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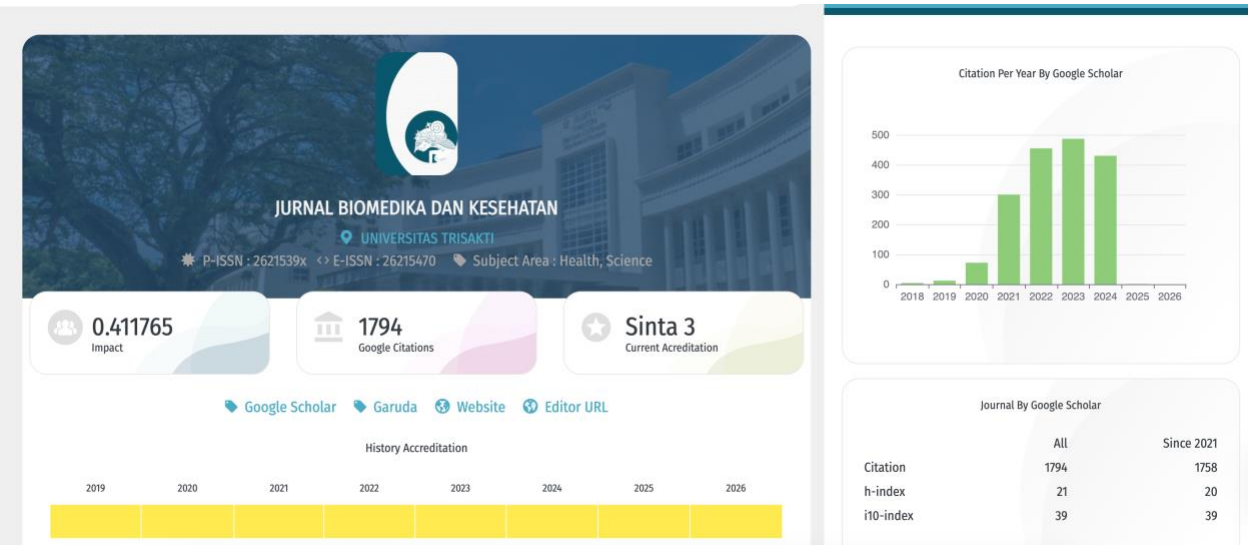

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ORIGINAL ARTICLE

Case-Control Study of Second-hand Smoke and Antenatal Care in Preterm Birth

Studi Kasus–Kelola Paparan Asap Rokok dan Kunjungan Antenatal pada Kejadian Kelahiran Prematur

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ABSTRACT

Background

Preterm birth remains one of the leading contributors to infant mortality in Indonesia. In addition, premature infants are more likely to develop diseases. Obstetric factors, such as parity and frequency of antenatal visits, as well as environmental factors, such as exposure to cigarette smoke, can influence the incidence of preterm birth. In Indonesia, parity remains high, and the frequency of antenatal visits varies by region, along with limited understanding of the dangers of second-hand smoke for fetuses. This study aims to analyze the relationship between parity, frequency of antenatal visits, and second-hand smoking, and the incidence of preterm birth.

Methods

This case-control study included pregnant women aged 20 – 35 years who gave birth to premature and preterm babies between January 2022 and December 2023 in hospitals. Pregnant women with hypertension during pregnancy, antepartum hemorrhage, *multiple* pregnancies, smoking, alcohol consumption, or postterm gestational age (>42 weeks) at birth were excluded from this study. Data on parity, secondhand smoking history, frequency of antenatal visits in the last pregnancy, and gestational age at childbirth were collected using a questionnaire. Medical records and Maternal – Child Health Books were used to confirm the data collected through questionnaires. The relationships and magnitudes of risk associated with parity, secondhand smoking, and frequency of antenatal care contacts with preterm birth were analyzed using the *Chi-Square Test*.

Results

Exposure to cigarette smoke (p=0.036; OR=2.727 [CI: 1.058 - 7.031]) and antenatal visits (p=0.033; OR=4.167 [CI: 1.046 - 16.605]) were associated with the incidence of preterm birth, whereas parity was not associated (p=0.251; OR=1.699 [CI: 0.685 - 4.209]) with the incidence of preterm birth.

Conclusions

Mothers exposed to cigarette smoke ≥ 5 sticks/day and with non-routine antenatal visits had a 2,727-fold and 4,167-fold increased risk of premature birth.

Keywords: Antenatal care contacts; Indonesia; Preterm birth; Second-hand smoking.

ABSTRAK

Latar Belakang

Kelahiran prematur masih merupakah salah satu penyumbang terbesar kematian bayi di Indonesia. Selain itu, bayi yang lahir prematur cenderung lebih mudah mengalami penyakit. Faktor kandungan (obstetrik) seperti jumlah paritas dan frekuensi kunjungan antenatal serta faktor lingkungan seperti paparan asap rokok dapat mempengaruhi kejadian kelahiran prematur. Di Indonesia, tingkat paritas masih tinggi dan frekuensi kunjungan antenatal masih bervariasi di tiap wilayah, serta pemahaman yang masih kurang mengenai bahaya paparan asap rokok dari lingkungan sekitar bagi janin. Penelitian ini bertujuan untuk menganalisa hubungan dan riskio jumlah paritas, frekuensi kunjungan antenatal, serta paparan asap rokok dari lingkungan dengan kejadian kelahiran prematur.

