

Determinants of autism spectrum disorder in children: A case-control study in Pontianak, West Kalimantan, Indonesia

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ABSTRACT

Introduction: Children with Autism Spectrum Disorder (ASD) who use the government's service facilities for children with special needs in Pontianak are increasing. This study aims to find out the determinants of ASD in Pontianak.

Material and Methods: This study investigates the determinants of ASD in children in Pontianak, West Kalimantan, using a case-control design. The study included 49 children diagnosed with ASD and 100 age-matched controls, with data collected through maternal questionnaires. The risk factors examined included gender, genetic factors, parental age, maternal health during pregnancy, perinatal risk factors, environmental exposures, and maternal habits. Data analysis using logistic regression.

Results: The results indicate a significantly higher likelihood of ASD in boys. Higher maternal education levels were also associated with increased ASD risk. Family history, particularly having siblings or relatives with ASD, emerged as a significant risk factor. Maternal anxiety during pregnancy doubled the risk of ASD, while frequent fruit consumption during pregnancy and exclusive breastfeeding were identified as protective factors. Exposure to vehicle fumes during pregnancy increased ASD risk. Turning off cell phones during sleep was also protective.

Conclusion: These findings highlight the need to address both genetic and environmental factors in ASD aetiology. Promoting healthy maternal habits and reducing harmful environmental exposures could potentially reduce ASD risk. Future research should focus on larger sample sizes and longitudinal studies to validate these findings and develop targeted interventions.

KEYWORDS:

Autism Spectrum Disorder (ASD); Case-Control Study; Child Health; Environmental Exposures; Maternal Health; Risk Factors

INTRODUCTION

Autism Spectrum Disorder (ASD) affects individuals through social communication difficulties, restricted interests, and repetitive behaviours from early life.¹ ASD encompasses

conditions like Autistic disorder, Rett disorder, Asperger syndrome, and pervasive developmental disorder.^{1,2} The term "spectrum" reflects the variability in symptoms and severity. ASD symptoms often manifest in the first year, though some children show developmental decline between 18 and 24 months.³

The prevalence of ASD in American children has increased significantly. In 2018, the CDC estimated 1 in 59 eight-year-olds had ASD, a rate that doubled over two decades.⁴ By 2023, this estimate rose to 1 in 36 children.⁵ Globally, 1 in 100 children are estimated to have ASD⁶, up from 1 in 160 children in 2015.⁷ The precise aetiology of ASD remains to be elucidated, although genetic factors are considered a significant contributor.^{8,9} Environmental factors, such as parental age, the fetal environment, perinatal risks, substance exposures, and psychosocial factors, are also considered risks.¹⁰ The exploration of these relationships remains an active area of research.

Understanding the increasing ASD prevalence is crucial to mitigating future risks. ASD significantly impacts life quality, contributing over 58 disability-adjusted life years (DALYs) per 100,000 population globally.⁷ This burden affects the quality of life for future generations. In Pontianak, the number of children diagnosed with ASD has increased, with 147 cases being reported between 2015 and 2020. This data was recorded by the Disability Service and Assessment Centre (DSAC) and the Main Clinic of Pontianak Psychiatric Hospital (PPH). On average, 20 new cases of ASD are recorded each year at these two units for children with special needs.¹¹ The causes of autism in Pontianak remain unstudied. This study aims to identify the relationship between risk factors and autism in Pontianak.

MATERIALS AND METHODS

Study Design

This study employed a case-control design to investigate the determinants of ASD in Pontianak, West Kalimantan. The research involved 49 children diagnosed with ASD and 100 age-matched controls without ASD.

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Participants

Participants comprised children aged 2 to 12 years who resided in Pontianak, with their data obtained from the Disability Services and Assessment Centre and Pontianak Psychiatric Hospital. Inclusion criteria required the participants to be biological children and residents of Pontianak. Exclusion criteria included instances where the patient had relocated, making their new address untraceable, as well as cases where the biological mother had passed away. Fig. 1 shows the data selection flow. Controls were defined as children of the same age as the cases, residing in proximity to them. The subjects of this research were the mothers of the children, who provided informed consent before participating.

