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Meta Analysis
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Effect of Maternal Obesity on Fetal Macrosomia: Meta-Analysis

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ABSTRACT

Background: Obesity is a condition that shows an imbalance between height and weight. Obesity in women poses a risk to future pregnancies and their pregnancy outcomes. One of the risks of pregnancy in obese women is the birth of babies with excess weight or macrosomia. Excess birth weight can increase the risk of death for both mother and baby. This study aims to examine the effect of obesity in pregnant women on child birth using macrosomia.
Subjects and Method: Meta-analysis was performed with the PRISMA flowchart using PubMed, Science Direct, and Google Schoolar databases. Keywords used ((maternal obesity OR obesity in pregnancy) AND (macrosomia OR large for gestational)). There were 11 studies with a cohort design published in 2012-2022 that met the inclusion criteria. Analysis was performed using Revman 5.3.
Results: There were 11 articles originating from three continents, namely Asia (2 studies from China, 2 from Saudi Arabia, 1 from Taiwan), the Americas (3 from the United States, 1 from Brazil), and the European continent (1 from Poland and 1 from Spanish). The heterogeneity of effect estimates between primary studies showed I^2 = 95% (p<0.001), so the analysis used the Random Effect Model (REM). Obese pregnant women had a 2.03 times risk of having a baby with macrosomia compared to pregnant women without obesity (aOR=2.03, 95% CI=1.88 to 2.18; p<0.001).
Conclusion: Obesity in pregnant women increases the risk of having a baby with macrosomia.

Keywords: maternal obesity, macrosomia.

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BACKGROUND

Obesity is a condition that shows an imbalance between height and weight due to excess fat tissue in the body resulting in excess body weight or obesity (Pellonpera et al., 2018). Obesity occurs if in one period of time more calories enter through food than are used to support the body's energy needs, which then excess energy will be stored as triglycerides in fat tissue (Pramudji, 2019). Globally, obesity is the third leading cause of chronic health problems and has more than doubled since 1980.

In 2017-2020, the prevalence of obesity

in adults reached 41.9%, an increase compared to 2015-2016, which was 39.6% in both men and women (CDC, 2020). The prevalence of obesity for the adult population in Indonesia based on the 2018 Basic Health Research was 21.8%, continuing to increase from 10.5% in 2007 and 14.8% in 2013. Based on gender characteristics, the prevalence of obesity in Indonesia is more prevalent in women, namely 29.3% consisting of women of childbearing age and pregnant women. This is higher when compared to the prevalence of obesity in men which reaches 14.5% (Ministry of Health, 2018).

According to Soltani et al. (2017), the proportion of overweight among pregnant women in Indonesia increased from 22.3% to 29.1%, while the proportion of obesity among pregnant women increased from 9.7% to 19.6% in the same time period. Women who are obese before pregnancy are at risk for future pregnancies and their pregnancy outcomes. One of the risks of pregnancy in women who are obese is the birth of babies with excess weight or macrosomia (Hermawan et al., 2020).

According to Beta (2019), macrosomia is a term that describes a baby born with a body weight > 4,000 grams. Pregnant women with excess weight increase the risk or complications in pregnancy such as hypertension, large fetal weight resulting in difficulties in childbirth (Jannah, 2012). Pregnant women who are obese can cause an increase in fetal glucose and insulin levels. Lipase in the placenta will affect triglyceride metabolism in the mother's blood and transfer free fatty acids as nutrients for fetal growth. Triglyceride levels will increase in obese pregnant women, this is related to excessive fetal growth through increased free fatty acids (Ouzounian et al., 2011).

Birth weight that exceeds normal can cause postpartum hemorrhage because the uterus stretches excessively and results in weak uterine contractions so that postpartum bleeding can occur. In addition, mothers who give birth to macrosomic babies have a risk of cesarean delivery, obstructed labor, shoulder dystocia, and asphyxia. Some of these risks, if not handled with appropriate and fast action, can threaten the life safety of the mother and baby.

According to the World Health Organization (WHO) in 2014, the incidence of macrosomia is increasing from year to year. In the last two to three decades, there has been an increase of around 15-25% in the proportion of women giving birth to large babies. The proportion of macrosomia in each population is around 5-20%. The highest prevalence is found in North European and North Atlantica countries, where macrosomic infants account for approximately 20% and 45% respectively.

