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Original Research Article

Retrospective analysis to predict preeclampsia by machine learning algorithms and its relation to neonatal outcome

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Abstract

Background: Preeclampsia is one of the most dangerous complications in pregnancy. It is characterised by hypertension, lower limb oedema, proteinuria, and thrombocytopenia. Preeclampsia can cause various complications that impact many body systems.
Aim and Objectives: The main aim of this study is to predict preeclampsia in mothers and find a possible relationship with neonatal outcomes.
Materials and Methods: This hospital-based retrospective case-control study involves 1231 pregnant women. They were randomly allocated into the testing (N=246) and training (N=985) groups, which were set at a ratio of 1:4. All medical records were analysed. Various machine learning models such as logistic regression (LR), K nearest neighbours (KNM), support vector machine (SVM), discriminant analysis (DA), extreme gradient boosting (EGB), and random forest (RF) algorithm were used to predict preeclampsia. The performance of these models was evaluated using standards such as accuracy, precision, recall, correct classification, misclassification, and F score using XLSTAT 2024.
Results: Out of the 1231 women, 368 were diagnosed with Preeclampsia. Factors such as kidney disease, blood pressure (BP) ≥ 120/80 mmHg in early pregnancy, chronic hypertension, family history of hypertension, and diabetes were found to be significant contributors to preeclampsia. The random forest model showed the highest performance.
Conclusions: Renal disease, chronic hypertension, family history of hypertension and diabetes and BP ≥120/80 mmHg early in pregnancy were the most important factors for predicting preeclampsia. The random forest model is the best feasible approach for screening and predicting preeclampsia because it helps obstetricians identify high-risk pregnancies and thus prevent adverse outcomes. Preeclampsia in mothers strongly affects neonatal outcomes, and this can result in a higher percentage of low birth weight, prematurity and intrauterine growth retardation.

Keywords: Pre-eclampsia; Prediction; Machine learning; Neonatal outcome.

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1. Introduction

Preeclampsia is one of the most dangerous complications in pregnancy. It is characterised by hypertension, lower limb oedema, proteinuria, and thrombocytopenia. Preeclampsia can cause various complications that impact many body systems. Preeclampsia has multiple risk factors, which include nullipara women, family history of hypertension, pregnancy-induced hypertension, advanced age, obesity, and diabetes mellitus, including gestational diabetes mellitus.[1] Preeclampsia typically develops in the third trimester of pregnancy.[2] 5 to 20% of preeclampsia cases can cause severe problems in mother and baby.[3] It has been studied that there is a strong association between preeclampsia and intrauterine growth restriction (IUGR). Preeclampsia women are at a high risk of developing intrauterine growth retardation.[4,5] Globally approx. 25% of babies born to mothers with preeclampsia experience growth restriction, while around a third are born prematurely.[6-8] Additionally, preeclampsia is linked to one in four infant deaths, particularly early newborn deaths. This condition is associated with poor infant outcomes such as low birth weight, prematurity, and severe birth asphyxia.[9,10] Predicting preeclampsia by calculating various risk factors early in pregnancy is very crucial as it will prevent further

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dangerous progression. Several studies have identified the factors that predict preeclampsia, such as clinical features, laboratory markers, and ultrasound markers. However, there is currently no consensus on the best method for predicting the possibility of preeclampsia. Although machine learning-based algorithms have been widely used in clinical research, there are few reports on their performance in predicting the risk factors of preeclampsia. This study aims to investigate the predictors of preeclampsia and develop risk factor prediction algorithms by comparing their performance. These findings will help clinicians identify high-risk cases to improve maternal and neonatal outcomes.

