Acute and Critical Care 2022 August 37(3):438-453
https://doi.org/10.4266/acc.2021.01501

Cardiopulmonary resuscitation of infants at birth: predictable or unpredictable?

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Background: Anticipating the need for at-birth cardiopulmonary resuscitation (CPR) in neonates is very important and complex. Timely identification and rapid CPR for neonates in the delivery room significantly reduce mortality and other neurological disabilities. The aim of this study was to create a prediction system for identifying the need for at-birth CPR in neonates based on Machine Learning (ML) algorithms.

Methods: In this study, 3,882 neonatal medical records were retrospectively reviewed. A total of 60 risk factors was extracted, and five ML algorithms of J48, Naïve Bayesian, multilayer perceptron, support vector machine (SVM), and random forest were compared to predict the need for at-birth CPR in neonates. Two types of resuscitation were considered: basic and advanced CPR. Using five feature selection algorithms, features were ranked based on importance, and important risk factors were identified using the ML algorithms.

Results: To predict the need for at-birth CPR in neonates, SVM using all risk factors reached 88.43% accuracy and F-measure of 88.4%, while J48 using only the four first important features reached 90.89% accuracy and F-measure of 90.9%. The most important risk factors were gestational age, delivery type, presentation, and mother's addiction.

Conclusions: The proposed system can be useful in predicting the need for CPR in neonates in the delivery room.

Key Words: cardiopulmonary resuscitation; data mining; feature selection; neonatal resuscitation; supervised learning

Original Article

Received: October 22, 2021
Revised: February 2, 2022
Accepted: February 17, 2022

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INTRODUCTION

Annually, around 1 million neonates worldwide die because of birth asphyxia [1]. According to the World Health Organization guideline on basic newborn resuscitation, although around one-fourth of neonatal mortality is due to birth asphyxia, effective cardiopulmonary resuscitation (CPR) at the moment of childbirth can prevent a large proportion approximately 30% of these deaths [2,3]. Most neonates enter from intrauterine to extrauterine life with no special assistance. However, less than 1% of all neonates [4] and around 0.1% of term neonates require advanced CPR at the moment of birth [5,6]. These statistics are much higher for preterm infants; 6%–7% of preterm neonates (gestational age [GA] <32 weeks) [7] and around 6%–10% of very low birth weight and extremely low birth weight infants require advanced CPR, i.e., chest compression with or without injecting epinephrine [8]. Many studies have been performed on CPR consequences, and mortality, neurological morbidity, neurodevelopmental impairment, lower motor scores, and retinopathy of prematurity (ROP) are more prevalent among preterm infants who have received CPR [7,9,10]. Thus, timely identification and rapid CPR of neonates in the delivery room can reduce neonatal mortality and morbidity [8].

Currently, at-birth CPR is suggested for neonates with asystole, profound bradycardia (heart rate <60 per minutes), and pulseless electrical activity despite effective ventilation. Absence of heart beat or other vital signs, which is recorded as zero APGAR (Appearance, Pulse, Grimace, Activity, Respiration), can also be used as a guideline for decision-making on beginning CPR [9]. Different studies have shown that the severity scoring systems have many limitations, and systems based on Machine Learning (ML) have better performance in prediction [11,12]. Accordingly, considering the importance of at-birth CPR, use of ML-based systems can be useful for anticipating the need for neonatal CPR. Application of ML algorithms in medicine, especially in neonatal medicine, has shown that these techniques have suitable performance in prediction and diagnosis.

Nevertheless, only a few studies have dealt with CPR in neonates, and most of these have a small set of samples and risk factors because of the challenges in data collection [13-17]. The aim of most studies is to identify the risk factors affecting the need for at-birth CPR [13,14,18-20]. Further, most studies have dealt with neonatal CPR in the Neonatal intensive care unit (NICU), although few of them have addressed at-birth CPR, due to examine at birth CPR, only antepartum factors should be considered. To the best of our knowledge, this is the first study on predicting the need for at-birth CPR in neonates using ML algorithms and considering a comprehensive set of maternal and prenatal risk factors. Accordingly, our aim is to design an ML-based clinical decision support system (CDSS) to predict the need for at-birth CPR in neonates based on maternal and fetal factors.

