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Machine Learning Algorithms for HELLP Syndrome Prediction: An Approach for early Detection

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Abstract: Machine learning (ML) techniques offer promising avenues for early prediction of HELLP syndrome in pregnancies, a condition associated with significant maternal and fetal morbidity. The main objective of this study is to propose a predictive model for HELLP syndrome, an obstetric syndrome, and to identify the most influential predictors for HELLP syndrome. For this purpose, we used data collected from the medical records of 266 pregnant women between 28 and 38 weeks of gestation. The variables studied are epidemiological, diagnostic, therapeutic, and evolutionary. The study sample included 49 women with Preeclampsia +Hellp Syndrome (PE+HELLP) and, 217 women with Preeclampsia and without Hellp (PE-HELLP). The proposed approach demonstrates robust performance in identifying pregnancies at risk of HELLP syndrome development through meticulous data preprocessing, feature selection, and model training. Validation on independent datasets underscores the model's generalizability and real-world applicability. Ethical considerations regarding patient privacy and algorithmic transparency are addressed, emphasizing the importance of responsible AI deployment in clinical settings. Our findings highlight the potential of ML-driven approaches to revolutionize prenatal care, enabling timely interventions and improved maternal-fetal health outcomes.

Keywords: *Hellp Syndrome, Machine Learning, Predictive Models, Making Decisions,* Pregnancy complications.

1. Introduction

HELLP syndrome, a complex and potentially life-threatening complication of pregnancy, presents a formidable challenge in obstetric care worldwide. First described by Weinstein in 1982, HELLP syndrome is characterized by hemolysis, elevated liver enzymes, and low platelet count [1]. It typically occurs in the third trimester but can also manifest earlier in pregnancy or postpartum, affecting approximately 0.2% to 0.6% of pregnancies [2], [3].

Despite decades of research and advances in maternal-fetal medicine, the etiology and pathogenesis of HELLP syndrome remain incompletely understood. The syndrome's unpredictable nature and nonspecific symptoms, which can mimic other pregnancy-related conditions such as preeclampsia, often lead to delays in diagnosis and initiation of appropriate treatment [4]. Consequently, HELLP syndrome poses substantial risks to maternal and fetal health, including maternal organ failure, placental abruption, and adverse perinatal outcomes[5].

Traditional methods for identifying individuals at risk of developing HELLP syndrome rely on clinical assessment, maternal history, and laboratory tests, including liver function tests and platelet counts[6]. However, these approaches may lack the sensitivity and specificity needed for early detection, underscoring the need for more accurate and reliable predictive tools.

In recent years, researchers have explored machine learning techniques to improve the prediction and management of diseas in general, and the prediction and management of pregnancy complications in particular, including HELLP syndrome. Schmidt et al. [7] investigated the use of machine learning algorithms, including logistic regression and decision trees, for predicting preeclampsia and related complications. [8] utilized machine learning techniques to predict the HELLP syndrome by incorporating clinical and paraclinical data. They concluded that the integration of machine learning-based algorithms in the first-trimester screening could improve the overall detection rate of these disorders. They demonstrated the feasibility of machine learning in early detection, achieving promising results in terms of predictive accuracy and performance metrics. Korachev et al. [9] investigated the use of machine learning models, including XG Boost and machine learning regression model, for predicting preeclampsia risk during the fisrt trimester. Through the analysis of maternal clinical parameters and laboratory data, the authors developed predictive models capable of identifying individuals at risk of developing HELLP syndrome, demonstrating the potential of machine learning in improving prenatal care. Moreira et al. [10] proposed the utilization of a neuro-fuzzy machine learning technique for predicting HELLP syndrome. By integrating clinical and laboratory variables, their predictive model achieved high accuracy in

