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Systematic Review
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Differences in Preeclampsia Characteristics Before and During the COVID-19 Pandemic: A Systematic Review

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ABSTRACT

Background: The COVID-19 pandemic has entered Indonesia since 2020 and has become a global pandemic. In the pre-pandemic period, Preeclampsia was one of the main causes of death of pregnant women in Indonesia. During the COVID-19 pandemic, the mortality rate of pregnant women and childbirth due to preeclampsia has the possibility of an increase. The cause of preeclampsia in pregnant women is not yet known. Early detection of risk factors and early treatment of preeclampsia are not carried out quickly and appropriately due to social restrictions due to the pandemic.
Subjects and Method: This study is a systematic review literature review conducted on selected databases (PubMed, Science Direcet, Unair Repository) with a publication year between 2017 and 2022. Literature uses Indonesian and English. The literature included was literature with cohort, cross sectional, and case control methods. The quality assessment of the literature was carried out using the EPHPP (Effective Public Health Practice Project).
Results: There were no significant differences in Preeclampsia characteristics i.e. age at pregnancy, parity, and BMI in both periods before and during the COVID-19 pandemic. However, differences were found that only existed in the period during the COVID-19 pandemic, namely comorbid diseases and previous history of preeclampsia.
Conclusion: In the period before and during the COVID-19 pandemic, pregnant women with preeclampsia did not show differences in outcomes in characteristics, but in the history of comorbid diseases and previous history of preeclampsia.

Keywords: preeclampsia, COVID-19, pregnant women, comorbidities.

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BACKGROUND

On March 11, 2020, the World Health Organization (WHO) has officially declared the extraordinary event of coronavirus or Coronavirus Disease 2019 (COVID-19) as a global pandemic. Initially, COVID-19 spread quickly in a short time in China, prompting the government to impose a strict lockdown.

With the speed of spread increasing exponentially, efforts to save public health are increasingly being intensified. Lockdown policies in this period are increasingly commonly used by various countries. In addition to lockdowns and travel bans, countries also implement border closures, enforce physical distancing through the closure of schools, offices, and restrictions on various activities that involve gathering large numbers of people (Ministry of Finance, 2021).

The Marwah et al. study(2022) pregnant women who are exposed to or infected with COVID-19 increase the risk factors for relatively more severe disease and require intensive care. Therefore, it is necessary to know the characteristics of PE mothers before and during the COVID-19 pandemic to prevent complications and risk of more severe diseases. According to Mendoza et al., (2020) COVID-19 during pregnancy is very closely related to preeclampsia, especially in nulipara women and pregnant women of very young age. The state of Indonesia has been exposed to COVID-19 since March 2020 and the social restrictions imposed by the government have proven to be effective in reducing the transmission of COVID-19. Preeclampsia / eclampsia is one of the main causes of maternal death in Indonesia. The cause of preeclampsia in pregnant women is not known for sure, although there have been several theories that try to explain that the cause of preeclampsia is placental ischemia. Preeclampsia is characterized by the onset of hypertension, edema and proteinuria as a result of a pregnancy that arises at more than 20 weeks of gestation. Preeclampsia/eclampsia is the second cause after bleeding as a specific direct cause of maternal death.

The high morbidity of preeclampsia incidence in pregnant women does not rule out the possibility that maternal and maternal mortality due to preeclampsia can also increase, especially during the COVID-19 pandemic, if early detection of risk factors and early treatment of preeclampsia are not carried out quickly and appropriately due to social restrictions due to the pandemic. This study aims to find out the description of preeclampsia characteristics before and during the COVID-19 pandemic.The high morbidity of preeclampsia incidence in pregnant women does not rule out the possibility that maternal and maternal mortality due to preeclampsia can also increase, especially during the COVID-19 pandemic, if early detection of risk factors and early treatment of preeclampsia are not carried out quickly and appropriately due to social restrictions due to the pandemic. This study aims to find out the description of preeclampsia characteristics before and during the COVID-19 pandemic.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic review , which is a method used to identify, evaluate, and interpret the results of existing studies that are relevant to a particular study question, topic or phenomenon.

2. Steps of Systematic Review

The study was conducted in stages:

1) Formulating PICO, namely Population: pregnant women in the period before and during the pandemic; Intervention: preeclampsia; Comparison: No preeclampsia; and Outcome: characteristics of preeclampsia (PE).
2) Next, determine the criteria for inclusion and exclusion, followed by a literature search. The literature used was obtained from search results on electronic databases in the form of: Airlangga University Repository, PubMed, and Science Direct

with a time range of literature or journals that have been published from 2017 - 2022.