MATERIALS AND METHODS

This retrospective study was conducted based on maternal, prenatal, and fetal data, with the aim of predicting the need for at-birth general/basic/advanced CPR in neonates. To develop the prediction model, ML algorithms were used. Also, the models were evaluated to examine the performance and determine the best model. Details related to the data, setting, method of development, and evaluation of the prediction models are presented in this section. All participants' parents provided written consent before loading the data into the registry.

KEY MESSAGES

- In the delivery room, timely neonatal cardiopulmonary resuscitation (CPR) could significantly reduce mortality and other neurological disabilities.
- Use of Machine Learning-based systems for predicting the need for at-birth CPR can be useful.

Data Source

The data were obtained through a neonatal registry system in Valiasr Hospital affiliated to Tehran University of Medical Sciences (TUMS) includes the information related to all neonates hospitalized in the NICU of Valiasr Hospital that has a grade of B3. The data related to the mother and fetus are entered into the registry by the person in charge. In this retrospective study, the data available in this registry were retrieved anonymously from March 2016 to March 2020. Consent forms were filled out by the father or mother of the infant before entering the data into the registry. Participant data were considered confidential, and no extra cost was imposed on our participants. The study was approved by the TUMS institutional review board (approval ID: IR.TUMS.VCR.REC.1398.591).

Identification of Neonatal CPR Risk Factors

Risk factors are identified according to the sixth edition of the *Textbook of neonatal resuscitation* [21] and the International Liaison Committee on Resuscitation (ILCOR) guidelines [22]. Three neonatologists were asked to review the list of risk

factors and add any factors not listed. Infertility information, sex, and delivery order of any appropriate infant in multiple gestation were added. According to experts' opinions, some variables (such as fetal problems and maternal chronic disease) were divided into smaller and more specialized subclasses. However, several identified risk factors were not recorded in the neonatal registry of Valisasr Hospital and were excluded. Figure 1 shows the process of risk factor identification.

Inclusion and Exclusion Criteria

All neonates hospitalized in the NICU from March 2016 to March 2020 were included in this study. Post-delivery data such as APGAR score, height, and weight of the neonate were excluded.

Definition

In this study, delivery room CPR and CPR immediately after birth were examined. CPR refers to any activity performed to simulate the cardiorespiratory activity of neonates who met the conditions of CPR according to the American Academy of Pediatrics (AAP) guidelines [23,24]. These activities can be categorized into two groups: basic CPR (use of oxygen mask, nasal continuous positive airway pressure (CPAP), and positive pressure ventilation (PPV) and advanced CPR (basic CPR plus epinephrine injection, chest compression, and intubation) [25]. In this study, basic, advanced, and general CPR were considered separately. The neonatal CPR protocol used in Iran is the newest version of the neonatal resuscitation program (NRP) developed by the AAP and the American Heart Association in 2020 [26]. Currently, the Ministry of Health is in charge of issuing NRP certificates. In our NICU, CPR procedures are performed by neonatologists, pediatric residents (second-year residents onwards), or neonatology fellows with NRP certification.

Steroid administration is considered the use of any type of fluorinated corticosteroid. Chorioamnionitis is defined by a maternal inflammatory response with neutrophilic infiltration of the chorionic plate or membranes with or without fetal inflammatory response [27]. Prenatal care adequacy is defined on the basis of the Kotelchuck Index [28]. Levels of "inadequate" and "intermediate" are considered as "no" outcomes, and "adequate" and "adequate plus" levels as "yes" results in the dataset used in this study.

Data Extraction and Preprocessing

After removing all identifiers, the data were extracted from the registry as a .sav file and classified into one of six groups: (1) Gestational risk factors: prenatal care, chorioamnionitis, steroid administration, and magnesium sulfate administration; (2) Maternal risk factors: age, hypertension (chronic, gestational, eclampsia), diabetes (chronic, gestational), addiction, human immunodeficiency virus (HIV), chronic disease history, history of abortion (less than 20 weeks), and intrauterine fetal death; (3) Female infertility: use of assisted reproductive techniques (ART), type of ART; (4) Accreta status: decollement/placenta abruption, vasa previa, previa, placenta accreta; (5) Fetal data: gender, GA, rank, and number of infants; intrauterine growth restriction; congenital problems diagnosed before birth; fetal hydrops; (6) Delivery risk factors: mode of delivery, prelabor rupture of membranes (PRoM), duration of PRoM, presentation, cord status, thick meconium, amniotic fluid status, and fetal heart rate during delivery.

