The Relationship of Age and Obesity with The Event of Preeclampsia in Pregnant Women

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ABSTRACT

Preeclampsia is a hypertensive disease in pregnancy which is systolic/diastolic 140/90 mmHg and proteinuria 300 mg/24 hours after 20 weeks gestation. According to WHO in 2015, the incidence of preeclampsia was 0,51%-38,4%. In Indonesia, preeclampsia and eclampsia cause 30%-40% of maternal deaths. Age and obesity are part of the risk factors for preeclampsia. This study aims to determine the relationship between age and obesity with the incidence of preeclampsia in pregnant women. It was conducted by systematic review with Meta-Analysis. Number of articles identified were 8.073 articles and included in the meta-analysis for 15 articles with details of 6 articles for age variable, 4 articles for obesity variable, and 5 articles for age and obesity variables. The results show that there is a relationship with the incidence of preeclampsia in selected journals with a combined effect size value at age of 2,280; [95% CI: 1,366-3,808, Z=3,151, *p*=0,002]; in obesity for 3,334; [95% CI: 1,839-6,043, Z=3,968, *p*=0,000]. It can be concluded that there was a greater relationship between obesity and the incidence of preeclampsia with SD (OR=3,334) compared to Age with the incidence of preeclampsia in pregnant women with SD (OR=2,280).

Keywords: Age, obesity, preeclampsia, pregnant women

INTRODUCTION

The United Nations Children's Fund (UNICEF) revealed that more than 290.000 women died from complications of pregnancy and childbirth in 2017 and there are 2,8 million pregnant women and newborns who die every year.[1] The achievement rate for reducing MMR in several ASEAN countries has reached the position of 40-60 per 100 live births. Data from the 2015 Inter-Census Population Survey (SUPAS), Indonesia still ranks 305 per 100.000 live births. Where MMR is based on the calculation of islands per 100 live births, namely Sumatra at 344, Java-Bali at 247, Kalimantan at 466, Sulawesi at 282, Nusa Tenggara, Maluku, and Papua at 489. According to data from the Indonesian Ministry of Health in 2015-2017, there has been a decline the number of cases of maternal death, where AKI in 2015 was 4.999 cases, in 2016 decreased by 4.912 cases and in 2017 decreased by 1.712 cases.[2] MMR according to data from the South Kalimantan Provincial Health Office in 2018 was 108,1 per

100.000 live births, 2019 was 92 per 100.000 live births, 2020 was 135 per live birth.[3]

Maternal Mortality Rate (MMR) in South Kalimantan in 2014 was 120 people caused by bleeding 33 people (27,5%), preeclampsia/eclampsia 34 people (28,3%), infection 3 people (2,5%), abortion 1 person (0,8%), others 49 people (40,8%). In 2015 there was a decrease in AKI as many as 89 people caused by bleeding 27 people (30,3%), preeclampsia/eclampsia 20 people (22,4%), infection 1 person (1,1%), circulatory disorders 8 people (8 ,9%), metabolic disorders 4 people (4,4%), others 29 people (32,5%).[4]

In Indonesia, preeclampsia and eclampsia are the causes of 30%-40% of maternal deaths, while in several hospitals in Indonesia, bleeding has shifted as the main cause of maternal death.[5] The World Health Organization (WHO) predicts that the incidence of preeclampsia in developing countries is higher than in developed countries, which is about 7 times. The incidence of preeclampsia in

high-income countries is 1,3%-6%, while in low-middle income countries it is 1,8% - 18%.[6]

Preeclampsia is a hypertensive disease caused by pregnancy which is characterized by hypertension with systolic/diastolic 140/90 mmHg and proteinuria 300 mg/24 hours after the 20th week of gestation. The edema criterion is no longer used as a diagnostic criterion because it is too common in normal pregnancies.[7]

Based on the results of research by age factor conducted by Andriyani (2012), Nisa et al (2018), Ermamilia et al (2020), Bardja (2020), and Putriana and Yenie[8] (2019), that there is a statistically significant relationship between age and the incidence of preeclampsia and it means that respondents at risky age have a greater chance of experiencing preeclampsia than those without risk. However, these results are not in line with the research of Sutrimah et al[9] (2015), Lusiana (2015), Mulastin dkk (2019), that there is no relationship between the age factor and the incidence of preeclampsia.

