Heliyon 11 (2025) e42679

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Prediction of pregnancy outcomes in women with systemic lupus erythematosus before pregnancy: Application of machine learning models

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ARTICLE INFO

Keywords:
Artificial intelligence
Machine learning
Pregnancy outcome
Data mining
Systemic lupus erythematosus
Neonate

ABSTRACT

Introduction: Fetal loss is possible during pregnancy in women with systemic lupus erythematosus (SLE). Predicting pregnancy outcomes for women with SLE can be an effective aid in providing consultation and treatment services. Therefore, this study aimed to develop a machine-learning model that could predict pregnancy outcomes before pregnancy in women with SLE.

Methods: The data of all pregnant women referred to the rheumatology center of Shariati Hospital and a specialized rheumatology clinic since 1980 were retrospectively collected from their medical records. Data collection was done by gathering 26 variables that affect pregnancy outcomes. Then, we used standard algorithms to select important features that affect pregnancy outcomes before pregnancy (11 different feature sets). A variety of machine learning algorithms were trained using both imbalanced and balanced datasets in Clementine and Weka software. Finally, the model with a higher area under the receiver operating characteristic curve (AUC) and F-score was selected to predict pregnancy outcomes.

Results: Out of 149 pregnancies, 46 pregnancies resulted in spontaneous abortion, while 103 pregnancies resulted in live birth. Compared with other models, the Chi-square automatic interaction detection (CHAID) decision tree was selected as the best-performing model with higher accuracy (93.5 %), specificity (92.9 %), sensitivity (93.8 %), precision (97 %), F-score (0.95), and AUC (0.96).

Conclusion: By using the CHAID decision tree to predict the outcome of pregnancy in women with SLE and extracted rules, it is possible to use appropriate methods that prevent spontaneous abortion and also provide timely consultation to women with SLE for making decisions to become pregnant.

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https://doi.org/10.1016/j.heliyon.2025.e42679
Received 30 August 2023; Received in revised form 11 February 2025; Accepted 12 February 2025
Available online 14 February 2025

1. Introduction

Systemic lupus erythematosus (SLE) is an inflammatory multisystem disease with unknown etiology in which autoantibodies are created against the body's antigens. This leads to inflammatory damage in various body organs, including the kidneys, blood-forming cells, nervous system and so on [1]. It seems that a set of genetic, environmental, and hormonal factors are among the causes of this disease [2]. Clinical symptoms and manifestations, laboratory signs, disease progress and prognosis are different from one patient to another [3]. These patients have to control their disease with self-care and continuous use of medicine throughout their lives [4].

The prevalence of this disease is higher in women, with a ratio of 15 to 1 [2]. Since the onset of this disease typically occurs during third and fourth decade of life, it predominantly affects women who are in their reproductive age [5,6]. These patients may experience high-risk pregnancies due to a combination of maternal factors (such as lupus flare-up, diabetes, and preeclampsia) and fetal risks (such as miscarriage, intrauterine fetal death, premature/preterm birth, intrauterine growth restriction, and congenital heart block) [5].

A meta-analysis of 16 studies in North America and Europe found that SLE is estimated to be 23.8 per 100,000 [3]. SLE is relatively common in Iran, with a reported prevalence of 40 per 100,000 people [7]. Numerous studies indicate that the disease is more prevalent in women, with the average age at diagnosis ranging from 37 to 50 years in women [3]. In Iran, 90 % of SLE cases are reported to be in women, and the average age of onset of this disease among Iranian women is reported to be around 21.5 years [7].

Women with SLE who are planning to become pregnant may have to deal with numerous risks for themselves and their unborn babies [8]. Any pregnancy may result in a live birth (full-term or premature/preterm) or fetal loss. Fetal loss can occur due to spontaneous abortion before the 20th week of pregnancy or intrauterine fetal death (stillbirth) after the 20th week of pregnancy [3,9]. Despite the advancements in the management of lupus patients, the disease is still associated with a significant risk of fetal loss in comparison to pregnant women without SLE [10]. Women with SLE experience fetal loss in approximately 20 % of pregnancies [11]. Some studies have reported that fetal loss occurs in 43.8 % of pregnancies [12]. A Chinese study found that these women experienced an 11.2 % rate of fetal death [9]. The prevalence of spontaneous abortion in women with SLE is approximately 14–35 %, which is higher than the prevalence in normal women, where it ranges from 7 to 12.5 %. Hence, pregnancy in these patients should be planned in advance and managed using approved medications at the time of proper control of the condition [5].

