



RISK FACTORS FOR SEVERE PREECLAMPSIA AT DR. WAHIDIN SUDIRO HUSODO HOSPITAL MOJOKERTO CITY IN 2021-2022

Enok Tuti Nurhayati¹, Dwi Izzati Budiono¹, Aditiawarman²

¹Midwifery Program, Faculty of Medicine, Airlangga University, Surabaya, Indonesia

²Maternal-Fetal Medicine Division, Obstetrics & Gynecology Department, Dr. Soetomo

Email : enok.tuti.nurhayati.2002@gmail.com

ABSTRACT	Keywords
<p>Background: Preeclampsia and eclampsia are major causes of morbidity and mortality during the perinatal period. The change from preeclampsia to severe preeclampsia can progress rapidly. The case of severe preeclampsia in Dr. Wahidin Sudiro Husodo Hospital, is very high. Purpose: To analyze the risk factors for severe preeclampsia at Dr. Wahidin Sudiro Husodo Hospital, Mojokerto City. Subjects and Methods: This study was conducted using an observational analytic quantitative method with an case control design. The sampling method used consecutive sampling. This study involved a total of 150 samples from two groups, consisting of pregnant women and laboring women. Results: The variables that had a significant relationship with the incidence of severe preeclampsia were age variables (p-value: 0.000; OR: 4.330; CI: 1.972-9.507), history of obesity (p-value: 0.000; OR: 15.460; CI: 5.255-45.483), history of preeclampsia (p-value: 0.001; OR: 7.579; CI: 2.127-27.006), history of diabetes mellitus (p-value: 0.012; OR: 11.385; CI: 1.419-91.352), and history of chronic hypertension (p-value: 0.000; OR: 6.945; CI: 2.931-16.456) were all significantly associated with the incidence of severe preeclampsia . the variables of age, history of obesity, and history of chronic hypertension met the final modeling in multivariate analysis. Conclusion: The history of obesity being the most dominant variable.</p>	<p>Severe preeclampsia, risk factors, history of obesity.</p>

INTRODUCTION

Preeclampsia and eclampsia are the leading causes of morbidity and mortality during the perinatal period (WHO, 2021). The most common cause of of death mothers in Indonesia based on the Death Registration System Litbangkes (2016) hypertension/preeclampsia/ eclampsia,bleeding, and infection (Kementrian Kesehatan, 2021). Efforts to reduce the maternal mortality rate (MMR) to 70 per 100 ,000 live births which is target number 3 from global Sustainable Development Goals (SDGs) (WHO, 2021). East Java Province is a province with a high

maternal mortality rate in Indonesia (Kementrian Kesehatan,2021). Mojokerto City is one of the cities with the highest maternal mortality rate in East Java province, and in the last five years there has been an almost three-fold increase in maternal mortality cases in 2021, with the most common cause of death being hypertension/preeclampsia.

Preeclampsia is a health problem that occurs during pregnancy and is characterized by an increase in blood pressure (> 140/90 mmHg) and the detection of protein in the urine (+2), but there are certain situations

where preeclampsia is not always accompanied by proteinuria. This condition starts to appear after 20 weeks of pregnancy. Serious complications associated with preeclampsia, including severe preeclampsia, HELLP syndrome (Hemolysis, Elevated Liver Enzymes, Low Platelet Count), and eclampsia, occur in approximately 5-6 deliveries out of every 1000 pregnancies (Feroz et al., 2020). Women who experience severe preeclampsia have a risk of serious complications that increases 3 to 25 times (Godana et al., 2021).

Severe preeclampsia based on the guidelines of the American College of Obstetricians and Gynecologists (ACOG) is a condition of preeclampsia with blood pressure (> 160/110 mmHg) on two separate occasions, with an interval of at least 4 hours and / or characterized by a decrease in platelet count (thrombocytopenia), impaired liver function, renal impairment, pulmonary edema, and the appearance of headache and visual disturbances. Factors that increase the risk of severe preeclampsia are nulliparity, multifetal pregnancy, preeclampsia in previous pregnancies, pregnancy interval, chronic hypertension, gestational diabetes, thrombophilia, BMI > 30, vulnerable age group, kidney disease, use of assisted reproductive technology, and antiphospholipid antibody syndrome. (Lisonkova et al., 2021).

