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Research

The Effect of Active Smoking of Pregnant Women on Premature Birth: A Meta Analysis

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ABSTRACT

Background: Smoking is a well-known major risk factor for premature death from cancer, cardiovascular disease, and chronic obstructive pulmonary disease. When a pregnant woman smokes, she puts herself and her baby at risk. This is because the developing fetus / baby in the mother's womb is in contact with the mother's bloodstream. Any chemical that the mother inhales or swallows can affect the fetus. This study aims to analyze the magnitude of the effect of active smoking on pregnant women with preterm labor by means of a meta-analysis study.
Subjects and Method: This was a systematic review and meta-analysis carried out by following the PRISMA flow diagram. The process of searching for articles is through a journal database which includes: PubMed, Springer Link, and Google Scholar by selecting articles published in 2005-2020. Keywords used include: "Maternal Smoking" OR "Smoking During Pregnancy" AND "Preterm Birth" OR "Premature" AND "multivariate" AND "AOR". The inclusion criteria were full paper articles with observational study design, articles in English, and multivariate analysis used with adjusted odds ratios. Articles that meet the requirements are analyzed using the Revmen 5.3 application.
Results: A total of 19 articles were reviewed in this study with a cross-sectional cohordant study design. A meta-analysis of 6 cohort studies showed that active smoking in pregnant women had a 1.34-fold increase in the incidence of preterm birth compared with nonsmoking pregnant women (aOR= 1.34; 95% CI= 0.14 to 5.80; p= 0.002). A meta-analysis of 5 cross-sectional studies showed that active smoking in pregnant women had a 1.29-fold increase in the incidence of preterm birth compared with nonsmoking pregnant women (aOR= 1.29; 95% CI= 0.89 to 4.54; p= 0.04).
Conclusion: Active smoking in pregnant women increases preterm labor.

Keywords: pregnant women smoking, premature labor, meta-analysis

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BACKGROUND

Smoking is a well-known major risk factor for premature death from cancer, cardiovascular disease, and chronic obstructive pulmonary disease (Arcavi, 2004). More than 7,000 chemicals are found in smoked tobacco, including through a pipe, and including at least 250 chemicals that can cause cancer and are known to be toxic. Globally, more than 22,000 people die from tobacco use or are exposed to secondhand smoke every day — one person every 4 seconds every day. Tobacco use affects almost all organs of the human body

(Giemza, 2004). The results of Arfaila-sufandi's study (2019) show a positive relationship between exposure to cigarette smoke and the incidence of cervical cancer and it is statistically significant. Women who were exposed to secondhand smoke were 12.57 times more likely to develop cervical cancer.

When a pregnant woman smokes, she puts herself and her baby at risk. Because the fetus, the developing baby in the mother's womb (womb), comes into contact with the mother's bloodstream, any chemicals that the mother inhales or swallows can affect the fetus (Delmas, 2005). Based on Indonesia's Health SDG Profile data, the prevalence of women who smoke in Indonesia is 4.5% (WHO, 2019). Data from Indonesian tobacco factsheet of women exposed to cigarette smoke at home is 52.7% (WHO, 2018).

WHO defines preterm birth as all births before the full 37 weeks of gestation, or less than 259 days from the first date of a woman's last menstrual period (WHO, 1977). Complications of preterm birth were the leading cause of death in children under 5 years globally in 2016, accounting for about 16% of all deaths, and 35% of deaths among newborns (UNICEF et al., 2017).

Listiani's study (2018) concluded that one of the determinants of neonatal mortality is prematurity, among other factors, asphyxia, low birth weight, and infection. In Susanti's study (2020) states that exposure to cigarette smoke can cause LBW. In addition, Sudaryanto's research (2019) states that smoking is a risk factor for hypertension in women.

In a study conducted by Azagba et al., (2020) found that the prevalence of smoking during pregnancy was 6.89% in 2017 in the United States. This study states that there are still quite a number of pregnant women who smoke during pregnancy.

Guo et al. (2019) showed that high concentrations of air pollution significantly influence the risk of adverse birth outcomes. However, further studies need to be done to focus more on smoking habits during pregnancy on risk factors for preterm birth.