Knowing the mutual relations between SLE and pregnancy outcome before pregnancy is crucial for providing appropriate counseling and care for women with SLE who decide to be pregnant [13]. Predicting possible adverse pregnancy outcomes can be an effective help for women with lupus before deciding to become pregnant. However, pregnant cases of SLE patients are extremely rare, which may limit our knowledge [14].

To effectively prevent fetal loss, it is essential to have a thorough understanding of the risk factors associated with it and their interrelationships. Several factors affect the outcome of pregnancy and each of them has a different degree of influence. There are also complicated relationships between some influencing risk factors and pregnancy outcomes, which cause complexity in decision-making regarding maternal care [2,3,5,6,8,12,15–22]. Some common predictors of adverse pregnancy outcomes in these patients include flare-up of SLE before pregnancy, proteinuria, thrombocytopenia, high blood pressure, positive Lupus Anti-Coagulant (LAC), high levels of IgG, anticardiolipin (aCL), previous history of fetal loss, kidney involvement, positive anti-dsDNA, younger age at disease onset, high CRP during pregnancy, positive anti-phospholipid antibody (APA), flare-up of SLE during pregnancy, unplanned pregnancy status, C3 hypocomplementemia and 24 h-urinary protein level [5,9,12,23–26].

Machine learning techniques can be applied to address this complexity. These techniques aim to determine the key variables, explore their relationships, and predict the target variable. Machine learning models can help the medical community in the diagnosis and prediction of diseases. Machine learning models are particularly useful in situations where the number of samples is small and/or the number of influential variables is high, as these models can reduce some of the limitations of traditional statistical methods [27]. In this regard, researchers developed many machine learning models in the field of reproductive medicine and neonatal care [28–30].

Based on the reasons mentioned, developing a model to early predict pregnancy outcomes in lupus women before deciding to become pregnant and implementing preventative measures, as well as timely management of women with lupus before pregnancy can greatly reduce adverse outcomes and physical and mental complications. In this regard, suitable predictive models are required. The majority of previous research has focused on determining the prevalence of pregnancy outcomes in women with lupus or identifying influential factors [5,11,12,24,25]. However, there have been limited studies on predicting pregnancy outcomes in lupus patients [9,14,26,27,31]. Out of these studies, two were conducted using logistic regression [9,26], two used artificial neural networks [14,31] and one utilized various machine learning methods [27]. Nevertheless, it is worth noting that all of these studies have been conducted to predict pregnancy outcomes for women with lupus using variables before and during pregnancy. As a result, the models presented in these studies cannot predict pregnancy outcomes before pregnancy. In other words, the developed models are only applicable to women with lupus during pregnancy. The present study proposes a model to predict pregnancy outcomes using only pre-pregnancy variables through various machine learning techniques.

2. Methods

2.1. Design

A retrospective study was conducted utilizing patients' medical records.

2.2. Setting and patients

Lupus is a disease closely related to the field of rheumatology. Pregnant women with lupus are subject to the supervision of both a gynecologist and a rheumatologist. Additionally, variables related to lupus (before pregnancy) are recorded in the medical records at rheumatology centers. Therefore, all pregnant women referred to the rheumatology center of Shariati Hospital and a specialized rheumatology center (Clinic) in Tehran, Iran, since 1980 were included in this study. We considered following inclusion and exclusion criteria. The medical records must contain data about influential risk factors before pregnancy to be included in the study. Furthermore, we only included singleton pregnancies. We also excluded patients with a high level of missing data in their medical records.

In the present study, sampling was not performed in order to access the maximum clinical data from the patients. All pregnant women who met the inclusion criteria and were referred to these rheumatology centers were included. The sampling strategy was based on pregnancy.

To gather data, a data collection form was designed after reviewing literature [3,11,15–17,20,32–61] and with the help of a rheumatologist. This form included all potentially influential variables in predicting pregnancy outcomes in lupus women before pregnancy. A well-trained researcher reviewed patients' medical records and recorded the values of these variables in this form. Subsequently, she entered the data into an Excel spreadsheet. She had a master's degree in medical informatics from a University of Medical Sciences. She was familiar with medical record review, data extraction, data analysis and medical terminologies.

