where the rates may differ due to genetic and environmental influences, is essential for guiding effective public health interventions and policies aimed at reducing the burden of CLP.

Despite extensive research into the etiology of CLP, the specific underlying factors contributing to the co-occurrence of these conditions are not yet fully understood. While isolated cleft lip and cleft palate have been linked to various genetic and environmental factors, the combined occurrence suggests a potentially unique set of influencing factors that warrant further investigation. Studies have often focused on isolated occurrences, leaving a gap in the understanding of the multifactorial influences that might specifically trigger the co-occurrence of CLP [7].

CLP may be caused by genetic as well as environmental factors. An example of environmental exposure is chlorinated solvent exposure during pregnancy, which is positively associated with CLP [8]. Several epidemiological studies suggest that exposure to chemicals such as pesticides may influence the occurrence of CLP [9]. In Lowa, South Sulawesi, Indonesia, the prevalence of mothers exposed to pesticides accounts for 35.4% of CLP cases, 32.1% of cleft palate cases, and 32.3% of the control group consisting of workers potentially exposed to pesticides during the critical period of pregnancy. Pesticides are suspected to cause a change in the quality of genetic factors in both maternal and paternal sufferers [10]. Spinder et al. found that maternal pesticide exposure significantly increased the risk of CLP in offspring by 1.7 times (OR = 1.7, 95% CI 1.0–3.1) [11]. Moreover, there is strong evidence that maternal smoking can increase the risk of oral clefts in the consumption of certain medications by mothers during pregnancy (such as corticosteroids and anticonvulsants) also shows a connection to cleft lip in their offspring [12].

The types and degree of environmental exposure are well dependent on the parent's residential environment as well as their occupation. Some habits (smoking, alcohol and caffeine consumption) are also suspected to have effect on CLP birth cases. Parental lifestyle choices, including smoking, alcohol consumption, and caffeine intake, have been implicated in the occurrence of CLP [13][14]. Maternal smoking, for example, has been consistently associated with an increased risk of these defects, likely due to the teratogenic effects of nicotine and other harmful substances in tobacco [15]. Similarly, excessive alcohol and caffeine consumption during pregnancy have been suggested to contribute to the risk of congenital anomalies, although the evidence is varied and remain inconclusive [13][14][16].

Therefore, this research aims to bridge existing knowledge gaps by examining several residential environmental factors and parental lifestyle choices as potential risk factors for the co-occurrence of CLP in Indonesia. Understanding these associations is critical for public health, as the findings can inform targeted interventions and preventative measures. The results may also serve as a basis for policy-making to mitigate exposure to environmental and lifestyle risks linked to CLP, and

raise community awareness about modifiable factors that could reduce the incidence of such birth defects. Odds ratios derived from multivariable logistic regression are used to measure the effects of these factors in this case-control epidemiological study.

2. METHODS

This study is an observational epidemiology study with a case-control design involving 213 participants, the parents of children with cleft lip only (CLO), cleft palate only (CPO), and CLP defect. The research sample selection was conducted using stratified random sampling, which aimed to ensure representation from various provinces in Indonesia.

2.1. Study Locations and Period

The research locations include several provinces in Indonesia, namely Banten, DKI Jakarta, West Java, Central Java, West Kalimantan, West Nusa Tenggara (NTB), Gorontalo, North Sulawesi, South Sulawesi, Central Sulawesi, Southeast Sulawesi, Maluku, North Maluku, and Central Papua. Respondent data were collected through online questionnaires and/or phone interviews. Primary data were collected from August 11 to October 23, 2023 from CLO, CPO, and CLP patients' parents in Indonesia.

2.2. Study Design

This study utilized a case-control design to explore the risk factors associated with the co-occurrence of CLP. The case group included children diagnosed with CLP, while the control groups comprised children with isolated CLO and CPO. This approach allows us to compare the risk factors associated with the more severe CLP condition against those associated with the less severe, isolated forms of clefting (CLO and CPO). This design was chosen due to the absence of a 'true' control group free of any cleft condition.