Metode

Penelitian ini merupakan studi kasus Kelola dengan menggunakan subjek Ibu hamil berusia 20 – 35 tahun yang melahirkan bayi prematur dan aterm dalam kurun waktu Januari 2022 – Desember 2023 di Rumah Sakit. Ibu hamil dengan hipertensi selama kehamilan, mengalami komplikasi perdarahan antepartum, kehamilan *multiple*, merokok, mengkonsumsi alkohol, pada kelahiran sebelumnya melahirkan bayi dengan usia gestasi *postterm* (>42 minggu) tidak diikutsertakan dalam penelitian ini. Kuesioner digunakan untuk mengumpulkan data jumlah paritas, riwayat paparan asap rokok dan frekuensi kunjungan antenatal pada kehamilan terakhir, serta usia gestasi saat melahirkan. Rekam medis dan Buku Kesehatan Ibu – Anak digunakan untuk konfirmasi data yang dikumpulkan melalui kuesioner. Hubungan dan besar risiko jumlah paritas, paparan asap rokok, frekuensi kunjungan antenatal terhadap kelahiran premature dianalisa menggunakan Uji *Chi-Square*.

Hasil

Paparan asap rokok (p=0,036;OR=2,727(CI:1,058 - 7,031)) dan kunjungan antenatal (p=0,033;OR=4,167(CI: 1,046 - 16,605)) berhubungan dengan kejadian kelahiran prematur, sedangkan jumlah paritas tidak berhubungan (p=0,251;OR=1,699(CI: 0,685 - 4,209) dengan kejadian kelahiran prematur.

Kesimpulan

Ibu yang terpapar asap rokok ≥ 5 batang/hari dan melakukan kunjungan antenatal tidak rutin memiliki risiko 2,727 kali dan 4,167 kali lebih besar untuk mengalami kelahiran prematur.

Kata Kunci: Indonesia; Kelahiran prematur; Kunjungan antenatal; Paparan asap rokok.

INTRODUCTION

A premature baby is a baby born before the expected gestational age, which is less than 37 weeks.[1] Globally, it is estimated that around 13.4 million babies were born prematurely, representing 9.9% of births in 2020.[2] According to a report by the Central Statistics Agency (BPS), Indonesia had an infant mortality rate of 16.8 per 1000 live births in 2018.[3] Premature birth is the leading cause of infant morbidity and mortality, resulting from the failure of various organ systems.[4] In Indonesia, premature birth is one of the leading causes of neonatal death.[5] Research by Herdiman J and Irwinda R reported 1011 premature births out of 2447 (41.32%) births at Dr. Cipto Mangunkusumo National Hospital during January - December 2014.

Several factors increase the risk of premature birth. Maternal factors include age at pregnancy, nutrition, and smoking habits during pregnancy, as well as environmental factors such as exposure to cigarette smoke during pregnancy.[8] Pregnant women generally know they need nutritious food intake during pregnancy,[9] and that they need to avoid alcohol consumption and smoking during pregnancy.[10] However, pregnant women sometimes pay less attention to the dangers of exposure to cigarette smoke from the surrounding environment during their pregnancy.[11] Indonesia has the highest number of smokers in Southeast Asia and ranks third worldwide.[12,13] The increase in the number of active smokers is related to the increase in the number of passive smokers, which is caused by the large number of active smokers who smoke at home.[12] Some chemicals in cigarettes, such as nicotine and carbon monoxide, can be transmitted

through the placenta in pregnant women to the fetus.[14,15] Exposure to these two compounds results in fetal hypoxia, which will increase the risk of premature birth.[16] Research conducted by Rang N. et al stated that there is a relationship between exposure to cigarette smoke during pregnancy and premature birth.[17] Wang L. et al also stated that pregnant women with husbands who are active smokers have a higher risk of premature birth.[18] However, research conducted by Tamura N. et al showed that there is a relationship between exposure to cigarette smoke during the first trimester of pregnancy and the incidence of premature birth.

Other factors that can influence preterm birth include obstetric factors, such as the frequency of antenatal visits and parity status. [20–22] Antenatal visits are part of government programs to prevent maternal and infant mortality in Indonesia.[23] The number of antenatal visits varies across regions in Indonesia.[24] Routine, high-quality antenatal visits reduce the risk of various pregnancy-related abnormalities, including conditions associated with preterm birth.[20,21] Pervin J. et al. found that three or more antenatal visits during pregnancy reduced the risk of preterm birth.[20] These results differ slightly from those of Melo EC. et al., which reported that mothers with more than six antenatal visits had a lower risk of preterm birth.[21] Another study by Ningsih NS. et al. found no association between antenatal visits and preterm birth.[25]

Maternal parity status, another obstetric factor, has been widely studied for its relationship to preterm birth. Contrary to previous research, these results were obtained. Research by Maharani E et al stated that primiparas have a higher risk of experiencing premature birth, while research by Koullali B et al found that the risk of premature birth was higher in nulliparous mothers and multiparous mothers with their fifth or more pregnancies.[22]

Results from previous studies differ. This study offers several novelties compared with previous studies, including the use of reliable secondary data (medical records and maternal and child health books) to corroborate several types of primary data collected, and the recruitment of research subjects beyond a single region. The purpose of this study was to analyze the effects of cigarette smoke exposure, parity status, and frequency of antenatal visits on the incidence of preterm birth among mothers aged 20-35 years.

