

PREDICTIVE VALUE OF THE SIGNS AND SYMPTOMS PRECEDING ECLAMPSIA: A SYSTEMATIC REVIEW

Legina Aromatika^{1*}, Teddy Nofriyadi¹, Mutia Juliana²

^{1*}Faculty of Medicine, University of Jambi, Indonesia

²Immanuel Institute of Health, Indonesia

***Corresponding Author:**

Leginaaromatika.dr@gmail.com

Abstract

Background: Malnutrition can be illness-related (one or more diseases or injuries directly result in nutrient imbalance), or it can be induced by environmental and behavioural variables associated with decreased nutrient intake and/or delivery. Comorbidities were shown to be related with child malnutrition in the study.

Aim: The goal of this study is to showed predictive value of the signs and symptoms preceding eclampsia.

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Result: In the PubMed database, the results of our search brought up 88 articles, whereas the results of our search on SagePub brought up 43 articles. The results of the search conducted for the last year of 2013 yielded a total 13 articles for PubMed and 7 articles for SagePub. In the end, we compiled a total of 12 papers, 9 of which came from PubMed and 3 of which came from SagePub. We included five research that met the criteria.

Conclusion: Visual abnormalities, epigastric discomfort, and headache are among of the most typically reported symptoms, however none of these were able to effectively predict or rule out the possibility of impending eclampsia.

Keyword: Delivery; Eclampsia; Magnesium sulphate; Pre-eclampsia.

INTRODUCTION

The life-threatening pregnancy condition known as eclampsia is defined as the onset of seizures during pregnancy that occurs simultaneously with a diagnosis of preeclampsia.¹ Eclampsia can lead to the premature delivery of the baby. Women who have been diagnosed with preeclampsia in the past are at an increased risk of developing eclampsia.² The hypertensive illnesses of pregnancy, which can include preeclampsia and eclampsia, are a common cause of maternal mortality, accounting for 10–15% of all direct maternal deaths around the world. These diseases can be fatal to both the mother and her unborn child.^{3–5}

In addition, eclampsia is linked to a greater maternal morbidity rate because of the increased risk of hypoxic–ischemic brain injury and seizure-related intracranial haemorrhage. Eclampsia is associated with an increased risk of both of these possible consequences.⁶ The estimated incidence of preeclampsia ranges from 16 to 69 instances per 10,000 people in low-to-middle income countries, whereas in high-income nations, the estimated incidence ranges from 2 to 8 cases per 10,000 people. In these countries, the incidence of eclampsia is significantly higher, which is true for a number of other maternal health issues as well.^{4,7,8}

Magnesium sulphate is the medicine of choice for treating and preventing eclampsia. It has been found to reduce the risk of eclampsia by more than 50 percent among women who have preeclampsia, which is the condition that comes before eclampsia.⁹ In the Magpie study, women with any kind of preeclampsia who were treated with magnesium sulphate had a 58% lower risk of developing preeclamptic complications. However, the number of patients that needed to be treated was 91 for all cases of preeclampsia, 61 for cases of preeclampsia with severe characteristics, and 101 for cases of preeclampsia with only hypertension and proteinuria.¹⁰

In addition, the risk of eclampsia is not restricted to only women who have preeclampsia; in fact, 15% of eclampsia cases occur in women who do not have hypertension, while 20% of instances occur among women who have modestly elevated blood pressure. Clinicians will give magnesium sulphate to women with preeclampsia only if they believe the woman is at danger for having an eclamptic seizure.⁹ However, there is a lack of clarity in the evidence that doctors can use to guide their decisions regarding which preeclamptic individuals are at heightened risk.¹¹ This research aims to demonstrate the predictive utility of the signs and symptoms that occur before eclampsia develops in a pregnant woman.

METHODS

The author of this study ensured that it was up-to-date and adhered to all of the standards in accordance with the guidelines provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This step is extremely significant since it validates the findings of the research and ensures that they are accurate. According to the findings of this study, there is a correlation between the indications and symptoms that occur before eclampsia. Examining previously conducted research on the topic is the method that will achieve this objective with the least amount of wasted time. Given the purpose of the essay, the focus of this section will be on the reasons why the issues discussed are significant.