2.3. Outcome and input variables and feature selection

The output variable was the pregnancy outcome in terms of live birth or spontaneous abortion. We conducted a review to identify the potential input variables (features) that may have an impact on pregnancy outcomes in women with lupus before pregnancy [3,11,15–17,20,32–63]. This review revealed 31 pre-pregnancy variables related to pregnancy outcomes in women with lupus (Table S1 in Supplement 1). However, five of these variables were not recorded in the patients' medical records. Therefore, we collected data from the remaining 26 variables and used standard feature selection algorithms available in Weka and Clementine software to select the most important features for machine learning. Moreover, important features were identified using univariate statistical test methods (Chi-square test for qualitative variables), mean comparison tests (Independent T-test and Mann-Whitney test for quantitative variables), as well as, binary logistic regression. We considered P_value$\leq$0.1 as an indicator for potentially influential variables. Two additional feature sets were created based on the results of these feature selection methods, one containing features identified as influential in at least three above-mentioned methods and another containing features identified as influential in at least four methods.

Table 1
Important variables for each feature selection algorithm.

Feature set	Method of feature selection	Included features
feature set 1	Cfs	Number of Children, Flare-up of lupus, Elevated blood pressure before pregnancy, APS Syndrome, Neuropathic problems, CRP before pregnancy, Anemia and leucopenia before pregnancy, Arterial thrombosis, Hydroxychloroquine dose before pregnancy
feature set 2	Consistency	Number of Children, Flare-up of lupus, Elevated blood pressure before pregnancy, APS Syndrome, History of abortion, Pulmonary problems, Cardiac problems, Neuropathic problems, VDRL, RF, CRP before pregnancy, ANA, Anemia and leucopenia before pregnancy, Lupus nephritis (before pregnancy), Hydroxychloroquine dose before pregnancy, Cyclophosphamides
feature set 3	Relief	Age, Flare-up of lupus, Elevated blood pressure before pregnancy, C3 before pregnancy, APS Syndrome, History of abortion, Cardiac problems, Neuropathic problems, RF, CRP before pregnancy, ANA, Anemia, and leucopenia before pregnancy, Lupus nephritis (before pregnancy), Cyclophosphamides
feature set 4	C5.0	Age, Flare-up of lupus, APS Syndrome, History of abortion, Platelets before pregnancy, Neuropathic problems, RF, CRP before pregnancy, AST before pregnancy, ALT before pregnancy, ANA, Anemia, and leucopenia before pregnancy, Lupus nephritis (before pregnancy), Hydroxychloroquine dose before pregnancy
feature set 5	CHAID	Age, Proteinuria before pregnancy, APS Syndrome, Neuropathic problems, VDRL, CRP before pregnancy, AST before pregnancy, Anemia, and leucopenia before pregnancy
feature set 6	QUEST	Number of Children, Proteinuria before pregnancy, Elevated blood pressure before pregnancy, C4 before pregnancy, APS Syndrome, History of abortion, Platelets before pregnancy, CRP before pregnancy, AST before pregnancy, ALT before pregnancy, Lupus nephritis (before pregnancy)
feature set 7	Binary Logistic Regression	Proteinuria before pregnancy, Flare-up of lupus, C3 before pregnancy, APS Syndrome, Platelets before pregnancy, CRP before pregnancy, Anemia and leucopenia before pregnancy, Hydroxychloroquine dose before pregnancy
feature set 8	Univariate analysis	The flare-up of lupus, APS Syndrome, CRP before pregnancy, Anemia and leucopenia before pregnancy, Hydroxychloroquine dose before pregnancy
feature set 9	The combined feature set 1	Age, Number of Children, Proteinuria before pregnancy, Flare-up of lupus, Elevated blood pressure before pregnancy, APS Syndrome, History of abortion, Platelets before pregnancy, Neuropathic problems, RF, CRP before pregnancy, AST before pregnancy, ANA, Anemia and leucopenia before pregnancy, Lupus nephritis (before pregnancy), Hydroxychloroquine dose before pregnancy
feature set 10	The combined feature set 2	The flare-up of lupus, Elevated blood pressure before pregnancy, APS Syndrome, History of abortion, Neuropathic problems, CRP before pregnancy, Anemia and leucopenia before pregnancy, Lupus nephritis (before pregnancy), Hydroxychloroquine dose before pregnancy
feature set 11	Main feature set	All 26 features

Table 1 shows the 11 feature sets developed in this study. The features selected for each method are detailed in Table S2 in Supplement 2.

