The Impact of Preeclampsia on Mothers and Perinatal

Lilin Turlina^{1*}, Mahalul Azam¹, Widya Hary Cahyati¹, Feddy Setyo Pribadi¹

¹Universitas Negeri Semarang, Central Java, Indonesia

Corresponding author: turlinalmg@students.unnes.ac.id

Abstract: Preeclampsia is an obstetric syndrome, a multisystem disorder affecting 2%-5% of pregnant women and a major contributor to both maternal and perinatal morbidity and mortality globally. This current study aimed to analyze the impact of preeclampsia on mothers and perinatal. This cross-sectional study was performed at Muhammadiyah Lamongan Hospital, using secondary data from January 2023 to February 2024. The sample was 192 delivering mothers, consisting of 96 delivering mothers with preeclampsia and 96 normal delivering mothers. The data were processed using multiple logistic regression. The statistical test showed that delivering mothers with preeclampsia had 85.7 times higher risk to undergo SC delivery (OR 85.706, 95% CI: 19,870 - 369,670), 5.5 times higher risk to deliver prematurely (OR 5.500, 95% CI: 2. 377 - 12,727), 4 times greater to deliver a baby with LBW or <2500 grams (OR 4,300, 95% CI: 1,971 - 9,383), 2 times higher to deliver a baby with APGAR Score < 7 in the first 5 minutes (OR 2,000, 95% CI: 1,116 -3,584). It is hoped that healthcare workers can carry out early detection for the prevention of preeclampsia and carry out immediate management to reduce morbidity and mortality in mothers and perinatal.

Keywords: Preeclampsia, The impact of preeclampsia, Mothers, Perinatal

INTRODUCTION

Preeclampsia (PE) according to the International Society for the Study of Hypertension in Pregnant (ISSHP) is defined as systolic blood pressure more than 140 mmHg and/or diastolic blood pressure more than 90 mmHg on at least two measurements 4 hours apart, or shorter than systolic blood pressure 160 mmHg or diastolic blood pressure 110 mmHg. Symptoms present in normotensive women during the 20th week of pregnancy with multiple symptoms such as protein urine, maternal organ dysfunction or uteroplacental dysfunction (Dimitriadis et al., 2023; Karrar & Hong, 2024; Poon et al., 2019a). PE is an obstetric syndrome, a multisystem disorder affecting 2%-5% of pregnant women and is a major contributor to maternal and perinatal morbidity and mortality worldwide, especially when it occurs in the early stages of pregnancy (Ansbacher-Feldman et al., 2022; Gómez-Jemes et al., 2022; Y.-X. Li et al., 2021; Liu et al., 2022; Poon et al., 2019b).

An estimated 4 million women worldwide are diagnosed with PE which causes 46,000 - 76,000 maternal deaths and 500,000 infant deaths each year (Chaemsaithong et al., 2022; Dimitriadis et al., 2023; Hedley et al., 2023; Kang et al., 2023; Leavey et al., 2015; Zheng et al., 2022). Globally, 10-15% of maternal deaths are statistically attributed to PE (Nair, 2018a; Ranjbar et al., 2023; Xue et al., 2023). Women in low- or middle-income and low-resource countries have a higher risk of developing PE

compared to women in high-resource countries. This is evident from the Global Burden of Disease (GBD) collaboration data in 2019 that the mortality rate in women aged 14 - 59 years due to hypertensive disorders of pregnancy is 50 times higher (Deshpande et al., 2021; Hedley et al., 2023; Poon et al., 2019b). In developing countries, the number of PE ranges from 1.8% to 16.7% (Ranjbar et al., 2023). In Sub-Saharan Africa, Maternal mortality over 5 years (2015-2020) is 22% (Musarandega et al., 2021). In the UK, PE contributes to 22 deaths and is the second most frequent cause of maternal mortality (Hackelöer et al., 2022). Nearly one-tenth of maternal deaths in Asia and Africa are caused by PE (Varghese et al., 2023).