METHODS

This is an observational analytical study with a case-control design. The cases were mothers who gave birth prematurely (<37 weeks), while the controls were mothers who gave birth at term (≥37 weeks). The study population comprised mothers aged 20-35 years who gave birth between January 2022 and December 2023 at three public hospitals in DKI Jakarta, Banten, and Central Java. Mothers with comorbid hypertension during pregnancy, multiple pregnancies, smoking habits, alcohol consumption, postterm birth (>42 weeks), and antepartum hemorrhage complications were excluded from this study. The ratio of cases to controls in this study was 1:1, and they were selected using consecutive non-random sampling. The sample size calculation included a 15% dropout rate, resulting in a total sample of 38 subjects. Cigarette smoke exposure criteria were divided into two groups: at-risk (exposure ≥5 cigarettes/day) and not at-risk (exposure <5 cigarettes/day). The frequency of antenatal visits was categorized as routine (minimum: 2 visits in the first trimester, 1 in the second trimester, and 3 in the third trimester) or non-routine (not meeting the routine criteria). Parity status, another variable analyzed in this study, was categorized into two groups: multiparous (having given birth more than once) and primiparous (having given birth once).

Materials and Instruments: This study used medical records, maternal and child health books, and questionnaires. Medical records were used to confirm gestational age at delivery and to document antepartum hemorrhage, multiple gestation, and hypertension during the last pregnancy. The maternal and child health book was used to confirm the number of antenatal visits, while the questionnaire was used to record smoking history, alcohol consumption during

pregnancy, and history of cigarette smoke exposure. Before the study began, the researchers provided informed consent, and respondents were asked to sign an assent form.

Data were analyzed using the chi-square test in the Statistical Package for the Social Sciences (SPSS) 27. The significance level was set at 5%. This study received ethical review by the Faculty of Medicine, Universitas Trisakti, under number 81//KER-FK/VII/2023, and obtained research permits from the three hospitals where the data were collected.

RESULTS

The subjects of this study were 76 mothers aged 20-35 years, 38 of whom had full-term births and 38 of whom had preterm births. This study found that among the 76 mothers, 60.5% had a high school education or equivalent, 77.6% were housewives, 59.2% were exposed to cigarette smoke (<5 cigarettes/day during pregnancy), 51.3% were multiparous, and 82.9% had undergone routine antenatal check-ups. Furthermore, of the 39 multiparous mothers, 1 mother had a history of preterm birth (2.56%).

Table 1. Respondent Characteristics (n=76)

Variable	Frequency (n=76)	Percentage (%)
Education Level		
Elementary School	7	9.2
Middle School	9	11.8
High School or Equivalent	46	60.5
Bachelor's Degree	14	18.4
Occupation		
Housewives	59	77.6
Civil servants	1	1.3
Private employees	10	13.2
Self-employed	4	5.3
Doctors	1	1.3
Teachers	1	1.3
Exposure to cigarette smoke during pregnancy		
No risk	45	59.2
Risky	31	40.8
Parity status		
Multipara	39	51.3
Primipara	37	48.7
Frequency of antenatal visits		
Routine	63	82.9
Not Routine	13	17.1

Table 2 shows that among subjects exposed to high-risk cigarette smoke (≥5 cigarettes/day) during pregnancy (64.5%), most experienced preterm birth, whereas the majority of those exposed to low-risk cigarette smoke (<5 cigarettes/day) gave birth to full-term babies (60.0%). The results showed an odds ratio (OR) of 2.727 for the association between cigarette smoke exposure and preterm birth. In addition, Table 2 shows that subjects with irregular antenatal visits mostly experienced preterm birth (76.7%), with an OR of 4.167.

Table 2. The Relationship between Exposure to Cigarette Smoke, Parity Status, History of Preterm Birth, and Antenatal Visits with the Incidence of Preterm Birth

Variable	Aterm N = 38(%)	Preterm N = 38(%)	Total	*p-value*	OR	CI
Exposure to cigarette smoke						
No risk	27(60.0)	18(40.0)	45	0.036*	2.727	1.058-7.031
Risky	11(35.5)	20(64.5)	29			
Parity status						
Multipara	22(56.4)	17(43.6)	38	0.251	1.699	0.685 – 4.209
Primipara	16(43.2)	21(56.8)	36			
Frequency of antenatal visits						
Routine	35(55.6)	28(44.4)	63	0.033*	4.167	1.046 – 16.605
Not routine	3(23.1)	10(76.9)	13			

*p<0,05; Chi-Square test.

DISCUSSION

Cigarettes contain various compounds that are harmful to pregnant women, such as nicotine and carbon monoxide, which can cause vasoconstriction, inflammation, and oxidative stress that play a role in premature birth.[14] Nicotine interferes with pregnancy by reducing blood flow to the uterus and causing changes in the blood vessels of the placenta.[26] The second compound, carbon monoxide from cigarette smoke, can circulate in the mother's blood and disrupt the bond between hemoglobin (Hb) and oxygen (O2), thereby causing a decrease in O2 distribution to fetal tissue.[27,28] Exposure to these two compounds inhibits fetal growth and development and reduces the mother's gestational age at delivery.[18] In addition, premature birth due to exposure to passive cigarette smoke occurs through the mechanism of oxidative stress, which then causes an increase in prostaglandin levels and increased sensitivity to oxytocin. [8,29]

This study found a relationship between cigarette smoke exposure and the incidence of preterm birth (p = 0.036), with an increased risk of preterm birth by 2.72 times among mothers exposed to cigarette smoke at ≥ 5 cigarettes/day during pregnancy. Previous research by Rang et al reported similar findings, showing that exposure to cigarette smoke during pregnancy increased the risk of preterm birth by 1.92 times.[17] Another study by Wang L. et al found a relationship between cigarette smoke exposure during pregnancy and preterm birth, with the risk increasing with the number of cigarettes consumed by the father at home (paternal smoking). [18] The findings in this study differ from those of Tamura N. et al, who reported no relationship between cigarette smoke exposure and the incidence of preterm birth. [19] This difference is likely due to the fact that Tamura N. et al assessed cigarette smoke exposure only in the first trimester of pregnancy, whereas this study did not differentiate the trimester of pregnancy when exposure occurred.