Based on data from the Mojokerto City Health Office in 2021 and 2022, there was an increase in cases of severe preeclampsia for 3 consecutive years. The number of cases of severe preeclampsia is still very high and still far from the safe category against preeclampsia. This is evidenced by several cases of maternal death due to severe preeclampsia, even to complications, including in 2019 and 2022 there were maternal deaths due to severe preeclampsia with pulmonary edema and in 2020 there were

cases of maternal death due to eclampsia and chronic hypertension.

Based on medical record data, severe preeclampsia cases were recorded at the Dr. Wahidin Sudiro Husodo Regional General Hospital in 2021 50 cases, and in 2022 it increased to more than 70 cases. One of the problems seen in the medical record data is that mothers with severe preeclampsia are predominantly referred patients. This implies that there is an increase in severe preeclampsia cases, but there is no visible change towards a better condition. The General Hospital is the health facility with the highest cases of severe preeclampsia in Mojokerto city, this is because the General Hospital is the facility with the highest number of cases of severe preeclampsia.

As the main referral health service in Mojokerto city, research on risk factors for severe preeclampsia at Dr. Wahidin Sudiro Husodo Regional General Hospital, is needed to serve as a reference for efforts to reduce maternal mortality (MMR) caused by severe preeclampsia in Mojokerto city.

METHOD

The research method used was an analytical observational study approach with an unmutate case-control hospital base design. The study subjects included all patients of pregnant women and delivery mothers, who were recorded in medical record data at Dr. Wahidin Sudiro Husodo Region General Hospital during the period January 2021 to December 2022. The size of the study sample was calculated using the case control design formula, and the minimum number of samples required was 136 for two groups, namely the case group and the control group. During the implementation of the study, a total of 150 samples were obtained, with 75 samples in the case group and 75 samples in the control group. The main objective of this study was to study, observe, and analyze the independent variables that act as risk factors in the

occurrence of severe preeclampsia. The dependent variable in this study was patients who experienced severe preeclampsia, while the independent variables consisted of risk factors such as maternal age, parity, history of obesity, history of chronic hypertension, and history of diabetes mellitus. The sampling method used was consecutive sampling, and medical record data collection was carried out during the June-August 2023 period at Dr. Wahidin Sudiro Husodo Region General Hospital. Data were collected using patient medical record data as the main instrument, and the collected data were then processed through various stages, including editing, coding, data entry, cleaning, and tabulating. Analysis of the research data involved several methods, including univariate analysis, bivariate analysis using the chi square test, and multivariate analysis with multiple logistic regression using the SPSS program. The aim was to identify the relationship between dependent and independent variables, and to determine the variables that have the most dominant influence on the risk of severe preeclampsia

RESULTS AND DISCUSSION

Over the past five years, there has been a very significant increase in cases of Severe Preeclampsia (PEB) at Dr. Wahidin Sudiro Husodo Hospital, Mojokerto City. This increase almost reached five times in the period 2021-2022. Mojokerto City, which is one of the three cities with the highest maternal mortality rate (MMR) in the country, has a significant increase in PEB cases.

East Java in 2021, faces a very serious situation. Maternal deaths can occur in severe situations, but the change from preeclampsia (PE) to severe preeclampsia (PEB) can be rapid, unexpected, and sometimes sudden (World Health Organization, 2021). The results of statistical test analysis using SPSS are outlined in the following table :