Another factor that is also closely related to the occurrence of preeclampsia is obesity.[10] The worldwide prevalence of obesity nearly tripled between 1975 and 2016.[11] In addition, it was also explained that the incidence of mild preeclampsia at the end of pregnancy was more commonly found in overweight or obese women. One way to identify the presence of overweight or obesity in adults is to use the Body Mass Index (BMI), which is categorized as obese if the BMI ≥25kg/m² for the Asia Pacific region.[11] Obesity is the fifth biggest risk that can cause global death. A study by Anjel in the United States on women of childbearing age showed that 24,5% of women aged 20-44 years had overweight nutritional status and 23% of them were obese.[12]

This gap or research is based on the results of research conducted by Nisa et al13 (2018), Ermamilia et al (2020), Pandiangan and Kusnanto (2017) and Perdana et al14 (2019), that there is a significant relationship between obesity and the incidence of preeclampsia in mothers pregnant. This research is following the theory which states that obesity is caused by many factors such as genetic factors, metabolic disorders, and excessive food consumption. . preeclampsia. 15 However, some of these studies are not in line with studies conducted by Yusrawati et al (2017), Pasca et al (2020), Mulastin et al (2019), Mustaghfiroh et al16 (2020) and Lisnawati and Rani (2020), that there is no significant relationship between obesity and the incidence of preeclampsia. Based on this, based on the description above, it can be seen that there are differences in results between one study and another where many studies have been conducted to determine the risk factors associated with preeclampsia in pregnant women, it is necessary to conduct research on the relationship between age and obesity with incidence of preeclampsia by meta-analysis.

This research's goal was to analyze the relationship of age and obesity with the event of preeclampsia in pregnant women.

METHOD

This study uses a meta-analysis study. Meta-analysis is a systematic study that uses statistical techniques to combine two or more results of a study so that new quantitative data are obtained. Meta-analysis is seen as a retrospective observational study, in the sense that the researcher only recapitulates the data without experimental manipulation. The stages of the research are as follows:

1. Identify Research Questions
   Identification of research questions is a question that is used as a basis for conducting a review. As a reference for formulating questions, you can use "SPIDER". SPIDER focuses less on intervention and more on research design and also focuses more on sample compared to population.

2. Research Protocol
   The research protocol in meta-analysis can use the concept of Preferred Reporting Items for Systematic Reviews and Meta Analysis (PRISMA).

3. Data Search Strategy
   The search strategy is carried out referring to the protocol that has been created and determines the location or source of the database for searching data and can involve other people to help review. Research data collection was carried out by researchers by browsing online journals, using SCOPUS, PubMed, Google Scholar and the Garuda Portal.

   The population in the Systematic Review and meta-analysis used is all free full-text articles and full-text national and international journals published on the Google Scholar database (in Indonesian and indexed by Sinta 1 to 4) and PubMed (in English for articles indexed by Scopus) that meet the criteria. retrieval of articles using the PRISMA method about the relationship between age and obesity with the incidence of preeclampsia in pregnant women (which is found in keywords).

   The sample consists of part of the population that can be used as research subjects through sampling. The sample in this systematic review and meta-analysis is the number of articles that were screened and

extracted in the previous stages. The sampling technique used is purposive sampling with predetermined inclusion criteria.

The variables that will be used in the research will consist of independent variables, namely age and obesity, and the dependent variable, namely the incidence of preeclampsia in pregnant women.