2.4. Data preprocessing

Only five variables out of 26 variables had missing data. The percentage of missing values for these variables is shown in Table 2. To impute missing data, we replaced the missing data with the mean of the classes (spontaneous abortion and live birth) for quantitative variables and class modes for qualitative variables.

2.5. Data balancing

Due to the imbalanced proportion of dataset in the classes, the Synthetic Minority Over-sampling Technique (SMOTE) was applied to balance the dataset [29,64,65].

2.6. Development and evaluation of machine learning models

We conducted training on various machine learning algorithms, including decision trees (C5, Chi-square automatic interaction detection (CHAID), classification and regression tree (CRT), J48, Random Trees), artificial neural networks (multi-layer perceptron (MLP), and radial basis function (RBF)), support vector machine (SVM), Bayesian network, AdaBoost and logistic regression using both balanced and imbalanced datasets. We trained models based on a 10-fold cross-validation process [29,64,66].

All the mentioned machine learning methods were implemented on 11 different feature sets in two modes of balanced and imbalanced datasets. Ultimately, the models were evaluated according to their accuracy, specificity, sensitivity, area under the receiver operating characteristic (ROC) curve (AUC), and F1-score. We selected the most optimal model based on the AUC and F1-score.

3. Results

3.1. Description of patients

The distribution of quantitative and qualitative variables based on pregnancy outcomes is shown in Table 3. Out of the 149 pregnancies studied, the outcome of 46 pregnancies (31 %) was spontaneous abortion and the outcome of 103 pregnancies (69 %) was a live birth.

3.2. Machine learning algorithms to predict pregnancy outcomes in lupus women

Eleven standard machine learning algorithms were implemented on 11 different feature sets using both balanced and imbalanced datasets. In total, 242 models were developed and compared, considering their performance. The evaluation results of the imbalanced datasets are presented in Table S3 in Supplement 2, while Table S4 presents the evaluation results of the models on the balanced datasets. The five most optimal models in the balanced and imbalanced datasets are presented in Table 4.

The ROC of the selected CHAID tree trained on imbalanced dataset is presented in Fig. 1. Furthermore, according to the results presented in Table 4, the CHAID tree in feature set 6 has the highest performance among balanced datasets. The ROC of this model on the balanced dataset is also presented in Fig. 2. According to the results, the CHAID decision tree performed better than other algorithms for predicting pre-pregnancy outcomes in women with SLE in feature set 9 using the imbalanced dataset (F-score = 0.95, AUC = 0.96).

The selected CHAID decision tree identified 13 out of 16 variables as being the most important variables in prediction of pregnancy outcome in women with SLE. These variables and their importance in prediction, are presented in Fig. 3. Furthermore, we extracted 27 rules from this CHAID decision tree. For instance, one rule states "If APS Syndrome = Negative AND Proteinuria≤81 AND CRP=Negative AND Lupus nephritis = Negative, then Output = Live birth". The other rules are provided in Table S5 in Supplement 3.

Table 2
Amount of missing values in two groups.

Variables	Missing data in Spontaneous abortion (%)	Missing data in Live birth (%)	Total (%)
CRP before pregnancy	7	13	20
Proteinuria before pregnancy	11	5	16
C3 before pregnancy	7	12	19
C4 before pregnancy	2	15	17
Platelets before pregnancy	3	4	7

Table 3
Distribution and comparison of different variables in two groups of live birth and spontaneous abortion.

