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Machine learning approach for the prediction of preeclampsia in a middle-income country

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Objective

To develop a first-trimester prediction model for preterm preeclampsia using maternal characteristics and locally developed multiple of medians for mean arterial pressure (MAP), uterine artery pulsatility index (UtA-PI), and serum placental growth factor (PlGF) using a machine-learning approach for variable selection.

Methods

Study design and participants: This prospective cohort of a non-selected population from Mexico City was developed exclusively for research in the first-level clinic Health Center Romero Rubio and at the Instituto Nacional de Perinatologia in Mexico City. Inclusion criteria were age >18 and singleton pregnancy at the 11-13.6-week scan. All patients categorized as high-risk of preeclampsia during screening were prescribed aspirin 150 mg daily. Only those patients who did not follow the prescription or with less than 50% adherence were included in the cohort. Outcomes: The primary outcome was the onset of preterm preeclampsia (pPE), defined as PE requiring delivery before 37 weeks of gestation. The secondary outcomes were the detection rate (DR) of early-onset preeclampsia (PE requiring delivery before 34 weeks of pregnancy (ePE)) and the DR of any type of preeclampsia (all-PE). Statistical analysis: Continuous variables were expressed as the median and interquartile range (IQR) and were compared between groups by the U-Mann Whitney test; categorical data were expressed as numbers and percentages and analyzed using the Chi-square or Fisher's exact test. For the machine learning approach, the dataset was split into a training set prepared from the data of 1068 pregnant women, a validation set of 914 pregnant women, and a test set of 1068 pregnant women, all of whom were independent population samples. An elastic net method was employed to identify the significant predictors of pPE. The calibration of the ML algorithm was assessed by the Hosmer-Lemeshow goodness-of-fit test. The performance of the models created was assessed at 10% false positive rates (FPR) and compared using the area under the curve (AUC). The models were centered at <37 weeks for the prediction of pPE, at <34 weeks for the prediction of ePE, and the prediction of any type of preeclampsia (all-PE).

Results

Description of the cohort and characteristics of the study population: The original cohort included 3,297 pregnant women, of whom 247 (7.49%) met exclusion criteria. Thus, 3050 pregnant women were contemplated in the final analysis. Among participants included for analysis, 124 (4.07%) developed PE, 83 (2.72%) were delivered before 37 weeks of gestation, and 21 (0.69%) developed early-onset preeclampsia. The pPE group showed higher maternal age, BMI, MAP, UtA-PI, and rates of pre-existing diabetes, chronic hypertension, antiphospholipid syndrome, family and personal history of PE, and lower serum PlGF concentrations when compared with the control group. Development of Machine Learning Model for Preeclampsia Prediction: The distribution of each biomarker was obtained, and the results were normalized to MoM values. The prediction model was developed using elastic nets. The training set was the input of an artificial neural network to predict pPE vs. no preeclampsia. During cross-validation, 36 elastic net models were built based on the training data in each run. Each model contained a subset of input features selected and regularized for subsequent cross-validation. A 10-fold cross-validation optimization model was performed and applied to the training set during the modeling process. The results of this analysis showed that PlGF, MAP, UtA-PI, BMI, antiphospholipid syndrome, PE in a previous pregnancy, pre-existing diabetes, smoking, spontaneous pregnancy, other drugs (cocaine or heroin), lupus, chronic hypertension, and maternal age were the most important input variables to predicting pPE. After fifty iterations comparing the performance of each model, the optimal stable training model exhibited an AUC of 0.868, 0.957, and 0.787 with a detection rate (DR) of 68.9%, 83.1%, and 50.6% at a 10% FPR for pPE, ePE, and all-PE respectively. The validation set was used for tuning hyperparameters to maximize the AUC; the validation model showed an AUC of 0.883, 0.958, and 0.776 for pPE, ePE, and all-PE, respectively, with a DR of 73.3%, 84.6%, and 48.1% at a 10% FPR. The Hosmer-Lemeshow test was non-significant (p=0.114), indicating that the machine-learning model predicted the probability of pPE, and the observed probability of pPE fit well.). The machine learning model was then applied to the test set and exhibited an AUC of 0.897, 0.963, and 0.778 for pPE, ePE, and all-PE, respectively, with a DR of 76.5%, 88.2%, and 50.1% at 10% FPR. The test set was utilized to test the impact of different factors on prediction accuracy. The highest contribution was provided by maternal characteristics, MAP, UtA-PI, and PlGF, with an AUC of 0.897 (95%CI, 0.839-0.937). Maternal characteristics alone exhibited an AUC of 0.769 (95%CI, 0.699-0.838) with a DR of 45.7%, similar to maternal characteristics plus MAP (DR of 45.8% at 10% FPR). The DR at 10% FPR of the combination of maternal characteristics, MAP, and UtA-PI was 56.5%; of maternal characteristics, MAP, and PlGF was 65.2%, and for the combination of maternal characteristics, MAP, UtA-PI, and PlGF, the DR was 76.5%. The AUC of the machine learning model for maternal characteristics and biomarkers for the prediction of ePE and all-PE was 0.963 (95%CI, 0.925-0.992) and 0.778 (95%CI, 0.722-0.834), respectively with a DR of 88.2% and 50.1% at 10% FPR.

Conclusion

Our study demonstrates a high performance of a machine learning model for predicting pPE and ePE employing locally developed MoMs for MAP, UtA-PI, and PlGF, and different maternal characteristics than previously developed models. Our results represent a step forward in designing and implementing algorithms to predict preeclampsia accurately in middle-income countries.