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identifying pregnant individuals at risk of developing HELLP syndrome, offering valuable insights for early intervention and management. The results are highly promising, with excellent performance. Melinte et al.[11] Presented a retrospective study to evaluate and compare four ML-based models using the Mississipi classification. These ML models include the Decision Tree model, Naïve Bayes model, K-nearest Neighbors model, and random forest, for predicting HELLP syndrome based on maternal demographic and clinical data. Their study demonstrated the potential of machine learning in the early detection and risk assessment of HELLP syndrome, highlighting the importance of leveraging predictive analytics for improving maternal-fetal health outcomes. Further, for preeclampsia prediction, various machine learning approaches were developed such as random forest (RF), decision trees (DT), gradient boosting (GB), naïve Bayes (NB), and support vector machine (SVM), with good predictive performance [12], [13]. Gomez et al.[14] Proposed a machine-learning model for predicting both pre-eclampsia and intrauterine growth restriction. By analyzing a comprehensive dataset of maternal clinical characteristics and laboratory parameters, the model occasionally failed to predict both disorders simultaneously; instead, it only predicted one of them. To enhance its performance, the model requires additional training data from pregnant women diagnosed with both disorders. This expanded dataset would enable the model to better learn the complexities and nuances of predicting these co-occurring conditions. Li et al.[15] developed predictive models for HELLP syndrome using various machine learning algorithms, including support vector machines, random Forest, learning regression, and gradient boosting. By analyzing a comprehensive dataset of maternal clinical characteristics and laboratory parameters, the authors demonstrated the efficacy of machine learning in identifying individuals at risk of HELLP syndrome.

The severity of HELLP syndrome is categorized using the Mississippi triple-class system, which takes into account platelet count (PLT), serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels, and lactate dehydrogenase (LDH) levels [16]. Class 1 HELLP syndrome represents the most severe form, characterized by PLT ≤ 50,000/mm3, AST or ALT ≥ 70 IU/L, and serum LDH ≥ 600 IU/L. Class 2 denotes a moderate form of HELLP syndrome, with platelet counts ranging between 50,000 and 100,000/mm3, AST or ALT ≥ 70 IU/L, and serum LDH ≥ 600 IU/L. Lastly, class 3 signifies the mildest form of HELLP syndrome, identified by platelet counts ranging between 100,000 and 150,000/mm3, AST or ALT ≥ 40 IU/L, and serum LDH ≥ 600 IU/L.

The main objective of the study is to develop a predictive model for HELLP syndrome, an obstetric syndrome, and to identify the most influential predictors for HELLP syndrome. This machine learning model is aimed to be used by care providers at the time of birth to provide individualized risk assessments to aid in clinical decision-making concerning the use of platelet and blood product transfusions and early delivery.

2. Materials And Method

2.1. Model Design

We have developed a machine-learning model to predict pregnancy outcomes. Particularly help syndrome. The data used was collected from the gynecology and obstetrics department, at Mother and Child Hospital of Setif, Algeria[17]. To report its results, we have followed the guidelines specified in the Guidelines for Developing and Reporting Machine Learning Predictive Models in Biomedical Research: A Multidisciplinary View[18].

The model was designed to make a prognosis of pregnancy outcomes. The under-prediction of the model can increase maternal and neonatal mortality and morbidity, while the overprediction can increase healthcare costs. We aim to avoid both scenarios but prioritize the prediction of pregnant women with a placental dysfunction disorder. The metrics used to evaluate the performance of the model were precision, recall, F1 score, and AUR-ROC. We defined a classifier that made predictions based on the most frequent label of the dataset.

2.2. Dataset

The real-world study population was recruited from pregnant women presenting with preeclampsia to the gynecology-obstetrics department of Mother and Child Hospital “Saadna Abdenour” of Setif, Algeria. Between June 2020 and June 2021[17]. Data were collected from the medical records of 266 patients with a pregnancy between 28 and 38 weeks of gestation. The variables studied are epidemiological, diagnostic, therapeutic, and evolutionary. All patients hospitalized with severe preeclampsia are included. The diagnosis was made on examination, clinical, biological, and radiological examinations Hepatic Doppler ultrasound. This data was entered into Excel and analyzed using the IBM SPSS modeler.

The study sample included 49 women with Preeclampsia +Hellp Syndrome (PE+HELLP) and, 217 women with Preeclampsia and without Hellp (PE-HELLP). With maternal age >=18 years old.