For the researchers to be allowed to take part in the study, they had to provide evidence that demonstrated they fulfilled the following requirements: 1) The study needs to be written in English and demonstrate that it has predictive value about the signs and symptoms that come before eclampsia in order for it to be published. 2) Works that were published after 2013 but were still in circulation at the time of the examination are eligible for consideration. Editorials, applications without a DOI, review articles that have already been published, and entries that are almost identical to journal papers that have already been published are examples of types of research that cannot be published.

We used between “predictive value”; “signs”; “symptoms”; and, “preceding eclampsia” as keywords. The search for studies to be included in the systematic review was carried out from July, 6th 2023 using the PubMed and SagePub databases by inputting the words: (*"predict"[All Fields] OR "predictabilities"[All Fields] OR "predictability"[All Fields] OR "predictable"[All Fields] OR "predictably"[All Fields] OR "predicted"[All Fields] OR "predicting"[All Fields] OR "prediction"[All Fields] OR "predictions"[All Fields] OR "predictive"[All Fields] OR "predictively"[All Fields] OR "predictiveness"[All Fields] OR "predictives"[All Fields] OR "predictivities"[All Fields] OR "predictivity"[All Fields] OR "predicts"[All Fields]*) AND (*"value"[All Fields] OR "values"[All Fields]*) AND (*"diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "signs"[All Fields] OR "diagnosis"[MeSH Terms] OR "signs"[All Fields]*) AND (*"diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "symptoms"[All Fields] OR "diagnosis"[MeSH Terms] OR "symptom"[All Fields] OR "symptom s"[All Fields] OR "symptomes"[All Fields]*) AND (*"preceded"[All Fields] OR "precedes"[All Fields] OR "preceding"[All Fields]*) AND (*"eclampsia"[MeSH Terms] OR "eclampsia"[All Fields] OR "eclampsias"[All Fields]*) AND (*y_10[Filter]*) AND (*clinicaltrial[Filter]*) used in searching the literature.

In the PubMed database, the results of our search brought up 88 articles, whereas the results of our search on SagePub brought up 43 articles. The results of the search conducted for the last year of 2013 yielded a total 13 articles for PubMed and 7 articles for SagePub. In the end, we compiled a total of 12 papers, 9 of which came from PubMed and 3 of which came from SagePub. We included five research that met the criteria.