Table 1 Variable analysis results of chi square test

Risk Factor	Severe Preeclampsia				p value	CI	OR 95 %
	Control		Case				
	N	%	N	%			
Age	<20,	3	42	1	14	0,000	1,97-4,33
	>35	2	,7 %	1	,7 %		
	20-35	4	,3 %	6	,3 %		
	Total	7	10 %	7	10 %		
Parity	Primiparus	3	42	3	44	1,000	0,49-0,947
	Multiparus	4	,3 %	4	56 %		
	Total	7	10 %	7	10 %		
	Total	5	0 %	5	0 %		
History Obesity	Yes	3	52	5	6,7 %	0,000	1,50-15,812
	No	3	48 %	7	93,3 %		
	Total	7	10 %	7	10 %		
	Total	5	0 %	5	0 %		
History Preeclampsia	Yes	1	24	3	4 %	0,001	2,12-7,270
	No	5	76 %	7	96 %		
	Total	7	10 %	7	10 %		
	Total	5	0 %	5	0 %		
History Chronic Hypertension	Yes	3	45	8	10,7 %	0,000	2,93-16,456
	No	4	54	6	89,4 %		
	Total	7	10 %	7	10 %		
	Total	5	0 %	5	0 %		
History Diabetes Mellitus	Yes	1	13	1	1,3 %	0,012	1,41-11,338
	No	6	86	7	98,7 %		
	Total	7	10 %	7	10 %		
	Total	5	0 %	5	0 %		

In table 1 above, it can be seen from the chi-square test analysis that the variables that have a p-value less than α (0.05) are age,

history of obesity, history of preeclampsia, history of chronic hypertension, and history of diabetes mellitus, so that these variables have a significant relationship with the incidence of severe preeclampsia at Dr. Wahidin Sudiro Husodo Region General Hospital.

a. Parity

The variable that did not have a significant association with the incidence of severe preeclampsia was parity, due to a p-value of 1.000, which was greater than $\alpha = 0.05$. This is due to the balanced number of primiparas and multiparas in the case and control groups in the research data. The results of this study are in line with research conducted by Jasda et al (2021) and Aryanti et al (2022) which state that parity has no significant relationship to the incidence of severe preeclampsia (PEB), but the results of this study are not in line with the theory that parity is associated with the incidence of severe preeclampsia, namely in nulliparous / primiparous mothers or mothers who have never given birth (ACOG, 2019).

b. Age

The results of the chi-square test analysis on the age variable showed a significant relationship with the incidence of severe preeclampsia (p-value: 0.000; OR: 4.33; CI: 1.972-9.507) and the risk was 4.3 times higher at high risk age (<20 and >35 years). These results are consistent with the results of the WHO survey (2019) and research by Ertiana and Wulan (2019) which showed that age <20 and >35 years were associated with a 5.4 times higher risk of severe preeclampsia. However, in contrast to research conducted by Sumampouw, et al (2019) stated that normal age (20-35 years) has a higher risk of developing severe preeclampsia. Severe Preeclampsia compared to susceptible ages (<20 and >35 years).

c. History of Obesity

The history of obesity variable also has a significant relationship with the incidence of PEB (p-value: 0.000; OR:

15.167; CI: 5.501-41.812) with a risk of 15 times higher in mothers who have a history of obesity before pregnancy. The results of a study conducted by Jeong, et al (2022) on Thai women showed that obesity before pregnancy increased the risk of PEB almost five times compared to normal weight before pregnancy. This confirms the importance of obesity history in the incidence of severe preeclampsia.

d. History of Preeclampsia in Previous Pregnancy

Previous history of preeclampsia was associated with PEB (p-value: 0.001; OR: 7.579; CI: 2.127-27.006) and it can be concluded that mothers who have a history of preeclampsia in previous pregnancies have a 7.5 times risk of increasing the incidence of PEB in subsequent pregnancies. The results of this study are similar to the ACOG guidelines (2019) and research conducted by Meazaw (2020) with a meta-analysis method involving six studies in various countries has shown a clear and strong correlation that a previous history of preeclampsia is one of the significant risk factors for the incidence of severe preeclampsia.