Based on the results of the 2017 Indonesian Demographic Health Survey (IDHS), data obtained that the incidence of babies born with excess weight or macrosomia in Indonesia has decreased by 0.5% compared to the previous 5 years. However, the macrosomia infant mortality rate increased by 0.1%. Meanwhile, birth complications experienced by mothers also increased from 35% to 41%.

Research shows that babies born to obese mothers are more at risk of experiencing macrosomia, while pregnant women with low body weight have an increased risk of giving birth to babies with LBW (Wahabi et al., 2021). Other studies suggest that the birth of babies with macrosomia is 2-3 times higher in obese pregnant women and found no relationship between obesity and the birth of babies with low birth weight (Soltani et al., 2017).

Another study that examined obesity in pregnant women with birth outcomes in infants found data that obesity in pregnant women had adverse effects such as babies

born with macrosomia (Avci et al., 2015). A similar study was conducted aiming to determine the relationship between body mass index (BMI) in mothers and pregnancy outcomes. The results of the study concluded that women with obesity have an increased risk of fetal macrosomia (Vince et al., 2020).

One of the primary studies conducted by Lewandowska et al. (2021), showed that obesity in mothers more than tripled the risk of giving birth to babies with macrosomia. Disorders that accompany obesity in pregnant women include chronic inflammation that can cause damage to the body and insulin resistance that cannot use blood sugar in the body properly, which can affect changes in the function of the placenta and its ability to distribute nutrients to the fetus.

The obesity epidemic that is prevalent in women will have an impact on future pregnancies and childbirth. This requires proper health services such as weight and height screening before or early in pregnancy to monitor and prevent future complications during pregnancy, childbirth, and complications in the baby being born. In addition, more comprehensive research is needed from various previous primary studies regarding the effect of obesity in pregnant women on the birth of babies with macrosomia.

This study aims to analyze and estimate the influence and risk of obesity in pregnant women on the birth of babies with macrosomia.

SUBJECTS AND METHOD

1. Study Design

This study used a systematic review and meta-analysis method. The data used are primary articles from databases such as PubMed, Google Schoolar, and Science Direct which were published in 2012-2022. Article searches were performed using the keywords “maternal obesity” OR “obesity in pregnancy” AND “macrosomia” OR “large for gestational”.

2. Steps of Meta-Analysis

1) Formulate research questions in the PICO format (Population, Intervention, Comparison, Outcome).
2) Search primary study articles from databases such as PubMed, Science Direct, and Google Schoolar
3) Perform screening by determining inclusion and exclusion criteria and conducting critical assessments.
4) Perform data extraction and analysis using RevMan 5.3 Software
5) Interpret the results and draw conclusions.

3. Inclusion Criteria

The inclusion criteria in this study were full text articles with cohort studies, research subjects were obese pregnant women, the size of the association used was OR, multivariate analysis was used with adjusted odds ratio (aOR), the outcome of the study was the birth of infants with macrosomia.

4. Exclusion Criteria

Exclusion criteria in this study were articles published before 2011, articles in languages other than English, analysis results reported in the form of bivariate analysis.

5. Operational Definition of Variable

Obesity is a condition resulting from the accumulation of body fat so that a person's weight far exceeds normal limits and can harm the body. Obesity is measured based on BMI examination.

Macrosomia is a baby born with a body weight >4,000 grams so that it can cause difficulties during delivery, especially when giving birth to the baby's shoulders. Diagnosis of macrosomia based on weight examination.

LBW babies are babies with birth weight <2,500 grams regardless of gestational age. Diagnosis of LBW is based on weight examination.

6. Instrument

The research was guided by the PRISMA flow chart and the quality assessment of research articles was carried out by the Critical Assessment Cohort Study published by JBI (The Joanna Briggs Institute 2020).

7. Data Analysis

Data analysis was performed using RevMan 5.3 Software. The results of the research are based on variations between studies with the fixed effect model or random effect model analysis. The fixed effect model is used when the consistency of heterogeneity (I^2) is <50%, while the random effect model is used when the consistency of heterogeneity (I^2) is >50%. Forest plots are used to describe effect sizes, while funnel plots describe whether or not there is publication bias.