Based on the above background, the researcher chose to use meta-analysis to expand the application of evidence from the results of previous primary studies, and was able to obtain the strongest empirical causality evidence on the relationship between variables, with a larger sample. Researchers want to conduct a meta-analysis study related to pregnant women who smoke actively against preterm birth. This topic is very important in view of the number of women who smoke which allows preterm birth. Therefore, a meta-analysis study is important in order to summarize and combine relevant studies on the influence of pregnant women who smoke on the incidence of preterm birth so that the results of the analysis can provide a summary based on evidence.

SUBJECTS AND METHOD

1. Study Design

This was a systematic review and meta-analysis carried out by following the PRISMA flow diagram. The process of searching for articles is carried out through a journal database which includes: PubMed, Springer Link, Google Scholar and Science Direct. The keywords used are: "Maternal Smoking" OR "Smoking During Pregnancy" AND "Preterm Birth" OR "Premature" AND "multivariate" AND "AOR"

2. Inclusion Criteria

The inclusion criteria for articles that can be reviewed are full paper articles with observational study design, articles in English, multivariate analysis used with adjusted odds ratios, the intervention given is

active smoking during pregnancy, study subjects are pregnant women, the outcome is preterm birth.

3. Exclusion Criteria

Exclusion criteria for articles included primary articles published where meta-analysis was carried out and statistical results reported in the form of a bivariate analysis.

4. Variable Operational Definition

The article search was carried out by considering the eligibility criteria defined using the PICO model. The population in the study was pregnant women with intervention in the form of active smoking, comparison with no smoking and outcomes in the form of preterm birth.

Premature is labor that occurs at 20 to 36 weeks of gestation, can be calculated from the first day of the last menstruation**.**

Smoking behavior is an act of burning cigarettes and then inhaling cigarette smoke using a pipe or cigarette and blowing it out so that it can cause smoke**.**

5. Instrument

The research stages followed the PRISMA flow diagram and the assessment of the quality of research articles using the Critical Appraisal Skills Program (CASP) for Cohort Study, Critical Appraisal Checklist for Cross-sectional Study (CEBMa, 2014).

6. Data Analysis

The data analysis process in this study was carried out using the Review Manager application (RevMen 5.3) to determine the effect size and heterogeneity of the study. The results of meta-analysis data processing are presented in the form of a forest plot and a funnel plot.

RESULTS

The process of searching for articles is carried out by PRISMA. The flow diagram can be seen in Figure 1.