A case-control epidemiology design is an ideal choice for studying rare diseases [17], especially when the focus is on the outcome (such as CLP cases) rather than a specific hypothesized cause, which could be more appropriately addressed by a cohort design. This study, which aims to establish associations between CLP cases and multiple

Table 2. Residential environment conditions contingency table (n = 213).

No	Risk Factor	Condition/Response	Cleft Lip & Palate	Cleft Lip/Palate
1	Floor	Soil & Cement	37	40
		Ceramic Tile (Ref.)	92	44
2	Roof	Zinc & Asbestos	58	52
		Clay tile roof (Ref.)	70	32
3	Cooking fuel	Firewood	22	22
		LPG/Kerosene (Ref.)	107	62
4	Proper Kitchen Ventilation	Yes	80	67
		No (Ref.)	49	17
5	Proximity to Industrial Site	Yes	26	6
		No (Ref.)	103	78
6	Water Source (Non-drinking purpose)	Rivers & Well (Direct Intake)	88	58
		Springs/Water Supply System (Ref.)	41	26
7	Water Source Complaints	Yes	29	7
		No (Ref.)	100	77
8	Drinking Water (Consumed)	Boiled/Filtered Water from Source	77	65
		Bottled/Commercial Refill Water (Ref.)	52	19

parental and residential factors, benefits from the case-control approach as it allows for the efficient assessment of multiple factors simultaneously [18]. This design is well-suited for exploring potential risk factors in a population where the condition of interest is relatively uncommon.

2.3. Data Collection

Data were obtained through online questionnaires and phone interviews from the Cleft Lip and Palate Patient Foundation (YPPCBL), which collaborated in this research. Institut Teknologi Bandung (ITB) sent a request to YPPCBL to collect data through interviews and questionnaire completion. After obtaining permission from each foundation and/or hospital, data collection commenced after explaining the background and purpose of the research to the patients' parents. Interviews and questionnaire completion proceeded after parental consent. To minimize potential sources of bias, interviews were conducted in the local language by trained personnel to ensure accurate data collection. A diverse sample from various regions of Indonesia was included to enhance the generalizability of findings.

We utilized data from 14 provinces and randomly selected participants from each province's pool of available parents. To ensure availability and consistency in responses, we only included parents who could be reached and agreed to participate in interviews. If participants did not respond to phone calls or messages, they were excluded from the study. Additionally, an exclusion criterion was applied: if one of the parents had passed away, the family was excluded due to the potential difficulty in obtaining accurate information from the remaining parent.

The study size was determined based on the prevalence of CLO, CPO, and CLP cases in Indonesia, aiming to achieve sufficient statistical power to detect significant associations between environmental and lifestyle factors and the risk of CLP. We included 213 respondents from 14 provinces to ensure a representative sample of the population. This sample size was considered adequate to provide reliable estimates and meaningful insights into the risk factors associated with CLP.

The questionnaire encompassed key areas, including the biodata of CLP patients (name, gender, and type of cleft/diagnosis), general information about the parents (names and addresses), and various aspects of parental habits such as active and passive smoking, alcohol and caffeine consumption, exposure to solvents, pesticides, chemicals, and radiation, use of drugs and medications, and exercise routines. Additionally, we assessed residential environment conditions, focusing on factors such as flooring, roofing, cooking fuel, ventilation, proximity to industrial sites, water sources for non-drinking purposes, water-related complaints, and drinking water sources. Respondents completed the questionnaire in approximately 15–20 min, and all interviews were conducted in the Indonesian language.

2.4. Data Processing and Analysis

A thorough data analysis was conducted to explore the association between parental and residential factors and the co-occurrence of CLP cases. Descriptive statistics were first used to summarize the characteristics of the study population and provide an overview of the distribution of variables. To assess the relationships between these factors and CLP, multivariable logistic regression was employed. This method was chosen to adjust for potential confounding factors, allowing for the calculation of odds ratios (ORs) that reflect the independent effect of each factor on the risk of CLP.