3) Literature search using Boolean Operators includes OR/AND/NOT. Each database has a different literature search procedure, so the term literature search is adapted to the database protocol.
4) Furthermore, the literature search process is reported in the PRISMA flow with the aim of explaining the search and screening process to be clear and systematic. Then an assessment of the quality of the literature selected in this study was carried out using EPHPP (Effective Public Health Practice Project. After that, the data that has been analyzed is extracted, collected and identified into a data collection sheet.
5) And the last one writes the results of the literature study described in the form of a narrative so that it is easy to understand the conclusions of the results of the study and the synthesis of the articles studied.

3. Inclusion Criteria

The inclusion criteria in this study are literature in English and Indonesian, full text literature, which is unlocked and can be accessed in full, the content of the article discusses the characteristics of preeclampsia during the pandemic and before the pandemic, the articles obtained are all by using cohort, cross sectional and case control methods for the study and the last study was conducted on humans.

4. Exclusion Criteria

The Exclusion Criteria used in this study ware that the study source comes from Non-Research Studies (Conference papers, bookc hapters, reports), and the second article that was published before 2017. And the last article with the systematic review study method, literature review, and meta analysis.

5. Operational Definition of Study

The mother's age is the mother's age when pregnant. Parity consists of nullipara and multipara. Nullipara is a mother who has never given birth to a child. Multipara, namely mothers who have given birth more than 1 time.

BMI is normal (18.5–24.9), overweight (25–29.9) and obese (≥30). History of **Comorbid Disease** is a disease that has been experienced such as DM, Hypertension, and Hep-B.

History of Preeclampsia/ eclampsia Previously, pregnant women who had experienced preeclampsia/ eclampsia before. COVID-19 is pregnant women with preeclampsia during COVID-19.

6. Study Instruments

The instrument used in data collection was to take a total of 9 international and national journals for analysis. The first data processing technique is to formulate the study topic, then determine the inclusion and exclusion criteria, then search for literature, assess the quality of literature, extract data and then analyze and finally write the results.

7. Data Analysis

Using EPHPP (Effective Public Health Practice Project).

RESULTS

1. Differences in Preeclampsia Characteristics Before and During the COVID-19 Pandemic.

Differences in the characteristics of preeclampsia before and during the COVID-19 pandemic were found in this systematic review. These differences have been evaluated from three case control studies, three cohort studies and one cross-sectional study. Based on the results of each study, the article presents various data consisting of variables that are in accordance with this study and variables are not needed from this study.

Table 1. Result of characteristics of preeclampsia before and during the COVID-19 pandemic

Author (Year)	Mother's Age	Parity	BMI	Comorbid Diseases	Previous PE/ Eclampsia History	Era	Results (Variation of PE characteristics before and during the COVID-19 pandemic)
Kartika et al. (2017)	<20>3 (n= 30) 20-35 (n= 104)	Primitive (n= 44) Multipara (n= 90)	Normal (n= 100) Obese (n= 34)	DM (n= 6) HT (n= 26)	Exist (n= 5)	During the COVID-19 pandemic	This study found that in pregnant women aged 20-35 years, nulipara women and women with abnormal BMI (>35kg) experienced the most PE. The history of comorbid diseases obtained in this study was only hypertension and DM. Previous history of PE is more than eclampsia.
Azmi et al. (2018)	<20>35 (n=35) 20-3 (n= 109)	Primitive (n= 96) Multipara (n= 41)	Normal (n= 73), Overweight (n= 30), Obese (n= 32)	N/A	N/A	Before the COVID-19 pandemic	This study found that pregnant women aged 20-35 years, multipara, and obesity have a high chance of contracting PE. Risk factors for severe preeclampsia in Dr. Soetomo in the pre-pandemic period are obesity, and a history of hypertension.
Perdana et al. (2018)	<20>35 (n= 47) 20-35 (n= 57)	Primitive (n= 46) Multipara (n= 66)	N/A	DM (n= 5) HT (n= 19)	N/A	Before the COVID-19 pandemic	This study found that the age of 20-35 years, nullipara, and abnormal BMI had the highest risk of contracting PE.
Palomo et al. (2022)	20-35 (n= 11)	Prima (n= 3) Multipara (n= 8)	. N/A	N/A	N/A	During the COVID-19 pandemic	This study found that, in the age range of 20 – 35 years, nullipara and abnormal BMI have a high risk of PE. This study also shows that the risk of PE is not higher than COVID-19 when viewed from the number and variables.
Palomo et al. (2022)	<20>35 (n= 213) 20-35= (n= 66)	Primipara (n= 147) Multipara (n= 132)	Overweight (n= 249) Obese (n= 30)	DM (n= 3) HT (n= 3)	Exist (n= 6)	During the COVID-19 pandemic	This study found that pregnant women aged >35 years, nullipara, BMI <30 who have a high risk of PE. The study also showed that COVID-19 symptomatic infection during pregnancy did not increase the high risk of pre-eclampsia