Data Collection

Data were collected using a structured questionnaire administered to the mothers. The questionnaire elicited information on the socio-demographic characteristics, including gender (male, female), children's age group (2-<5 years, 5-12 years), birth weight (<2500 grams, ≥2500 grams), gestational age (preterm, term), caesarean section (yes, no), maternal age at pregnancy (<30 years, ≥30 years), paternal age at pregnancy (≤40 years, >40 years), mother's education (primary to middle education ≤12 years, higher education >12 years), father's education (primary to middle education ≤12 years, higher education >12 years), maternal occupation during pregnancy/working outside home (yes, no), and residence during pregnancy (Pontianak, outside Pontianak). We also asked 18 factors associated with ASD, such as whether the child had siblings with ASD (yes, no), relatives with a history of ASD (yes, no), the mother's habit of consuming vegetable and fruit during pregnancy (3 times/week – every day, never-seldom), exposed to smoke from forest and land fires (yes, no), exposed to smoke from forest and land fires when baby <6 months (yes, no). Maternal exposure to vehicle fumes during pregnancy was determined through self-reported data collected via structured interviews. Mothers were asked about their daily activities, including time spent near traffic, commuting habits, and whether they regularly passed or stayed near busy roads. Responses were used to classify daily exposure to vehicle emissions. Exposed to vehicle fume during pregnancy (3 times/week – every day, never-seldom), whether the mother living with smoker, experienced hypertension, hyperemesis, bleeding, and anxiety during pregnancy (yes, no), the baby experience fever – seizure when <2 years old (yes, no), whether the mother provided exclusive breastfeeding (yes, no). Exposure to television and cell phones was assessed through parental interviews. Parents were asked to report the age at which their child was first exposed to these devices. Additionally, they were asked whether this exposure began before or after the child was diagnosed with ASD. This information was used to explore potential temporal relationships between media exposure and ASD development. Mothers were also asked whether they turned off their cell phones when sleeping at night with their children.

Statistical Analysis

Data were analysed using multivariate and bivariate methods. The chi-square test was used to examine the

association between each risk factor and ASD. Logistic regression was conducted to identify the most significant risk factors for ASD, providing adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Health Research Ethics Committee (HREC) of Politeknik Kesehatan Kemenkes Pontianak (No. 58/KEPK-PK.PKP/III/2022). Informed consent was obtained from all participants.

Data Management

To ensure confidentiality, the data were anonymised and analysed using appropriate statistical software to verify the reliability and validity of the findings. Adherence to rigorous ethical standards ensured compliance with established guidelines.

RESULTS

Table I represent the sociodemographic characteristics of the respondents. Among the 11 observed variables, four sociodemographic variables had a significant relationship with the incidence of ASD: gender, maternal education, maternal employment outside the home, and maternal residence during pregnancy. Table II shows five related factors that had a significant relationship in the bivariate analysis. These variables were a family history of ASD, maternal fruit consumption habits during pregnancy, exposure to vehicle exhaust during pregnancy, anxiety during pregnancy, and turning off mobile phones while sleeping.

The results indicate a significant difference in gender distribution between cases and controls. Boys were found to have a seven times higher risk of developing ASD compared to girls (OR: 7.04, 95% CI: 2.888–17.179; $p < 0.05$). Even after adjusting for other variables as seen in Table III, boys are eight times as likely to develop ASD (OR: 8.08, 95% CI: 2.93–22.21; $p < 0.05$). Maternal education level emerged as a significant risk factor. Mothers with a higher education level (>12 years) were more likely to have a child with ASD (OR: 2.492, 95% CI: 1.237–5.020; $p < 0.05$). After adjusting for other variables in the multivariate analysis in Table III, mothers with more than 12 years of education had almost a sixfold increased risk of having a child with ASD (OR: 5.96, 95% CI: 2.26–15.70; $p < 0.05$). Furthermore, employed mothers showed an increased risk, although this factor did not remain significant after adjusting for other variables. Living in Pontianak city during pregnancy was a protective factor (OR = 0.216, 95% CI: 0.045–0.860; $p < 0.05$), but this variable was no longer significant after adjusting for other variables.