Variables	Values	Spontaneous abortion N (%)	Live birth N (%)
Quantitative Variables			
Number of Children	No child	35 (23.5)	70 (47)
	One child	9 (6.0)	26 (17.4)
	More than one child	2 (1.3)	7 (4.8)
Flare-up of lupus	Yes	4 (2.7)	2 (1.3)
	No	42 (28.0)	101 (68.0)
Elevated blood pressure before pregnancy	Yes	5 (3.3)	20 (13.4)
	No	41 (27.5)	83 (55.7)
APS[a] Syndrome	Positive	10 (6.7)	5 (3.3)
	Negative	36 (24.2)	98 (65.8)
History of abortion	Negative	28 (18.8)	69 (46.3)
	One time	9 (6.0)	13 (8.7)
	Two times	3 (2.0)	10 (6.7)
	Three times	3 (2.0)	9 (6.0)
	More than three times	3 (2.0)	2 (1.3)
Pulmonary problems	Positive	3 (2.0)	6 (4.0)
	Negative	43 (28.9)	97 (65.1)
Cardiac problems	Positive	13 (8.7)	23 (15.4)
	Negative	33 (22.1)	80 (53.7)
Neuropathic problems	Positive	8 (5.4)	26 (17.4)
	Negative	38 (25.5)	77 (51.7)
VDRL[b]	Positive	4 (2.7)	6 (4.0)
	Negative	42 (28.0)	97 (65.1)
RF[c]	Positive	5 (3.3)	5 (3.3)
	Negative	41 (27.5)	98 (65.8)
CRP[d] before pregnancy	Positive	11 (7.4)	6 (4.0)
	Negative	35 (23.5)	97 (65.1)
ANA[e]	Positive	36 (24.2)	79 (53.0)
	Negative	10 (6.7)	24 (16.0)
Anemia and leucopenia before pregnancy	Positive	22 (15.0)	33 (22.0)
	Negative	24 (16.0)	70 (47.0)
Pulmonary Embolism	Positive	2 (1.3)	2 (2.3)
	Negative	44 (29.5)	101 (68.0)
Thrombophlebitis	Positive	2 (1.3)	2 (1.3)
	Negative	44 (29.5)	101 (68.0)
Arterial thrombosis	Positive	0 (0.0)	2 (1.3)
	Negative	46 (31.0)	101 (68.0)
Lupus nephritis (before pregnancy)	Negative	28 (18.8)	55 (36.9)
	First degree	5 (3.3)	10 (6.7)
	Second degree	1 (0.7)	7 (4.8)
	Third degree	6 (4.0)	14 (9.4)
	Forth degree	6 (4.0)	17 (11.4)
Cyclophosphamides	Yes	16 (10.7)	41 (27.5)
	No	30 (20.1)	62 (41.6)
Variables	**Values**	**Spontaneous abortion (mean ± SD)**	**Live birth N (%) (mean ± SD)**
Qualitative Variables			
Age	18–40	29.07 ± 4.758	28.19 ± 4.655
Proteinuria before pregnancy	0–1560	197.74 ± 306.141	121.26 ± 221.654
C3 before pregnancy	28–214	105.22 ± 31.687	101.32 ± 33.057
C4 before pregnancy	3–108	21.46 ± 6.991	23.00 ± 15.561
Platelets before pregnancy	69000–452000	223500.00 ± 70260.389	235398.06 ± 64565.871
AST[f] before pregnancy	6–50	21.50 ± 8.978	22.11 ± 6.388
ALT[g] before pregnancy	3–60	21.74 ± 10.368	19.38 ± 8.882
Hydroxychloroquine dose before pregnancy (mg)	0–400	169.57 ± 105.661	228.88 ± 228.88

[a] Anti-Phospholipid Antibody Syndrome.
[b] Venereal Disease Research Laboratory.
[c] Rheumatoid factor.
[d] C-reactive protein.
[e] Antinuclear Antibody.
[f] Aspartate Aminotransferase.
[g] Alanine Aminotransferase.

Table 4
Evaluation results of five of the best models.