The number of maternal deaths in Indonesia tends to increase every year, but decreased in 2022, which amounted to 3,572 deaths, while in 2021 it was 7,389 deaths and in 2020 it was 4,627 deaths. The most common cause of maternal death in 2022 was hypertension in pregnancy with 801 cases (Kementrian Kesehatan RI, 2022). In 2021, maternal deaths due to PE were 1,077 cases (Kementrian Kesehatan RI, 2021) and in 2020, maternal deaths due to PE reached 1,110 cases (Kementrian Kesehatan RI, 2020). The Maternal Mortality Rate (MMR) in East Java in 2022 decreased compared to the previous two years. In 2020, the MMR in East Java was 98.40 per 100,000 live births, and in 2021 it was 234.7 per 100,000 live births, while in 2022 it managed to fall to 93.00 per 100,000 live births. The two highest causes of maternal mortality in East Java are hypertension in pregnancy (24.45%) and bleeding (21.24%) (Dinas Kesehatan Jawa Timur, 2022). Meanwhile, in 2021, the three highest causes of maternal mortality in 2021 were hypertension in pregnancy, which amounted to 9.62% (123 cases), bleeding at 9.38% (120 cases), and other causes at 68.18% (872 cases) (Dinas Kesehatan Jawa Timur, 2021).

The pathogenesis and underlying etiology of PE, both premature and full term are still unknown and delivery is the procedure to terminate pregnancy in pregnant women diagnosed with PE (Aljameel et al., 2023; Dimitriadis et al., 2023; S. Li et al., 2020; Yun et al., 2023a). The two-stage PE model proposes that PE is caused by placental dysfunction leading to impaired trophoblast invasion and differentiation (Dimitriadis et al., 2023; Garrido-Giménez et al., 2023; Nair, 2018b). However, many risk factors have been identified to be associated with PE (Dimitriadis et al., 2023), both clinical and historical risk factors (Henderson et al., 2017). Risk factors for PE have been proposed by several clinical guidelines such as the National Institute for Health and Excellence, the American College of Obstetricians and Gynecologists, the Society of Obstetricians and Gynecologists of Canada, and the World Health Organization. These risk factors include maternal age, parity, previous history of PE, pregnancy interval, reproductive technology, family history of PE, obesity, race and ethnicity, and (Awor et al., 2023; Dimitriadis et al., 2023; Giannakou, 2021; Henderson et al., 2017; Y. Li et al., 2021; Melinte-Popescu et al., 2023; Poon et al., 2019b; Yun et al., 2023b).

Proceedings of International Conference on Health Science, Practice, and Education

PE can be distinguished into early-onset PE, which happens sometime after 34 weeks of gestation, and the more common late-onset PE occurred at or after 34 weeks of development. (Xue et al., 2023). PE contains a non-negligible frequency and causes advanced systemic complications and long-lasting sequelae for the mother (Kang et al., 2023). Maternal complications related to PE incorporate placental abruption and acute kidney injury. In serious cases, PE causes life-threatening eclamptic seizures and hemolysis, raised liver enzymes, and HELLP syndrome (Garrido-Giménez et al., 2023; Jhee et al., 2019). Mothers also have the potential to suffer from fatal pathological manifestations including hypertension, protein urine, liver rupture, acute pulmonary syndrome, pulmonary edema, cardiovascular disease, metabolic disorders, renal failure, and neurological disorders, as well as delivery by surgery (Sectio caesarean/SC) (Dimitriadis et al., 2023; He et al., 2021; Pham et al., 2023; Poon et al., 2019b; Ratnik et al., 2022).

PE is also related to a number of perinatal and neonatal complications including mortality (Dimitriadis et al., 2023). The complications involve intrauterine fetal death, intrauterine growth restriction, premature birth, low birth weight, low APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score, respiratory distress syndrome, high hospitalization rate and stillbirth (Dimitriadis et al., 2023; Garrido-Giménez et al., 2023; He et al., 2021; Henderson et al., 2017; Y. Li et al., 2021; Melinte-Popescu et al., 2023; Ratnik et al., 2022; Sufriyana et al., 2020; Xue et al., 2023).