Author (Year)	Mother's Age	Parity	BMI	Comorbid Diseases	Previous PE/ Eclampsia History	Era	Results (Variation of PE characteristics before and during the COVID-19 pandemic)
Nobrega et al., 2022	<20>3 (n= 2) 20-35 (n= 9)	Primitive (n= 3) Multipara (n= 8)	N/A	DM (n= 6) HT (n= 1) Hep-B (n= 1)	Exist (n= 5)	During the COVID-19 pandemic	This study shows that the age of mothers >35 years, multipara and obesity is higher at risk of contracting PE. The study also shows that COVID-19 in early pregnancy has the potential to be a risk factor for PE during pregnancy, such as hypertension, Hep-B, and DM.
Marwah et al. (2022)		Primitive (n= 18) Multipara (n= 20)	N/A	N/A	N/A	During the COVID-19 pandemic	This study shows that the age range of 20 – 35 years, and multipara are the highest causes of PE. The study also found that pregnant women with pre-eclampsia infected with COVID-19 have relatively more severe illnesses, and require more intensive care, in addition to high maternal and infant morbidity.
Wulandari et al. (2020)	<20>35 (n= 36) 20-35 (n= 44)	Primitive (n= 51) Multipara (n= 69)	N/A	DM (n= 21) HT (n= 71)	Exist (n= 13)	Before the COVID-19 pandemic	This study shows that in the age range of 20 – 35 years, nullipara is the highest cause of PE. This study also mentions that risk factors for PE in pregnant women are hypertension and DM.
Chaiworapongsa et al. (2022)	<20>35 (n=115) 20-35 (n= 143)	N/A	N/A	DM (n= 5) HT (n= 19)	Exist (n= 182)	During the COVID-19 pandemic	This study shows that the age range of 20 – 35 years, multipara, and abnormal BMI (overweight and obese) are the highest causes of PE. This study states that pregnant women with PE have a history of comorbid diseases (HT and DM). This study mentions a small sample that has a previous history of PE.

DISCUSSION

1. Mother's Age with Preeclampsia Incidence

In both study periods, before the COVID-19 pandemic, journals number 2, 3 and 8, and during the COVID-19 pandemic, journals number 1, 4, 7 and 9 stated that pregnant women in the age range of 20-35 years experienced the most PE. However, on the contrary, journals number 5 and 6 periods during the COVID-19 pandemic present that, data on pregnant women aged > 35 years who experienced a lot of PE. According to Wardhana et al. (2021) states that preeclampsia is still the main cause of maternal death in developing countries, including in Indonesia".

In both study periods, before the COVID-19 pandemic, journals number 1, 2 and 3, and during the COVID-19 pandemic journals number 4, 5, 7, 8 and 9 stated that pregnant women in the age range of 20-35 years experienced the most PE. The most common occurrence of preeclampsia is found at the age of 20 – 29 years (Bilano, 2014). However, on the contrary, journal number 6 of the period during the COVID-19 pandemic presents that, data on pregnant women aged > 35 years who have experienced a lot of PE. The results of the study on age above are in line with Nursal et al. (2015) The risk of developing preeclampsia is higher for pregnant women who are early and late reproductive age, namely adolescents and over 35 years old.

2. Maternal Parity with Preeclampsia Incidence

The results of the study period during the COVID-19 pandemic in Table 1, journal numbers 1, 4, and 5 show that the parity of nullipara mothers or mothers who have never experienced a previous pregnancy experience the most PE. The same results were also shown in journals numbers 3 and 8 in the period before the COVID-19 pandemic. However, contrary to other studies, both the period before and during the COVID-19 pandemic, journals numbers 2, 6, 7, and 9 actually presented data that multipara parity or mothers who did not experience the first pregnancy experienced PE.

The results of the study period during the COVID-19 pandemic in Table 1, journal numbers 9, 4, and 5 show that the parity of nullipara mothers or mothers who have never experienced a pregnancy before experience the most PE. The same results were also shown in journal numbers 2 and 3 in the period before the COVID-19 pandemic. However, contrary to other studies, both the period before and during the COVID-19 pandemic, journals numbers 1, 6, 7, and 8 actually presented data that multipara parity or mothers who did not experience their first pregnancy experienced PE.

Nullipara has an immunological mechanism, namely the formation of blocking antibodies against placental antigens so that it triggers hypertension to preeclampsia. The placenta antigen in primipara is not perfect, and will be even more perfect in the next pregnancy (Renita, 2018). The results of the above study on parity are in line with Opitasari and Andayasari (2014), that the incidence of preeclampsia is more experienced by nullipara women or women who have never given birth. Some of the journals above state primipara for mothers who have never given birth, but in this systematic review study the definition of nullipara is the same as primipara.