2.3. Selected Features and Data Preprocessing

The features provided in the dataset included maternal characteristics, Neonatal Characteristics, pregnancy characteristics, biological tests, platelet measures, and Doppler measures of the Hepathic Arterie Portal vein, we collected 24 features. All features are listed and described see Table 1.

Table 1. Selected Features

Feature	***Description***
Group	Two possible groups: Preeclampsia with HELLP (PE+HELLP) and Preeclampsia without HELLP (PE-HELLP).
Neonatal Characteristics	
Weight	Neonatal Weight in grams
Maternal Characteristics	
Maternal age	Patient age
Gestite	Number of pregnancies
Parity	Number of times that a woman has delivered a fetus, regardless of whether the child was born alive or was stillborn
Previous Cesarian Section	Number of previous cesarian section
SAP	Systolic Arterie Pressure
DAP	Diastolic Arterie Pressure
Biological Tests	***Hepatic Enzymes (ASAT, ALAT), Platelets Numeration, Proteinearea***
AST (ASAT)	Serum Aspartate aminoTransferase AST
ALT (ALAT)	ALanine aminoTransferase ALT level
Platelets	Platelets Count
Urine PRT	Proteinearea
Pregnancy Characteristics	
Gestational Age (AG)	Fetus Age at the time of data collection.
Hepathic Arterie Portal vein Doppler Measures	
Cross sectional AH	Cross sectional Hepathic Arterie.
Velocity AH	Velocity of Hepathic Arterie. Unit: cm/s
Blood flow AH	Blood flow of Hepathic Arterie. Unit: L/mn
Ir resistance AH	Resistance index of Hepathic Arterie
Beam angle AH	Beam angle of Hepathic Arterie
Cross sectional PV	Cross sectional Portal Vein
Velocity PV	Velocity Portal Vein. Unit: cm/s
Blood flow PV	***Blood flow of the Portal Vein. Unit: L/mn***
Beam angle PV	Beam angle Portal Vein
Total flow	The total flow is the Sum of the Blood flow of the Hepathic Arterie and the Blood flow of the Portal Vein. Total flow= Blood flow AH+ Blood flow PV
Interval-d	The interval between Doppler day and delivery days

The data were divided into training (80%) and testing (20%) sets to facilitate model evaluation. To guard against overfitting, all models underwent 5-fold cross-validation. Following cross-validation on both training and testing data, the models' predictive performance will assess based on the training outcomes. Key metrics including: accuracies, area under the receiver operating characteristic curve (AUROC) values, precision, and F1 scores will comput and compare across HELLP syndrome and its class 1, 2, and 3 subgroups, respectively. The results will graphically present.

2.4. Exploratory Analysis

A total of 266 patients were included in the analysis of this study and were divided into two groups: those who developed HELLP syndrome (49 patients, group 1), and those who did not develop HELLP syndrome (217 patients, group 2). The dataset contains 24 features as mentioned above. The dataset values could be inferred in the preprocessing stage. The target value was biclass. There were two categories: PE+HELLP and PE-HELLP.

During the exploratory data analysis, it was detected that the problem could be treated as a multi-class. The pregnant patients affected by HELLP syndrome (group 1 of 49 patients), were subsequently divided into the following subgroups according to the Mississippi

classification: subgroup 1 (Class 1, n = 15), subgroup 2 (Class 2, n = 25), and subgroup 3 (Class 3, n = 9). See Table 2.

Table 2: HELLP Syndrome classes

	EFFECTIF	POURCENTAGE
INF 50000	15	30.612 %
50000-100000	25	51.020 %
SUP 100000	9	18.367%
TOTAL	49	100 %

The PE±HELLP classes truly depended on the presence or absence of PE or HELLP. Thus, we defined two binary tags as output: PE+HELLP as (1), and PE-HELLP as (0).

All characteristics were numerical, except gestate, parity, and previous cesarian, which were considered categorical variables. Doppler ultra sound mesearments is relevant in the early detection of HELLP Syndrome. We studied the distribution of those variables for each class to prove their relevance.