Another study by Andriani H and Kuo HW also found no association between paternal cigarette smoke exposure and preterm birth. [30] The association between cigarette smoke exposure and preterm birth was apparent only when analyzing the number of cigarettes smoked (groups >20 cigarettes/day) [30] These findings suggest that the impact of cigarette smoke exposure on preterm birth is influenced by the number of cigarettes smoked by people in the pregnant woman's home environment, particularly the father of the fetus. Differences between the results of Andriani H and Kuo HW's study and this study include the fact that the data in Andriani H and Kuo HW's study came from parents of children aged 0-5 years and relied solely on the mother's recollection of the child's gestational age. This study used more accurate data by including mothers who had given birth within the past year and medical records to confirm gestational age at delivery.

Parity is often associated with an increased risk of preterm birth. Primiparous mothers have a higher risk of preterm birth than multiparous mothers. Maharani A. et al. reported a 2,978-fold increased risk of preterm birth among primiparous mothers. This is because primiparous mothers have an increased risk of gestational hypertension, fetal distress, and oligohydramnios.

Another study by Dasa TT. et al. found that multiparous mothers with five or more pregnancies (grand multiparity) had an increased risk of preterm birth. The different results in this study are likely due to the lack of differentiation between multiparous mothers with 2–4 births (low multiparity) and those with more than 4 births (grand multiparity). [32] These results differ from the study by Waldenstrom U. et al., which reported that the risk of preterm birth was not influenced by maternal parity status, but that the risk increased with maternal age. [33]

This study found no association between parity status and preterm birth but observed a higher number of preterm births among primiparous mothers, with a 1.699-fold increased risk compared to multiparous mothers. This difference from previous studies is likely due to the fact that this study included only mothers aged 20–35 years, considered the ideal gestational age. [23] This suggests that maternal age may play a significant role in preterm birth, both in primiparous and multiparous mothers.

Another obstetric risk factor examined in this study was a history of preterm birth in multiparous mothers. The mechanism by which a history of preterm birth increases the risk of preterm birth in subsequent pregnancies remains unclear.[34] Previous research by Alijahan R. et al. reported a relationship between the two, with an odds ratio of 12.7.[34]

Another study by Tingleff T. et al. also reported that a history of preterm birth in the first pregnancy was a major risk factor for preterm birth in the second pregnancy.[35] The discrepancy between these results may be due to other factors causing preterm birth, such as gestational hypertension and placental abnormalities, not being excluded in the previous study. Furthermore, only one subject out of 38 multiparous mothers had a history of preterm birth in this study, so the relationship between the two variables remains unclear. This study did not analyze the relationship between a history of preterm birth and preterm birth because it included both primiparous and multiparous mothers. Primiparous mothers did not have a history of preterm birth.

In addition to the three factors above, irregular antenatal visits can also influence the risk of premature birth.[21,36] Antenatal visits aim to prevent, diagnose early, and treat various health problems, including obstetric complications that occur during pregnancy.[37] At each antenatal visit, pregnant women are examined by a doctor or other health professional.[38] Antenatal visits are conducted from the first to the third trimester: two in the first trimester, one in the second, and three in the third. [23] This study found that the majority of mothers who did not have regular antenatal visits gave birth to premature babies (76.9%). This finding indicates that routine antenatal care plays an important role in reducing the risk of premature birth. Baldewsingh GK. et al., found a relationship between antenatal care visits (ANC) and gestational age.[39] That study used a different limit for routine antenatal care visits than this study, namely, 8 visits.[39]

Another study by Hoque AM. et al. also supports the results of this study. The results of this study stated that mothers who did not attend antenatal visits and those with a low number of antenatal visits (1-3 visits) had a 6.7-fold higher risk (95% CI 2.7-16.9) and a 3.4-fold higher risk (95% CI 1.8-6.6) of experiencing preterm birth, respectively. [40] The findings of this study differ from those of Ningsih NS. et al. [25]. The difference in results between this study and the study by Ningsih NS. et al. may be due to the cross-sectional design of the Ningsih NS. et al. study, which resulted in an uneven distribution between the preterm and term birth groups.

Premature birth is associated with increased infant mortality and can affect future health and development.[4] Infant survival rates and future child well-being can be improved by addressing or avoiding factors known to influence preterm birth, such as exposure to five or more cigarettes per day and irregular antenatal visits.

This study used a questionnaire to collect primary data, while medical records and maternal and child health cards were used for secondary data collection and to confirm some of the primary data obtained from the questionnaire. This demonstrates the robustness and accuracy of some of the data used in this study. However, this study still has limitations.

One limitation is that this study did not differentiate between pregnant women who were not exposed to cigarette smoke at all and those exposed to low-risk cigarette smoke (1-4 cigarettes/day). Furthermore, this study did not differentiate between cigarette smoke exposure at home, at work, or in other locations, even though exposure at home and at work may be more intense than in other locations. This study also assessed cigarette smoke exposure only by the number of cigarettes smoked per day, without measuring the amount of carbon monoxide inhaled by pregnant women from cigarettes. Data on cigarette smoke exposure in this study were collected via a questionnaire that relied on subjects' recall, which could introduce recall bias. Another limitation of this study is that all subjects were mothers who gave birth in hospitals.

In Indonesia, many mothers still have midwives assist with their deliveries, both in private midwife practices (29%) and at home (16%) [24] This situation affects the study results, which may not be representative of the entire Indonesian population. Furthermore, the data analysis shows wide confidence intervals, indicating substantial variation and uncertainty in the data.