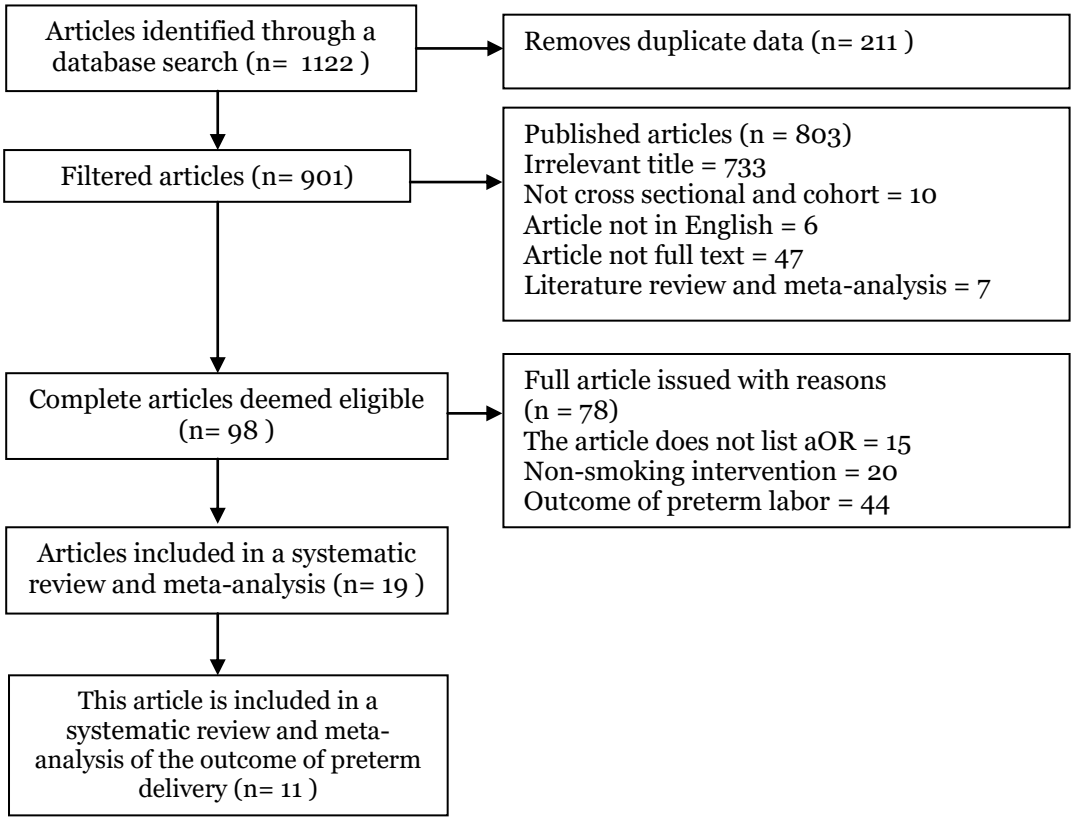

Figure 1. PRISMA flow diagram

Primary studies related to the effect of active smoking on pregnant women on preterm labor consisted of 5 studies from the Asian continent, 2 studies from the continent of Europe, and 4 studies from the continent of North America. Figure 2 shows the areas where articles were drawn according to the inclusion criteria. Next, the researcher conducted an assessment of the quality of the articles (Tables 1 and 2). Table 3 shows that there are 6 cohort study articles and 5 cross-sectional study articles as evidence of the association of the effect of active smoking in pregnant women on preterm birth.

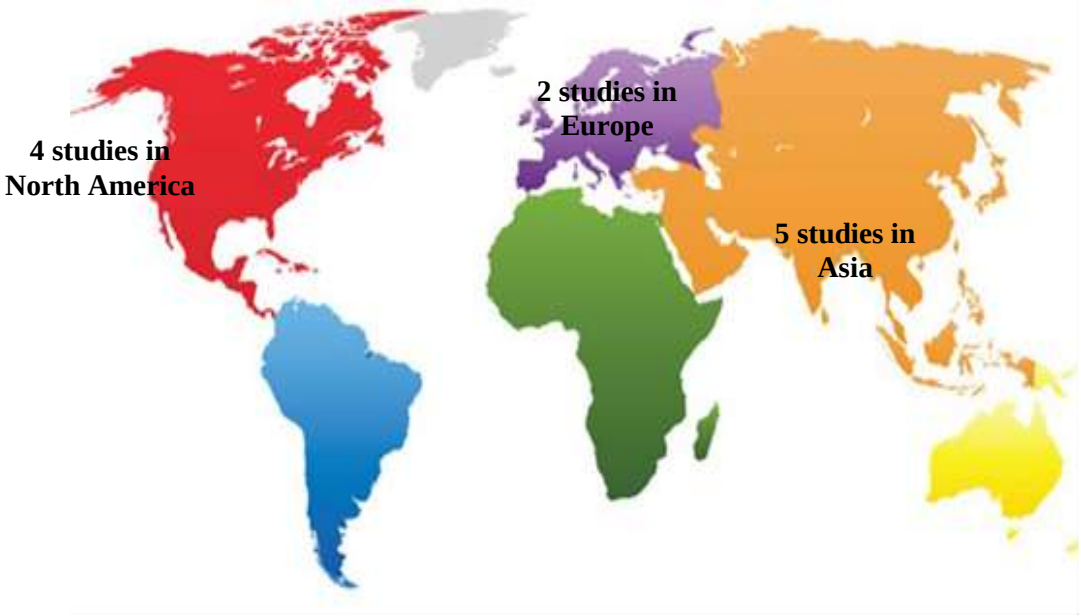

Figure 2. Map of the research area

Table 1. Assessment of Research Quality using the Critical Appraisal Skills Program for Cohort Study