Various efforts are made to reduce maternal mortality due to PE. One of these efforts is to conduct screening and early detection in pregnant women with <20 weeks of gestation. (Juwita et al., 2022). PE screening is an important component of antenatal care worldwide (Thomas et al., 2023). PE screening can be performed based on maternal characteristics and medical history, biophysical markers (uterine artery doppler and MAP) and biomarkers. (Marić et al., 2022). The Regulation of the Minister of Health of the Republic of Indonesia No. 21 of 2021 concerning Health Services, pregnant women should at least do integrated antenatal care 6 times with a standard antenatal service of 10 T. Through regular ANC, early detection of abnormalities9090 suffered by pregnant women can be carried out and management of abnormalities / diseases / disorders in pregnant women immediately or make referrals to health care facilities in line with the existing system. This is one of the efforts to prevent an increase in maternal and perinatal morbidity and mortality rates (Kementerian Kesehatan RI, 2021).

METHOD

This study used descriptive analytic research with a cross sectional approach. The research was conducted at Muhammadiyah Lamongan Hospital. The data were collected using secondary data from the labor register of Muhammadiyah Lamongan Hospital from January 2023 to February 2024. The sample used was 192 delivering mothers consisting of 96 delivering mothers with a diagnosis of

880

preeclampsia and 96 normal delivering mothers. The data were analyzed using multivariate analysis with multiple logistic regression.

RESULTS

 Table 1. Demographic Characteristics of Delivering Mothers at Muhammadiyah Lamongan Hospital in 2024

No.	Variable	Case Group	(with PE)	Control Group (without PE)		
		f	%	f	%	
1.	Age - < 20 years	1	1,04	0	0	
	- 20 – 35 years	71	73.96	84	87.50	
	 > 35 years 	24	25	12	12.50	
2.	Parity					
	- Primiparous	40	41.67	29	30.21	
	- Multiparous	50	52.03	60	62.50	
	- Grande multiparous	6	6.25	7	7.29	

It can be perceived that the age of mothers in both the case and control groups was in the range of 20 - 35 years (73.96% and 87.50%). As for maternal parity data, both case and control groups were multiparous (50% and 62.50%). In general, there was no significant difference in demographic data between the case and control groups.

No.	Variable	wit	with PE without PE		out PE	Sig	Exp B)	95% CI
	-	f	%	f	%			
1.	End of pregnancy - Mature	64	66.67	88	91.67	<0.001	5.500	2.377 – 12.727
	- Premature	32	33.33	8	8.33			
2.	Types of delivery - Spontaneous	2	2.08	62	64.58	<0.001	85.706	19.870 – 369.670
	- SC	94	97.92	34	35.42			
3.	Birth weight - > 2500 gram	64	66.67	86	89.58	<0.001	4.300	1.971 – 9.383
	- ≤ 2500 gram	32	33.33	10	10.42			
4.	APGAR Score - ≥ 7	49 47	51.04	64 32	66.67	0.020	2.000	1.116 -3.584
	1	41	40.30	JZ	55.55			

 Table 2. The impact of Preeclampsia on Mother and Perinatal in Muhammadiyah Lamongan Hospital in 2024

Data on Table 2 showed that there were no significant frequency differences in the variables of end of pregnancy, birth weight, APGAR Score and IUFD. In the type of delivery, almost all mothers with preeclampsia ended their pregnancy with SC (97.92%). Meanwhile, based on the logistic regression statistical test, it can be perceived that delivering mothers with preeclampsia had a significantly higher chance of complications. Pregnant women with preeclampsia had a 5.5 times higher risk of preterm delivery (OR 5,500, 95% CI: 2,377 - 12,727). Delivering mothers with preeclampsia were 85.7 times more likely to undergo SC delivery (OR 85.706, 95% CI: 19,870 - 369,670). Pregnant women with preeclampsia had a 4 times greater risk of delivering a baby with a low birth weight or <2500 grams (OR 4.300, 95% CI: 1.971 - 9.383). Delivering mothers with preeclampsia had a 2 times higher risk of delivering an infant with APGAR score less than 7 in the first 5 minutes (OR 2,000, 95% CI: 1,116 -3,584).