As demonstrated in Table II, a total of 18 variables were identified as potentially correlating with the incidence of ASD. However, subsequent analysis revealed that only 6 of these variables exhibited a significant relationship. The presence of a family history of ASD in children was found to be a significant predictor of the development of ASD, with an odds ratio of 3.525 (95% confidence interval: 1.177–10.561; $p < 0.05$). This indicates that children with a family history of

Table I: Socio-demographic characteristics

Variable	Categories	Case n = 49	Control n =100	Unadjusted OR (CI 95%)
		n (%)	n (%)	
Gender	Male / Female	42 (86) / 7 (14)	45 (45) / 55 (55)	7.04 (2.888 – 17.179)*
Children’s age	2-<5 ys / 5-12 ys	15 (31) / 34 (69)	25 (25) / 75 (75)	1.324 (0.621 - 2.823)
Birth weight	<2500 g / ≥2500 g	6 (12) / 43 (48)	9 (9) / 91 (91)	1.411 (0.472 – 4.216)
Gestational age	Preterm / Term	2 (4) / 47 (96)	6 (6) / 94 (94)	0.668 (0.064 - 3.924)
Caesarean section	Yes / No	14 (29) / 35 (71)	27 (27) / 73 (73)	1.081 (0.505 – 2.315)
Maternal age	<30 ys / ≥30 ys	26 (53) / 23 (47)	57 (57) / 43 (43)	0.853 (0.429 – 1.695)
Paternal age	≤40 ys / >40 ys	21 (43) / 28 (57)	47 (47) / 53 (53)	0.846 (0.425 – 1.684)
Mother’s education	>12 ys / ≤12 ys	27 (55) / 22 (45)	33 (33) / 67 (67)	2.492 (1.237 – 5.020)*
Father’s education	>12 ys / ≤12 ys	20 (43) / 29 (57)	45 (45) / 55 (55)	0.843 (0.422 – 1.685)
Working outside	Yes / No	19 (39) / 30 (61)	21 (21) / 79 (79)	2.382 (1.126 – 5.041)*
Residence during pregnancy	Pontianak / Outside Pontianak	41 (84) / 8 (16)	96 (96) / 4 (4)	0.216 (0.045 – 0.860)*