Questions of the checklist	Publication (Author and Year)					
	Ratnasiri et al. (2018)	Ion et al,. (2015)	Ko et al. (2013)	Miyake et al. (2013)	Suzuki et al. (2008)	Jaddoe et al,. (2008)
Does this research address clearly focused issues?	1	1	1	1	1	1
Is the cohort research method appropriate for answering research questions?	1	1	1	1	1	1
Are there enough subjects to determine that the findings were not by chance?	1	1	1	1	1	1
Is the selection of cohorts based on objective and validated criteria?	1	1	1	1	1	1
Is the cohort representative of the defined population?	1	1	1	1	1	1
Was there sufficient follow-up?	0	0	1	1	1	1
Are objective and unbiased results criteria used?	1	1	1	1	1	1
Is the method of measuring active smoking in pregnant women validated?	1	1	1	1	1	1
Is the effect size practically relevant?	1	1	1	1	1	1
Are there any confidence intervals given?	1	1	1	1	1	1
Have the confounding factors been taken into account, such as the age of the pregnant woman, the weight of the pregnant woman, the lifestyle (alcohol consumption)?	1	1	1	1	1	1
Can the results be applied to your research?	1	1	1	1	1	1
Total	11	11	12	12	12	12

Note: Yes = 1, No = 0

Table 2. Assessment of Research Quality using the Critical Appraisal for Cross-sectional Study

Question of checklist	Publication (Author and Year)				
	Adibelli et al. (2020)	Ju et al. (2018)	Robl et al. (2012)	Wang et al. (2020)	Kondracki et al. 2019
Does this objective clearly address the research focus / problem?	1	1	1	1	1
Is the cross-sectional research method suitable for answering research questions?	1	1	1	1	1
Is the method of selecting research subjects clearly written?	1	1	1	1	1
Does the sampling method lead to bias (selection)?	0	0	0	0	0
Does the research sample taken represent the designated population?	1	1	1	1	1
Was the sample size based on pre-study considerations?	1	1	1	1	1
Was a satisfactory response achieved?	1	1	1	1	1
Are the research instruments valid and reliable?	1	1	1	1	1
Is statistical significance assessed?	1	1	1	1	1
Are confidence intervals given for the main outcome?	1	1	1	1	1
Are there any confounding factors that have not been taken into account, such as the age of the pregnant woman, the weight of the pregnant woman, the lifestyle (alcohol consumption)?	0	0	0	0	0
Are the results applicable to your research?	1	1	1	1	1
Total	10	10	10	10	10

Note: Yes = 1, No= 0

Table 3. Description of the primary study meta-analysis of the effect of active smoking in pregnant women on preterm birth

Primary Study	Country	Study Design	Sample	P Population	I Intervention	C Comparison	O Outcome
Ratnasiri, 2018	California	Cohort	435,280	Pregnant mother	Active smoking during pregnancy	Do not smoke	Premature Birth
Ion, 2015	UK	Cohort	13,359	Pregnant mother	* Active and passive smoking during pregnancy	Do not smoke	Premature Birth
Ko, 2013	Taiwan	Cohort	24,200	Pregnant mother	Active smoking during pregnancy	Do not smoke	LBW, * Premature Birth, SGA
Jaddoe, 2008	Netherlands	Cohort	7,098	Pregnant mother	* Active and passive smoking during pregnancy	Do not smoke	LBW and * Premature Birth
Suzuki, 2008	Japan	Cohort	1,329	Pregnant mother	Smoking while pregnant	Do not smoke	LBW, Premature Birth, SGA
Miyake, 2013	Japan	Cohort	1,565	Pregnant mother	* Active and passive smoking	Do not smoke	LBW, * Premature Birth, SGA
Adibelli, 2020	Turkey	Cross-Sectional	217	Pregnant mother	* Smoking during pregnancy, Passive Smokers	Do not smoke	LBW, * Premature Birth, and other Fetal Complications
Wang, 2020	Shanghai	Cross-Sectional	8,586	Pregnant mother	* Smoking during pregnancy, secondhand smoke	Do not smoke	LBW and * Premature birth
Kondracki, 2019	United States of America	Cross-Sectional	130,060	Pregnant mother	Active smoking during pregnancy	Do not smoke	* Premature Birth
Ju, 2018	Hawaii	Cross-Sectional	20,061	Pregnant mother	Demographics of pregnant women and unhealthy lifestyles, * Active smoking during pregnancy	Demographics of pregnant women and healthy lifestyles	LBW and * Premature Birth
Robl, 2012	Kentucky	Cross-Sectional	270,886	Pregnant mother	Smoking while pregnant	Do not smoke	LBW and * Premature Birth