2.5. Model Training

Learning from multi-label data can be accomplished through various strategies, including data transformation, adaptation of conventional classification methods, and employing ensemble classifiers [19]. This study specifically focuses on the data transformation and method adaptation approach. The data transformation technique involves utilizing transformation methods to convert the original multi-label data into one or multiple binary or multiclass datasets. Conversely, the adaptation approach entails modifying existing classification algorithms to handle multi-label data, generating multiple outputs instead of a singular one [19]. Decision Tree Classifier, Extra Tree Classifier, Random Forest Classifier, and K-Nearest Neighbors Classifier are among the models that can be adjusted for multi-label classification purposes.

The clinical variables considered in this evaluation comprised demographic information such as age, gestate, parity, Previous Cesarian Section , and Hepatic Enzymes (ASAT, ALAT), Platelets Numeration, Proteinearea, along with obstetrical comorbidities and a history of pathological conditions (such as Hepathic Arterie Portal vein, Doppler Ultarsound and Blood flow of the Portal Vein). Additionally, paraclinical data including the APRI score, systolic arterial pressure (SAP), and diastolic arterial pressure (DAP) were incorporated into the analysis.

2.6. Model Validation

After training the models, we proceed to assess their performance using the test set. Model selection was evaluated through various metrics including AUC ROC (Area Under the Receiver Operating Characteristic Curve), accuracy (the proportion of instances correctly classified by the model), precision (the ratio of correctly identified positive cases to all cases identified as positive), recall (the proportion of actual positive cases correctly identified by the model), F1 score (the harmonic mean of precision and recall), and Hamming loss (the proportion of misclassifications).

To provide a comprehensive evaluation for each label, label-based measures were employed. Two options were considered: macro-average and micro-average. In the macro-average approach, the metric is computed independently for each label, assigning equal weight to all labels. Conversely, micro-average metrics aggregate contributions from all labels to compute an average metric. For our evaluation, we adopted the macro-average version of recall, precision, and F1 score [20].

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}} \quad (1)$$

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \quad (2)$$

$$\text{Recall} = \frac{TP}{\text{TP} + \text{FN}} \quad (3)$$

$$\text{F1 score} = \frac{2 * \text{TP}}{2 * \text{TP} + \text{FP} + \text{FN}} \quad (4)$$

3. Results

In our prospective study, we assessed a cohort of 266 pregnant patients. Their clinical and paraclinical characteristics are outlined in Table 4, and categorized into two groups: individuals who developed HELLP syndrome (group 1, comprising 49 patients), and those who did not develop HELLP syndrome (group 2, comprising 213 patients).

3.1. Doppler ultrasound measurements

In Doppler ultrasound measurements, we observed important differences between two groups PE+HELLP and PE-HELLP. The hepatic artery pulsatility index is elevated compared to normal in preeclamptic women; this elevation is greater in the preeclampsia group complicated by HELLP syndrome with an average of 1.88 vs 1.67. See Figure 2.

In the Blood Flow quantification, there is a significant reduction in hepatic flow in the PE+HELLP group. This reduction is more important in hepatic arterie flow as shown in figure 3.