Further research can be conducted using a cohort study design to assess the causal relationship between cigarette smoke exposure, antenatal visits, and preterm birth. This cohort design can also minimize recall bias. Furthermore, quantitative measurements of carbon monoxide levels inhaled by pregnant women are needed to determine the threshold levels of this compound that influence the incidence of preterm birth. Selecting a broader range of research subjects, including mothers who deliver with midwives, is also recommended to better reflect population conditions in Indonesia.

CONCLUSION

Exposure to cigarette smoke exceeding five cigarettes per day and irregular antenatal visits can increase the risk of preterm birth. These findings suggest that maternal exposure to a certain level of environmental cigarette smoke is associated with preterm birth. However, further research is needed to determine the causal relationship between cigarette smoke exposure, antenatal visit frequency, and preterm birth.

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AUTHORS CONTRIBUTION

These are the author's contributions to the paper: Conceptualization, formal analysis, methodology, project administration, validation, writing the original draft, review, and editing: AHZ, KK. Data curation, investigation, resources, software, supervision: AHZ. Visualization: KK. All authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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ORIGINAL ARTICLE

Case-Control Study of Second-hand Smoke and Antenatal Care in Preterm Birth

Studi Kasus-Kelola Paparan Asap Rokok dan Kunjungan Antenatal pada Kejadian Kelahiran Prematur

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ABSTRACT

Background

Preterm birth remains one of the leading contributors to infant mortality in Indonesia. In addition, premature infants are more likely to develop diseases. Obstetric factors, such as parity and frequency of antenatal visits, as well as environmental factors, such as exposure to cigarette smoke, can influence the incidence of preterm birth. In Indonesia, parity remains high, and the frequency of antenatal visits varies by region, along with limited understanding of the dangers of second-hand smoke for fetuses. This study aims to analyze the relationship between parity, frequency of antenatal visits, and second-hand smoking, and the incidence of preterm birth.

Methods

This case-control study included pregnant women aged 20 – 35 years who gave birth to premature and preterm babies between January 2022 and December 2023 in hospitals. Pregnant women with hypertension during pregnancy, antepartum hemorrhage, *multiple* pregnancies, smoking, alcohol consumption, or postterm gestational age (>42 weeks) at birth were excluded from this study. Data on parity, secondhand smoking history, frequency of antenatal visits in the last pregnancy, and gestational age at childbirth were collected using a questionnaire. Medical records and Maternal – Child Health Books were used to confirm the data collected through questionnaires. The relationships and magnitudes of risk associated with parity, secondhand smoking, and frequency of antenatal care contacts with preterm birth were analyzed using the *Chi-Square Test*.

Results

Exposure to cigarette smoke (p=0.036; OR=2.727 [CI: 1.058 - 7.031]) and antenatal visits (p=0.033; OR=4.167 [CI: 1.046 - 16.605]) were associated with the incidence of preterm birth, whereas parity was not associated (p=0.251; OR=1.699 [CI: 0.685 - 4.209]) with the incidence of preterm birth.

Conclusions

Mothers exposed to cigarette smoke ≥ 5 sticks/day and with non-routine antenatal visits had a 2,727-fold and 4,167-fold increased risk of premature birth.

Keywords: Antenatal care contacts; Indonesia; Preterm birth; Second-hand smoking.

ABSTRAK

Latar Belakang

Kelahiran prematur masih merupakah salah satu penyumbang terbesar kematian bayi di Indonesia. Selain itu, bayi yang lahir prematur cenderung lebih mudah mengalami penyakit. Faktor kandungan (obstetrik) seperti jumlah paritas dan frekuensi kunjungan antenatal serta faktor lingkungan seperti paparan asap rokok dapat mempengaruhi kejadian kelahiran prematur. Di Indonesia, tingkat paritas masih tinggi dan frekuensi kunjungan antenatal masih bervariasi di tiap wilayah, serta pemahaman yang masih kurang mengenai bahaya paparan asap rokok dari lingkungan sekitar bagi janin. Penelitian ini bertujuan untuk menganalisa hubungan dan riskio jumlah paritas, frekuensi kunjungan antenatal, serta paparan asap rokok dari lingkungan dengan kejadian kelahiran prematur.

Metode

Penelitian ini merupakan studi kasus Kelola dengan menggunakan subjek Ibu hamil berusia 20 – 35 tahun yang melahirkan bayi prematur dan aterm dalam kurun waktu Januari 2022 – Desember 2023 di Rumah Sakit. Ibu hamil dengan hipertensi selama kehamilan, mengalami komplikasi perdarahan antepartum, kehamilan *multiple*, merokok, mengkonsumsi alkohol, pada kelahiran sebelumnya melahirkan bayi dengan usia gestasi *postterm* (>42 minggu) tidak diikutsertakan dalam penelitian ini. Kuesioner digunakan untuk mengumpulkan data jumlah paritas, riwayat paparan asap rokok dan frekuensi kunjungan antenatal pada kehamilan terakhir, serta usia gestasi saat melahirkan. Rekam medis dan Buku Kesehatan Ibu – Anak digunakan untuk konfirmasi data yang dikumpulkan melalui kuesioner. Hubungan dan besar risiko jumlah paritas, paparan asap rokok, frekuensi kunjungan antenatal terhadap kelahiran premature dianalisa menggunakan Uji *Chi-Square*.

Hasil

Paparan asap rokok (p=0,036;OR=2,727(CI:1,058 - 7,031)) dan kunjungan antenatal (p=0,033;OR=4,167(CI: 1,046 - 16,605)) berhubungan dengan kejadian kelahiran prematur, sedangkan jumlah paritas tidak berhubungan (p=0,251;OR=1,699(CI: 0,685 - 4,209) dengan kejadian kelahiran prematur.