DISCUSSION

Preeclampsia causes maternal and perinatal morbidity and mortality and still a main problem in obstetrics and public health. In the current study, it was found that preeclampsia was greatly associated with the adverse pregnancy outcomes, including premature birth (OR 5,500), SC delivery (OR 85,706), LBW (OR 4,300) and APGAR score <7 in the first 5 minutes (OR 2,000). Additionally, these findings are in accordance with the previous studies, in which poor pregnancy outcomes was higher in pregnant women with preeclampsia. Sutan et al. (2022) revealed that pregnant women with preeclampsia in Greater Kuala Lumpur Malaysia had a significantly greater chance of premature incidence (adjOR 6,214), instrumental and cesarean delivery (adjOR 4,320), LBW (adjOR 7,873), 5-minute APGAR score <7 (adjOR 3,158) and the admission to NICU by adj OR 8,778 (Sutan et al., 2022). A retrospective cohort study employing medical data in the United States revealed that pregnant women with preeclampsia had a risk of cesarean delivery (OR 1.61 and 1.99), premature birth (OR 2.22 and 5.37), respiratory distress syndrome (OR 2.39 and 4.19) and LBW (OR 3.64 and 9.61). Mothers and newborns to mothers with preeclampsia or superimposed preeclampsia experienced more adverse outcomes when it was compared to mothers without preeclampsia (Bromfield et al., 2023).

The results of another study also mentioned that, out of 204 neonates, about 16 (7.84%) newborns weighed <2.5 kg, while 26 (12.7%) and 27 (13.2%) newborns with the first and fifth minute Apgar scores <7 (Godana et al., 2023). Preeclampsia during pregnancy is related to placental dysfunction in early pregnancy. This will lead to placental hypoxia and placental ischemia, which may eventually lead to fetal growth disorders (Dimitriadis et al., 2023). The subsequent impact of placental insufficiency on fetal development is complex and caused by many factors. However, The main impacts may be located

882

in placental respiratory failure and fetal hypoxemia, in which both of them resulted in intrauterine growth retardation and its impacts which includes prematurity (Wardinger & Ambati, 2024).

PE during pregnancy is also associated with SC delivery. In accordance with previous studies, PE is associated with cesarean section and the likelihood of cesarean section in women with preeclampsia is significantly higher compared to normal pregnant women (OR: 8.11, p<0.001). SC is chosen by obstetricians for women with PE to save the lives of both mother and baby. Through SC the pregnancy can be terminated immediately (Das et al., 2023). Preeclampsia in pregnant women is in relation to adverse perinatal outcomes for mother and baby. Preeclampsia, superimposed preeclampsia, and chronic hypertension are associated with a risk of stillbirth, premature birth, LBW, NICU admission, and cesarean delivery. Preeclampsia in pregnant women is also a risk factor for postpartum preeclampsia. The severe health risks of preeclampsia for both mother and perinatal emphasize the need for prevention and management to prevent complications.

CONCLUSION

Preeclampsia is an important health problem that affects and leads to both maternal and perinatal morbidity and mortality. Pregnant women who experience preeclampsia have a high risk of delivering premature babies, delivering with SC, delivering babies with LBW and with APGAR score less than 7 in the first 5 minutes. These results may be useful to provide information to health workers regarding efforts to prevent the occurrence of preeclampsia, especially in mothers with high risk and immediate treatment for mothers who have experienced preeclampsia to avoid complications both in mothers, fetuses and newborns.

REFERENCES

- Aljameel, S. S., Alzahrani, M., Almusharraf, R., Altukhais, M., Alshaia, S., Sahlouli, H., Aslam, N., Khan, I. U., Alabbad, D. A., & Alsumayt, A. (2023). Prediction of Preeclampsia Using Machine Learning and Deep Learning Models: A Review. *Big Data and Cognitive Computing*, 7(1). https://doi.org/10.3390/bdcc7010032.
- Ansbacher-Feldman, Z., Syngelaki, A., Meiri, H., Cirkin, R., Nicolaides, K. H., & Louzoun, Y. (2022). Machine-learning-based prediction of pre-eclampsia using first-trimester maternal characteristics and biomarkers. *Ultrasound in Obstetrics and Gynecology*, 60(6), 739–745. https://doi.org/10.1002/uog.26105.
- Awor, S., Abola, B., Byanyima, R., Orach, C. G., Kiondo, P., Kaye, D. K., Ogwal-Okeng, J., & Nakimuli, A. (2023). Prediction of pre-eclampsia at St. Mary's hospital lacor, a low-resource setting in northern Uganda, a prospective cohort study. *BMC Pregnancy and Childbirth*, 23, 1–10. https://doi.org/https://doi.org/10.1186/s12884-023-05420-z.