e. History of Comorbidities

History of comorbidities of chronic hypertension and diabetes mellitus had a significant association with the incidence of History of chronic hypertension (p-value: 0.000; OR: 6.945; CI: 2,931-16.456) has a risk of 6.9 times that of mothers who do not have a previous history of chronic hypertension, which is the same as that of mothers who do not have a history of chronic hypertension (2020) noted that pregnant women in Nigeria who had a history of chronic hypertension experienced more than a 2- fold increase in the risk of PEB. History of diabetes mellitus (p-value: 0.012; OR: 11.385; CI: 1 .419-91.352) has a 11.3 times higher risk of experiencing PEB, this result is in line with research conducted by Yang and Wu (2022) which states that HAPO (international cohort study) which has a 11.3 times higher risk of

experiencing severe preeclampsia, involving 23,316 pregnant women from nine countries. This study proved the relationship between blood glucose levels and severe preeclampsia. In addition, there is research conducted by Eka Wulandari (2021) with the results of her research that the history of comorbidities does not have a significant relationship with the incidence of PEB, this difference is due to the place and there are differences in research subject criteria.

Table 2 Multivariate analysis results

Multivariate Analysis		P value	Exp(B)	CI
Step 1	Age of Respondent	0,049	2,709	1,006-7,296
	History of Obesity	0,000	14,897	4,979-44,571
	History of Preeclampsia	0,281	2,321	0,503-10,714
	History of Diabetes Mellitus	0,067	8,323	0,859-80,644
	History of Chronic Hypertension	0,003	4,843	1,709-13,724
	Constant	0,000	0,210	
Step 2	Age of Respondent	0,028	2,972	1,128-7,832
	History of Obesity	0,000	15,535	5,216-46,271
	History of Diabetes Mellitus	0,062	8,664	0,900-83,364
	History of Chronic Hypertension	0,001	5,770	2,122-15,690
		Constant	0,000	0,213
Step 3	Age of Respondent	0,007	3,657	1,437-9,306
	History of Obesity	0,000	15,460	5,255-45,483
	History of Chronic Hypertension	0,001	5,568	2,088-14,848
		Constant	0,000	0,230

In table 2 above, the results of multivariate analysis using multiple logistic regression showed that the variable history of obesity before pregnancy was the most dominant variable in the incidence of severe preeclampsia with a risk of 15 times higher. experienced severe preeclampsia in mothers with a history of obesity before pregnancy compared to mothers who were not obese.

Age and history of chronic hypertension were variables included in the final modeling of multivariate analysis.

CONCLUSIONS

The variables of age, history of obesity, history of preeclampsia, history of diabetes mellitus and history of chronic hypertension are significant risk factors for the incidence of severe preeclampsia (PEB) at Dr. Wahidin Sudiro Husodo Region General Hospital, Mojokerto City in the 2021-2022 period, and history of obesity is the most dominant variable.

For future research, additional factors related to the mother's life can be developed, such as the frequency and quality of ANC visits, the mother's education level, early marriage factors, economic conditions, and support provided by family and husband. Dr. Wahidin Sudiro Husodo Region General Hospital can make promotive and preventive efforts to the community regarding severe preeclampsia, as well as optimizing screening in patients with risk factors in an effort to prevent complications in the mother even to death.

REFERENCES

- ACOG. (2019). Gestational Hypertension and Preeclampsia. *MCN The American Journal of Maternal/Child Nursing*, 44(3), 170. <https://doi.org/10.1097/NMC.0000000000000523>
- Almasi-Hashiani, A., Omani-Samani, R., Mohammadi, M., Amini, P., Navid, B., Alizadeh, A., Khedmati Morasae, E., & Maroufizadeh, S. (2019). Assisted reproductive technology and the risk of preeclampsia: an updated systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, 19(1), 149. <https://doi.org/10.1186/s12884-019-2291-x>