Kesimpulan

Ibu yang terpapar asap rokok ≥ 5 batang/hari dan melakukan kunjungan antenatal tidak rutin memiliki risiko 2,727 kali dan 4,167 kali lebih besar untuk mengalami kelahiran prematur.

Kata Kunci: Indonesia; Kelahiran prematur; Kunjungan antenatal; Paparan asap rokok.

INTRODUCTION

A premature baby is a baby born before the expected gestational age, which is less than 37 weeks.[1] Globally, it is estimated that around 13.4 million babies were born prematurely, representing 9.9% of births in 2020.[2] According to a report by the Central Statistics Agency (BPS), Indonesia had an infant mortality rate of 16.8 per 1000 live births in 2018.[3] Premature birth is the leading cause of infant morbidity and mortality, resulting from the failure of various organ systems.[4] In Indonesia, premature birth is one of the leading causes of neonatal death.[5] Research by Herdiman J and Irwinda R reported 1011 premature births out of 2447 (41.32%) births at Dr. Cipto Mangunkusumo National Hospital during January - December 2014.[6]

Several factors increase the risk of premature birth. Maternal factors include age at pregnancy, nutrition, and smoking habits during pregnancy, as well as environmental factors such as exposure to cigarette smoke during pregnancy.[8] Pregnant women generally know they need nutritious food intake during pregnancy,[9] and that they need to avoid alcohol consumption and smoking during pregnancy.[10] However, pregnant women sometimes pay less attention to the dangers of exposure to cigarette smoke from the surrounding environment during their pregnancy.[11] Indonesia has the highest number of smokers in Southeast Asia and ranks third worldwide.[12,13] The increase in the number of active smokers is related to the increase in the number of passive smokers, which is caused by the large number of active smokers who smoke at home.[12] Some chemicals in cigarettes, such as nicotine and carbon monoxide, can be transmitted

through the placenta in pregnant women to the fetus.[14,15] Exposure to these two compounds results in fetal hypoxia, which will increase the risk of premature birth.[16] Research conducted by Rang N. et al stated that there is a relationship between exposure to cigarette smoke during pregnancy and premature birth.[17] Wang L. et al also stated that pregnant women with husbands who are active smokers have a higher risk of premature birth.[18] However, research conducted by Tamura N. et al showed that there is a relationship between exposure to cigarette smoke during the first trimester of pregnancy and the incidence of premature birth.

Other factors that can influence preterm birth include obstetric factors, such as the frequency of antenatal visits and parity status. [20–22] Antenatal visits are part of government programs to prevent maternal and infant mortality in Indonesia.[23] The number of antenatal visits varies across regions in Indonesia.[24] Routine, high-quality antenatal visits reduce the risk of various pregnancy-related abnormalities, including conditions associated with preterm birth.[20,21] Pervin J. et al. found that three or more antenatal visits during pregnancy reduced the risk of preterm birth.[20] These results differ slightly from those of Melo EC. et al., which reported that mothers with more than six antenatal visits had a lower risk of preterm birth.[21] Another study by Ningsih NS. et al. found no association between antenatal visits and preterm birth.[25]

Maternal parity status, another obstetric factor, has been widely studied for its relationship to preterm birth. Contrary to previous research, these results were obtained. Research by Maharani E et al stated that primiparas have a higher risk of experiencing premature birth, while research by Koullali B et al found that the risk of premature birth was higher in nulliparous mothers and multiparous mothers with their fifth or more pregnancies.[22]

Results from previous studies differ. This study offers several novelties compared with previous studies, including the use of reliable secondary data (medical records and maternal and child health books) to corroborate several types of primary data collected, and the recruitment of research subjects beyond a single region. The purpose of this study was to analyze the effects of cigarette smoke exposure, parity status, and frequency of antenatal visits on the incidence of preterm birth among mothers aged 20-35 years.

METHODS

This is an observational analytical study with a case-control design. The cases were mothers who gave birth prematurely (<37 weeks), while the controls were mothers who gave birth at term (≥37 weeks). The study population comprised mothers aged 20-35 years who gave birth between January 2022 and December 2023 at three public hospitals in DKI Jakarta, Banten, and Central Java. Mothers with comorbid hypertension during pregnancy, multiple pregnancies, smoking habits, alcohol consumption, postterm birth (>42 weeks), and antepartum hemorrhage complications were excluded from this study. The ratio of cases to controls in this study was 1:1, and they were selected using consecutive non-random sampling. The sample size calculation included a 15% dropout rate, resulting in a total sample of 38 subjects. Cigarette smoke exposure criteria were divided into two groups: at-risk (exposure ≥5 cigarettes/day) and not at-risk (exposure <5 cigarettes/day). The frequency of antenatal visits was categorized as routine (minimum: 2 visits in the first trimester, 1 in the second trimester, and 3 in the third trimester) or non-routine (not meeting the routine criteria). Parity status, another variable analyzed in this study, was categorized into two groups: multiparous (having given birth more than once) and primiparous (having given birth once).

Materials and Instruments: This study used medical records, maternal and child health books, and questionnaires. Medical records were used to confirm gestational age at delivery and to document antepartum hemorrhage, multiple gestation, and hypertension during the last pregnancy. The maternal and child health book was used to confirm the number of antenatal visits, while the questionnaire was used to record smoking history, alcohol consumption during

pregnancy, and history of cigarette smoke exposure. Before the study began, the researchers provided informed consent, and respondents were asked to sign an assent form.