Bromfield, S. G., Ma, Q., DeVries, A., Inglis, T., & Gordon, A. S. (2023). The association between

hypertensive disorders during pregnancy and maternal and neonatal outcomes: a retrospective claims analysis. *BMC Pregnancy and Childbirth*, 23(1), 1–10. https://doi.org/10.1186/s12884-023-05818-9.

- Chaemsaithong, P., Sahota, D. S., & Poon, L. C. (2022). First trimester preeclampsia screening and prediction. *American Journal of Obstetrics and Gynecology*, 226(2), S1071 S1097.e2. https://doi.org/10.1016/j.ajog.2020.07.020.
- Das, S., Maharjan, R., Bajracharya, R., Shrestha, R., Karki, S., Das, R., Odland, J. Ø., & Odland, M. L. (2023). Pregnancy outcomes in women with gestational hypertension and preeclampsia at Paropakar Maternity and Women's Hospital, Nepal: A retrospective study. *PLoS ONE*, *18*(6 June), 1–11. https://doi.org/10.1371/journal.pone.0286287.
- Deshpande, J. S., Sundrani, D. P., Sahay, A. S., Gupte, S. A., & Joshi, S. R. (2021). Unravelling the potential of angiogenic factors for the early prediction of preeclampsia. *Hypertension Research*, *1*. https://doi.org/10.1038/s41440-021-00647-9.
- Dimitriadis, E., Rolnik, D. L., Zhou, W., Estrada-Gutierrez, G., Koga, K., Francisco, R. P. V., Whitehead, C., Hyett, J., da Silva Costa, F., Nicolaides, K., & Menkhorst, E. (2023). Pre-eclampsia. *Nature Reviews Disease Primers*, 9(1). https://doi.org/10.1038/s41572-023-00417-6.
- Dinas Kesehatan Jawa Timur. (2021). Daftar Isi. *Profil Kesehatan Jatim* 2021, 3(1). https://doi.org/10.21831/dinamika.v3i1.19144.
- Dinas Kesehatan Jawa Timur. (2022). No. In *Profil Kesehatan Jatim* 2022 (Vol. 5, Issue 1). https://revistas.ufrj.br/index.php/rce/article/download/1659/1508%0Ahttp://hipatiapress.com/hpjour nals/index.php/qre/article/view/1348%5Cnhttp://www.tandfonline.com/doi/abs/10.1080/095007997 08666915%5Cnhttps://mckinseyonsociety.com/downloads/reports/Educa.
- Garrido-Giménez, C., Cruz-Lemini, M., Álvarez, F. V., Nan, M. N., Carretero, F., Fernández-Oliva, A., Mora, J., Sánchez-García, O., García-Osuna, Á., Alijotas-Reig, J., & Llurba, E. (2023). Predictive Model for Preeclampsia Combining sFIt-1, PIGF, NT-proBNP, and Uric Acid as Biomarkers. *Journal* of Clinical Medicine, 12(2), 431. https://doi.org/10.3390/jcm12020431.
- Giannakou, K. (2021). Prediction of pre-eclampsia. In *Obstetric Medicine* (Vol. 14, Issue 4, pp. 220–224). SAGE Publications Inc. https://doi.org/10.1177/1753495X20984015.
- Godana, A., Tesi, S., Nigussie, S., & Dechasa, M. (2023). Perinatal outcomes and their determinants among women with eclampsia and severe preeclampsia in selected tertiary hospitals, Eastern Ethiopia. *Pregnancy Hypertension*, 34(February), 152–158. https://doi.org/10.1016/j.preghy.2023.11.005.
- Gómez-Jemes, L., Oprescu, A. M., Chimenea-Toscano, Á., García-Díaz, L., & Romero-Ternero, M. del C. (2022). Machine Learning to Predict Pre-Eclampsia and Intrauterine Growth Restriction in Pregnant Women. *Electronics*, *11*(19), 3240. https://doi.org/https://doi.org/10.3390/electronics11193240.
- Hackelöer, M., Schmidt, L., & Verlohren, S. (2022). New advances in prediction and surveillance of preeclampsia: role of machine learning approaches and remote monitoring. *Archives of Gynecology and Obstetrics*. https://doi.org/10.1007/s00404-022-06864-y.