- Aryanti, R., Aisyah, S., & Anggraini, H. (2022). The Relationship of Knowledge , Parity and Anxiety With the Event of Severe Preeclampsia in Hospital General of Wood Area 2021. *Science Midifery*, 10(2), 857–862.
- Brown, M. A., Magee, L. A., Kenny, L. C., Karumanchi, S. A., McCarthy, F. P., Saito, S., Hall, D. R., Warren, C. E., Adoyi, G., & Ishaku, S. (2018). The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertension*, 13, 291–310. <https://doi.org/https://doi.org/10.1016/j.preghy.2018.05.004>
- Cervilla-Muñoz, E., Galeano-Valle, F., Villarreal-Paul, G., Enríquez-Gómez, A., De-Santos-Belinchón, S., Del-Toro-Cervera, J., & Demelo-Rodríguez, P. (2022). HELLP syndrome complicated by subcapsular liver hematoma and pulmonary embolism: An extremely rare case report and literature review. *Thrombosis Update*, 8, 100115. <https://doi.org/https://doi.org/10.1016/j.tru.2022.100115>
- Chandrasekaran, S., & Simon, R. (2020). Hepatic Complications in Preeclampsia. *Clinical Obstetrics and Gynecology*, 63(1), 165–174. <https://doi.org/10.1097/GRF.00000000000000501>
- Charan, J., & Biswas, T. (2013). How to calculate sample size for different study designs in medical research? *Indian Journal of Psychological Medicine*, 35(2), 121–126. <https://doi.org/10.4103/0253-7176.116232>
- Ernawati, E., Erliana, E., Sulistono, A., Joewono, H. T., Akbar, M. I. A., Wicaksono, B., Gumilar, K. E., Sarjana, M. P., Cininta, N., Aryananda, R., Etika, R., Purnomo, W., Abdullah, N., Gumilar, E., Dekker, G., & Aditiawarman, A. (2018). Expectant management of severe preeclampsia in a developing country: Maternal outcomes and perinatal survival. *Pregnancy Hypertension*, 13, S19. <https://doi.org/https://doi.org/10.1016/j.preghy.2018.08.058>
- Ertiana, D., & Wulan, S. R. (2019). Hubungan Usia dengan Kejadian Preeklamsia pada Ibu Hamil di RSUD Kabupaten Kediri Tahun 2018. *Midwifery Jurnal Kebidanan*, 5(2), 1–7. <https://doi.org/10.21070/mid.v5i2.2765>
- Feroz, A., Saleem, S., & Seto, E. (2020). Exploring perspectives, preferences and needs of a telemonitoring program for women at high risk for preeclampsia in a tertiary health facility of Karachi: A qualitative study protocol. *Reproductive Health*, 17(1), 1–7. <https://doi.org/10.1186/s12978-020-00979-8>
- Godana, A., Dessalegn, D., Adem, F., & Edessa, D. (2021). Treatment outcomes and determinants of eclampsia and severe preeclampsia among pregnant women admitted to selected tertiary hospitals in ethiopia: A cohort study. *International Journal of Women's Health*, 13, 781–791. <https://doi.org/10.2147/IJWH.S321128>
- Handayani, E. D. (2022). Umur Dan Paritas Terhadap Kejadian Preeklamsi Berat Pada Ibu Hamil Di UGD Kebidanan. *Jurnal Abdi Kesehatan dan Kedokteran*, 1(1), 6–11. <https://doi.org/10.55018/jakk.v1i1.2>