CI, confidence interval; OR, odds ratio; *= significant at p<0.05

Table II: Associated factors

Variable	Categories	Case n = 49	Control n =100	Unadjusted OR (CI 95%)
		n (%)	n (%)	
Siblings with ASD	Yes / No	5 (10) / 44 (90)	2 (2) / 98 (98)	5.498 (0.860 – 59.84)
Relative with ASD	Yes / No	9 (18) / 40 (82)	6 (6) / 94 (94)	3.525 (1.177 – 10.561)*
Vegetable consumption	Never-seldom / 3 times a week-everyday	13 (27) / 36 (73)	16 (16) / 84 (84)	1.896 (0.827 – 4.345)
Fruit consumption	Never-seldom / 3 times a week-every day	26 (53) / 23 (47)	74 (74) / 26 (26)	0.397 (0.194 – 0.814)*
Exposed to smoke from forest and land fires	Yes / No	6 (12) / 43 (88)	23 (23) / 77 (77)	0.467 (0.177 – 1.236)
Exposed to smoke from forest and land fires when baby <6 months	Yes / No	4 (8) / 45 (92)	17 (17) / 83 (83)	0.436 (0.101 – 1.449)
Exposed to vehicle fume during pregnancy	3 times a week-everyday / Never-seldom	18 (37) / 31 (63)	21 (21) / 79 (79)	2.184 (1.027 – 4.644)*
Living with smoker	Yes / No	22 (45) / 27 (55)	50 (50) / 50 (50)	0.815 (0.410 – 1.618)
Hypertension	Yes / No	4 (8) / 45 (92)	14 (14) / 86 (86)	0.548 (0.124 – 1.882)
Hyperemesis	Yes / No	22 (45) / 27 (55)	58 (58) / 42 (42)	0.590 (0.296 – 1.175)
Bleeding during pregnancy	Yes / No	4 (8) / 45 (92)	6 (6) / 94 (94)	1.389 (0.274 – 6.198)
Anxiety during pregnancy	Yes / No	19 (39) / 30 (61)	22 (22) / 78 (78)	2.245 (1.067 – 4.727)*
Fever – seizure when baby <2 years old	Yes / No	8 (16) / 41 (84)	8 (8) / 92(92)	2.244 (0.788 – 6.391)
Exclusive breastfeeding	Yes / No	27 (55) / 22 (45)	76 (76) / 24 (24)	0.388 (0.187 – 0.801)*
Exposed to Television	Yes / No	40 (82) / 9 (18)	85 (85) / 15 (15)	0.784 (0.316 – 1.944)
Exposed to cellphone	Yes / No	35 (71) / 14 (29)	83 (83) / 17 (17)	0.512 (0.228 – 1.151)
Turn off the cell phone when sleep	Yes / No	13 (27) / 36 (73)	54 (54) / 46 (46)	0.308 (0.146 – 0.649)*

CI, confidence interval; OR, odds ratio; *= significant at p<0.05

Table III: Multivariate analysis

Variable	Adjusted OR (CI 95%)	Significant
Gender	8.08 (2.93 – 22.21)	*
Mother’s education	5.96 (2.26 – 15.70)	*
Fruit consumption	0.25 (0.09 – 0.67)	*
Exclusive breastfeeding	0.32 (0.13 – 0.79)	*
Turn off the cell phone when sleep	0.27 (0.11 – 0.66)	*