Dataset	Model	Feature set	Accuracy %	Specificity %	Sensitivity %	Precision	F-score	AUC
Imbalanced	CHAID	**9**	**93.5**	**92.9**	**93.8**	**0.97**	**0.95**	**0.96**
	Random Trees	5	89.1	72.2	100.0	0.85	0.92	0.94
	CHAID	11	89.1	85.7	90.6	0.94	0.92	0.94
	Random Trees	9	89.1	71.4	96.9	0.89	0.93	0.88
	CHAID	5	82.6	61.1	96.4	0.79	0.87	0.90
Balanced	CHAID	**6**	**89.3**	**96.2**	**83.3**	**0.96**	**0.89**	**0.93**
	Random Trees	4	85.7	93.1	77.8	0.91	0.84	0.95
	Multi-layer Perceptron	4	88.2	91.3	85.4	0.92	0.88	0.94
	Multi-layer Perceptron	6	85.6	91.3	80.6	0.91	0.86	0.93
	CHAID	2	83.9	92.3	76.7	0.92	0.84	0.93

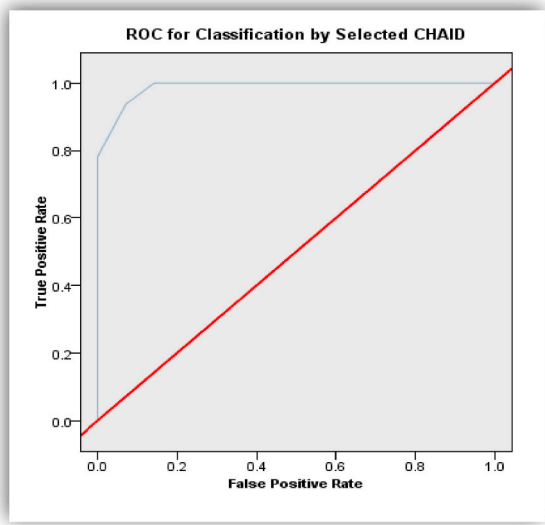

Fig. 1. ROC of selected CHAID tree for imbalanced dataset.

4. Discussion

A recent review indicates that the non-invasive prenatal test is valuable screening tool to detect different diseases in the first trimester of pregnancy [67]. In this regard, artificial intelligence and machine learning models have been widely used in many fields of medicine to help providers with decision making, and predict clinical outcomes based on the initial features. The fields of reproductive medicine will be greatly impacted by artificial intelligence [30]. Furthermore, at beginning of pregnancy or in the first trimester, we can analyze the data using machine learning to predict pregnancy outcomes. In this regard, Medenica et al. have conducted a comprehensive review that focuses on clinical AI applications for infertility and show that AI could be applied in many field of infertility of women and men and predict the outcome of infertility treatment [30]. Another study indicated that ML models are capable of predicting pregnancy based on the quality of oocytes, with a success rate of around 60 % [30]. Other researchers developed a web-based decision support system to predict survival of neonates in NICU. They implemented the system in a NICU to externally validate the system. They found that the system were able to accurately predict survival of neonates with an accuracy of 97.02 %, and F-score of 0.984. Their external validation showed an accuracy of 98.91 % and F-score of 0.993 [28]. In another study, researchers applied machine learning to predict neonatal deaths. They developed different models and found that the highest AUC was for SVM and Ensemble models (0.98). The highest accuracy, sensitivity and F-score were also achieved for the SVM model with 0.94, 0.95 and 0.96, respectively [29]. These studies use machine learning and data related to early stages of pregnancy or delivery to predict the outcomes.

In the present study, various machine learning models were presented to predict pregnancy outcomes in women with lupus before pregnancy. The results indicate that the CHAID decision tree model with an AUC of 0.96 and an F-score of 0.95 was effective in predicting pregnancy outcomes in this population. The selected decision tree operates in such a way that the specialists or other users enter the 16 variables of a woman with lupus required for the CHAID decision tree, and the decision tree provides a result according to the values of all the entered variables and the decision rules. The result will be either "spontaneous abortion" or "live birth" and the

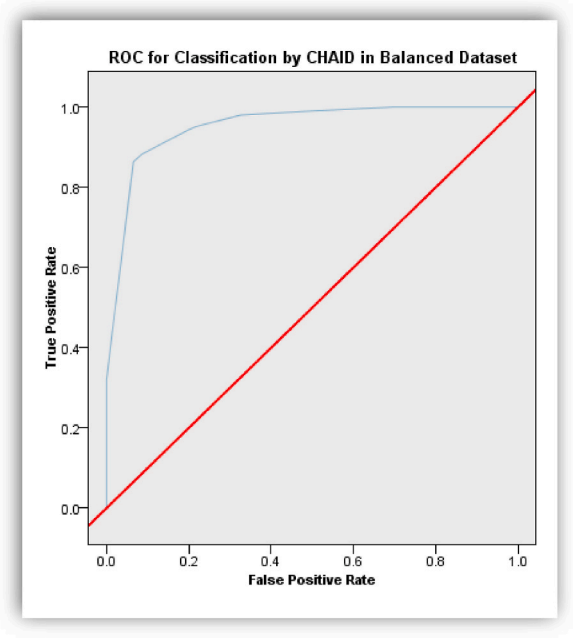

Fig. 2. ROC of CHAID tree for balanced dataset.