RESULTS

The data used comes from primary article searches from databases such as PubMed, ScienceDirect, Google Schoolar from 2012-2022. Article searches were performed using the keywords "maternal obesity" OR "obesity in pregnancy" AND "macrosomia" OR "large for gestational". The process of selecting and reviewing articles is carried out using the PRISMA flowchart. The flow of searching for articles in the PRISMA flowchart can be seen in Figure 1.

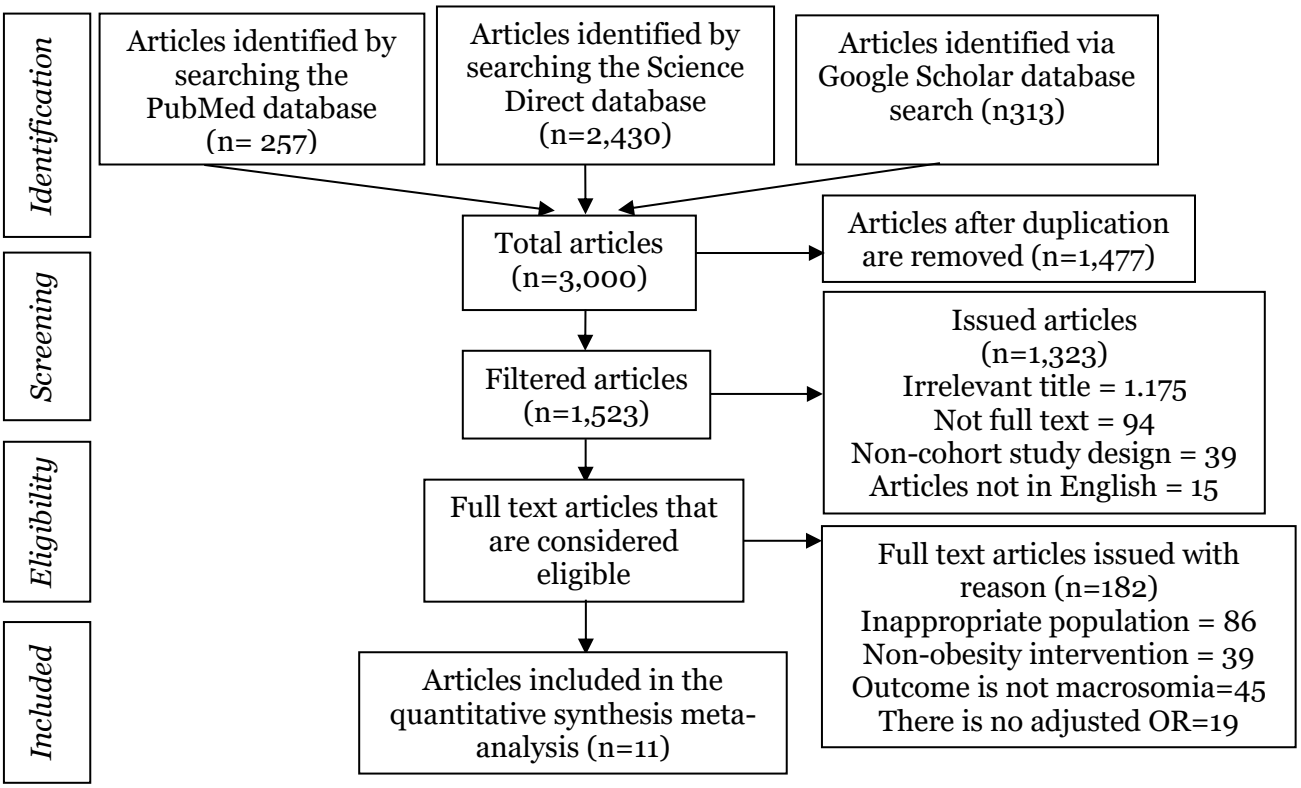

Figure 1. Prism Flow Diagram Results

The initial article search results obtained a number of 3,000 articles. After the process of removing duplicate articles, 1,523 articles were obtained. Then there were 11 articles that met the requirements for a full-text review. Full text articles included in the exclusion criteria are due to the following reasons:

1) The intervention from the observational study is not obesity but other diseases such as gestational diabetic mellitus, hy-

pertensive, and polycystic ovarian syndrome.
2) Outcome is not macrosomia, but premature birth, childbirth bleeding, and stunting.
3) Do not include the aOR value from the results of multivariate logistic regression analysis.