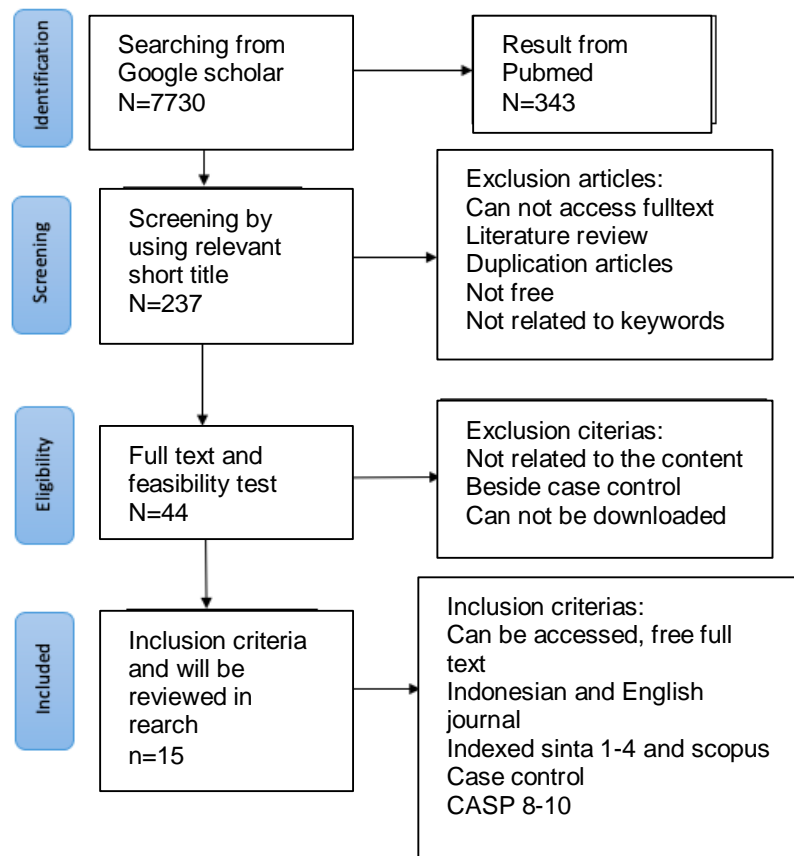The process of journal screening was mentioned in figure below:

Figure 1. Research Protocol

Combining the results of the various studies is the most decisive step in the meta-analysis. The basic unit of the meta-analysis study is the effect size, so to answer the research problem formulation, calculations are used with the analysis technique of the magnitude of the relationship (effect size).

Data analysis in this study was carried out at the time of conducting research, because data processing will be related to drawing conclusions. This study uses thematic analysis. in identifying patterns or determining themes through data collected by research (Braun & Clarke, 2006). There are 3 stages that are passed including:

1. Compare: find similarities between several literatures.
2. Contrast: find differences between several literatures and draw conclusions.
3. Criticize: give your own opinion based on the sources you read.

RESULT AND DISCUSSION

This study is related to the number of published studies relating to the relationship between age and obesity with the incidence of preeclampsia in pregnant women so that a meta-analysis study was carried out to obtain strong conclusions. This is done by following the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) using PRISMA diagrams to identify the amount of literature and track studies that meet the meta-analysis criteria. The PRISMA stages go through 4 (four) stages, including: identification, screening, eligibility, and inclusion (Klepinowski, Limanówka and Sagan, 2020). The search was carried out on 2 (two) database sources, namely Google Scholar and PubMed with a range of 2011-2020. Variables in this research based on 2 theories (Dahlan et. al. 2020) and Endeshaw et. al. (2016) and then age and obesity as the risk factors of preeclampsia.

The relationship of age with the incidence of preeclampsia in pregnant women

The number of journals combined to analyze the relationship between age and the incidence of preeclampsia in pregnant women is 11 studies.
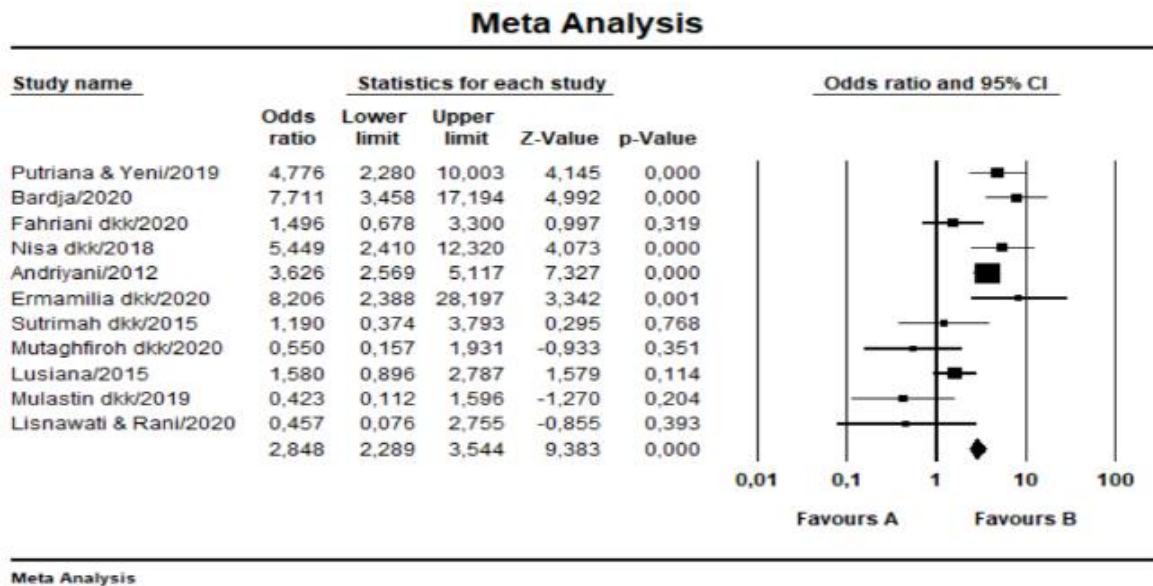
Figure 2. Graph of Forest Plot Random Effect Model of the Relationship of Age with the Incidence of Preeclampsia in Pregnant Women