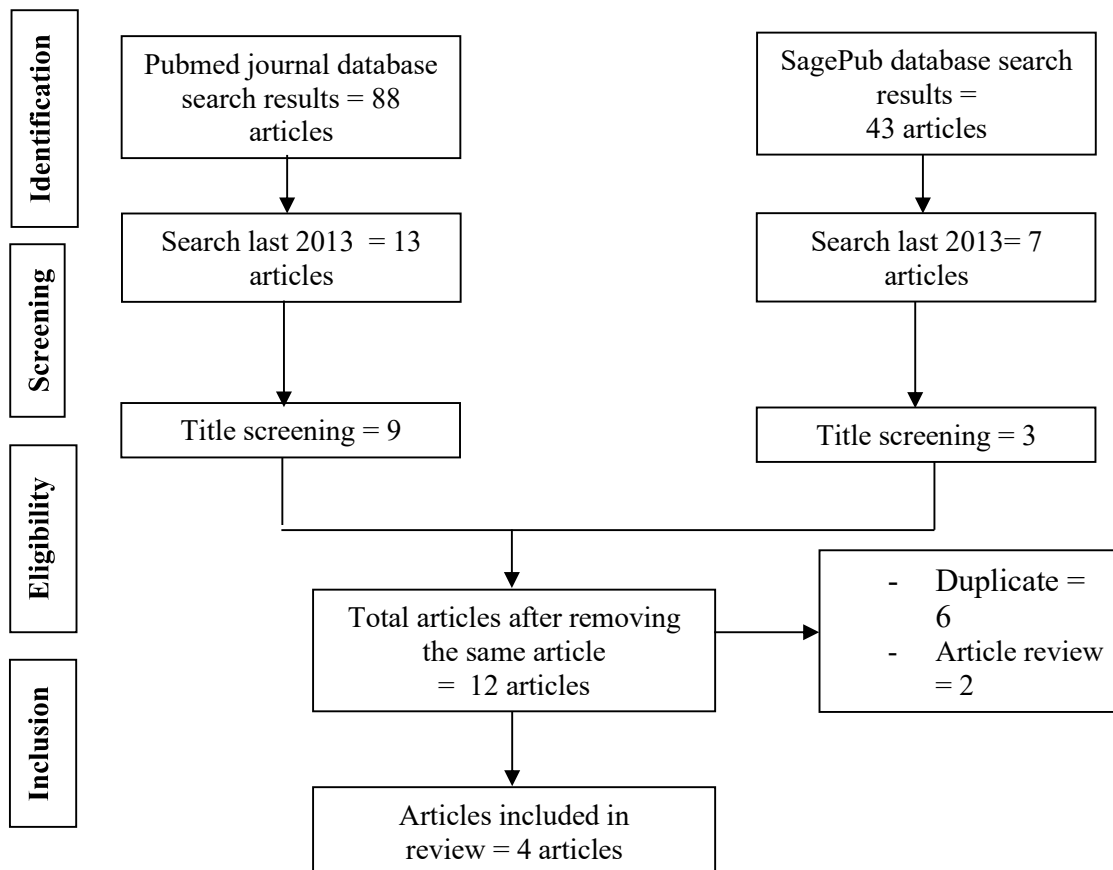


Figure 1. Article search flowchart

In order to evaluate the reliability of the study, we looked at both the abstract and the title of it. They examined a significantly larger number of historical records. This finding is supported by a number of other investigations that utilised the same methodology. In order to comment, you need to utilise an original form of the English language that has never been seen before in print. In the systematic review, the only works that were considered for inclusion were those that met the predetermined criteria for inclusion. The number of search results that are displayed has been reduced. Insufficient time spent investigating and analysing. This section presents the results of the evaluation. The research paper includes detailed information about the subjects, authors, date, place, topic, and parameters of the study. The name of the author as well as the publishing date are both included in the article. Any duplicates that Endnote discovered were deleted. The article titles and abstracts that were provided were reviewed by two different raters. Their in-depth papers were analysed in order to assess whether or not the research could be carried out and to acquire relevant data. In addition to GWAS, conferences and research have been centred on the examination of a variety of other health concerns. The results of the evaluation led the assessors to their conclusion. Before making their decision about which papers to explore, each author read the abstracts and titles of all of the research that were accessible. After then, an assessment will be made of every eligible article that satisfies the inclusion requirements. Following the completion of the initial lesson on the fundamentals, we will select review topics. Articles of inquiry and critical analysis are chosen using this methodology.

RESULT

In the PubMed database, the results of our search brought up 88 articles, whereas the results of our search on SagePub brought up 43 articles. The results of the search conducted for the last year of 2013 yielded a total 13 articles for PubMed and 7 articles for SagePub. In the end, we compiled a total of 12 papers, 9 of which came from PubMed and 3 of which came from SagePub. We included five research that met the criteria.

Maraschini, et al (2022)¹² showed multiple pregnancies (RR = 4.51; p <0.001) and pregnancies made possible by fertility treatments (RR = 3.03; p <0.001) were linked to an increased risk of eclampsia. Almost 30% of women with preeclampsia took magnesium sulphate to prevent an eclamptic fit, and 89% of women who had an eclamptic fit took magnesium sulphate to treat it. For antepartum cases, the time between the first fit and the birth was 62 minutes, and for intrapartum cases, it was 10 minutes. About a third of the women had at least one other serious problem, and one mother died. 13.3% of the babies had a serious illness. There were two deaths of foetuses and one death of a newborn.

Melese, et al (2019)¹³ showed that 46.5% of babies born to mothers with severe preeclampsia or eclampsia did not have a good result. It shows that the number of unfavourable perinatal outcomes was high, which means that we have a responsibility to suggest ways to improve health care so that these problems can be prevented and fixed. Variables that were linked to bad perinatal outcomes were the mother's level of education (adjusted odds ratio [AOR] = 6.6, 95% confidence interval [CI] = 1.32–10.03), her number of children (AOR = 8.3, 95% CI = 6.27–27.02), her gestational age in weeks (AOR = 9.6, 95% CI = 2.18–18.65), and the time she took a drug (AOR = 3.8, 95% CI = 1.81–8.07).