The odds ratios were accompanied by 95% confidence intervals (CIs) to ensure the precision and reliability of the estimates. The statistical significance of the associations was determined by p-values obtained from the logistic regression model. This approach provides a more accurate assessment of the risk factors by accounting for the influence of other variables in the model. All analyses were carried out using IBM SPSS Statistics software, version 22.

3. RESULTS AND DISCUSSIONS

The questionnaire distributed to the participants resulted in 213 residential environment condition data and 213 parental data (both on fathers and mothers) regarding their lifestyle. The basic main

Table 3. Paternal lifestyle history contingency table (n = 213).

No	Paternal			
	Risk Factor	**Response**	**Cleft Lip & Palate**	**Cleft Lip/Cleft Palate**
1	Active Smoking	Yes	81	48
		No	48	36
2	Passive Smoking	Yes	78	37
		No	51	47
3	Alcohol Consumption	Yes	8	6
		No	121	78
4	Caffeine Consumption	Yes	84	37
		No	45	47
5	Industrial Solvent Exposure	Yes	41	6
		No	88	78
6	Pesticide Exposure	Yes	12	7
		No	117	77
7	Radiation Exposure	Yes	95	21
		No	34	63
8	Household Chemical Exposure	Yes	14	3
		No	115	81
9	Workout Routine	Yes	106	71
		No	23	13
10	Drugs or Medication	Yes	8	1
		No	121	83

characteristics of the respondents, namely the gender of the patients (children) and the cleft types, are presented in Table 1. The majority of cases of CLP defects are male (57%), while 91 other patients or 43% are female. Among all patients, the highest case was CLP with as much as 129 cases (61%). The second highest and the lowest were CL only and CP only, with as much as 47 (22%) and 37 cases (17%), respectively.

The primary data obtained from the questionnaire responses are presented in Tables 2, 3, and 4. There were a total of 8 residential environment risk factors and 10 parental lifestyle (for both paternal and maternal) risk factors assessed. All of the risk factor questions present a binary choice, specifically a Yes/No choice for the parental lifestyle questions and some of the residential environment risk factors. For other residential environment risk factor questions requiring a description of their condition, a basic binary choice is given, describing common residential environment conditions in Indonesia. Furthermore, an "other" option is also provided for these questions, requiring the respondents to elaborate further with a short answer. However, none of the respondents chose the "other" options, resulting in dichotomous responses for each of the risk factor questions. There were no missing data in our records for this study. All questionnaire responses were complete, allowing for a

comprehensive analysis of all collected data without the need for imputation or exclusion due to incomplete records.

3.1. Residential Environment

The inclusion of each residential environmental factor in this study is based on the known underlying epidemiologic associations between these factors and CLP. Exposure to various air pollutants is known to cause several health effects, including reproductive issues in both males and females [19][20], disruption of fetal growth [21], and congenital malformations [22][23]. The first five residential environmental factors assessed (flooring, roofing, cooking fuel, ventilation, and proximity to industrial sites) correspond to this main exposure factor, airborne pollutants. Based on the questionnaire responses, some respondents use ceramic tiles for their flooring. However, others, especially those living in rural parts of Indonesia, use hard, raw, unpolished cement for flooring. Additionally, some houses in rural areas have uncovered soil as their flooring. These types of floors are harder to clean and facilitate exposure to dust for the residents [24][25]. Furthermore, some houses use old metal zinc and asbestos roofing, which might cause exposure to dust and airborne asbestos [26], unlike houses with clay tile roofing. Respondents who utilize wood fuel for cooking might be exposed to various indoor air pollutants [27], compared to those who use LPG or kerosene stoves. Proper ventilation, however, might facilitate better air circulation and reduce the risk of high concentrations of indoor air pollutants [28]. Finally, proximity to industrial sites may affect ambient air quality, further putting nearby residents at risk of exposure [29]. Therefore, the main hypothesis is that these residential environmental factors, corresponding to parental exposure to air pollutants, have a significant association with the co-occurrence of cleft lip and cleft palate defects.