The forest plot above shows the odds ratio of each study (black box) to its confidence interval (horizontal line). The combined odds ratio is represented in the form of diamonds (black color).

Table 1. Effect Size of Combined Research

		Effect Size and 95% CI			Significant Test	
Model	Number of Research	Combined Effect	Lower limit	Upper limit	Z	P
Random	11	2.280	1.366	3.808	3.151	0.002

It can be seen in table 1. The value with the combined effect of the results of the analysis of these eleven studies is 2.280 with a confidence interval of 1.366-3.808. The combined effect also produces a Z value of 3.151 and a p value of 0.002. Because the p value < 0.05, this means that there is a significant relationship between age and the incidence of preeclampsia in pregnant women.

This study is a meta-analysis study that analyzes the relationship between age and the incidence of preeclampsia in pregnant women. Many studies have analyzed the relationship between age and the incidence of preeclampsia in pregnant women. For this reason, statistical analysis was carried out using meta-analysis, so that new quantitative data were obtained with a larger sample size and more accurate conclusions could be drawn. The results of journal searches from various sources ultimately resulted in fifteen (15) studies that met the inclusion criteria and which could be analyzed into a meta-analysis using the CMA3 statistical application.

Fifteen (15) studies were analyzed involving 1,650 research samples from the total number of samples in each research study. Of the 11 studies, 5 research studies stated that there was an association between age and the incidence of preeclampsia in pregnant women with a total sample of 1,086. For 6 research studies that stated there was no association between age and the incidence of preeclampsia in pregnant women with a total sample of 564.

The quality of the data on the relationship between age and the incidence of preeclampsia in pregnant women with a sample of relevant journal searches (n = 11) can be seen from the heterogeneity (p = 0.000, p<0.05 and I²=76.3%) so the Random Effect Model is used. The

results of this random effect model assume that the 11 journals come from heterogeneous data. Because it has a heterogeneity value at the I²>50%, which means that the articles analyzed have various types of data.

In Table 1. the correlation of age with the incidence of preeclampsia in pregnant women, the effect size value of each study with a certain confidence interval of 11 studies resulted in a value of p = 0.002 (p <0.05), meaning that there is a significant correlation between age and the incidence of preeclampsia in pregnant women. The combined effect size value of the analysis results on the correlation of age with the incidence of preeclampsia in pregnant women is 2.280 with a wide confidence interval (95%CI) lower limit of 1.366-3.808, meaning that the age factor in pregnant women has a greater chance of 2.280 times the risk of preeclampsia.

The results of this analysis prove that age affects the incidence of preeclampsia in pregnant women. Based on the OR values, several studies of the forest plot images showed that there was a relationship between age and the incidence of preeclampsia in pregnant women. Pregnant women who have a risk of developing preeclampsia tend to be found in mothers who have an age range of <20 years and >30 years compared to those aged 20-35 years.

This is in line with the results carried out by Putriana and Yenie (2019), the OR value obtained = 4.776 (2.280-10.003), Bardja (2020), with OR = 7.711 (3.458-17.194), Nisa et al (2018) with OR = 5.449 (2.410-12.320), Andriyani (2012) with OR = 3.626 (2.569-5.117), and Ermamilia et al (2020) with OR = 8.206 (2.388-28.197).