- He, B., Liu, Y., Maurya, M. R., Benny, P., Lassiter, C., Li, H., Subramaniam, S., & Garmire, L. X. (2021). The maternal blood lipidome is indicative of the pathogenesis of severe preeclampsia. *Journal of Lipid Research*, 62, 100118. https://doi.org/10.1016/j.jlr.2021.100118.
- Hedley, P. L., Hagen, C. M., Wilstrup, C., & Christiansen, M. (2023). The use of artificial intelligence and machine learning methods in early pregnancy pre-eclampsia screening: A systematic review protocol. *PLOS ONE*, *18*(4), e0272465. https://doi.org/10.1371/journal.pone.0272465.
- Henderson, J. T., Thompson, J. H., Burda, B. U., & Cantor, A. (2017). Preeclampsia screening evidence report and systematic review for the US preventive services task force. JAMA - Journal of the American Medical Association, 317(16), 1668 – 1683. https://doi.org/10.1001/jama.2016.18315.
- Jhee, J. H., Lee, S. E. S., Park, Y., Lee, S. E. S., Kim, Y. A., Kang, S.-W., Kwon, J.-Y., & Park, J. T. (2019). Prediction model development of late-onset preeclampsia using machine learning-based methods. *PLOS ONE*, *14*(8), e0221202. https://doi.org/10.1371/journal.pone.0221202.
- Juwita, A., Yani, E. R., & Yudianti, I. (2022). Skrining Preeklamsia dengan Metode Pengukuran Mean Arterial Pressure (MAP) Preeclampsia Screening with Mean Arterial Pressure (MAP). Research Article, 8(1), 82–90. file:///D:/JURNAL KEBIDANAN MIDWIFERIA/JURNAL MIDWIFERIA/TH 2022/APRIL/TYPESETT PDF/AYU JUWITA/Midwiferia Jurnal Kebidanan %7C https://midwiferia.umsida.ac.id/index.php/midwiferia.
- Kang, J., Hwang, S., Lee, T., Ahn, K., Seo, D. M., Choi, S. J., & Uh, Y. (2023). Prediction Model for Pre-Eclampsia Using Gestational-Age-Specific Serum Creatinine Distribution. *Biology*, *12*(6), 816. https://doi.org/https://doi.org/10.3390/biology12060816.

Karrar, S. A., & Hong, P. L. (2024). Preeclampsia.

- Kementerian Kesehatan RI. (2021). PMK No. 21 Tahun 2021. *Menteri Kesehatan Republik Indonesia Peraturan Menteri Kesehatan Republik Indonesia*, 879, 2004–2006.
- Kementrian Kesehatan RI. (2020). Health Information Systems. In *Profil Kesehatan Indonesia 2020* (Vol. 48, Issue 1). https://doi.org/10.1524/itit.2006.48.1.6.

Kementrian Kesehatan RI. (2021). Profil Kesehatan Indonesia 2021. In Pusdatin.Kemenkes.Go.Id.

Kementrian Kesehatan RI. (2022). Profil Kesehatan Kesehatan Indonesia 2022.