The next three residential environment factors pertain to water. According to interview results, in areas where clean water services are not available from public water companies, communities typically use groundwater (wells), river water, and mountain spring water. The issue that arises is the poor quality of water, which often appears brownish and has an unpleasant odor, particularly for water from wells and polluted rivers. Using this water, even for non-drinking purposes (e.g. bathing), may cause several health issues [30]. The respondents were also asked to report any complaints or dissatisfaction they currently have regarding their water source. As much as 29% of CLP patients' parents and 9% of CLO and CPO patients' parents reported at least one concern regarding their water source, which may indicate impurities in the water. Lastly, for residential environmental factors, the respondents reported on their source of drinking water. Some regularly consume commercial bottled or refill water, while others treat their water source for non-drinking purposes using filtration and boiling methods.

The analysis results for each residential environment risk factor are summarized in Table 5. The OR, phi correlation, and p-values of each factors in logistic regression represent the risk and association between the risk factors and the co-occurrence of cleft lip and cleft palate. Three out of eight residential environmental factors were significantly associated with the outcomes at $p < 0.05$ (kitchen ventilation, proximity to industrial sites, and consumed drinking water source). Two additional factors showed marginal significance at $p < 0.1$ (floor material and water source complaints).

The OR result confirms the hypothesized increased risk of having children with CLP for parents with close proximity to industrial site (OR = 3.595, 95% CI:1.029 - 12.558) and decreased risk for those who have a proper ventilation in the kitchen (OR = 0.245, 95% CI:0.096 - 0.624). Both factors demonstrated statistically significant associations with CLP cases ($p < 0.05$). The OR result for cooking fuel also confirms the hypothesized increased risk for families using firewood to cook (OR = 1.78, 95% CI: 0.641 – 4.943), although not statistically significant ($p = 0.268$). For flooring and roofing, the results were counter-hypothetical. The residential conditions that were presumed unhealthy turned out being protective based on odds ratio, such as soil and cement flooring (OR = 0.41, 95% CI:0.167 – 1.005) and also zinc and asbestos roofing (OR = 0.708, 95% CI:0.3 – 1.675), although the association for the floor – CLP is only marginally significant ($p = 0.051$) and the association is insignificant for roof – CLP ($p = 0.432$).

The confirmed, hypothesized effects of proximity to industrial sites, ventilation, and the use of firewood as cooking fuel require further investigation and validation. There are many aspects of these factors that need clearer answers. For instance, how close are the homes of parents who answered 'yes' to living near industrial sites? What is the actual airflow rate in the homes of those who reported having proper ventilation? Additionally, the potential harmful effects of indoor air pollutants from firewood combustion could be exacerbated by poor ventilation. The counter-hypothetical results regarding flooring and roofing suggest that the relationship between residential environmental factors and the occurrence of CLP might be more complex than previously understood. One possible explanation for these findings is the potential presence of confounding factors that were not accounted for in this study. For instance, households with soil or cement flooring, and zinc or asbestos roofing, might also have other characteristics that contribute to a lower risk of CLP, such as healthier dietary habits [31][32] or genetic factors [33] that were not measured. This underscores the importance of considering cultural and contextual factors when assessing environmental health risks to rule out biases and other potential confounding factors. Therefore, these five residential environment factors corresponding to exposure to air pollutants warrant further research and are compelling subjects for future studies.

The three water-related factors yielded mixed OR results. The source of water for non-drinking purposes showed no notable association with CLP cases in this study, with an OR of 1.062 (95% CI:

Table 4. Maternal lifestyle history contingency table (n = 213).

No	Maternal			
	Risk Factor	**Response**	**Cleft Lip & Palate**	**Cleft Lip/Cleft Palate**
1	Active Smoking	Yes	2	2
		No	127	82
2	Passive Smoking	Yes	65	20
		No	64	64
3	Alcohol Consumption	Yes	4	2
		No	125	82
4	Caffeine Consumption	Yes	26	13
		No	103	71
5	Industrial Solvent Exposure	Yes	5	2
		No	124	82
6	Pesticide Exposure	Yes	20	7
		No	109	77
7	Radiation Exposure	Yes	85	17
		No	44	67
8	Household Chemical Exposure	Yes	21	2
		No	108	82
9	Workout Routine	Yes	100	69
		No	29	15
10	Drugs or Medication	Yes	18	2
		No	111	82

Table 5. Residential environment factors odds ratio and correlation result.