Data were analyzed using the chi-square test in the Statistical Package for the Social Sciences (SPSS) 27. The significance level was set at 5%. This study received ethical review by the Faculty of Medicine, Universitas Trisakti, under number 81//KER-FK/VII/2023, and obtained research permits from the three hospitals where the data were collected.

RESULTS

The subjects of this study were 76 mothers aged 20-35 years, 38 of whom had full-term births and 38 of whom had preterm births. This study found that among the 76 mothers, 60.5% had a high school education or equivalent, 77.6% were housewives, 59.2% were exposed to cigarette smoke (<5 cigarettes/day during pregnancy), 51.3% were multiparous, and 82.9% had undergone routine antenatal check-ups. Furthermore, of the 39 multiparous mothers, 1 mother had a history of preterm birth (2.56%).

Table 1. Respondent Characteristics (n=76)

Variable	Frequency (n=76)	Percentage (%)
Education Level		
Elementary School	7	9.2
Middle School	9	11.8
High School or Equivalent	46	60.5
Bachelor's Degree	14	18.4
Occupation		
Housewives	59	77.6
Civil servants	1	1.3
Private employees	10	13.2
Self-employed	4	5.3
Doctors	1	1.3
Teachers	1	1.3
Exposure to cigarette smoke during pregnancy		
No risk	45	59.2
Risky	31	40.8
Parity status		
Multipara	39	51.3
Primipara	37	48.7
Frequency of antenatal visits		
Routine	63	82.9
Not Routine	13	17.1

Table 2 shows that among subjects exposed to high-risk cigarette smoke (≥5 cigarettes/day) during pregnancy (64.5%), most experienced preterm birth, whereas the majority of those exposed to low-risk cigarette smoke (<5 cigarettes/day) gave birth to full-term babies (60.0%). The results showed an odds ratio (OR) of 2.727 for the association between cigarette smoke exposure and preterm birth. In addition, Table 2 shows that subjects with irregular antenatal visits mostly experienced preterm birth (76.7%), with an OR of 4.167.

Table 2. The Relationship between Exposure to Cigarette Smoke, Parity Status, History of Preterm Birth, and Antenatal Visits with the Incidence of Preterm Birth

Variable	Aterm N = 38(%)	Preterm N = 38(%)	Total	*p-value*	OR	CI
Exposure to cigarette smoke						
No risk	27(60.0)	18(40.0)	45	0.036*	2.727	1.058- 7.031
Risky	11(35.5)	20(64.5)	29			
Parity status						
Multipara	22(56.4)	17(43.6)	38	0.251	1.699	0.685 – 4.209
Primipara	16(43.2)	21(56.8)	36			
Frequency of antenatal visits						
Routine	35(55.6)	28(44.4)	63	0.033*	4.167	1.046 – 16.605
Not routine	3(23.1)	10(76.9)	13			

*p<0,05; Chi-Square test.

DISCUSSION

Cigarettes contain various compounds that are harmful to pregnant women, such as nicotine and carbon monoxide, which can cause vasoconstriction, inflammation, and oxidative stress that play a role in premature birth.[14] Nicotine interferes with pregnancy by reducing blood flow to the uterus and causing changes in the blood vessels of the placenta.[16] The second compound, carbon monoxide from cigarette smoke, can circulate in the mother's blood and disrupt the bond between hemoglobin (Hb) and oxygen (O2), thereby causing a decrease in O2 distribution to fetal tissue.[17,18] Exposure to these two compounds inhibits fetal growth and development and reduces the mother's gestational age at delivery.[18] In addition, premature birth due to exposure to passive cigarette smoke occurs through the mechanism of oxidative stress, which then causes an increase in prostaglandin levels and increased sensitivity to oxytocin.[8,19]

This study found a relationship between cigarette smoke exposure and the incidence of preterm birth (p = 0.036), with an increased risk of preterm birth by 2.72 times among mothers exposed to cigarette smoke at ≥ 5 cigarettes/day during pregnancy. Previous research by Rang et al reported similar findings, showing that exposure to cigarette smoke during pregnancy increased the risk of preterm birth by 1.92 times.[17] Another study by Wang L. et al found a relationship between cigarette smoke exposure during pregnancy and preterm birth, with the risk increasing with the number of cigarettes consumed by the father at home (paternal smoking).[18] The findings in this study differ from those of Tamura N. et al, who reported no relationship between cigarette smoke exposure and the incidence of preterm birth.[19] This difference is likely due to the fact that Tamura N. et al assessed cigarette smoke exposure only in the first trimester of pregnancy, whereas this study did not differentiate the trimester of pregnancy when exposure occurred.

Another study by Andriani H and Kuo HW also found no association between paternal cigarette smoke exposure and preterm birth.[20] The association between cigarette smoke exposure and preterm birth was apparent only when analyzing the number of cigarettes smoked (groups >20 cigarettes/day)[20] These findings suggest that the impact of cigarette smoke exposure on preterm birth is influenced by the number of cigarettes smoked by people in the pregnant woman's home environment, particularly the father of the fetus. Differences between the results of Andriani H and Kuo HW's study and this study include the fact that the data in Andriani H and Kuo HW's study came from parents of children aged 0-5 years and relied solely on the mother's recollection of the child's gestational age. This study used more accurate data by including mothers who had given birth within the past year and medical records to confirm gestational age at delivery.

Parity is often associated with an increased risk of preterm birth. Primiparous mothers have a higher risk of preterm birth than multiparous mothers. Maharani A. et al. reported a 2,978-fold increased risk of preterm birth among primiparous mothers. This is because primiparous mothers have an increased risk of gestational hypertension, fetal distress, and oligohydramnios.