The outcome variable is whether CPR is performed for a baby in the delivery room. The general, basic, and advanced resuscitation levels are considered separately as outcomes. The data set contained approximately 7% missing values, which were imputed by the multiple imputation method.

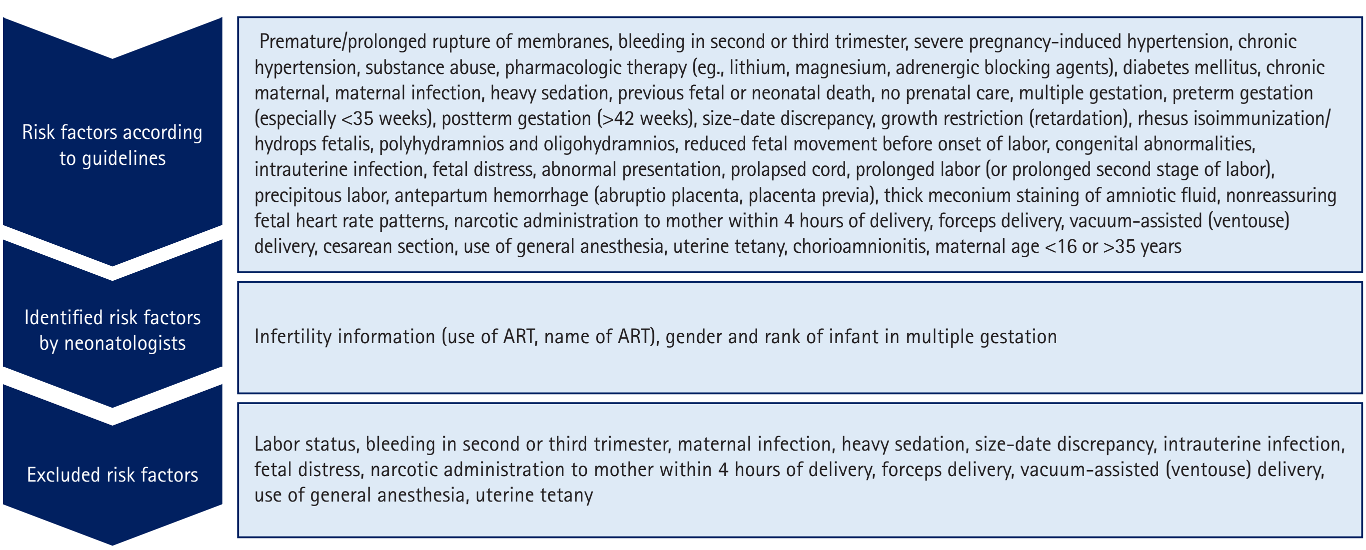

Figure 1. Identification of the neonatal cardiopulmonary resuscitation risk factors. ART: assisted reproductive techniques.

Prediction Model Construction

When a study is associated with a large number of interdependent factors and there is a need to categorize records into two classes, one of the simplest and most effective methods is the binary classifier [29]. Therefore, to develop the prediction model for the need for at-birth general/basic/advanced CPR, ML algorithms of J48, multilayer perceptron, support vector machine (SVM), Naïve Bayesian (NB) and random forest were used. All algorithms were performed with the original data set. Next, Feature Selection (FS) techniques were used to determine the importance of each attribute in predicting type of CPR. As a result, only relevant attributes were involved in the data mining process, which improved predictive accuracy and reduced processing time. For this purpose, filter FS algorithms including relief and correlation-based feature selection (CFS) and wrapper methods using classifiers SVM, J48, and NB were used (Table 1). These methods consider feature dependencies as well as predictive ability of attributes. As a result, feature subsets with less inter-correlation but high correlation to the outcome are preferred [30-33]. Then, the risk factors were organized based on the total importance resulting from implementing the five FS algorithms. Based on the ordered list of variables, various data subsets were created, and ML algorithms were implemented on both the original data set and these data subsets.

Statistical Analysis and Performance Measurements

For continuous data, mean, range, and standard deviation were reported, while frequency and percentage were reported for discrete data. To investigate the distribution of variables in the two groups (neonates receiving CPR vs. those not receiving CPR), independent samples t-test, chi-square, Fisher exact, and Mann-Whitney tests were used. The significance levels for all tests were set at $P<0.05$. All statistical analyses were performed using IBM SPSS ver. 20.0 (IBM Corp., Armonk, NY, USA). After analyzing the role of risk factors in predicting the outcome and developing the prediction models for need for at-birth general/basic/advanced CPR, the performance of the developed models was evaluated based on accuracy, precision, sensitivity, specificity, and F-measure criteria as well as the 10-fold cross validation method. The role of variables was analyzed using the FS algorithms in WEKA software. Development and assessment of models were performed using R v3.4.1 (R Foundation, Vienna, Austria).