OR = Odds Ratio; CI = Confidence Interval; * = significant at p<0.05

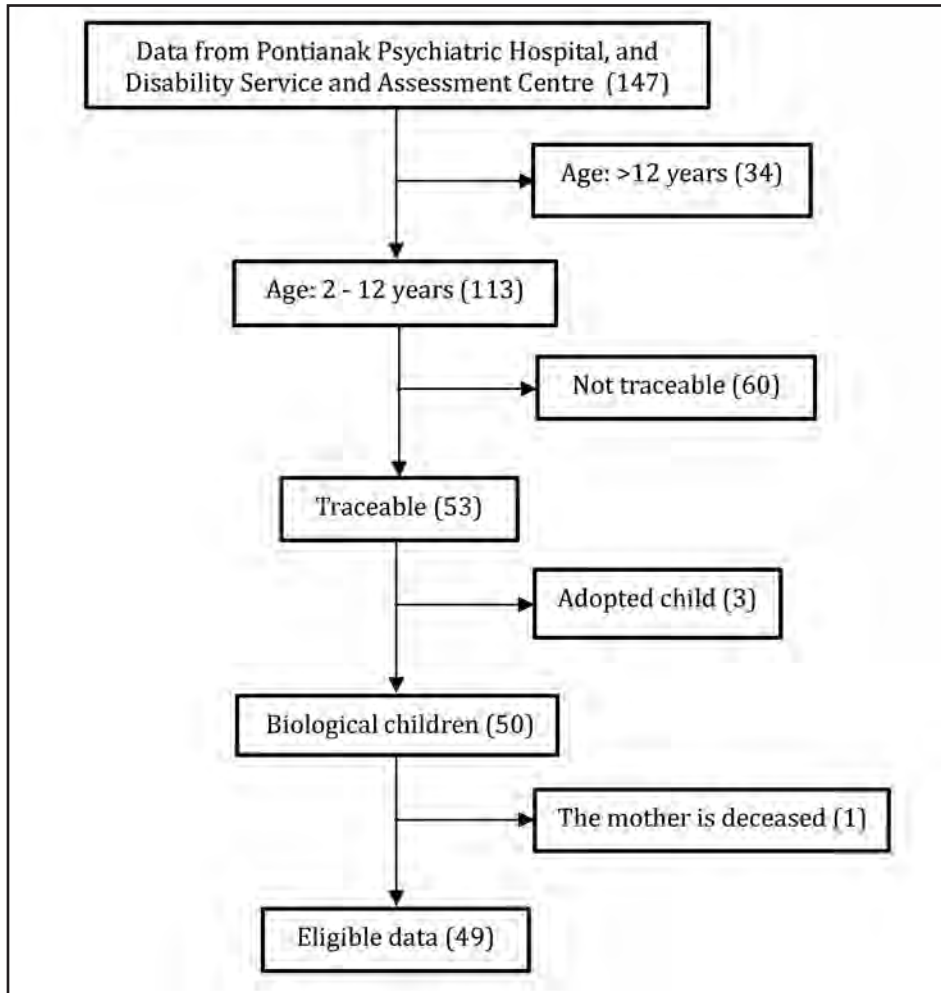


Fig. 1: Data selection flowchart

ASD are 3.5 times more likely to develop the condition themselves. Following adjustment for other variables, the relationship between this variable and the outcome was not found to be significant. The study identified the mother's consumption of fruit during pregnancy as a significant protective factor, with an odds ratio of 0.397 (95% CI: 0.194-0.814; $p < 0.05$). Following adjustments for confounding variables, this dietary habit remained a protective factor for the development of ASD (odds ratio [OR]: 0.25; 95% confidence interval [CI]: 0.09-0.67; $p < 0.05$).

Exposure to vehicle exhaust, occurring three times a week to every day, in pregnant women was identified as a risk factor for ASD (OR: 2.184; 95% CI: 1.027 – 4.644; $p < 0.05$). However, following the adjustment for other variables, this association was no longer observed. Conversely, maternal anxiety during pregnancy has been demonstrated to double the risk of offspring developing ASD. However, following the adjustment for other variables, this anxiety was no longer found to be a causal factor. Exclusive breastfeeding has been identified as a protective factor against the development of ASD (OR: 0.388; 95% CI: 0.187-0.801; $p < 0.05$). Following adjustment for other confounding variables, this variable maintains its protective factor status against the

development of ASD (OR: 0.32; 95% CI: 0.13-0.79). Furthermore, the act of mothers turning off their mobile phones while sleeping with their babies has been shown to be a protective factor against the development of ASD (OR: 0.308; 95% CI: 0.146-0.649; $p < 0.05$), and this remains the case after adjusting for other variables (OR: 0.27; 95% CI: 0.11-0.66; $p < 0.05$).

DISCUSSION

One of the most significant findings was the increased risk of ASD in boys. Boys were found to be seven times more likely to develop ASD compared to girls, and this remained significant even after adjusting for other variables. This gender disparity is well-documented in the literature, with numerous studies indicating a higher prevalence of ASD in males.^{12,13} The exact reasons for this discrepancy are not entirely understood, but hypotheses include differences in brain development, hormonal influences, and genetic factors.⁸ Research suggests that boys might be more susceptible to ASD due to sex-linked genetic factors and differential brain development pathways influenced by sex hormones such as testosterone. Additionally, genetic studies have found that boys are more likely to inherit mutations associated with ASD.⁸

Understanding these mechanisms is crucial for developing gender-specific interventions and supports.