- Leavey, K., Bainbridge, S. A., & Cox, B. J. (2015). Large Scale Aggregate Microarray Analysis Reveals Three Distinct Molecular Subclasses of Human Preeclampsia. *PLoS One*, *10*(2). https://doi.org/https://doi.org/10.1371/journal.pone.0116508.
- Li, S., Li, H., Li, C., He, X., & Wang, Y. (2020). Development and Validation of a Nomogram for Predicting the Risk of Pregnancy-Induced Hypertension : 00(00), 1–10. https://doi.org/10.1089/jwh.2020.8575.
- Li, Y.-X., Shen, X.-P., Yang, C., Cao, Z.-Z., Du, R., Yu, M.-D., Wang, J.-P., & Wang, M. (2021). Novel electronic health records applied for prediction of pre-eclampsia: Machine-learning algorithms. *Pregnancy Hypertension*, *26*, 102–109. https://doi.org/10.1016/j.preghy.2021.10.006.

- Li, Y., Shen, X. X.-P., Yang, C., Cao, Z. Z.-Z. Z. Z.-Z., Du, R., Yu, M.-D. M. M.-D., Wang, J. J.-P. J., & Wang, M. (2021). Novelelectronic health records applied for prediction of pre-eclampsia: Machinelearning algorithms. *Pregnancy Hypertension*, 26, 102–109. https://doi.org/https://doi.org/10.1016/j.preghy.2021.10.006.
- Liu, M., Yang, X., Chen, G., Ding, Y., Shi, M., Sun, L., Huang, Z., Liu, J., Liu, T., Yan, R., & Li, R. (2022). Development of a prediction model on preeclampsia using machine learning-based method: a retrospective cohort study in China. *Frontiers in Physiology*, 13. https://doi.org/10.3389/fphys.2022.896969.
- Marić, I., Contrepois, K., Moufarrej, M. N., Stelzer, I. A., Feyaerts, D., Han, X., Tang, A., Stanley, N., Wong, R. J., Traber, G. M., Ellenberger, M., Chang, A. L., Fallahzadeh, R., Nassar, H., Becker, M., Xenochristou, M., Espinosa, C., De Francesco, D., Ghaemi, M. S., ... Aghaeepour, N. (2022). Early prediction and longitudinal modeling of preeclampsia from multiomics. *Patterns*, *3*(12). https://doi.org/10.1016/j.patter.2022.100655.
- Melinte-Popescu, A.-S., Vasilache, I.-A., Socolov, D., & Melinte-Popescu, M. (2023). Predictive Performance of Machine Learning-Based Methods for the Prediction of Preeclampsia—A Prospective Study. *Journal of Clinical Medicine*, *12*(2), 418. https://doi.org/10.3390/jcm12020418.
- Nair, T. M. (2018a). Statistical and artificial neural network-based analysis to understand complexity and heterogeneity in preeclampsia. *Computational Biology and Chemistry*, 75, 222–230. https://doi.org/https://doi.org/10.1016/j.compbiolchem.2018.05.011.
- Nair, T. M. (2018b). Statistical and artificial neural network-based analysis to understand complexity and heterogeneity in preeclampsia. *Computational Biology and Chemistry*, 75, 222–230. https://doi.org/10.1016/j.compbiolchem.2018.05.011.
- Pham, H. Van, Long, C. K., Phan, H. K., & Ha, Q. T. (2023). A Fuzzy Knowledge Graph Pairs-Based Application for Classification in Decision Making: Case Study of Preeclampsia Signs. *Information*, *14*(2), 104. https://doi.org/https://doi.org/10.3390/info14020104.
- Poon, L. C., Shennan, A., Hyett, J. A., Kapur, A., Hadar, E., Divakar, H., McAuliffe, F., da Silva Costa, F., von Dadelszen, P., McIntyre, H. D., Kihara, A. B., Di Renzo, G. C., Romero, R., D'Alton, M., Berghella, V., Nicolaides, K. H., & Hod, M. (2019a). The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *International Journal of Gynecology and Obstetrics*, 145(S1), 1 33. https://doi.org/10.1002/ijgo.12802.
- Poon, L. C., Shennan, A., Hyett, J. A., Kapur, A., Hadar, E., Divakar, H., McAuliffe, F., da Silva Costa, F., von Dadelszen, P., McIntyre, H. D., Kihara, A. B., Di Renzo, G. C., Romero, R., D'Alton, M., Berghella, V., Nicolaides, K. H., & Hod, M. (2019b). The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *International Journal of Gynecology and Obstetrics*, 145(S1), 1–33. https://doi.org/10.1002/ijgo.12802.
- Ranjbar, A., Taeidi, E., Mehrnoush, V., Roozbeh, N., & Darsareh, F. (2023). Machine learning models for predicting pre-eclampsia: A systematic review protocol. *BMJ Open*, *13*(9). https://doi.org/10.1136/bmjopen-2023-074705.