2. Material and Methods

This retrospective case-control study was conducted at the Obstetrics and Gynaecology Department of Chandulal Chandrakar Memorial Medical College from October 2017 to March 2020. The study included pregnant women who received antenatal care and delivered at the hospital. The inclusion criterion was pregnant women who gave birth at the hospital, while the exclusion criteria were pregnancies terminated before 28 weeks. The institutional ethics committee approved the study. The hospital's medical records were acquired to get all maternal information. This information included maternal age, pre-pregnancy body mass index (BMI primigravida or multipara, multiple pregnancies, history of preeclampsia, hypertension in early pregnancy, family history of hypertension and diabetes mellitus, in vitro fertilisation, essential hypertension, diabetes mellitus, gestational diabetes mellitus and kidney disease. The women were divided into training and testing groups using the data sampling technique in XLSTAT 2024. The ratio of 4:1. These sets were further divided into cases and controls, with the case group comprising pregnant women diagnosed with preeclampsia and the control group comprising pregnant women without preeclampsia. Continuous variables were presented as means ± standard deviations, and statistical tests were performed to compare categorical variables. A Welch t-test was done for quantitative variables, and a chi-square test was done for qualitative variables. The statistical significance level was set at $P<0.05$. Logistic regression analyses were done to identify independently associated risk factors and a logistic regression model for predicting preeclampsia was created using these risk factors. Machine learning techniques were employed to predict disease risk using XLSTAT 2024. The data was randomly split into two samples 80% of the observations were used to train the model and 20% for validation. Various methods were used for analysis, including logistic regression, random forests, K nearest neighbours, support vector machine, discriminant analysis, and extreme gradient boosting. Performance metrics such as accuracy, precision, recall, correct classification, misclassification, and F score were assessed. The primary outcome was identifying the risk factors for preeclampsia during the perinatal period, while the secondary outcome was the neonatal outcome.

3. Observations and Results

Table 1 summarises the characteristics of all participants. Out of the 1231 women, 358 were diagnosed with Preeclampsia. There were no differences between the training and testing sets (all $P>0.05$).

Table 1: Showing clinical characteristics of study participants in training and testing group

Clinical Characteristics	Training group (n = 985)	Testing group (n = 246)	n	p-value
AGE, mean (sd)	30.8 (5.61)	30.9 (5.74)	1231	0.79
BMI, mean (sd)	24.4 (3.85)	24.9 (3.71)	1231	0.087
Abnormal Pregnancy	193 (20%)	44 (18%)	237	0.54
In Vitro Fertilisation	88 (8.9%)	18 (7.3%)	106	0.42
BP≥120/80	267 (27%)	77 (31%)	344	0.19
Essential Hypertension	79 (8%)	23 (9.3%)	102	0.5
DM/GDM	63 (6.4%)	15 (6.1%)	78	0.86
Family History of DM,	260 (26%)	61 (25%)	321	0.61
Family History of HTN	257 (26%)	68 (28%)	325	0.62
Multiple Pregnancy	88 (8.9%)	18 (7.3%)	106	0.42
Preeclampsia	289 (29%)	69 (28%)	358	0.69
Primigravida	484 (49%)	132 (54%)	616	0.2
Multipara	501 (51%)	114 (46%)	615	
Renal disease	10 (1%)	4 (1.6%)	14	0.5

Table 2: Clinical characteristics of the groups according to cases and controls

Clinical Characteristics	Training Group (N=985)			Testing Group (N=246)		
	Cases (n = 289)	Controls (n = 696)	p-value	Cases (n = 69)	Controls (n = 177)	p-value
AGE, mean (SD)	30.4 (5.81)	31.0 (5.52)	0.18	29.4 (5.71)	31.5 (5.67)	0.014
BMI, mean (SD)	24.6 (3.88)	24.4 (3.84)	0.49	25.2 (3.88)	24.7 (3.65)	0.37
Abnormal Pregnancy	63 (22%)	130 (19%)	0.26	12 (17%)	32 (18%)	0.9
In Vitro Fertilisation	24 (8.3%)	64 (9.2%)	0.66	8 (12%)	10 (5.6%)	0.11
BP≥120/80	163 (56%)	104 (15%)	<0.001	47 (68%)	30 (17%)	<0.001
Essential Hypertension	66 (23%)	13(1.9%)	<0.001	20 (29%)	3 (1.7%)	<0.001
DM/GDM	16 (5.5%)	47 (6.8%)	0.48	8 (12%)	7 (4%)	0.036
Family History of DM	91 (31%)	169 (24%)	0.019	22 (32%)	39 (22%)	0.11
Family History of HTN	133 (46%)	124 (18%)	<0.001	34 (49%)	34 (19%)	<0.001
Multiple Pregnancy	26 (9%)	62 (8.9%)	0.96	9(13%)	9 (5.1%)	0.031
Primigravida	149 (52%)	335 (48%)		36 (52%)	96 (54%)	
Multipara	140(48%)	361(52%)	0.33	33 (48%)	81 (46%)	0.77
Renal disease	6(2.1%)	4 (0.57%)	0.072	3(4.3%)	1 (0.56%)	0.068