Maternal education level was another significant factor, with mothers having higher education levels (>12 years) being more likely to have children with ASD. This finding is consistent with studies from various regions, including Bangladesh, Bradford, and San Francisco, which also reported higher ASD prevalence in children of highly educated parents.¹⁴⁻¹⁶ One possible explanation is that highly educated parents might be more vigilant and capable of seeking a diagnosis for their children. Moreover, it is hypothesised that highly educated mothers may experience elevated levels of stress and anxiety, which may have a detrimental effect on fetal development. The association between higher maternal education and increased ASD risk may also reflect a heightened awareness and access to diagnostic services among educated parents. It has been hypothesised that such parents may adopt a more proactive stance in seeking evaluations for developmental concerns, thereby resulting in enhanced detection rates.¹⁴ Moreover, the stress associated with high-achieving environments could contribute to neurodevelopmental risks.¹⁰ The initial finding that working mothers were at higher risk of having children with ASD did not remain significant after adjusting for other variables. This suggests that while maternal occupation may contribute to stress and lifestyle factors, it is not a standalone risk factor for ASD. Previous studies have shown mixed results regarding maternal employment and ASD risk, indicating that other underlying factors such as workplace stress and environmental exposures might play a role.¹⁰

It is acknowledged that the respondents in this study were Pontianak residents; however, it is possible that they did not reside there during their pregnancy. The present study found that being a mother in Pontianak during pregnancy was a protective factor for ASD. This is attributable to the fact that Pontianak is the capital of West Kalimantan Province and possesses superior health facilities in comparison to other regions within West Kalimantan, including antenatal care and the early detection of child developmental disorders. It has been demonstrated that mothers residing in Pontianak have more convenient access to educational resources and antenatal care. The hypothesis that stronger social support in urban environments such as Pontianak can help mothers manage stress during pregnancy is one that merits further investigation, given its potential as a risk factor for ASD.¹⁷ Furthermore, it is hypothesised that mothers residing in Pontianak may possess certain demographic characteristics (e.g., higher education, optimal reproductive age) that indirectly contribute to a reduced risk of ASD.

A family history of ASD was identified as a significant risk factor, with children having siblings or relatives with ASD being at a higher risk. This finding is consistent with the genetic predisposition theory, which posits that heritable genetic mutations contribute significantly to the risk of developing ASD.^{8,9} Studies have shown that siblings of children with ASD are more likely to be diagnosed with the disorder, and familial studies suggest that genetic factors account for a large proportion of ASD cases.^{18,19} Genetic studies indicate that specific gene mutations and

chromosomal abnormalities increase ASD risk. For example, polymorphisms in genes like Dopa Decarboxylase and Dopamine Receptor-1 have been linked to ASD.²⁰ Additionally, the presence of interstitial duplications in certain chromosomal regions has been associated with the disorder.²¹ These genetic determinants underscore the importance of genetic counseling and early screening for families with a history of ASD.

Conversely, frequent fruit consumption during pregnancy and exclusive breastfeeding were identified as protective factors against ASD. Regular fruit consumption during pregnancy has been linked to better neurodevelopmental outcomes in children.²² Fruits are rich in essential vitamins, antioxidants, and phytochemicals, which can promote healthy brain development and reduce oxidative stress. Consumption of fruits and vegetables during pregnancy can prevent postpartum depression²³, while postpartum depression was found to be associated with the incidence of autism and mental retardation in children.²⁴

Maternal exposure to vehicle exhaust fumes during pregnancy, with exposure levels ranging from three times per week to daily, has been demonstrated to double the likelihood of offspring being diagnosed with ASD. The study also demonstrated that working mothers exhibited a nearly equal risk of having a child with ASD. This phenomenon can be attributed to the increased likelihood of exposure to vehicle exhaust fumes among working mothers. Vehicle exhaust fumes contain various hazardous substances, including the pollutants of concern in this instance are carbon monoxide (CO), nitrogen oxides (NO_x), sulfur dioxide (SO₂) and fine particulate matter (PM_{2.5}). These substances have the capacity to enter the body of a pregnant woman through inhalation, exerting an effect on placental function, oxygen circulation, and fetal brain development.¹¹ The potential neurotoxic effects of vehicle emissions are supported by research showing that exposure to high levels of air pollution during pregnancy is associated with increased ASD risk.¹⁰ This finding emphasizes the need for public health measures to reduce pregnant women's exposure to pollutants.