3. Body Mass Index with Preeclampsia Incidence

The results of the study showed that both the period before and during the COVID-19 pandemic, all journal issues presented data that pregnant women with abnormal BMI (overweight, and obese) who had a high risk of PE. However, 2 journals number 7 during the pandemic and 8 before the COVID-19

pandemic do not present data on the BMI of pregnant women who experience PE.

The results of the study showed that both the period before and during the COVID-19 pandemic, all journal issues presented data that pregnant women with abnormal BMI (overweight, and obese) who had a high risk of PE. However, 2 journals number 7 during the pandemic and 3 before the COVID-19 pandemic did not present data on the BMI of pregnant women who experienced PE.

4. Hypertension with Preeclampsia Incidence

In the study period during the COVID-19 pandemic, journals numbers 1, 6 and 9 presented data that mothers with preeclampsia had risk factors for comorbid diseases, namely hypertension. ". In the study period during the COVID-19 pandemic, journals number 2 and 8 presented the same data, that mothers with PE during the COVID-19 pandemic had a risk factor for comorbid diseases, namely Hypertension. Hypertension and diabetes mellitus are factors that cause preeclampsia. According to Akbar et al. (2019) stated that chronic hypertension in pregnancy in Indonesia is the main risk of poor maternal and perinatal output factors.

In the study period during the COVID-19 pandemic, journals numbers 9, 6 and 8 presented data that mothers with preeclampsia had risk factors for comorbid diseases, namely hypertension. Chronic hypertension in pregnancy in Indonesia is the main risk of poor maternal and perinatal output factors (Akbar et al., 2019). In the study period during the COVID-19 pandemic, journals number 2 and 8 presented the same data, that mothers with PE during the COVID-19 pandemic had a risk factor for comorbid diseases, namely hypertension.

5. Diabetes Mellitus with Preeclampsia Incidence

In the study period during the COVID-19 pandemic, journals numbers 1, 6 and 9 presented data that pregnant women with preeclampsia had risk factors for comorbid diseases, namely DM. The same data that pregnant women withpreeclampsia have risk factors for comorbid DM disease only exists in one of the three journals, namely number 8. The two comorbid diseases above obtained from various studies both before and during the COVID-19 pandemic, hypertension and DM are factors that cause preeclampsia in pregnant women. As for Hep-B comorbid disease, it was only presented in journal number 6 in the period during the COVID-19 pandemic.

In the study period during the COVID-19 pandemic, journals numbers 1, 6 and 9 presented data that pregnant women with preeclampsiahad risk factors for comorbid diseases, namely DM. The same data that pregnant women withpreeclampsia have risk factors for comorbid disease DM only exists in one of three journals, namely number 8.The two comorbid diseases above obtained from various studies both before and during the COVID-19 pandemic, hypertension and DM are the factors that cause preeclampsia in pregnant women. As for Hep-B comorbid disease, it was only presented in journal number 6 in the period during the COVID-19 pandemic. A study conducted by Baschat in 2014, stated that a history of preeclampsia, hypertension, diabetes are risk factors for preeclampsia.

6. Previous History of Preeclampsia-/Eclampsia with Preeclampsia Occurrence

In a study in the period during the COVID-19 pandemic, journal number 7 stated that pregnant women with those exposed to or infected with COVID-19 increased risk factors for the disease which were relatively more severe and required intensive care. However, contrary to study journals numbers 4 and 5 which are also in the period

during the COVID-19 pandemic, that pregnant women with PE who are infected or experiencing symptoms of COVID-19 do not increase the risk of Preeclampsia.

Pregnant women with Preeclampsia who have a previous history of Preeclampsia/ eclampsia, are only obtained from period study data during the COVID-19 pandemic. Meanwhile, in the period before the COVID-19 pandemic, it was not obtained. Nofiyana (2020) explained that pregnant women with a history of preeclampsia in previous pregnancies can experience hypertension or even preeclampsia in subsequent pregnancies.

In a study in the period during the COVID-19 pandemic, journal number 7 stated that pregnant women with those exposed to or infected with COVID-19 increased risk factors for the disease which were relatively more severe and required intensive care. However, contrary to study journals numbers 4 and 5, which were also in the period during the COVID-19 pandemic, that pregnant women with infected PE or experiencing symptoms of COVID-19 did not increase the risk of Preeclampsia. Common signs and symptoms of COVID-19 infection include symptoms of acute respiratory distress, fever, cough, shortness of breath and feeling tired. Some patients may experience pain and aches, nasal congestion, runny nose, headache, conjunctivitis, sore throat, diarrhea, loss of smell and smell (anosmia) and skin rash (Ministry of Health of the Republic of Indonesia, 2020).

AUTHOR CONTRIBUTION

In this study, Aditiawarman and Rahayu Kusuma collaborated to create a conceptual framework and study methodology. Rahayu Kusuma collects data. Rahayu Kusuma, Aditiawarman, and Atika collaborated to analyze the data.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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