Table 3: Risk factors for preeclampsia with multivariate logistic regression analysis

Clinical Characteristics	p-value	Odds ratio (95% CI)
Age, mean (SD)	0.019	0.973(0.941-1.005)
BMI, mean (SD)	0.798	0.986(0.940-1.035
Abnormal Pregnancy	0.764	0.968 (0.589-1.592)
In Vitro Fertilisation	0.173	1.013(0.509-2.015)
BP≥120/80	<0.0001	13.862(8.970-21.420)
Essential Hypertension	<0.0001	14.104(6.761-29.420)
Diabetes Mellitus	0.271	0.583(0.224-1.520)
Family History		
Diabetes Mellitus	<0.0001	0.373(0.232-0.598)
Hypertension	<0.0001	3.492(2.362-5.162)
Multiple Pregnancy	0.008	0.393(0.190-0.814)
Primigravida	0.665	0.830(0.580-1.189)
Renal disease	0.031	11.202(2.803-44.770)

In the training group, compared with the controls, the cases had a higher occurrence of essential hypertension (23% vs. 1.9%, P<0.001), BP ≥120/80 mmHg (56% vs. 15%, P<0.001), family history of diabetes mellitus (31% vs. 24%, P=0.019), and family history of hypertension (46% vs. 18%, P<0.001). There were differences in the mean age group in the testing group (p=0.014). Compared with the control group, the cases had a higher occurrence of essential hypertension (29% vs. 1.7%, P<0.001), BP ≥120/80 mmHg (68% vs.17%, P<0.001), family history of hypertension (60% vs. 13%, P<0.001), diabetes mellitus (12% vs 4%, p=0.036) and multiple pregnancy (13% vs 5.1% p=0.031) (**Table 2**).

Table 3 shows various risk factors and their relation to preeclampsia calculated by the multivariate logistic regression analysis. Age, BP ≥120/80 mmHg in early pregnancy, essential hypertension, multiple pregnancy, renal disease, family history of hypertension and diabetes significantly contributed to preeclampsia.

Table 4: Performance metrics of various machine learning algorithms

Performance metrics	Logistic regression	Random forests	Extreme Gradient Boosting	K Nearest Neighbors	SVM	Discriminant Analysis
Accuracy	0.744	0.825	0.805	0.626	0.728	0.553
Precision	0.759	0.829	0.811	0.678	0.739	0.659
Recall	0.910	0.934	0.928	0.849	0.922	0.699
Correct classification	183.000	203.000	198.000	154.000	179.000	136.000
Misclassification	63.000	43.000	48.000	92.000	67.000	110.000
F-score	0.827	0.878	0.865	0.754	0.820	0.678

Table 5: Neonatal outcomes of cases and controls

Neonatal Outcomes	Training Group (N=985)	Testing Group (N=246)	p-value	Training Group (N=985)			Testing Group (N=246)		
				Cases (n=289)	Controls (n=696)	p-value	Cases (n=69)	Controls (n=177)	p-value
Prematurity	98(9.9%)	29(11.7%)	0.46	65(22.5%)	33(4.7%)	<0.001	17(24.6%)	12(6.7%)	<0.001
Low birth weight	232(23.5%)	62(25.2%)	0.64	133(46%)	99(14.2%)	<0.001	33(47.8%)	29(16.4%)	<0.001
IUGR	77(7.8%)	21(8.5%)	0.80	44(15.2%)	33(4.7%)	<0.001	11(15.9%)	10(5.6%)	<0.001
NICU admission	159(16.1%)	44(17.8%)	0.57	90(31.1%)	69(9.9%)	<0.001	23(33.3%)	21(11.8%)	<0.001
Perinatal Asphyxia	53(5.4%)	11(4.4%)	0.67	26(8.9%)	27(3.8%)	<0.001	7(10.1%)	4(2.2%)	<0.001
Neonatal Mortality	45(4.5%)	14(5.7%)	0.56	35(12.1%)	10(1.4)	<0.001	10(14.4%)	4(2.2%)	<0.001

A summary table containing several indices computed on the validation sample corresponding to these methods. When the prediction performance matrices of each model were compared, the RF model was shown to perform the best. According to the statistical Misclassification computed on the validation sample, the best model is coloured green in the table above. The Accuracy, precision, recall correct classification, misclassification, and f scores were 0.825, 0.829, 0.934, 203, 43 and 0.878 respectively. (**Table 4**).