Table 1. The literature include in this study

Author	Origin	Method	Participant	Result
Maraschini, 2022 ¹²	Italy	Case-control, prospective	109 cases	According to the findings of this study, the rate of preeclampsia is rather low in Italy, and when it does occur, timely treatment with antihypertensive medications and magnesium sulphate helps to both prevent and treat subsequent seizures.
Melese, 2019 ¹³	Ethiopia	Cross sectional study	456 severe preeclamptic and eclamptic mothers	This study showed that 46.5% of babies born to mothers with severe preeclampsia or eclampsia did not have a good result. It shows that the number of unfavourable perinatal outcomes was high, which means that we have a responsibility to suggest ways to improve health care so that these problems can be prevented and fixed.
Taweasuk, 2014 ¹⁴	Thailand	Case-control, retrospective	138,261 births	The risk factors of the development of eclampsia compared to mild preeclampsia are maternal age <20 years, antenatal care (ANC) <4 visits, deep tendon reflex (DTR) ≥3+, serum uric acid ≥6 mg/dL, serum creatinine ≥0.9 mg/dL, and serum SGOT ≥44 IU/L.
Raghuraman, 2014 ¹⁵	Haiti	Cohort retrospective	1,743 mothers	At this facility in Haiti, the rates of preeclampsia and the complications that are associated with it, such as eclampsia and placental abruption, as well as maternal death and stillbirth, are high. These kind of data are absolutely necessary for the development of preeclampsia-complication-prevention strategies that are specific to an area.

Taweasuk, et al (2014)¹⁴ showed the risk factors that were significantly associated with eclampsia compared to mild preeclampsia after using multivariate logistic regression analysis were maternal age <20 years (aOR = 4.8, 95% confidence interval (CI) = 1.7 to 14), antenatal care (ANC) <4 visits (aOR = 3.4, 95% CI = 1.2 to 9.1), deep tendon reflex (DTR) ≥3+ (aOR = 15.1, 95% CI = 5.3 to 42.7), serum uric acid ≥6 mg/dL (aOR = 8.3, 95% CI = 3.5 to 19.8), serum creatinine ≥0.9 mg/dL (aOR = 18, 95% CI = 4.8 to 67.5), and serum glutamate oxaloacetate transaminase (SGOT) ≥44 IU/L (aOR = 15.9, 95% CI = 5.6 to 45.3).

Raghuraman, et al (2014) showed 16.6% mothers were found to have preeclampsia or eclampsia. Almost all (95.0%) of the preeclampsia patients who were brought to the hospital had severe preeclampsia. There were 83 people with eclampsia, which was 30.7%, and 61 of them, or 73.4%, had it before they gave birth. There were 48 stillbirths, which is 17.8%, and 5 deaths of mothers, which is 1.9%. Compared to women with antepartum preeclampsia, people with antepartum eclampsia were younger, more likely to be first-time moms, and had less prenatal care. Antepartum eclampsia was linked to the separation of the placenta and the death of the mother.

DISCUSSION

Eclampsia is a pregnancy complication that is uncommon but potentially fatal. It can occur in women who have preeclampsia as well as in women whose blood pressure is normal. Pregnant women tend to and easily experience preeclampsia if they have the following predisposing factors: nullipara, multiple pregnancies, age <20 or >35 years, history of preeclampsia-eclampsia in previous pregnancies, family history of preeclampsia-eclampsia, kidney disease, hypertension and pre-existing diabetes mellitus, and obesity.¹⁶

Circulating proangiogenic factors secreted by the placenta include vascular endothelial growth factor (VEGF) and placental growth factor (PlGF). Antiangiogenic factors include soluble receptor tyrosine kinase I (sFlt-1) (otherwise known as soluble VEGF receptor type I) and soluble endoglin (sEng). VEGF and PlGF promote angiogenesis by interacting with the VEGF receptor family. Although both growth factors are produced by the placenta, serum PlGF levels increase much more significantly in pregnancy.¹⁶

Because eclampsia is such a rare disorder, there have only been a handful of studies done to investigate how clinical

symptoms might be used to predict the risk of developing the condition. We came across mostly retrospective studies, almost all of which suffered from serious methodological shortcomings and posed a significant danger of being biased. In addition, there was a significant amount of variation amongst the research due to the diverse study designs, people, and environments. It was found that there were a total of 28 signs and symptoms.¹⁷