However, it is not in line with the research conducted by Fahriani et al (2020) with the OR value =1.496 (0.678-3.300), Sutrimah et al (2015) with OR= 1.190 (0.374-3.793), Mustaghfiroh et al (2020) with OR= 0.550 (0.157-1.931), Lusiana (2015) with OR= 1.580 (0.896-2.787), Mulastin et al (2019) with OR= 0.423 (0.112-1.596) and Lisnawati and Rani (2020) with OR= 0.457 (0.076-2.755), stated that there was no relationship between age and the incidence of preeclampsia in pregnant women. Based on the results above, most of the mother's age is in the age range that is not at risk, namely 20-35 years. According to Saifuddin[17] (2010), The age of 20-35 years is a safe age from the risk of complications in pregnancy and childbirth.

Grouping by age is one of the important factors in maternal and child health programs in Indonesia. This does not rule out the possibility that preeclampsia can occur at risky maternal ages (20-35 years). Thus, all pregnant women, both at risky age (20-35 years) and not at risk (<20 years and >35 years) must undergo intensive pregnancy monitoring in order to minimize risk factors that occur through regular Ante Natal Care (ANC) regularly.

Teenage pregnancies under the age of 20 years have a risk, one of which is preeclampsia. Women at the age of <20 years the state of the reproductive organs is not ready to accept pregnancy.[19] The risk of pregnancy in mothers who are too young usually arises because they are not ready psychologically or physically. Psychologically, usually a teenager is not ready to become a mother. Physically, usually the reproductive organs of adolescents are not mature enough to bear the burden of pregnancy where the organs of the womb are still weak.[20,21] In contrast to pregnancy at a good reproductive age where the woman's physical condition is in prime condition. The uterus is able to provide maximum protection or conditions for pregnancy. The reproductive age of a woman is 20-35 years. This reproductive age is the safest period for pregnancy and childbirth because at that age the risk of complications during pregnancy is lower.[22]

Women over 35 years of age are more prone to various health problems, one of which is hypertension and preeclampsia.[7] This is due to changes in the tissues of the womb and birth canal are no longer flexible as well as blood vessels, also due to blood pressure that increases with age, causing oedema and proteinuria. The age of 35 years is actually not considered vulnerable, but at this age the reproductive ability begins to decline so that age> 35 years is considered the phase to stop a pregnancy.[20] At this age there is physical weakness and changes in connective tissue and the obstetrician and birth canal are no longer flexible so that it becomes a trigger factor for preeclampsia and also has a risk of suffering from chronic hypertension which will continue to be superimposed preeclampsia when pregnant.[20,23]

Based on the results of research conducted by Fahriani et al (2020), it states that from the results of research on productive age 20-35 years there are still 49 pregnant women who experience preeclampsia due to mothers experiencing other risk factors that can cause the risk of preeclampsia such as multiple pregnancies, a history of previous preeclampsia and there are other diagnoses in mothers such as anemia, molahidatidosa, hyperemesis gravidarum, polyhydramnios, oligohydramnios and premature rupture of membranes (KPD).

Age grouping is an important factor in maternal and child health programs in

Indonesia. This does not rule out the possibility that preeclampsia can occur at an at-risk maternal age (20-35 years). Thus, all pregnant women both at risk (20-35 years) and not at risk (<20 years and >35 years) must be carried out intensive pregnancy monitoring in order to minimize risk factors that occur through regular Ante Natal Care (ANC) visits.