No	Risk Factor	Odds Ratio (95% CI), Adjusted	p-values
1	Floor	0.41 (0.167 – 1.005)	0.051**
2	Roof	0.708 (0.300 – 1.675)	0.432
3	Cooking fuel	1.78 (0.641 – 4.943)	0.268
4	Proper Kitchen Ventilation	0.245 (0.096 - 0.624)	0.003*
5	Proximity to Industrial Site	3.595 (1.029 – 12.558)	0.045*
6	Water Source (Non-drinking purpose)	1.062 (0.468 – 2.409)	0.886
7	Water Source Complaints	2.841 (0.876 – 9.211)	0.082**
8	Drinking Water (Consumed)	0.39 (0.160 - 0.950)	0.038*

Note: *p-value < 0.05; **p-value < 0.10

0.468–2.409) and a p-value of 0.886, indicating no statistically significant relationship. However, the other two factors were more closely associated with CLP risk. Parents with concerns or dissatisfaction about their water source had an estimated 2.841 times greater risk (95% CI: 0.876–9.211) of having a child with CLP, though this result was marginally significant (p = 0.082). In contrast, parents who used treated water from rivers and wells had a statistically significant lower risk of CLP compared to those who consumed commercial bottled or refill water (OR = 0.39, 95% CI: 0.16–0.95, p = 0.038), suggesting a potential protective effect.

The findings suggest that the perceived quality of water sources may play a significant role in the risk of CLP. Studies have shown that contaminants in water sources can affect fetal development and pregnancy outcomes. For example, research by Stayner et al. found that exposure to contaminated water during pregnancy was associated with an increased risk of congenital abnormalities [34]. Similarly, Delpla et al. demonstrated that dissatisfaction with water quality might correlate with actual pollutants that can have adverse health effects [35]. The marginal significance of this result suggests that the association and corresponding OR between these two factors warrant further investigation and validation.

The counterintuitive finding that treated water users have a lower risk than those using commercial bottled water may reflect socio-economic or behavioral factors not captured in this study. It is possible that those who treat their own water are more vigilant about overall hygiene and environmental health, thus reducing their overall risk [36]. Moreover, it is essential to consider the quality and management of commercial water refill depots relied on by the respondents, which may vary widely. Further research is needed to explore the specific contaminants in the water sources and their direct impact on CLP development. Detailed water quality testing and longitudinal studies could provide more definitive insights into the relationship between water source quality and congenital defects.

3.2. Parental Lifestyle

There are a total of 10 parental lifestyle factors assessed in this study. The first four factors (active and passive smoking, alcohol consumption, and caffeine consumption) correspond to parental exposure to these substances (tobacco smoke, alcohol, and caffeine) based on their consumption habit in daily life. The next four factors (exposure to industrial solvents, pesticides, radiation, and household chemicals) correspond to parental exposure to these substances in their occupation or in their house. The last two factors (workout routine and drugs/medication consumption) correspond to personal health practices. The initial hypothesis is that, except for the workout routine, all other factors may increase the risk of having children with CLP, compared to CLO/CPO.

The analysis results for each parental lifestyle risk factor are summarized in Table 6. The OR, phi correlation, and p-values of each factors in logistic

regression represent the risk and association between the parental lifestyle risk factors and the co -occurrence of cleft lip and cleft palate. Only three factors (maternal active smoking, paternal passive smoking, and paternal radiation exposure) were found to have an effect on the risk of CLP with marginal significance.

The OR results for the first four factors present a mixed confirmation of the hypotheses. While no factor shows a statistically significant association with CLP at the 5% level, a few show marginal significance. For instance, maternal active smoking, though not statistically significant at the conventional 5% level, shows marginal significance (OR = 0.052, 95% CI: 0.002 - 1.09, p = 0.057). Paternal passive smoking also exhibits marginal significance with an increased risk of CLP (OR = 2.309, 95% CI: 0.897 - 5.942, p = 0.083).