The majority of studies are designed to be retrospective, it is impossible to analyse symptoms other than those asked about or actively reported. Because of this, so it is probable that the finding of symptoms that are not previously generally associated with eclampsia will be hampered. Data support the theory, as vision abnormalities, pain in the epigastric region, and headaches were the symptoms that were reported the most frequently throughout all of the trials.¹⁷

Two very important symptoms of preeclampsia, namely hypertension and proteinuria, are abnormalities that are usually not recognized by pregnant women. By the time complaints such as headaches, visual disturbances or epigastric pain begin to appear, the disorder is usually severe.¹⁶ Preeclampsia clinical manifestations can be heterogeneous, diagnosing preeclampsia may not be established directly. The final diagnosis of gestational hypertension can only be made in retrospect. Mild to moderate preeclampsia may be asymptomatic. Many cases are detected through routine prenatal screening.^{18,19}

Preeclampsia in previous pregnancies is associated with recurrence in subsequent pregnancies. A history of gestational hypertension or preeclampsia should greatly raise clinical suspicion. Patients with preeclampsia with severe manifestations exhibit end-stage organ dysfunction and may complain of the following: headache, altered mental status, blindness, dyspnea, distention, epigastric or right upper quadrant abdominal pain, malaise, edema present in many pregnant women oedema of the limbs or face which is indicative of preeclampsia. Preeclamptic edema occurs by a different mechanism similar to angioneurotic edema.^{20,21}

Arteriolar vasospasm causes preeclampsia, therefore high blood pressure is the most dependable early warning indication. BP > 90 mm Hg is unhealthy, however diastolic pressure is a better predictive indication. Preeclampsia in women begins with rapid weight gain. Preeclampsia is suspected if weight gain surpasses 1 kg per week or 3 kg per month. Fluid retention causes sudden and severe weight gain, which can always be detected before non-dependent edema symptoms like swollen eyes, hands, or feet appear.^{19,21,22}

When present, these signs brought to a slight increase in the risk of eclampsia developing. The investigations found that vision abnormalities, pain in the epigastric region, and headaches were the most common symptoms overall. Severe preeclampsia is commonly linked with these symptoms. However, none of these tests were reliable in predicting eclampsia since they had poor to moderate test characteristics. An improvement in the ability to forecast eclampsia is essential to lowering the rates of maternal morbidity and mortality associated with this potentially fatal condition.²¹

Eclampsia is a clinical diagnostic that is characterised by the presence of new-onset generalised tonic-clonic seizures in a woman who has preeclampsia. On occasion, however, eclampsia can be the first manifestation of preeclampsia in some cases. The clinical findings may include posterior reversible encephalopathy syndrome, which is characterised by headaches, disorientation, visual problems, and seizures. This syndrome is caused by vasogenic edema that is largely localised in the posterior cerebral hemispheres.¹⁸

If there were more accurate predictors that had a higher level of sensitivity, then there would be a reduction in the number of cases of eclamptic convulsions. If there were more accurate predictors with a higher level of specificity, it would be possible to direct the most appropriate treatment and resources towards the people who were in the most desperate need of them. These two parameters would, when combined, have the effect of reducing the variability of magnesium sulphate prophylaxis.^{19,21,22}

Daily nonstress testing and ultrasonography should check oligohydramnios and foetal movement. To ensure foetal growth, 2-week foetal growth checks should be done. Repeat a 24-hour protein urine sample. Before 34 weeks, foetal lung maturity requires corticosteroids. Ultrasound assesses IUGR. Umbilical artery transabdominal Doppler ultrasonography checks blood flow. Other foetal artery Doppler ultrasonography is unproven. Monoscopes, Dopplers, and ultrasounds measure foetal heart rate. Test liver function, blood count, uric acid, and LDH. Patients should report headaches, visual anomalies, epigastric pain, and reduced foetal movement.¹⁸

CONCLUSION

Visual abnormalities, epigastric discomfort, and headache are among of the most typically reported symptoms, however none of these were able to effectively predict or rule out the possibility of impending eclampsia.