Table 5 shows the neonatal outcomes in training and testing groups. There were no differences between the two groups. In the training group, prematurity (22.5% vs 4.7%), low birth weight (46% vs14.2%), NICU admission (31.1% vs 9.9%), IUGR(15.2% vs 5.7%), perinatal asphyxia (8.9% vs 3.8%) and neonatal mortality(12.1% vs 1.4%) were higher in cases as compared with controls.($p<0.001$). In the testing group, prematurity (24.6% vs 6.7%), low birth weight (47.8% vs16.4%), NICU admission (33.3% vs 11.8%), IUGR(15.9% vs 5.6%), perinatal asphyxia (10.1% vs 2.2%) and neonatal mortality (14.4% vs 2.2%) were higher in cases as compared with controls.($p<0.001$)

4. Discussion

Predicting preeclampsia remains a challenge for obstetricians, with significant maternal and neonatal mortality rates. Based only on maternal risk factors, conventional screening methods have low prediction accuracy and are currently used in low-income countries. Recent advances in screening methods lead to increased prediction but come with limitations such as limited parameters and high human and financial resources required.

Previous studies have identified several factors associated with an increased incidence of PE, including maternal age ≥35 years, family history of hypertension or DM, chronic hypertension, GDM, and pre-pregnancy BMI ≥30 kg/m^2.[11-14] Our study found that renal disease, chronic hypertension, family history of hypertension and diabetes and BP ≥120/80 mmHg early in pregnancy were the most important factors for predicting preeclampsia.

Chronic hypertension is a lifetime disease that affects the function of various organs in the body, and this is dangerous for life. A similar finding by Bori Boonhirunsarn et al. showed 43.3% of preeclampsia in pregnant women with essential hypertension.[15] Nie et al. performed logistic regression and found that a history of preeclampsia and a lack of systemic antihypertensive treatment (OR = 8.983, 95% CI: 7.735 -9.933, $P < 0.001$) were risk factors for the occurrence of chronic hypertension complicated by preeclampsia.[16]

Conti-Ramsden et al. found that 15% of women admitted to the hospital had pregnancy-related AKI-related kidney disease.[17] A new finding in this study was a higher number of

women with Kidney disease had a history of hypertensive disorder in a previous pregnancy. Preeclampsia is four times more common in women with a prior episode of AKI by Tangren et al. Thus, underlying renal disease is also involved in recurrent preeclampsia and AKI.[18]

Jhee et al. recorded higher systolic and diastolic blood pressure early in the pregnancy in preeclampsia as compared to average patients.[19] In our study, blood pressure ≥120/80 mmHg early in pregnancy was a significant predictor of preeclampsia, similar to the above findings. Another study finds that women with systolic BP ranging from 120 to139 mmHg and Diastolic BP ranging from 80 to 89 mmHg in early pregnancy are at increased risk for preeclampsia.[20] Various studies found that the prophylactic low-dose aspirin reduces the risk for preeclampsia.[21,22] Another study found an increased risk of preeclampsia in nulliparous women with increased blood pressure and hypertension stage 1 in the first trimester.[23]

Various studies in Brazil and Sweden found that hypertension in a mother and sister were risk factors for a woman to develop severe preeclampsia.[24,25] In our study, a family history of diabetes and hypertension was associated with an increased risk of preeclampsia. Similarly, another study found that a family history of hypertension and diabetes was associated with maternal and paternal diabetes and hypertension.[26]