High maternal anxiety during pregnancy was associated with a doubled risk of having a child with ASD. This finding is supported by other research indicating that maternal stress and anxiety can impact fetal brain development and increase the risk of neurodevelopmental disorders.¹⁰ The physiological mechanisms behind this association may involve stress hormones such as cortisol, which can cross the placenta and affect fetal development.

Exclusive breastfeeding was another protective factor, reducing the risk of ASD. Breastfeeding provides essential nutrients and fosters a strong mother-child bond, which is crucial for cognitive and emotional development.^{25,26} Breast milk contains bioactive compounds that support brain development and immune function, potentially mitigating the risk of neurodevelopmental disorders. The protective role of exclusive breastfeeding has been documented in several studies. A systematic review and meta-analysis reported that breastfeeding reduces the risk of ASD by 58%, and exclusive

breastfeeding can reduce the risk by 76%.²⁵ The bonding and interaction during breastfeeding are believed to enhance social and cognitive development, crucial areas impacted in ASD.²⁷

Interestingly, the study found that turning off cell phones during sleep was a protective factor against ASD. While the exact mechanism is unclear, it is hypothesised that electromagnetic radiation from cell phones may affect brain development. Studies on animal models have shown behavioral changes due to prolonged exposure to electromagnetic fields.²⁸ Further research is needed to confirm this finding and understand the underlying mechanisms.

Implications for Public Health

The findings of this study have significant public health implications. Identifying modifiable risk factors for ASD can inform prevention strategies and interventions. For instance, promoting healthy maternal habits such as regular fruit consumption and exclusive breastfeeding can potentially reduce the risk of ASD. Public health campaigns can also raise awareness about the impact of environmental exposures, such as air pollution and electromagnetic radiation, on fetal development. Public health initiatives should focus on educating expectant mothers about the benefits of a nutritious diet and the importance of reducing exposure to environmental toxins. Programs aimed at improving air quality and minimizing pollutant exposure during pregnancy could significantly impact ASD prevalence rates.

Limitations and Future Research

Notwithstanding the insightful information this study offered, a number of limitations must be noted. The results may not be as broadly applicable as they could be because of the tiny sample size. To corroborate these findings, more research with broader sample sizes and a more varied population is required. Furthermore, the study used self-reported data, which is prone to bias in recollections. To improve the accuracy of the findings, objective measurements of exposure and health consequences should be incorporated into future studies.

Longitudinal studies are needed to establish temporal relationships between risk factors and ASD development. Furthermore, while the study identified several significant risk factors, the complex interplay between genetic and environmental factors in ASD aetiology warrants further investigation. Longitudinal research can provide more robust evidence on the causal relationships between risk factors and ASD.

CONCLUSION

This study identified several significant risk factors for ASD in Pontianak, including gender, maternal education, family history, maternal health, and environmental exposures. These findings align with existing literature and highlight the importance of both genetic and environmental factors in the aetiology of ASD. The protective effects of healthy maternal habits, such as regular fruit consumption and exclusive breastfeeding, underscore the potential for preventive strategies. Addressing environmental exposures and

promoting healthy maternal behaviors can mitigate the risk of ASD and improve neurodevelopmental outcomes in children. Future research should focus on elucidating the mechanisms underlying these associations and developing targeted interventions to reduce the burden of ASD.

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Author contributions were assigned following the CRediT Taxonomy:

Fathmawati Fathmawati contributed to Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, and Funding acquisition.

Dini Fitri Damayanti contributed to Methodology, Investigation, and Writing – review & editing.

Fara Chitra contributed to Methodology, Investigation, Data curation, Project administration, Supervision, and Writing – review & editing.

Ayu Rafiony contributed to Methodology and Writing – review & editing.

Ismi Ardhini contributed to Methodology, Investigation, and Writing – review & editing.

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