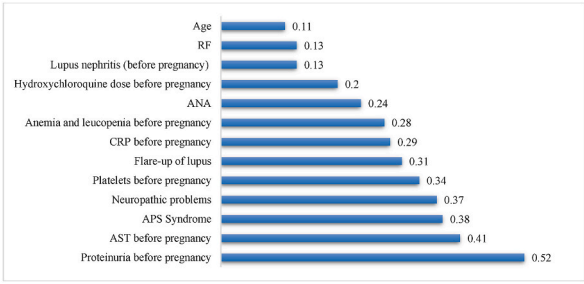

Fig. 3. Predictor importance score of CHAID tree (Target: Outcome of pregnancy).
RF= Rheumatoid factor.
ANA = Antinuclear Antibody.
CRP= C-reactive protein.
APS = Anti-Phospholipid Antibody Syndrome.
AST = Aspartate Aminotransferase.

probability of this prediction.

Various machine learning methods have been extensively used to predict the mode of delivery, assess the possible risks to the woman during pregnancy, and predict pregnancy outcomes. For example, in the research conducted by Gómez-Jemes, a machine learning model was presented to predict high-risk pregnancies, especially preeclampsia and fetal growth restriction. The data from 95 pregnant women with preeclampsia and intrauterine growth restriction was trained using different algorithms. The most optimal model on the imbalanced data had an AUC-ROC of 0.87 and a recall of 0.89 [68].

Recent studies have explored the potential of machine learning algorithms for lupus patients. For example, Bikdeli et al. (2023) conducted a study that utilized these algorithms to identify clusters of patients with similar clinical histories and laboratory results. Additionally, they investigated maternal and prenatal outcomes for patients with SLE, proposing a risk assessment model tailored to this population. They used 21 maternal and perinatal features to cluster data through the application of a self-organizing map (SOM). This approach created five distinct clusters, enabling the categorization of pregnancy outcomes in SLE women into high-risk, medium-risk, and low-risk categories [69]. Additionally, Sanchez et al. (2022) conducted a study aimed at designing and developing the prototype of SLE-T2T, a web-based application that recommends suitable treatment for managing patients with lupus based on patient-entered data [70].

There are numerous studies on pregnancy outcome prediction using machine learning; however, there is limited research on predicting pregnancy outcomes in SLE patients. Paydar et al. (2015) found that an MLP neural network had a better performance in

predicting pregnancy outcomes (live birth and spontaneous abortion) in the first trimester compared to an RBF neural network [31]. Wu et al. (2019) developed a regression model to predict fetal loss in SLE women at the early stages of pregnancy. The study sample size was 338, with a fetal loss rate of 11.2 %. They classified patients into two groups: low-risk (0–3) and high-risk (>3). The sensitivity, specificity, the AUC and accuracy of their model were 60.5 %, 93.3 %, 0.829 and 90 %, respectively.

Hao et al. (2023) developed machine learning-based prediction models for predicting adverse pregnancy outcomes in women with SLE. Researchers used data from 51 pregnant women and 288 variables related to before and during pregnancy. They found that the random forest model had the best performance in predicting adverse pregnancy outcomes. The MLP neural network model was ranked second [27].

In another study, an artificial neural network was used to predict fetal loss among 469 pregnancies (fetal loss rate = 10.4 %). The ANN showed a sensitivity of 94 %, an accuracy of 81 %, and an F-score of 0.50 [14]. In a study, a regression model was applied to predict adverse pregnancy outcomes, including fetal loss among 116 pregnancies. This study reported an AUC of 0.948, sensitivity of 93.5 %, specificity of 85.19 %, and accuracy of 89.6 % [26]. Our proposed model has higher accuracy, sensitivity, F-score, and AUC in comparison with recent studies. Moreover, it can predict pregnancy outcomes before pregnancy due to the consideration of only pre-pregnancy variables.