The results that met the qualitative requirements were reviewed again to determine the articles that met the quantitative requirements. There were 11 articles that met the requirements for inclusion in the meta-analysis. This study on the effect of obesity in pregnant women on the birth of babies with macrosomia consists of 11 articles originating from 3 continents namely Asia, Europe and America. There were 5 studies originating from the Asian continent (2 from China, 2 from Saudi Arabia, 1 from Taiwan), there were 2 studies from the European continent (1 study from Poland and 1 study from Spain), there were 3 studies from the Americas (3 from United States, 1 from Brazil). The distribution of the descriptions of the study areas can be seen on the map of the research areas (Figure 2).

Figure 2. Map of the Research Area

Table 1. Critical Appraisal Checklist for Cohort Study the Effect of Obesity in Pregnant Women on the Birth of Babies with Macrosomia

Author	Question Criteria											
	1	2	3	4	5	6	7	8	9	10	11	Total
Donghua et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	22
Fayed et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	22
Hung et al. (2016)	2	2	2	2	2	1	2	2	2	2	2	21
Lewandowska (2021)	2	2	2	2	2	2	2	2	2	2	2	22
Marshall et al. (2018)	2	2	2	2	1	2	2	2	2	2	2	21
Melchor et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	22
Ratnasiri et al. (2019)	2	2	2	2	1	2	2	2	2	2	2	21
Schneider et al. (2019)	2	2	2	2	1	2	2	2	2	2	2	21
Snowden et al. (2016)	2	2	2	2	2	2	2	2	2	2	2	22
Wahabi et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	22
Zhang et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	22

The quality assessment of the primary study was carried out using the Critical Appraisal

Checklist for Cohort Study published by The Joanna Briggs Institute (JBI, 2020). Critical appraisal is carried out with the aim of evaluating scientific articles so that the feasibility of the articles as research samples can be determined. Critical appraisal is also used to assess the validity of an article. The 11 research quality assessment criteria (Table 1).

Description and questions:

1 =Were the two groups similar and recruited from the same population?
2 = Whether the exposure is measured the same to determine the exposed group and the non-exposed group??
3 = Whether exposure is measured in a valid and reliable way?
4 = Are confounding factors identified?
5 = Were strategies for dealing with confounding factors stated?
6 = Were the group/ participants independent of the outcome at the start of the study (or at the time of exposure)?
7 = Are the results measured in a valid and reliable way?
8 = Was follow-up time reported and long enough for results to occur?
9 = Was follow-up complete, and if not, were reasons for missing follow-up explained and explored?
10 = Were strategies to address incomplete follow-up in place??
11 = Whether appropriate statistical analysis was used?

Answer Score Description*:*

2 = Yes
1 = No
0 = Unclear

Table 2 is a summary of observational study articles using a cohort study design as a source of meta-analysis of the effect of maternal obesity on the birth of infants with macrosomia. In the summary of the primary research, there are differences in the number of samples. The smallest number of intervention samples was 913 and the largest number of samples were 4,621,082 samples.

Table 2. Summary of Source Articles (Summary Source) Effects of Obesity in Pregnant Women on the Birth of Babies with Macrosomia