REFERENCE

- [1]. Tranquilli A, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. Vol. 4, Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health. Elsevier; 2014. p. 97–104.
- [2]. Peraçoli JC, Borges VTM, Ramos JGL, Cavalli R de C, Costa SH de AM, Oliveira LG de, et al. Preeclampsia/eclampsia. Rev Bras Ginecol e Obs. 2019;41:318–32.
- [3]. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Heal. 2014 Jun;2(6):e323–33.
- [4]. Sibai BM. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol. 2005;105(2):402–10.
- [5]. Luealon P, Phupong V. Risk factors of preeclampsia in Thai women. J Med Assoc Thai. 2010 Jun;93(6):661–6.
- [6]. Osungbade KO, Ige OK. Review Article Public Health Perspectives of Preeclampsia in Developing Countries : Implication for Health System Strengthening. 2011;2011.
- [7]. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies.

- Nat Rev Nephrol [Internet]. 2019;15(5):275–89. Available from: <https://doi.org/10.1038/s41581-019-0119-6>
- [8]. Papageorghiou AT, Deruelle P, Gunier RB, Rauch S, García-May PK, Mhatre M, et al. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. *Am J Obstet Gynecol*. 2021 Sep;225(3):289.e1-289.e17.
- [9]. Bartal MF, Sibai BM. Eclampsia in the 21st century. *Am J Obstet Gynecol*. 2022;226(2):S1237–53.
- [10]. Group MTFSC. The Magpie Trial: a randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years. *BJOG An Int J Obstet Gynaecol*. 2007;114(3):300–9.
- [11]. Erez O, Romero R, Jung E, Chaemsaithong P, Bosco M, Suksai M, et al. Preeclampsia and eclampsia: the conceptual evolution of a syndrome. *Am J Obstet Gynecol*. 2022;226(2):S786–803.
- [12]. Maraschini A, Salvi S, Colciago E, Corsi E, Cetin I, Lovotti M, et al. Eclampsia in Italy: A prospective population-based study (2017–2020). *Pregnancy Hypertens* [Internet]. 2022;30:204–9. Available from: <https://www.sciencedirect.com/science/article/pii/S2210778922001131>
- [13]. Melese MF, Badi MB, Aynalem GL. Perinatal outcomes of severe preeclampsia/eclampsia and associated factors among mothers admitted in Amhara Region referral hospitals, North West Ethiopia, 2018. *BMC Res Notes* [Internet]. 2019;12(1):147. Available from: <https://doi.org/10.1186/s13104-019-4161-z>
- [14]. Taweesuk P, Tannirandom Y. Clinical and laboratory parameters associated with eclampsia in Thai pregnant women. *J Med Assoc Thai*. 2014;97(2):139–46.
- [15]. Raghuraman N, March MI, Hacker MR, Modest AM, Wenger J, Narcisse R, et al. Adverse maternal and fetal outcomes and deaths related to preeclampsia and eclampsia in Haiti. *Pregnancy Hypertens An Int J Women's Cardiovasc Heal*. 2014;4(4):279–86.
- [16]. Wiknjosastro H, Prawirohardjo S, Wiknjosastro H, Prawirohardjo S. Ilmu Kebidanan. PT. Bina Pustaka. Jakarta. Jakarta: Yayasan Bina Pustaka Sarwono Prawirohardjo; 2015.
- [17]. Berhan Y, Berhan A. Should magnesium sulfate be administered to women with mild pre-eclampsia? A systematic review of published reports on eclampsia. *J Obstet Gynaecol Res*. 2015;41(6):831–42.
- [18]. Task Force on Hypertension in Pregnancy. [Guideline] American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists. *Obs Gynecol*. 2013;122(5):1122–31.
- [19]. Fox R, Kitt J, Leeson P, et al. Preeclampsia: Risk Factors, Diagnosis, Management, and the Cardiovascular Impact on the Offspring. *J Clin Med*. 2019;8(10):1625.
- [20]. Cunningham FG, Leveno KJ, Bloom SL. *Williams Obstetri*. 25th ed. New York: The McGraw-Hill Companies; 2020.
- [21]. Lagana AS, Favilli A, Triolo O, et al. Early serum markers of pre-eclampsia: are we stepping forward? *J Matern Fetal Neonatal Med*. 2015;23:1–5.
- [22]. Cooray SD, Edmonds SM, Tong S, et al. Characterization of symptoms immediately preceding eclampsia. *Obs Gynecol*. 2011;118(5):995–9.