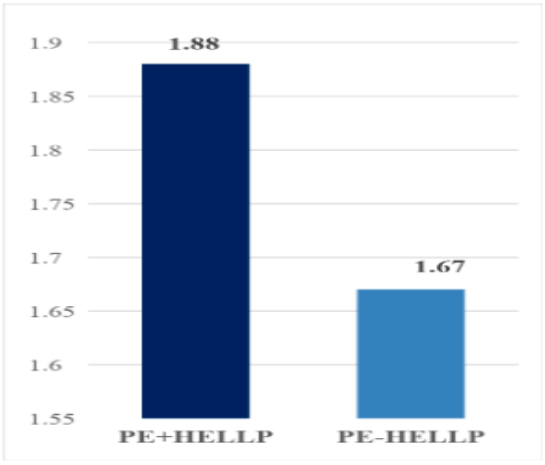

Fig 1. Hepatic artery pulsatility index

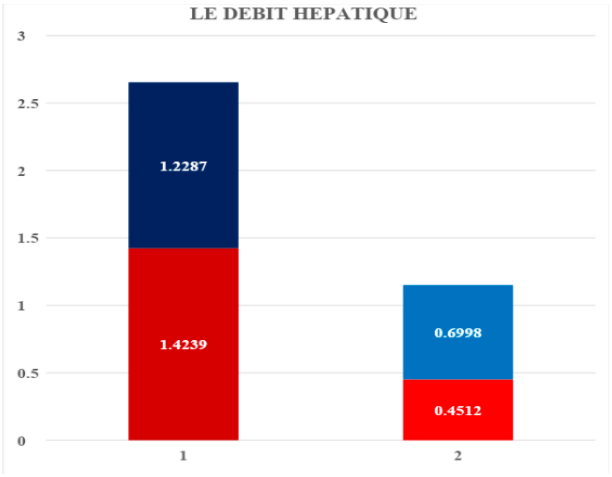

Fig 2. Distribution of Debit hepatic according to PE+/- HELLP syndrome groups

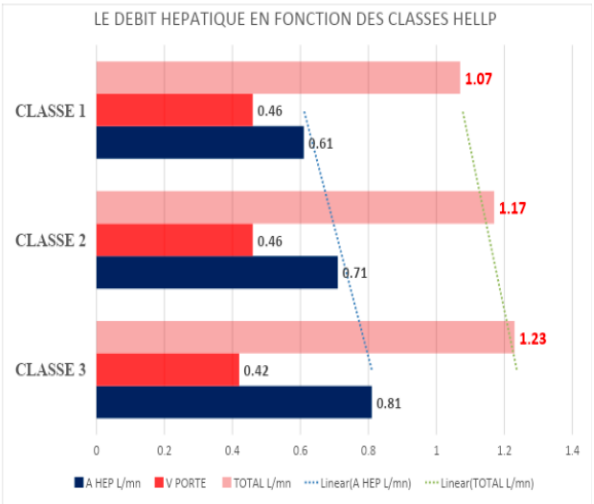

Fig 3. Average hepatic blood flow according to HELLP syndrome classes

The decrease in hepatic blood flow is more significant with progression from HELLP syndrome from class 3 to class 1 with a more pronounced decrease in the hepatic artery component see Figure 4.

APRI

APRI(aspartate-aminotransferase to platelet ratio index) was calculated using the following formula: [AST (IU/l) / AST (upper limit of normal - IU/l) / platelet count (109/l)] × 100. The APRI score, which is an assessment method of dividing AST by platelet count, has been traditionally used to diagnose liver cirrhosis. It was described in 2003 as an accurate predictor of the degree of liver fibrosis in patients with HCV.

Distribution of patients by their apri according to PE±HELLP groups (figure 4). Distribution of patients by their apri according to HELLP syndrome classes (figure 5).