The protective effect (OR<1) result of the maternal smoking factor is surprising, for there are no possible, plausible explanation to this result and thus this result must be interpreted carefully. The small sample size, especially mothers who confirm smoking (only 2 in both CLO/CPO and CLP groups) might be the cause for the counterintuitive result. For the passive smoking factor especially from paternal side, result aligns with existing research that suggests environmental exposures, such as passive smoking, may increase the risk of CLP [37]. Passive smoking's potential mechanism might involve indirect exposure to harmful chemicals in tobacco smoke, which could adversely affect fetal development [38] and male fertility [39]. However, these findings regarding smoking, given their borderline significance, warrant further investigation to confirm these associations and clarify the potential dose-response relationships. Active smoking on paternal side, passive smoking on maternal side, and caffeine & alcohol intake on both maternal and paternal sides did not show significant associations with CLP in this study, possibly due to reporting biases, the relatively small sample size, or variations in exposure levels. Further research on these factors is also needed to explore their impact more deeply, particularly in relation to different degrees of exposure and their impact on CLP risk.

The OR results for the next four factors (exposure to industrial solvents, pesticides, radiation, and household chemicals) present mixed findings with no statistically significant associations but marginal significance for radiation exposure. Paternal exposure to radiation shows a marginally significant association with an increased risk of CLP (OR = 3.489, 95% CI: 0.828 - 14.703, p = 0.089), suggesting a potential link worth further exploration. However, exposure to industrial solvents (such as gasoline, paint thinner, etc.), pesticides, and household chemicals (such as cleaning agents) from both parental sides did not show significant associations with CLP.

The hypothesized association between these parental past exposure factors and CLP risk is based on the known underlying mechanisms that may involve genotoxic effects of these substances, which can lead to DNA damage and disruption of normal fetal development [40][41]. Previous study by Chevrier et al. suggested that maternal occupational exposure to organic solvents during pregnancy might contribute to the etiology of oral clefts [42]. Radiation exposure is known to cause mutations and chromosomal abnormalities, which could explain the high odds ratios observed [43]. Maternal radiation exposure during pregnancy can lead to direct damage to the developing embryo's cells, potentially resulting in congenital malformations, including CLP [44]. Radiation exposure in males might also cause reproductive issues by damaging sperm DNA, further increasing the risk of having children with congenital malformations [45][46].

While the marginal significance of paternal radiation exposure suggests potential reproductive health impacts, possibly through sperm DNA damage that could increase congenital malformation risk, the other factors including industrial solvent and pesticide exposure did not display notable odds ratios or significant p-values. The lack of significant findings for these factors might be due to several reasons, such as the small sample size or insufficient exposure levels among respondents and difficulty in confirming the answers. Household chemical exposure from both parental sides also did not yield a significant association, which may similarly reflect low exposure frequency or variability in household chemical use. Overall, the findings imply that while there may be some influence of environmental

exposures, particularly radiation, further research is necessary to clarify the role of these exposures in the etiology of CLP. Further studies with more detailed exposure assessments are required to confirm these associations and investigate potential relationships.

The OR results for the last two factors, parental workout routine and drugs/medication use, did not show significant associations with CLP cases. Both paternal and maternal workout routines displayed no significant correlation with CLP risk (paternal OR = 0.412, 95% CI: 0.132 - 1.289, p = 0.128; maternal OR = 1.14, 95% CI: 0.392 - 3.313, p = 0.81). Similarly, no significant association was observed for drug or medication use from either parent (paternal OR = 2.607, 95% CI: 0.147 - 46.309, p = 0.514; maternal OR = 1.453, 95% CI: 0.225 - 9.38, p = 0.694). These findings suggest that neither lifestyle factor, within the context of this study, had a notable impact on the risk of having children with CLP.

Although previous research has hypothesized that the use of certain medications taken during pregnancy could increase the risk of congenital anomalies such as CLP through teratogenic effects [47][48], the results here do not support this link in a statistically significant manner. The lack of association between workout routine and CLP was also somewhat unexpected, as it was thought that regular physical activity could promote better reproductive health and fetal development. Regular physical activity is known to improve overall

Table 6. Parental lifestyle factors odds ratio and correlation result.