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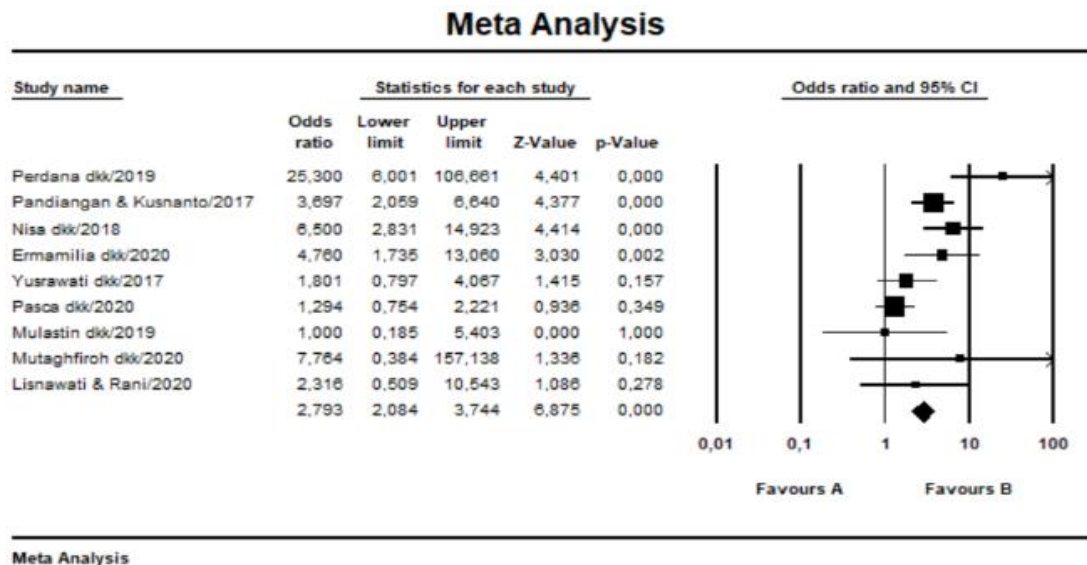
Figure 3. Forest Plot Graph Random Effect Model Relationship of Obesity with the Incidence of Preeclampsia in Pregnant Women

The forest plot 2. above shows the odds ratio of each study (black box) to its confidence interval (horizontal line). The combined odds ratio is represented in the form of diamonds (black color).

Table 2. Effect Size of Combined Research

	Effect Size and 95% CI				Significant Test	
Model	Number of Research	Combined Effect	Lower limit	Upper limit	Z	P
Random	9	3,334	1,839	6,043	3,968	0,000

It can be seen in table 2. The combined effect value from the results of the analysis of these nine studies is 3.334 with a confidence interval of 1.839-6.043. The combined effect also produces a Z value of 3.968 and a p value = 0.000. Because the p value < 0.05, this means that there is a significant relationship between obesity and the incidence of preeclampsia in pregnant women.

Nine (9) studies were analyzed involving 1,144 research samples from the total number of samples in each research study. Of the 9 studies, 4 of them stated that there was an association between obesity and the incidence of preeclampsia in pregnant women with a total sample of 588. For 5 research studies that stated there was no association between obesity and the incidence of preeclampsia in pregnant women with a total sample of 556.

The quality of the data on the relationship between obesity and the incidence of preeclampsia in pregnant women with a sample of relevant journal searches (n = 9) can be seen from the heterogeneity (p = 0.001, p<0.05 and I²=68.9%) so that the Random effect model is used. The results of this random effect model assume that the 9 journals come from heterogeneous data because they have a heterogeneity value at the value of I² > 50%, which means that the articles analyzed have various types of data.

In Figure 2, the forest plot graph of the relationship between obesity and the incidence of preeclampsia in pregnant women, the effect size value of each study with a certain

confidence interval from the 9 studies resulted in a p value = 0.000 (p <0.05), meaning that there was a significant relationship between obesity and the incidence of obesity. preeclampsia in pregnant women. The combined effect size value from the analysis of the relationship between obesity and the incidence of preeclampsia in pregnant women is 3.334 with a wide confidence interval (95% CI) of 1.839-6.043 which means that the obesity factor in pregnant women has a greater chance of 3.334 times the risk preeclampsia.

The results of this analysis prove that obesity affects the incidence of preeclampsia in pregnant women. Based on the OR values of several studies from forest plot images, the four studies showed that there was a relationship between obesity and the incidence of preeclampsia in pregnant women. Pregnant women who have a risk of preeclampsia tend to be found in women who have excessive nutritional status or obesity compared to pregnant women with normal weight. This is in line with the results conducted by Perdana et al (2019), where the OR value = 25.300 (6.001-106.661), Pandiangan and Kusnanto (2017) with OR = 3.697 (2.059-6.640), Nisa et al (2018) with OR = 6.500 (2.831-14.923), dan Ermamilia et al (2020) with OR = 4.760 (1.735-13.060).