- Ratnik, K., Rull, K., Aasmets, O., Kikas, T., Hanson, E., Kisand, K., Fischer, K., & Laan, M. (2022). Novel Early Pregnancy Multimarker Screening Test for Preeclampsia Risk Prediction. *Frontiers in Cardiovascular Medicine*, 9. https://doi.org/10.3389/fcvm.2022.932480.
- Sufriyana, H., Wu, Y.-W., & Su, E. C.-Y. (2020). Prediction of Preeclampsia and Intrauterine Growth Restriction: Development of Machine Learning Models on a Prospective Cohort. *JMIR Medical Informatics*, 8(5), e15411. https://doi.org/10.2196/15411.
- Sutan, R., Aminuddin, N. A., & Mahdy, Z. A. (2022). Prevalence, maternal characteristics, and birth outcomes of preeclampsia: A cross-sectional study in a single tertiary healthcare center in greater Kuala Lumpur Malaysia. *Frontiers in Public Health*, 10. https://doi.org/10.3389/fpubh.2022.973271
- Thomas, G., Syngelaki, A., Hamed, K., Perez-Montaño, A., Panigassi, A., Tuytten, R., & Nicolaides, K. H. (2023). Preterm preeclampsia screening using biomarkers: combining phenotypic classifiers into robust prediction models. *American Journal of Obstetrics & Gynecology MFM*, 5(10), 101110. https://doi.org/https://doi.org/10.1016/j.ajogmf.2023.101110.
- Varghese, B., Jala, A., Meka, S., Adla, D., Jangili, S., Talukdar, R. K., Mutheneni, S. R., Borkar, R. M., & Adela, R. (2023). Integrated metabolomics and machine learning approach to predict hypertensive disorders of pregnancy. *American Journal of Obstetrics & Gynecology MFM*, 5(2), 100829. https://doi.org/https://doi.org/10.1016/j.ajogmf.2022.100829.

Wardinger, J. E., & Ambati, S. (2024). Placental Insufficiency.

- Xue, Y., Yang, N., Gu, X., Wang, Y., Zhang, H., & Jia, K. (2023). Risk Prediction Model of Early-Onset Preeclampsia Based on Risk Factors and Routine Laboratory Indicators. *Life*, *13*(8), 1648. https://doi.org/10.3390/life13081648.
- Yun, S. J., Kim, W. J., Choi, S. K., Kim, S. M., Shin, J. E., Kil, K. C., Kim, Y. H., Wie, J. H., Kim, H. W., Hong, S., & Ko, H. S. (2023a). Prediction of Pregnancy-Associated Hypertension Using a Scoring System: A Multicenter Cohort Study. *Life*, *13*(6), 1330. https://doi.org/https://doi.org/10.3390/life13061330.
- Yun, S. J., Kim, W. J., Choi, S. K., Kim, S. M., Shin, J. E., Kil, K. C., Kim, Y. H., Wie, J. H., Kim, H. W., Hong, S., & Ko, H. S. (2023b). Prediction of Pregnancy-Associated Hypertension Using a Scoring System: A Multicenter Cohort Study. *Life*, 13(6), 1330. https://doi.org/https://doi.org/10.3390/life13061330.
- Zheng, D., Hao, X., Khan, M., Wang, L., Li, F., Xiang, N., Kang, F., Hamalainen, T., Cong, F., Song, K., Qiao, C., Song, K., & Qiao, C. (2022). Comparison of machine learning and logistic regression as predictive models for adverse maternal and neonatal outcomes of preeclampsia: A retrospective study. *Frontiers in Cardiovascular Medicine*, 9. https://doi.org/10.3389/fcvm.2022.959649