Author (Year)	Countri	Sample	Population	Intervention	Comparison	Outcome
Donghua et al. (2021)	China	431,412	Pregnant women aged 20-24 years	Obese (BMI >30kg/m²)	Normal weight	Macrosomia
Hung et al. (2016)	Taiwan	10,973	Pregnant women aged <20 to >40 years	Thin (BMI <18.5 kg/m²) Excess Weight (BMI 25-29 kg/m²) Obese (BMI >30kg/m²)	Normal weight	Macrosomia
Fayed et al. (2022)	Saudi Arabia	7,029	Pregnant women aged 20-35 years	Thin (BMI <18.5 kg/m²), Excess weight (BMI 18.5-29.9kg/m²), Obese (BMI >30kg/m²)	Normal weight	Macrosomia
Lewandowska et al. (2021)	Poland	912	Pregnant women aged 18-45 years	Obese (BMI >30kg/m²)	Not Obese	Macrosomia
Marshall et al. (2018)	The USA	317,144	Pregnant women aged <35 years	Obese (BMI >30kg/m²)	Not Obese	Macrosomia
Melchor et al. (2019)	Spain	16,609	Pregnant women aged 30-45 years	Thin (BMI <18.5 kg/m²) Excess Weight (BMI 25-29 kg/m²)	Normal weight	Macrosomia

Author (Year)	Countri	Sample	Population	Intervention	Compa-rison	Out-come
Ratnasiri et al. (2019)	The USA	4,621,082	Pregnant women aged 25-30 years	Obese (BMI >30kg/m²) Thin (IMT 18.5-24.9 kg/m²), Excess Weight (BMI 25.0-29.9 kg/m²), Obese (BMI >30kg/m²)	Normal weight	Macro-somia
Schneider et al. (2019)	Brazil	1,464	Pregnant women aged 20-30 years	Thin (BMI 18.5-24.9 kg/m²), Excess Weight (BMI 25-29.9 kg/m²), Obese (BMI >30kg/m²)	Normal weight	Macro-somia
Snowden et al. (2016)	The USA	386,407	Pregnant women aged <35 years	Obese (BMI >30kg/m²)	Not Obese	Macro-somia
Wahabi et al. (2021)	Saudi Arabia	2,447	Pregnant women aged 20-35 years	Thin (BMI 18.5-24.9 kg/m²), Excess Weight (BMI 25-29.9 kg/m²), Obesity (BMI >30kg/m²)	Normal weight	Macro-somia
Zhang et al. (2021)	China	3,731	Pregnant women	Thin (BMI <18.5 kg/m²), Excess Weight (BMI 24-27.9 kg/m²), Obese (BMI >28kg/m²)	Normal weight	Macro-somia

After critical appraisal, the data in the article was analyzed using RevMan 5.3 software. Interpretation of the results of the meta-analysis process can be seen through the forest plot. Figure 3. which shows the results that obesity in pregnant women affects the birth of macrosomic babies and is statistically significant. Pregnant women who are obese have a 2.03 times the risk of giving birth to babies with macrosomia compared to pregnant women who are not obese (aOR= 2.03, 95% CI = 1.88 to 2.18; p<0.001). Forest plot shows heterogeneity of research data I2 = 95%. So the analysis uses the Random Effect Model (REM).