* Variables entered in the meta-analysis

Foest plot

Interpretation of the results from the meta-analysis process can be seen through a forest plot. Figure 3 shows that active smoking in pregnant women increases the incidence of preterm birth. The meta-analysis of the cohort study showed that active smoking in pregnant women increased the incidence of preterm delivery by 1.34 times compared to preterm births that were not affected by active smoking in pregnant women (aOR= 1.34, 95% CI= 1.11-1.62, p = 0.002). The heterogeneity of the research data shows I^2 = 58% so that the distribution of the data is stated to be homogeneous (random effect model). The results of the meta-analysis of cross-sectional studies showed that active smoking in pregnant women could increase the incidence of preterm birth by 1.29 times compared to the incidence of preterm birth which was not influenced by active smoking in pregnant women (aOR= 1.29, 95% CI= 1.01-1.63, p= 0.04). The heterogeneity of the research data shows I^2= 97% so that the distribution of the data is stated to be heterogeneous (random effect model).

Funnel Plot

A funnel plot is a plot that depicts the estimated effect size of each study on the estimate of its accuracy which is usually the standard error. Figure 4 shows the existence of publication bias which is indicated by the asymmetry of the plot location on the right and left sides, not forming an inverted funnel. On the right side there are 3 plots which are located far apart, on the left side there are 4 plots which are located adjacent to 2 plots that are far apart, and there are 2 plots in the middle. The plot on the right side of the graph appears to have a standard error (SE) between 0 and 0.5. The plot on the left side of the graph has a standard error (SE) between 0 and 1. Bias also occurs from an unbalanced distance between studies on both the right and left of the funnel plot.

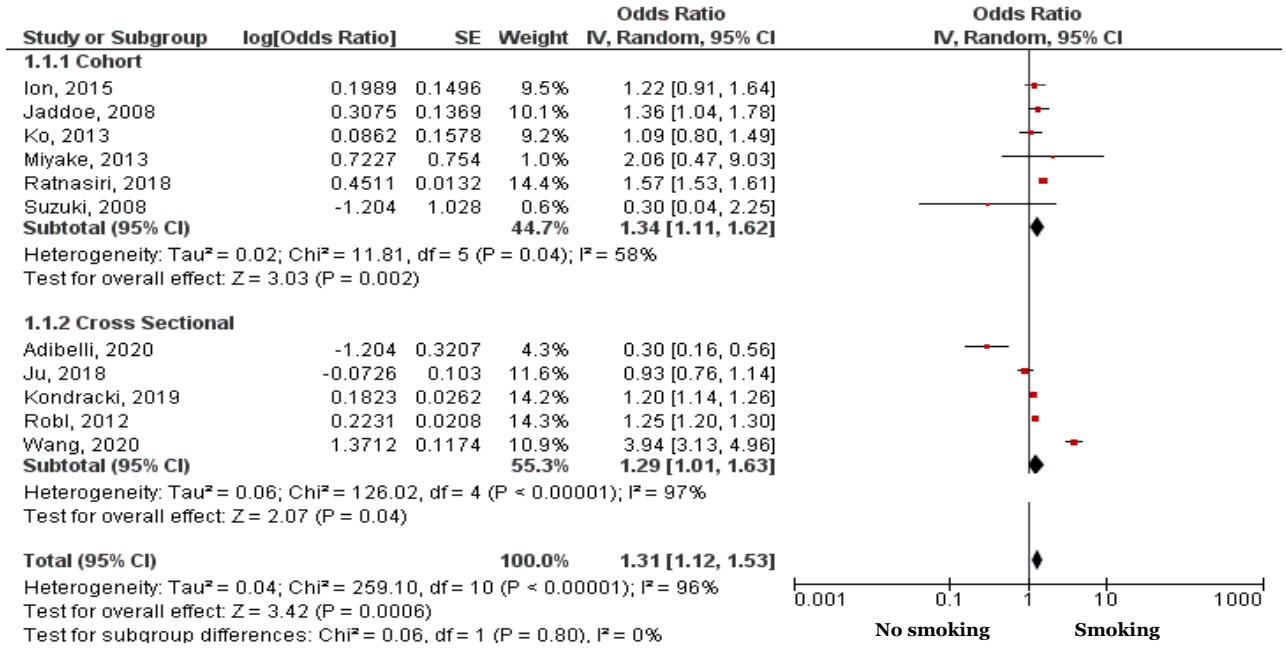

Figure 3. Forest plot of the effect of active smoking on pregnant women on preterm birth