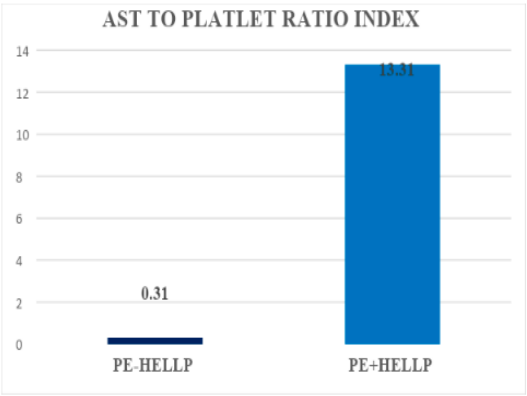

Fig 4. APRI and PE±HELLP group

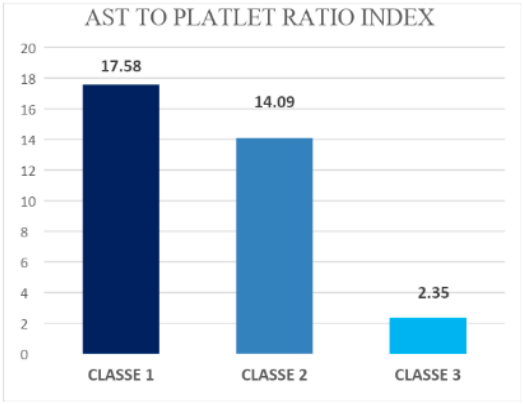

Fig 5. APRI and HELLP classes

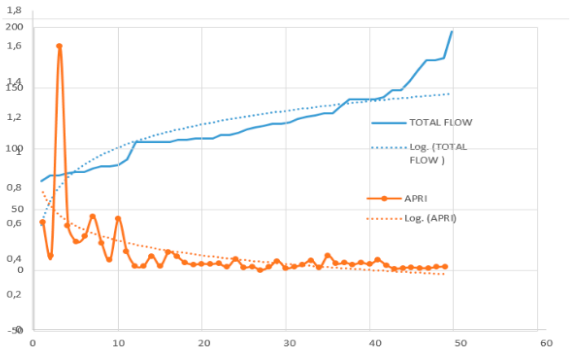

Fig 6. APRI en fonction du debit sanguin hepatic total

The lower hepatic blood flow, the more severe HELLP syndrome resulting in a high APRI reflecting greater hepatic cytolysis as shown in Figure 6.

3.2. Hellp Syndrome Severity

The severity of HELLP syndrome is categorized using the Mississippi classification (Tri-class) with AST, Platelets, and APRI Score, as shown in table 3.

Table 3. Distribution according to HELLP classes

BIOLOGICAL PARAMETER	*CLASS 1 (n=15)*	*CLASS 2 (n=25)*	*CLASS 3 (n=9)*
AST	237,07	175,37	94,77
PLATELETS	39,66	75,28	118,33
APRI SCORE	17,58	14,09	2,35

We note the APRI score is proportional to the degree of severity of the HELLP, increasing with more hepatic cytolysis and deep thrombocytopenia.
Given the multiple life-threatening complications of this syndrome, it is vital to offer individualized care and to try to identify potential predictive factors for the severity and progression of the disease. Superior predictive performance of the APRI (aspartate-aminotransferase to platelet ratio index) score compared to serum AST levels in terms of sensitivity (82.6% versus 71.7%), but not specificity (87.6% versus 91.2%) for the prediction of HELLP syndrome.

4. Discussion

The HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count) is a rare and dramatic pregnancy-related condition. often complicated by cerebral edema and multi-organ failure. HELLP syndrome is characterized by the presence of microangiopathic hemolytic anemia, elevated liver enzymes, low platelet count, and is associated with severe clinical complications leading to maternal organ failure or death. It can worsen within hours, and affected patients complain of abdominal pain, nausea, and vomiting, hence the adage that any abdominal pain with vomiting in the third trimester is a HELLP until proven otherwise. Additionally, patients exhibit increased blood pressure and proteinuria. The most feared complication is liver rupture. There are certain risk factors for the occurrence of HELLP syndrome such as hypertension, overweight, or multiple pregnancies.

The risk of recurrent HELLP syndrome in subsequent pregnancies exists.

Given the multiple potentially life-threatening complications of this syndrome, it is vital to offer individualized management and try to identify potential predictors of disease severity and progression.

5. Conclusion

The development of a machine learning model for predicting HELLP syndrome in pregnancies represents a significant advancement in maternal healthcare. Our study demonstrates the potential of leveraging computational techniques to enhance early detection and management of this life-threatening condition.

Through comprehensive data collection, rigorous preprocessing, and model training, we have successfully constructed a predictive model capable of identifying pregnancies at increased risk of developing HELLP syndrome. The model exhibits promising performance metrics, providing healthcare providers with valuable insights to facilitate timely interventions and improve maternal and fetal outcomes.

Looking ahead, as future work, we will train, validate, and evaluate the model proposed using the maximum number possible of machine learning models: Decision Trees (DT), Random Forest (RF), and Naive Bayes (NB) models and k-Nearest Neighbors (KNN) and others models to achieve optimal performance in predicting HELLP syndrome.

Conflicts of interest

The authors declare no conflicts of interest.

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