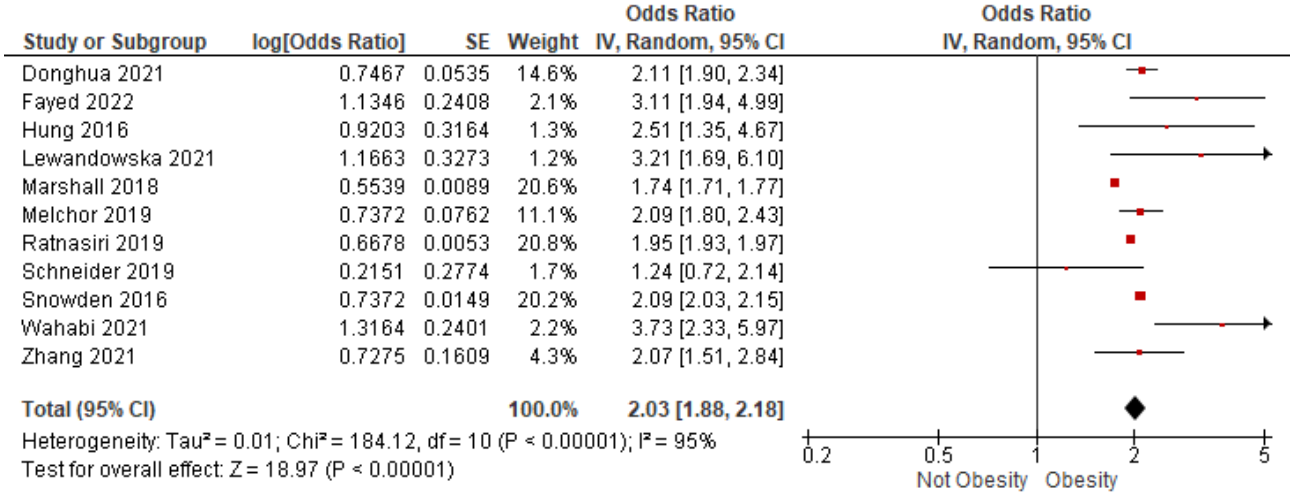

Figure 3. Forest Plot Effect of Obesity in Pregnant Women on the Birth of Babies with Macrosomia

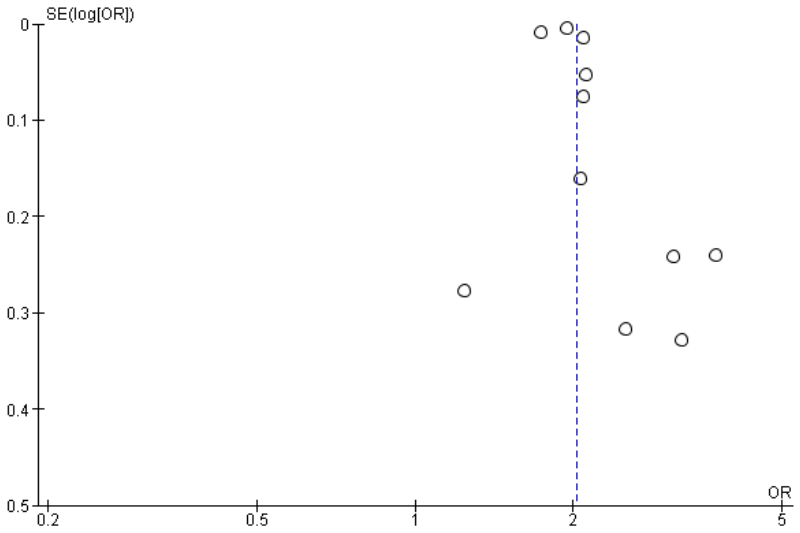

Figure 4. Funnel Plot Effect of Obesity on Pregnant Women on the Birth of Babies with Macrosomia

The results of the funnel plot can be seen in Figure 4. which shows the distribution of effect estimates between studies is not symmetrical, that is, there is more distribution on the right side of the average vertical line of effect estimates than on the left, where there are 4 plots on the right, 5 plots in the middle, and 2 plots on the left. Thus, this funnel plot indicates publication bias, because the distribution of effect estimates is more to the right of the average vertical line of estimates, the publication bias tends to overestimate the actual effect.

DISCUSSION

Macrosomia is a newborn or neonatal with a body weight exceeding the normal limit, which is >4,000 grams. One of the factors causing the birth of babies with macrosomia is obesity experienced by the mother (Cunningham et al., 2014). According to Manuaba (2007), the greatest danger when giving birth to a baby with macrosomia is permanent disturbance of the brachial plexus with all its motor effects, vital disturbances which result in mild, severe asphyxia to death, and disorders of the baby's neck joints.

There are 11 primary study articles with cohort studies which are a source of meta-analysis of the relationship of obesity in pregnant women to births of babies with macrosomia. Based on the results of the synthesis of 11 primary studies that were carried out systematic review and meta-analysis showed that there was high heterogeneity between experiments (I^2=95%; p<0.001), so the analysis used the Random Effect Model (REM). This heterogeneity is based on the varying sample sizes between studies and the asymmetric distribution between the left and right plots in the funnel plot.

The hypothesis in this study is that obesity in pregnant women can affect the birth of babies with macrosomia. Obesity in pregnant women can increase the risk of having a baby with macrosomia. This is in accordance with the research results which can be seen from the forest plot. The forest plot in this study revealed that pregnant women who were obese were 2.03 times more likely to give birth to babies with macrosomia than mothers who were not obese (aOR= 2.03; 95% CI= 1.88 to 2.18; p<0.001). This meta-analysis uses research that has controlled for confounding

factors or confounding factors which can be seen from the inclusion criteria, namely the results of multivariate analysis in the form of adjusted odds ratio (aOR).