Another study by Dasa TT. et al. found that multiparous mothers with five or more pregnancies (grand multiparity) had an increased risk of preterm birth. The different results in this study are likely due to the lack of differentiation between multiparous mothers with 2–4 births (low multiparity) and those with more than 4 births (grand multiparity). [32] These results differ from the study by Waldenstrom U. et al., which reported that the risk of preterm birth was not influenced by maternal parity status, but that the risk increased with maternal age. [33]

This study found no association between parity status and preterm birth but observed a higher number of preterm births among primiparous mothers, with a 1.699-fold increased risk compared to multiparous mothers. This difference from previous studies is likely due to the fact that this study included only mothers aged 20–35 years, considered the ideal gestational age. [33] This suggests that maternal age may play a significant role in preterm birth, both in primiparous and multiparous mothers.

Another obstetric risk factor examined in this study was a history of preterm birth in multiparous mothers. The mechanism by which a history of preterm birth increases the risk of preterm birth in subsequent pregnancies remains unclear.[34] Previous research by Alijahan R. et al. reported a relationship between the two, with an odds ratio of 12.7.[34]

Another study by Tingleff T. et al. also reported that a history of preterm birth in the first pregnancy was a major risk factor for preterm birth in the second pregnancy.[35] The discrepancy between these results may be due to other factors causing preterm birth, such as gestational hypertension and placental abnormalities, not being excluded in the previous study. Furthermore, only one subject out of 38 multiparous mothers had a history of preterm birth in this study, so the relationship between the two variables remains unclear. This study did not analyze the relationship between a history of preterm birth and preterm birth because it included both primiparous and multiparous mothers. Primiparous mothers did not have a history of preterm birth.

In addition to the three factors above, irregular antenatal visits can also influence the risk of premature birth.[21,36] Antenatal visits aim to prevent, diagnose early, and treat various health problems, including obstetric complications that occur during pregnancy.[37] At each antenatal visit, pregnant women are examined by a doctor or other health professional.[38] Antenatal visits are conducted from the first to the third trimester: two in the first trimester, one in the second, and three in the third. [13] This study found that the majority of mothers who did not have regular antenatal visits gave birth to premature babies (76.9%). This finding indicates that routine antenatal care plays an important role in reducing the risk of premature birth. Baldewsingh GK. et al., found a relationship between antenatal care visits (ANC) and gestational age.[39] That study used a different limit for routine antenatal care visits than this study, namely, 8 visits.[39]

Another study by Hoque AM. et al. also supports the results of this study. The results of this study stated that mothers who did not attend antenatal visits and those with a low number of antenatal visits (1-3 visits) had a 6.7-fold higher risk (95% CI 2.7-16.9) and a 3.4-fold higher risk (95% CI 1.8-6.6) of experiencing preterm birth, respectively. [40] The findings of this study differ from those of Ningsih NS. et al. [25]. The difference in results between this study and the study by Ningsih NS. et al. may be due to the cross-sectional design of the Ningsih NS. et al. study, which resulted in an uneven distribution between the preterm and term birth groups.

Premature birth is associated with increased infant mortality and can affect future health and development.[4] Infant survival rates and future child well-being can be improved by addressing or avoiding factors known to influence preterm birth, such as exposure to five or more cigarettes per day and irregular antenatal visits.

This study used a questionnaire to collect primary data, while medical records and maternal and child health cards were used for secondary data collection and to confirm some of the primary data obtained from the questionnaire. This demonstrates the robustness and accuracy of some of the data used in this study. However, this study still has limitations.

One limitation is that this study did not differentiate between pregnant women who were not exposed to cigarette smoke at all and those exposed to low-risk cigarette smoke (1-4 cigarettes/day). Furthermore, this study did not differentiate between cigarette smoke exposure at home, at work, or in other locations, even though exposure at home and at work may be more intense than in other locations. This study also assessed cigarette smoke exposure only by the number of cigarettes smoked per day, without measuring the amount of carbon monoxide inhaled by pregnant women from cigarettes. Data on cigarette smoke exposure in this study were collected via a questionnaire that relied on subjects' recall, which could introduce recall bias. Another limitation of this study is that all subjects were mothers who gave birth in hospitals.

In Indonesia, many mothers still have midwives assist with their deliveries, both in private midwife practices (29%) and at home (16%) [24] This situation affects the study results, which may not be representative of the entire Indonesian population. Furthermore, the data analysis shows wide confidence intervals, indicating substantial variation and uncertainty in the data.

Further research can be conducted using a cohort study design to assess the causal relationship between cigarette smoke exposure, antenatal visits, and preterm birth. This cohort design can also minimize recall bias. Furthermore, quantitative measurements of carbon monoxide levels inhaled by pregnant women are needed to determine the threshold levels of this compound that influence the incidence of preterm birth. Selecting a broader range of research subjects, including mothers who deliver with midwives, is also recommended to better reflect population conditions in Indonesia.

CONCLUSION

Exposure to cigarette smoke exceeding five cigarettes per day and irregular antenatal visits can increase the risk of preterm birth. These findings suggest that maternal exposure to a certain level of environmental cigarette smoke is associated with preterm birth. However, further research is needed to determine the causal relationship between cigarette smoke exposure, antenatal visit frequency, and preterm birth.

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AUTHORS CONTRIBUTION

These are the author's contributions to the paper: Conceptualization, formal analysis, methodology, project administration, validation, writing the original draft, review, and editing: AHZ, KK. Data curation, investigation, resources, software, supervision: AHZ. Visualization: KK. All authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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