The main aim of this study is to detect preeclampsia in mothers as early as pregnancy. Our critical finding is that while applying machine learning, the Random Forest Algorithm prove to be the most feasible way to screen for risk factors of preeclampsia early in the pregnancy. Many more studies are needed to validate its clinical applicability. The pathogenesis of preeclampsia is complex, and the exact aetiology is still not clear.[27,28] Several studies have been done to find the predictive risk factors to detect preeclampsia early, such as clinical features and biochemical and USG markers. Early identification of risk factors is crucial to start preventive therapy against preeclampsia. Since some risk factors appear only in late pregnancy, we must identify the early indicators. Accurate and complete maternal information early in the second trimester is essential for prediction of preeclampsia. However, it is impossible to find out all the risk factors during antenatal examination and biochemical tests are routinely not done for screening in low-income countries. So, an hour is needed to develop a precise, conceptual, knowledge-based operational tool for obstetricians to detect preeclampsia as early as possible in the second trimester. The Random Forest algorithm provided the best performance with the highest accuracy. Therefore, the Random Forest algorithm must be applied as a primary screening tool for predicting preeclampsia in future studies.

Chen et al. found that the RF model is the most feasible screening approach for predicting PE in the early second trimester of pregnancy.[29] Pregnant women's family history of hypertension, increased BMI, BP ≥130/80 mmHg in the second trimester, chronic hypertension, and duration of hypertension can be used as predictors for preeclampsia. In another study by Liu et al., prediction models for preeclampsia were designed.[31] The random forest (RF) model was the most accurate, with an accuracy of 0.74 and a recall rate of 0.42. The AUC of the RF model was 0.86, the precision was 0.82, and the F score was 0.17. Similarly, Martínez-Velasco et al.[30] uses various machine-learning algorithms to predict the occurrence of preeclampsia. Finally, random forest (RF) has the highest accuracy, specificity, and sensitivity, with values of 0.8530, 0.8614, and 0.6846, respectively. Other studies found extra gradient boosting the most accurate model.[31-33] One study found the SVM algorithm paired with the highest accuracy at 93%.[34]

When analysing neonatal outcomes, we observed that neonates born to preeclampsia mothers had a significantly higher percentage of prematurity, intrauterine growth retardation and low birth weight. Additionally, early neonatal deaths occurred in about 13.5% of these neonates, all of whom were born to women with preeclampsia. Among these early neonatal deaths, one was due to severe birth asphyxia. Pregnancy-induced hypertension, like chronic hypertension, has been linked to impaired fetal growth, resulting in low birth weight and its associated complications.[36] Low birth weight is a common consequence of preeclampsia due to fetal under-nutrition caused by inadequate blood flow from the mother to the placenta, leading to growth retardation and various fetal health issues such as prematurity and mortality.[35,37] As a result, low birth weight, prematurity and perinatal asphyxia cases are seen increased in women with preeclampsia. Newborn babies of mothers with preeclampsia usually have poor outcomes like prematurity, intrauterine growth retardation, low birth weight, birth asphyxia and the need for admission to the neonatal intensive care unit (NICU). Also, the number of NICU admissions was significantly higher for neonates born to mothers with preeclampsia compared to those born following a normal pregnancy.

Every study has some limitations, and we have also. Our study had fewer cases than the control group, so we needed more cases to predict preeclampsia accurately. We only included maternal history in the characteristics. We did not include laboratory and radiological markers in our study. It is essential to establish a comprehensive scoring system and conduct prospective studies to validate the accuracy of the prediction models based on the weightage of each risk factor for preeclampsia.

5. Conclusions

The RF model may be a practical screening approach for predicting preeclampsia (PE) in the early second trimester of pregnancy. Indicators such as pregnant women's family history of hypertension, blood pressure (BP) of ≥120/80 mmHg in early pregnancy, and chronic hypertension can be

used to assess the risk of PE. However, large-scale studies are needed to validate its clinical applicability. Maternal preeclampsia has a significant effect on infant outcomes, remarkably increasing the incidence of low birth weight and prematurity. Therefore, the association of preeclampsia with adverse outcomes and increased perinatal morbidity and mortality requires a more collaborative approach to care rather than the current practice of single-speciality obstetric care.

6. Source of Funding

None.

7. Conflict of Interest

None.

8. Ethical Approval

Ethical No.: CCMCD/273/OL/2021.

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