No	Risk Factors		Odds Ratio (95% CI), Adjusted	p-values
1	Active Smoking	P	0.823 (0.344 – 1.972)	0.662
		M	0.052 (0.002 – 1.09)	0.057*
2	Passive Smoking	P	2.309 (0.897 – 5.942)	0.083*
		M	1.584 (0.594 - 4.222)	0.358
3	Alcohol Consumption	P	0.337 (0.051 - 2.202)	0.256
		M	2.03 (0.213 - 19.362)	0.539
4	Caffeine Consumption	P	1.194 (0.474 – 3.005)	0.706
		M	0.719 (0.233 - 2.22)	0.566
5	Industrial Solvent Exposure	P	2.087 (0.575 – 7.576)	0.263
		M	0.641 (0.04 – 10.359)	0.754
6	Pesticide Exposure	P	0.621 (0.088 - 4.361)	0.632
		M	1.281 (0.202 – 8.127)	0.793
7	Radiation Exposure	P	3.489 (0.828 - 14.703)	0.089*
		M	1.991 (0.467 – 8.481)	0.352
8	Household Chemical Exposure	P	1.8 (0.215 - 15.092)	0.588
		M	4.216 (0.543 - 32.751)	0.169
9	Workout Routine	P	0.412 (0.132 - 1.289)	0.128
		M	1.14 (0.392 - 3.313)	0.81
10	Drugs or Medication	P	2.607 (0.147 - 46.309)	0.514
		M	1.453 (0.225 - 9.38)	0.694

health, reduce stress, and enhance circulation, which could positively influence reproductive health and fetal development [49][50]. However, this study's results indicate that neither regular exercise nor the use of medications during pregnancy has a clear, measurable effect on CLP risk. Further studies with larger sample sizes and more detailed exposure data on medication types and physical activity levels are needed to explore these factors more comprehensively. Understanding the potential risks and benefits of medications, as well as how parental health practices like exercise influence congenital outcomes, remains a crucial area for future research.

4. CONCLUSIONS

The findings of this study contributed knowledge on the multifaceted factors influencing the incidence of CLP births in Indonesia. Through a comprehensive analysis of residential environmental factors and parental lifestyles, significant associations with CLP incidence have been identified. Residential environmental factors such as proximity to industrial areas, ventilation, and drinking water source emerged as significant risk factors for CLP, while unexpected protective effects were observed for certain flooring materials, with marginal significance. These findings underscore the importance of considering environmental exposures in residential settings to mitigate CLP risk. Additionally, some parental factors were found to be linked with CLP cases with marginal significance, specifically maternal active smoking, paternal passive smoking, and paternal radiation exposure. These results emphasize the need for parental health interventions and lifestyle modifications to reduce CLP risk. However, it is essential to acknowledge the limitations of this study. The heavy reliance on self-reported data through questionnaires introduces the potential for recall bias and misclassification. Additionally, while each results in the analysis are adjusted through multivariable regression, the study may not have fully accounted for certain confounding variables, such as genetic predispositions and other unmeasured environmental exposures, which could impact the results. The absence of exposure validation methods, such as environmental monitoring or biomarker analysis, further limits the accuracy of the findings. Future research should aim to address these limitations by incorporating more robust study designs, including objective exposure assessments and genetic screening, to enhance the validity of the results. The study's findings contribute to the growing body of literature on CLP etiology and highlight the necessity for continued research in this field. Future studies should explore the mechanisms underlying the observed associations and investigate additional environmental and parental factors influencing CLP incidence.

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethical Committee of Padjadjaran University, Protocol No: 882/UN6.KEP/EC/2023.

INFORMED CONSENT

Informed consent was obtained from all respondents included in this study. Each participant signed a consent form agreeing to their participation and the use of their data for research purposes. The authors state that there is no detailed identification (name, characteristics, photos, and other information) of the respondents who are presented in the manuscript of this paper, all respondents related to this study have been anonymized.

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