- Ives, C. W., Sinkey, R., Rajapreyar, I., Tita, A. T. N., & Oparil, S. (2020). Preeclampsia—Pathophysiology and Clinical Presentations: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, 76(14), 1690–1702. <https://doi.org/10.1016/j.jacc.2020.08.014>
- Jaimcharyatam, N., Na-Rungsri, K., Tungsanga, S., Lertmaharit, S., Lohsoonthorn, V., & Totienchai, S. (2019). Obstructive sleep apnea as a risk factor for preeclampsia-eclampsia. *Sleep & Breathing = Schlaf & Atmung*, 23(2), 687–693. <https://doi.org/10.1007/s11325-018-1758-8>
- Jasda, A., Gusrianti, E., Program, N. S., Polytechnic, H., The, O., Of, M., Tanjungpinang, H., & Info, A. (2021). RISK FACTORS FOR SEVERE PRE-ECLAMPSIA IN PREGNANT WOMEN IN RIAU ISLANDS 2019. *International Journal of Social Science*, 1(1), 49–56.
- Jena, M. K., Sharma, N. R., Petitt, M., Maulik, D., & Nayak, N. R. (2020). Pathogenesis of Preeclampsia and Therapeutic Approaches Targeting the Placenta. *Biomolecules*, 10(6). <https://doi.org/10.3390/biom10060953>
- Jeong, D. E., Hyun, S. M., Cho, I., Lee, K.-N., Ahn, K., Ji Kim, H., Yoon Park, J., & Oh, K. J. (2022). The association between maternal pre-pregnancy body mass index and pregnancy outcomes of preeclampsia. *Taiwanese Journal of Obstetrics and Gynecology*, 61(3), 441–446. <https://doi.org/https://doi.org/10.1016/j.tjog.2022.03.008>
- Karrar SA, Hong PL. Preeclampsia. [Updated 2023 Feb 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK570611/> diakses pada 7 agustus 2023
- Kattah, A. (2020). Preeclampsia and Kidney Disease: Deciphering Cause and Effect. *Current Hypertension Reports*, 22(11), 91. <https://doi.org/10.1007/s11906-020-01099-1>
- Kaur, H., & Kolli, M. (2021). Acute Pulmonary Edema in Pregnancy - Fluid Overload or Atypical Pre-eclampsia. In *Cureus* (Vol. 13, Nomor 11, hal. e19305). <https://doi.org/10.7759/cureus.19305>
- Kementrian Kesehatan RI. 2021. Peringatan Hari Preeklamsia Sedunia 2021. <https://ayosehat.kemkes.go.id/peringatan-hari-preeklamsia-sedunia-2021> di akses tanggal 1 april 2023.
- Lisonkova, S., Bone, J. N., Muraca, G. M., Razaz, N., Wang, L. Q., Sabr, Y., Boutin, A., Mayer, C., & Joseph, K. S. (2021). Incidence and risk factors for severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome, and eclampsia at preterm and term gestation: a population-based study. *American Journal of Obstetrics and Gynecology*, 225(5), 538.e1-538.e19. <https://doi.org/10.1016/j.ajog.2021.04.261>
- Luna, S. D., & Martinovic, T. C. (2023). Hipertensión y embarazo: revisión de la literatura. *Revista Médica Clínica Las Condes*, 34(1), 33–43. <https://doi.org/https://doi.org/10.1016/j.rmclc.2023.01.006>
- Malone, S. L., Yahya, R. H., & Kane, S. C. (2022). Reviewing Accuracy of First

- Trimester Screening for Preeclampsia Using Maternal Factors and Biomarkers. *International Journal of Women's Health*, 14(August), 1371–1384.
<https://doi.org/10.2147/IJWH.S283239>
- Meazaw, M. W., Chojenta, C., Muluneh, M. D., & Loxton, D. (2020). Systematic and meta-analysis of factors associated with preeclampsia and eclampsia in sub-Saharan Africa. *PloS One*, 15(8), e0237600.
<https://doi.org/10.1371/journal.pone.0237600>
- Michalczyk, M., Celewicz, A., Celewicz, M., Woźniakowska-Gondek, P., & Rzepka, R. (2020). The Role of Inflammation in the Pathogenesis of Preeclampsia. *Mediators of Inflammation*, 2020, 3864941.
<https://doi.org/10.1155/2020/3864941>
- Mou, A. D., Barman, Z., Hasan, M., Miah, R., Hafsa, J. M., Das Trisha, A., & Ali, N. (2021). Prevalence of preeclampsia and the associated risk factors among pregnant women in Bangladesh. *Scientific Reports*, 11(1), 1–9.
<https://doi.org/10.1038/s41598-021-00839-w>
- Phillips, J., Nathan, E., & Graham, D. (2023). Preeclampsia in women with lupus – Influence of aspirin and hydroxychloroquine on pregnancy outcome. *Pregnancy Hypertension*, 31, 14–16.
<https://doi.org/https://doi.org/10.1016/j.preghy.2022.11.006>
- Phipps, E. A., Thadhani, R., Benzing, T., & Karumanchi, S. A. (2019). Preeclampsia: pathogenesis, novel diagnostics and therapies. *Nature Reviews. Nephrology*, 15(5), 275–289.
<https://doi.org/10.1038/s41581-019-0119-6>
- Persson M, Cnattingius S, Wikström AK, Johansson S. Maternal overweight and obesity and risk of pre-eclampsia in women with type 1 diabetes or type 2 diabetes. *Diabetologia*. 2018 Oct;59(10):2099-105. doi: 10.1007/s00125-016-4035-z. Epub 2018 Jul 1. PMID: 27369871; PMCID: PMC5016540.
- POGI. 2016. Pedoman Pengelolaan Hipertensi Dalam Kehamilan Di Indonesia. Edisi 2, Semarang : Himpunan Kedokteran Feto Maternal POGI
- Pratiwi, A. M., & Fatima. (2019). *PATOLOGI KEHAMILAN* (Pustaka Baru Press (ed.)). Pustaka Baru Press.
- Preeclampsia: Basic, Genomic, and Clinical. (2018). Jerman: Springer Nature Singapore.
- Skoura, R., Andronikidi, P.-E., Anastakis, D., Petanidis, S., Orovou, E., Tzitiridou, M., & Eskitzis, P. (2022). Antiphospholipid Syndrome and Preeclampsia in Pregnancy: A Case Report. In *Cureus* (Vol. 14, Nomor 8, hal. e28458).
<https://doi.org/10.7759/cureus.28458>
- Stern EM, Blace N. Ophthalmic Pathology of Preeclampsia. [Updated 2022 Oct 24]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK576389/>
- Sudjai, D. (2023). Association of pre-pregnancy body mass index with early- and late-onset severe preeclampsia. *European Journal of Obstetrics & Gynecology and Reproductive Biology*: X, 19, 100223.