Assessment of nutritional status in pregnant women can be done by examining the condition of pregnant women, while monitoring nutritional status in pregnant women can be done by conducting routine Ante Natal Care (ANC) examinations. Obesity is a multifactorial disease, and a risk factor for preeclampsia. This is in accordance with the theory that the greater a person's weight, the more blood there is in the body and the more difficult it is for the heart to pump blood, therefore preeclampsia can occur (Junior et al. 2014). This condition may be related to oxidative stress, inflammation and altered vascular function. Vascular neutrophil infiltration and extensive vascular inflammation have been reported in preeclamptic pregnant women and overweight women .[15]

Preeclampsia has similar characteristics of dyslipidemia to obesity. It is thought that obese women with abnormal lipid levels have a higher risk of developing preeclampsia. Obesity is usually accompanied by oxidative stress, which results from inflammatory reactions and an increase in free fatty acids. Diet is also thought to contribute to oxidative stress, as obese patients usually have low levels of antioxidants in the blood. Dyslipidemia in obesity is usually characterized by increased triglycerides and free fatty acids, and decreased HDL (high density lipoprotein), while LDL (low density lipoprotein) levels may be normal or slightly elevated. Free fatty acids can trigger oxidative stress and also contribute directly to insulin resistance.[24]

However, it is not in line with research conducted by Yusrawati et al (2017), Pasca et al (2020), Mulastin et al (2019), Mustaghfiroh et al (2020), and Lisnawati and Rani (2020), stating that there is no relationship between obesity and the incidence of preeclampsia in pregnant women. Although obesity is well correlated with several obstetric morbidities such as preeclampsia, gestational diabetes and macrosomia and the proportion is quite high, but in the study of Pasca et al (2020), especially in preeclampsia, it was found that obesity status before pregnancy did not have a significant impact on this complication. This suggests that the condition of obesity during pregnancy is more important than the status of obesity before pregnancy.[25]

The limitation of this research is that the search for research articles only uses three databases, namely Google Scholar, PubMed. The study design in this article related to the relationship between age and obesity is case control. In addition, in this meta-analysis, there is no limitation on the number of research subjects in the article, while it is known that the weights are directly proportional to the research subjects and inversely proportional to the variation.

The results of this meta-analysis indicate a publication bias. Publication bias is caused because the primary study data used tend to be published data which usually shows significant data, while insignificant data tends not to be published. Another factor that can cause the bias to be high in the effect size is language bias where the selected articles are only in Indonesian and English according to those mastered by the researcher. In addition, there is an availability bias where researchers choose research articles that are more accessible.[18]

CONCLUSION

The results of the study from 11 journals for the age variable were 5 journals (45.4%) which stated that there was a relationship and 6 journals (54.6%) stated that there was no relationship. The results of the meta-analysis with the heterogeneity test resulted in an I-squared value of 76.358 and a p value of 0.000, with a combined OR value of 2.280 and a 95% confidence interval (1.366-3.808). The result of the combined p-value of 0.002 means that there is a relationship between age and the incidence of preeclampsia in pregnant women.

The results of studies from 9 journals for the obesity variable as many as 4 journals (44.4%) stated that there was a relationship and 5 journals (55.6%) stated that there was no relationship. The results of the meta-analysis with the heterogeneity test resulted in an I-squared value of 68.953 and a p value of 0.001, with a combined OR value of 3.334 and a 95% confidence interval (1.839-6.043). The results of the combined p-value of 0.000, these results state that there is a relationship between obesity and the incidence of preeclampsia in pregnant women.