The impact of SLE and its complications for a mother and her baby have been studied in different studies with different results. In Wu et al. study, renal disorders and hematological disorders were found as important risk factors for predicting the overall risk of fetal loss [9]. Zamani et al. found that high levels of C-reactive protein (CRP) during pregnancy, renal involvement and anti-phospholipid antibody (APA) positivity are the predictors of adverse pregnancy outcomes in SLE patients. The risk of adverse pregnancy outcome especially abortion is higher when the APS syndrome is positive in a SLE woman [12]. Moreover, absence of remission for at least six months before conception, preexisting lupus nephritis, active disease at conception, and antiphospholipid antibody syndrome were found in Makarm study et al. Their study revealed a statistically significant decrease in adverse events among pregnant patients taking hydroxychloroquine (HCQ) and Low-molecular-weight heparin (LMWH) [26]. Janardana et al. [24] introduced HCQ, a history of lupus nephritis, antiphospholipid antibody positivity, disease activity as influential risk factors. When pregnancy happens during a stable disease, the probability of a major flare during pregnancy is minimized. HCQ use was associated with a lower risk of flare in SLE patients who were in remission at the time of conception [24]. Our CHAID decision tree also consistently considered these variables as the influential factors to predict pregnancy outcomes.

Patient management should be planned accordingly to provide optimum care and support for the SLE woman and her baby. The counseling and care of SLE patients before and during pregnancy requires identifying the risk factors for adverse outcomes. This study demonstrated that 13 variables are more important than others in predicting pregnancy outcomes before pregnancy. Therefore, the status of these risk factors should be checked by a specialist before planning a pregnancy to assess the risk of fetal loss. Moreover, the importance score of variables should be considered while assessing the risk. The physician is capable of assessing the level of risk based on the rules extracted from the selected decision tree and the confidence level of each rule.

5. Limitations and strengths

In this study, a variety of machine learning algorithms were used on different feature sets, which is one of the strengths of the study. Furthermore, unlike the previous models, our model is capable of predicting adverse outcomes before pregnancy. With a low prevalence worldwide, pregnancy in women with lupus is a rare condition [8,14], so the small number of samples used to train and test the models is one of the weak points of our study. In this regard, it is recommended to use more data in future studies. In addition, our data were collected from two centers. Developing models based on a dataset that is collected from more diverse healthcare settings is also recommended. Additionally, we were unable to conduct an external validation study to confirm our model in other settings. Other evaluations are needed to confirm the external validity and safety [71,72] of this model in clinical practice.

6. Conclusion

It is essential to predict adverse pregnancy outcomes in women with SLE in order to minimize their risks. Application of artificial intelligence has a great potential in health care, especially in the field of gynecology and midwifery. Machine learning models can help improve the health of pregnant women by closely monitoring their health in order to reduce maternal and perinatal complications and mortality through early detection of these outcomes. According to the findings of our study, it can be concluded that the CHAID decision tree with appropriate input features, can prove to be a valuable tool in predicting pregnancy outcomes in women with SLE before pregnancy. Therefore, by using this decision tree to predict the outcome of pregnancy before planning pregnancy, providers can recommend patients the necessary advices about maternal risks for the better management of the condition.

CRediT authorship contribution statement

Khadijeh Paydar: Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Abbas Sheikhtaheri:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Ethics declaration

This study was reviewed and approved by the Research Ethics Committee at the Iran University of Medical Sciences with the approval number: IR.IUMS.REC.1398.978 dated 2019/12/16. The Research Ethics Committee at the Iran University of Medical Sciences waived informed consent because this study was conducted retrospectively based on reviewing patients' medical records.

Data availability statement

The patient data that has been used is confidential and not available publicly. The data can be requested from corresponding author based on reasonable request.

Funding

This study was financially supported by the Iran University of Medical Sciences (98-3-37-15724).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors sincerely appreciate the support provided by the personnel of the Rheumatology Research Center of Tehran University of Medical Sciences, the Shariati Hospital, and the specialized clinic for data collection. We also would like to thank Digital Health and Artificial Intelligence in Medicine Research Unit at Iran University of Medical Sciences.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2025.e42679.

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