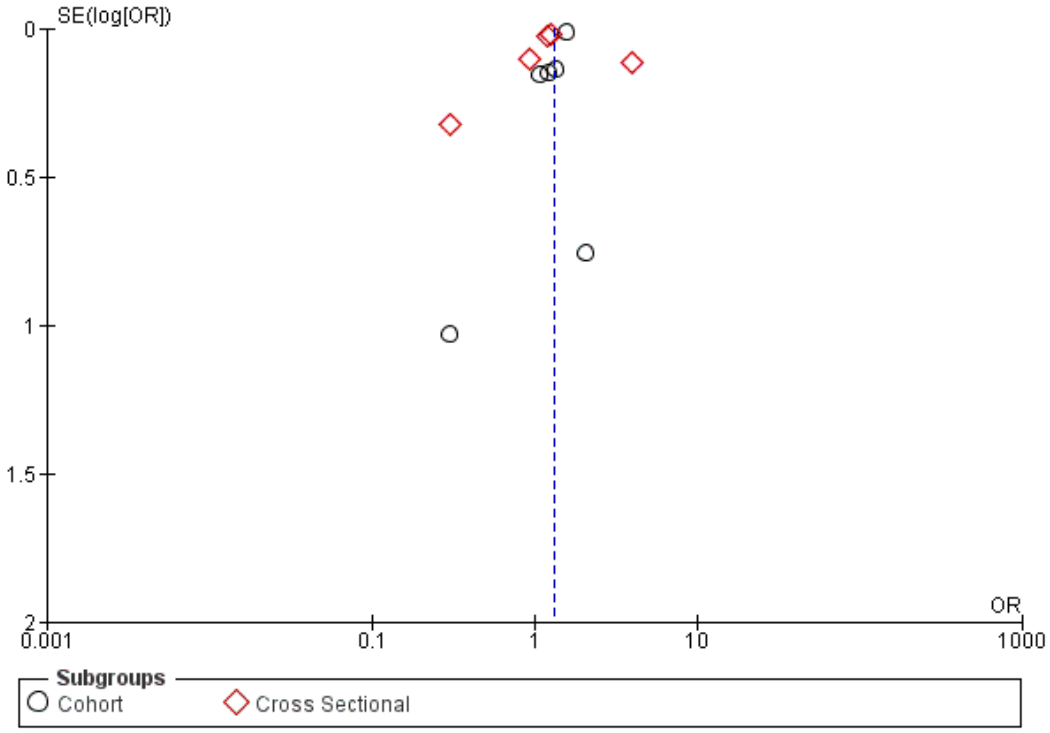

Figure 4. Funnel plot of the effect of active smoking on pregnant women on preterm birth

DISCUSSION

This systematic review and meta-analysis research raises the theme of the effect of active smoking on pregnant women on preterm labor. The independent variable which was analyzed by pregnant women was active smoking. The dependent variable in this systematic review and meta-analysis was preterm delivery. The results of the primary study carried out by systematic studies and meta-analyzes show an epidemiological study design with a larger population sample, with different demographic characteristics in different countries so as to provide a basis for concluding that active smoking has a statistical effect on the incidence of low birth weight and birth weight. premature birth.

Smoking is a well-known major risk factor for premature death from cancer, cardiovascular disease, and chronic obstructive pulmonary disease. Smoking also appears to be a major risk factor for respiratory tract and other systemic infections (Arcavi, 2004). When a pregnant woman smokes, she puts herself and her baby at risk. Because the fetus, the developing baby in the mother's womb (womb), comes into contact with the mother's bloodstream, any chemicals that the mother inhales or swallows can affect the fetus (Delmas, 2005). The results of the primary study analysis carried out by systematic review and meta-analysis showed that studies that met the analysis criteria were found in Africa 3 studies, Asia 6 studies, Europe 3 studies, Australia 1, North America 5 and South America 1 study.