The results of this study are supported by another study conducted by Donghua et al., (2021) which suggested that pregnant women who are obese will have a detrimental effect on their pregnancy outcomes. Obese pregnant women are 2.11 times more likely to give birth to babies with macrosomia compared to mothers who are not obese. The results of this study were statistically significant with results (aOR=2.11, 95% CI= 1.90 to 2.35; p<0.001). Obese women experience increased blood volume and cardiac output and increased blood pressure during pregnancy. In obese pregnant women, insulin resistance occurs which causes metabolic disorders, resulting in increased availability of nutrients for the fetus so that it receives large amounts of glucose through the placenta and causes hyperinsulinemia and accelerated fetal growth. The larger size of the fetus also increases the difficulty for vaginal delivery.

A similar study was conducted by Fayed et al. (2022) which showed that obesity increased the risk of delivering a baby with macrosomia (aOR= 3.11; 95% CI= 1.94 to 4.99; p<0.001). The birth of babies with excess body weight is associated with maternal and neonatal complications such as postpartum hemorrhage, birth canal injuries, shoulder dystocia and fractures at birth. This is in line with the theory put forward by Jannah (2012), that pregnant women with excess weight increase the risk or complications of pregnancy such as difficulties in childbirth. The results of this study were also supported by research by Hung et al. (2016), in their research which stated that women with obesity are more likely to give birth to macrosomic babies compared to women who have normal weight (aOR= 2.51; 95% CI= 1.35 to 4.64; p <0.001).

One of the primary studies conducted by Lewandowska et al. (2021) showed that obese mothers more than tripled the risk of having a baby with macrosomia (aOR=3.21; 95% CI = 1.69 to 6.1; p<0.001). Disorders that accompany obesity in pregnant women include chronic inflammation that can cause damage to the body, oxidative stress, epigenetic changes, and insulin resistance which cannot properly use blood sugar in the body, which can affect changes in placental function and its ability to transfer nutrients. from mother to fetus.

Similar study was also conducted by Marshall et al. (2018), who suggested that an increase in BMI is strongly associated with macrosomia. Pregnant women with obesity are at risk of giving birth to babies with macrosomia 1.74 times. The results of this study were statistically significant with the results (aOR= 1.74; 95% CI= 1.71 to 1.77; p<0.05). Study conducted by Melchor et al., (2019), shows that a higher BMI is associated with a greater degree of macrosomia. Obese pregnant women are at risk (aOR=2.09; 95% CI 1.80 to 2.42).

The primary study was conducted by Schneider et al. (2019) which suggested that an increase in BMI in pregnant women was associated with an increase in neonatal weight. Obese pregnant women were 1.95 times more at risk of having a baby with macrosomia (aOR=1.95; 95% CI 0.72 to 2.14; p=0.42). In addition, pregnant women with obese BMI show a higher likelihood of complications during delivery, such as cesarean section, heavy bleeding, and hypertension. Study conducted by Snowden et al. (2016) who conducted research on pregnant women based on differences in race or ethnicity obtained the result that obesity in pregnant women is a risk factor for macrosomia in all racial/ethnic groups. Pregnant women with obesity from all racial/ ethnic groups have 2.09 times the risk of giving birth to babies with macrosomia (aOR= 2.09; 95% CI= 2.03

to 2.15).

The study results in this systematic review and meta-analysis are in accordance with the hypothesis that obesity in pregnant women is associated with the birth of macrosomic babies. Pregnant women with obesity increase the risk of having a baby with macrosomia. This is also in accordance with the theory expressed by Irianto (2014) that uncontrolled weight gain in pregnant women will result in babies whose weight is not controlled both in the womb and at birth. Excessive nutritional intake in pregnant women can result in excessive weight gain, large baby sizes, and can also cause pre-eclampsia (pregnancy poisoning), and the baby will be more at risk of having health problems.

AUTHORS CONTRIBUTION

Vilia Ayu Kumalasari is the main researcher who selects topics, searches for and collects study data. Rita Benya Adriani and Bhisma Murti analyzed the data and reviewed atudy documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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