20th World Congress in Fetal Medicine

Performance of a machine learning approach to predict preterm preeclampsia

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Objective

This study aimed to develop a simplified preterm preeclampsia prediction model using machine learning, with clinical and laboratory data from Mexican pregnant women at the first-trimester screening ($11\text{-}13^{+6}$ weeks gestation).

Methods

This prospective cohort of a non-selected population from Mexico City was developed exclusively for research purposes in a first-level clinic Health Center Romero Rubio, and at the Instituto Nacional de Perinatologia in Mexico City. The primary outcome was the detection rate (DR) of pPE by the machine learning model in Mexican population. Secondary outcomes were the DR of the logistic regression model for predicting preterm pre-eclampsia (pPE) and the compared performance between both models. 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. 75/25 training and validation data sets were created for the machine learning approach. An elastic net method was employed to identify the significant predictors of pPE. The elastic net is a calibrated method that linearly combines ridge and lasso regression and typically outperforms classic regression methods because it lets to accomplish both shrinkage and automatic selection of predictors. Since the automatic selection of predictors is achieved by penalty, no previous subset selection must be performed, thereby reducing the variance and instability of the prediction model; this is an advantage over previous methods. The automatic selection of predictors through elastic net results in a simpler and sparse model that includes only a subset of variables, this improves the interpretation of the model. Ten-fold cross-validation was used to determine the shrinkage parameter of the elastic net. The traditional model was created by nested logistic regression adding anthropometric variables, serum, and ultrasound biomarkers to a previous model integrated by maternal medical history variables using a stepwise method for variable selection. The performance of the models created was assessed at 5%, 10%, and 15% false positive rates (FPR) and compared using the area under the curve (AUC). The calibration of ML algorithm was assessed by Hosmer-Lemeshow goodness-of-fit test. Both models were centered at 37 weeks for the prediction of pPE [StataCorp. 2020]. A p-value <0.05 was considered significant.

Results

A total of 3067 pregnant women were enrolled in the original cohort, and 247 women (8.05%) were excluded due to incomplete data. Among the included women, 115 (4.07%) developed PE, and 72 of them (2.6%) were delivered before 37 weeks of gestation. The distribution of each biomarker was obtained, and the results were normalized to MoM values. The prediction model was developed using elastic nets. 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 that were selected and regularized for subsequent cross-validation. During the modeling process, a 10-fold cross-validation optimization model was performed and applied to the training set. 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, lupus, chronic hypertension, and maternal age were the most important input variables to predict pPE, and unlike the FMF model, PAPP-A was not a selected variable by the elastic net. After fifty iterations comparing each model performance, the optimal stable training model exhibited an AUC of 0.870. Similarly, the validation model showed an AUC of 0.905 with a detection rate (DR) of 0.768 at FPR of 15%. 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. For comparison, we fitted a traditional prediction model via nested logistic regression using the same covariates. This logistic model exhibited an AUC of 0.902, DR of 0.762, and FPR of 15%. We expect similarity in the performance of both methods because the majority of variables with the most influence in the prediction (antiphospholipid syndrome, history of preeclampsia, preexisting diabetes, spontaneous pregnancy, lupus, chronic hypertension, and maternal age) are categorical.

Conclusion

Our study demonstrates that machine learning is a simplified method for predicting pPE and identified PlGF as the most important marker in Mexican women. Once validated, testing it in an external cohort, this machine learning model could be implemented in primary care.