Wagijo et al., (2017) stated that the effects of smoking on maternal health during pregnancy are physiological symptoms such as tachycardia, increased nausea and vomiting, fatigue and anorexia, as well as an increased risk of spontaneous abortion, premature rupture of membranes, preterm labor, and hypertension. According

to Leppee et al., (2012) the impact on the fetus appears to be fetal toxicity, neurotoxicity, increased risk of Down's Syndrome, intrauterine death, fetal development retardation, low birth weight, sudden infant death syndrome, and an increased risk of congenital malformations.

This systematic and meta-analysis study used research that controlled for confounding factors which could be seen from the study inclusion requirements, namely using multivariate analysis and the statistical result reported was the adjusted odd ratio (aOR). According to Murti (2018), confounding factor is the mixing of estimates of the relationship between exposure and the disease under study, by other factors that are related, both to disease and exposure. Confounding factors influence the relationship or effect of exposure to the occurrence of disease that the study estimates (estimated) are not the same as the relationship or effect that actually occurs in the target population, or the study results are invalid (incorrect).

Estimates of the combined association of the effect of active smoking on pregnant women with preterm labor were processed using the RevMan 5.3 application with the generic inverse variance method. This method is used to analyze data in the form of: rate, time-to-event, hazard ratio, ordinal scale, adjusted estimate, difference difference of mean or ratio of mean (Anulus et al. 2019). The results of the systematic review and meta-analysis of this study are presented in the form of forest plots and funnel plots.

The forest plot is a diagram that shows visually the amount of variation (heterogeneity), CI, the average between the results of the studies examined in the meta-analysis. A funnel plot is a diagram in meta-analysis used to demonstrate possible publication bias. The funnel plot shows the relationship between the effect size of the study and the sample size of the various studies studied, which can be measured in a number of different ways (Murti, 2018)

The effect of active smoking in pregnant women on premature labor

There were 11 observational studies consisting of 6 cohort studies and 5 cross-sectional studies as a source of meta-analysis of the effect of active smoking in pregnant women on preterm labor. Analyzes were performed with subgroups of each observational study design. The meta-analysis of the cohort study showed that the effect of active smoking on pregnant women increased the risk of preterm labor by 1.34 times compared to preterm delivery that was not affected by active smoking in pregnant women (aOR= 1.34, 95% CI= 1.11-1.62, p= 0.002). Meanwhile, the meta-analysis of a cross-sectional study showed that the effect of active smoking in pregnant women on preterm labor increased the risk by 1.29 times compared to preterm labor which was not influenced by active smoking in pregnant women (aOR= 1.29, 95% CI= 1.01-1.63, p= 0.04) .

The results of a meta-analysis conducted by Shah and Bracken, (2000) that mothers who smoked during pregnancy increased 1.27 times the incidence of preterm labor compared to nonsmokers (aOR 1.27 95% CI 1.21-1.33). Study by Andriani et al., (2014) states that carbon monoxide causes a strong vasoconstrictor (narrowing of the blood vessels) of the placental vessels and can integrate with oxygen to form carboxyemo-globins, which can limit the amount of oxygen supplied to the fetus and cause low oxygenation of fetal tissues. .

In the study of Jaddoe et al., (2007) the effect of drinking alcohol on preterm birth showed that mothers who consumed alcohol during pregnancy increased 1.20 times the incidence of preterm labor com-

pared to mothers who did not consume alcohol (aOR 1.20, 95% CI 0.16- 9.17) . This suggests that it is necessary to control for confounding variables such as "consumption of alcoholic beverages during pregnancy" in order to determine their true effect on the target population.

AUTHOR CONTRIBUTION

Imam Setya Arifian is the main researcher who plays a role in coordinating the research, conducting all stages of the research, and completing the research paper. Vitri Widyaningsih played a role in developing ideas, research designs, and research hypotheses and Hanung Prasetya played a role in compiling the research framework, processing research data, representing the results of research analysis, and preparing research papers.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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