REFERENCES

1. Unicef. Laporan PBB. Untuk Pertama Kalinya Angka Perempuan Dan Anak Yang Bertahan Hidup Capai Tingkat Tertinggi, 2019.
2. Agung. AKI di Indonesia Masih Tinggi, 2019. https://www.ugm.ac.id/id/berita/17548-aki-di-indonesia-masih-tinggi, diakses 06 Maret 2021.
3. Dinas Komunikasi dan Informatika Provinsi Kalimantan Selatan. Data Dinas Kesehatan Provinsi Kalimantan Selatan AKI. Jumlah Kematian Ibu, 2021. (online), (https://data.kalselprov.go.id/?r=JmlKematianibu/index, diakses Diakses pada Kamis, 06 Mei 2021.
4. Dinas Kesehatan Provinsi Kalimantan Selatan. Profil Kesehatan Provinsi Kalimantan Selatan Tahun 2016. Banjarmasin, 2016.
5. Yulianti L, Fikawati S. Pre-Eklampsia Berat Di RSUDBayu Asih Purwakarta, Jurnal Kesehatan Masyarakat Nasional Vol. 3, No. 1, Agustus 2008; 39-44.
6. POGI. PNPK Diagnosis dan Tatalaksana Preeklampsia. 2016;1–48
7. Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC, Hauth JC, Wens KD. Obstetri Williams. Edisi ke-21. Alih Bahasa oleh Andry Hartono, Y. Joko Suyono, Brahm U. Pendit. Jakarta: EGC; 2005.
8. Putriana Y, Yenie H. Faktor-Faktor yang Berhubungan dengan Kejadian Pre Eklamsia pada Sebuah Rumah Sakit di Provinsi Lampung. Jurnal Ilmiah Keperawatan Sai Betik, 2019; 15(1): 31-42.
9. Sutrimah S, Mifbakhudin M, Wahyuni D. Faktor-faktor yang Berhubungan dengan Kejadian Preeklampsia pada Ibu Hamil di Rumah Sakit Roemani Muhammadiyah Semarang. Jurnal Kebidanan, 2015; 4(1): 1-10.
10. Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, *et al.* Obesity, obstetric complications and cesarean delivery rate–a population based screening study. Am J ObstetGynecol, 2004;190(4):1091-7.
11. World Health Organization. Obesity and overweight, 2020. Tersedia dari: URL: HYPERLINK https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight
12. Vahratian A. Prevalence of overweight and obesity among women of childbearing age: results from the 2002 National Survey of Family Growth. Matern Child Health J, 2009;13:268–273.
13. Nisa R, Kartasurya M, Fatimah S. Asupan Vitamin D yang Rendah, Obesitas dan Paparan Asap Rokok merupakan Faktor Risiko Preeklampsia Di Puskesmas Indramayu Tahun 2017. Jurnal Manajemen Kesehatan Indonesia, 2018; 6(3): 204-209.
14. Perdana RA, Surya IGP, Sanjaya IH. Obesitas dan resistensi insulin merupakan faktor risiko terjadinya preeklampsia. Medicina, 2019; 50(3): 493-497.
15. Nursal DGA, Tamela P, Fitrayeni F. Faktor Risiko Kejadian Preeklampsia pada Ibu Hamil di RSUP Dr. M. Djamil Padang Tahun 2014. Jurnal Kesehatan Masyarakat Andalas, 2015; 10(1): 38–44.
16. Mustaghfiroh L, Sari N, Prima RP. Usia, Gravida, Status Gizi, dan Riwayat Hipertensi Berhubungan dengan Kejadian Preeklampsia. Jurnal Ilmiah Permas: Jurnal Ilmiah STIKES Kendal, 2020; 10(1): 41-50.
17. Saifuddin AB. Ilmu Kebidanan. Jakarta: PT Bina Pustaka Sarwono Prawiroharjo, 2009.
18. Retnawati H dkk. Pengantar Analisis Meta. Yogyakarta: Parama Publishing, 2018.
19. Manuaba IAC dan Manuaba IBGF. Pengantar Kulian Obstetri. Jakarta: EGC, 2007.
20. Kurniasari D dab Arifandini F. Hubungan Usia, Paritas dan Diabetes Mellitus pada Kehamilan dengan Kejadian Preeklanpsia pada Ibu Hamil di Wilayah Kerja Puskesmas Rumbia Kabupaten Lampung Tengah. Jurnal Kesehatan Holisik, 2015; 9(3): 142-150.
21. Najati N, Gojazadeh M. Maternal and Neonatal Complication in Mothers Aged Under 18 Years. PMC Journal, 2010; 4: 219-222.
22. Novianti H. Pengaruh Usia dan Paritas Terhadap Kejadian Pre Eklamsia di RSUD Sidoarjo. Jurnal Ilmiah Kesehatan, 2016; 9(1): 25-31.
23. Yogi ED, Hariyanto, Sombay E. Hubungan Antara Usia dengan Preeklamsia pada

IbuHamil di Poli KIA RSUD Kefamenanu Kabupaten Timor Tengah Utara. Jurnal Delima Harapan, 2014; 3(2): 10-14.

24. Roberts, et all. The Role of Obisity in Peeclampsia, National Institutes of Health (NIH) Public Accss, 2011; 50(3): 6-10.

25. Yuniarti F, Wijaya W, Ivantarina D. Analisis Perilaku Kesehatan dan Faktor Risiko Kejadian Preeklampsia pada Ibu Hamil di Poliklinik Obstetri Gynekologi RSUD Kabupaten Kediri. Journal of Issues in Midwifery, 2017; 1(3): 1-17.