<https://doi.org/https://doi.org/10.1016/j.eurox.2023.100223>

Sumampouw Claudia Meinda, Tendean, H. M. M., & Freddy W. Wagey. (2019). Gambaran Preeklampsia Berat Dan Eklampsia Ditinjau Dari Faktor Risiko di RSUP Prof. DR. R. D. Kandou Manado. *Jurnal Medik dan Rehabilitasi (JMR)*, 1(3), 1–5.

Szczepanski, J., Griffin, A., Novotny, S., & Wallace, K. (2020). Acute Kidney Injury in Pregnancies Complicated With Preeclampsia or HELLP Syndrome. *Frontiers in Medicine*, 7, 22. <https://doi.org/10.3389/fmed.2020.00022>

Varrias, D., Spanos, M., Kokkinidis, D. G., Zoumpourlis, P., & Kalaitzopoulos, D. R. (2023). Venous Thromboembolism in Pregnancy: Challenges and Solutions. *Vascular Health and Risk Management*, 19, 469–484. <https://doi.org/10.2147/VHRM.S404537>

WHO. (2011). Prevention and treatment of pre-eclampsia and eclampsia. In *Journal of Steroid Biochemistry & Molecular Biology* (Vol. 97).

WHO. (2021). WHO recommendations on antiplatelet agents for the prevention of pre-eclampsia. In *Seminars in Thrombosis and Hemostasis* (Vol. 37, Nomor 2, hal. 137–140). <https://doi.org/10.1055/s-0030-1270340>

Wu, C.-T., Kuo, C.-F., Lin, C.-P., Huang, Y.-T., Chen, S.-W., Wu, H.-M., & Chu, P.-H. (2021). Association of family history with incidence and gestational hypertension outcomes of preeclampsia. *International Journal of Cardiology Hypertension*, 9, 100084. <https://doi.org/https://doi.org/10.1016/j.ijchy.2021.100084>

Wulandari, E. S., Ernawati, E., & Nuswantoro, D. (2021). Risk Factors of Preeclampsia With Severe Features and Its Complications. *Indonesian Midwifery and Health Sciences Journal*, 5(1), 29–37. <https://doi.org/10.20473/imhsj.v5i1.2021.29-37>

Yang, Y., & Wu, N. (2022). Gestational Diabetes Mellitus and Preeclampsia: Correlation and Influencing Factors. *Frontiers in Cardiovascular Medicine*, 9, 831297. <https://doi.org/10.3389/fcvm.2022.831297>