Clinical Decision Support System Design

After selecting the best algorithm for predicting the need for delivery room CPR in neonates, the system user interface was designed based on the best prediction model for the need for at-birth CPR in Visual Studio platform 2015.

RESULTS

A total of 3,882 infants with an average birth weight of 2,500.81 g (standard deviation [SD], 889.107 g; range, 400–5,250 g) was included in the study according to the inclusion/exclusion criteria (Figure 2). Of these, 2,011 (51.8%) received delivery room CPR. Overall, 1,909 infants (49.18%) received basic CPR, and 510 (13.14%) received advanced CPR. The frequency of

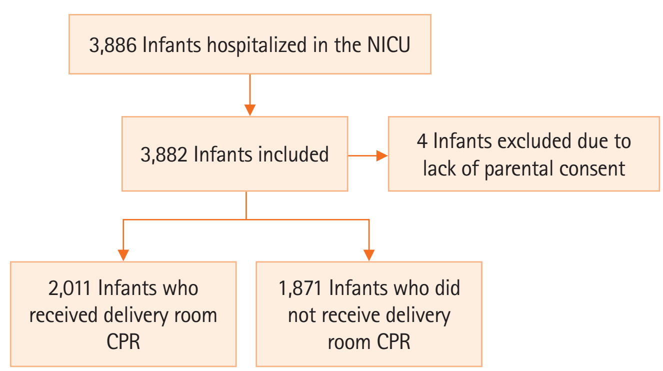

Figure 2. Flowchart of patient selection. NICU: neonatal intensive care unit; CPR: cardiopulmonary resuscitation.

Table 1. Characteristics of FS methods

Type of FS method	Evaluation algorithm	Weka class name	Parameters tuning
Filter	Attribute evaluation using relief	ReliefFAttributeEval	
	Correlation-based feature selection evaluation	CfsSubsetEval	
Wrapper	Subset evaluation by using a user-specified classifier and separate held-out test set	ClassifierSubsetEval	Classifier=SVM
	Subset evaluation by using a user-specified classifier and internal cross-validation	WrapperSubsetEval-weka.classifiers.trees.J48	Classifier=J48
	Subset evaluation by using a user-specified classifier and internal cross-validation	WrapperSubsetEval-weka.classifiers.bayes.NaiveBayes	Classifier=NB

FS: feature selection; SVM: support vector machine; NB: Naïve Bayesian.

CPR types was as follows: nasal CPAP (n=1,120, p=28.8%), PPV (n=891, p=22.9%), oxygen mask (n=723, p=18.6%), intubation (n=494, p=12.7%), chest compression (n=86, p=2.2%), and epinephrine injection (n=68, p=1.7%). Data are shown in Table 2.

To develop a prediction model for need for at-birth general/basic/advanced CPR, ML algorithms were used. The results obtained from applying these algorithms to the original data set are shown in Figure 3. Based on all performance criteria, the SVM method demonstrated the best performance for predicting the need for at-birth general and basic CPR (Figure 3A and B). The J48 method demonstrated comparable results. As in Figure 3C, the performance of the J48 technique was better than that of the other models in predicting advanced CPR. However, the NB method had the highest specificity.

In the next step of simulation, FS algorithms were employed. For this, the two filter FS algorithms of relief and CFS were implemented with the three wrapper methods of SVM, J48, and NB. Then, for each risk factor, the total importance resulting from implementing the five FS algorithms was calculated. The rank resulting from the FS algorithms as well as the average rank for each attribute in predicting the types of CPR are presented in Table 3. The average rank was calculated using the following relation, where r_i represents the rank of variable in the i^{th} feature selection algorithm.

Average rank: $(r_1+r_2+\ldots+r_5)/5$

According to Table 3, GA is the most important risk factor for predicting all types of CPR. Also, the average ranks of "maternal kidney disease," "thyroid disorders," and "decollement/placenta abruption" were lowest in predicting general, basic, and advanced CPR, respectively. For each type of resuscitation, the variables were sorted based on average rank, and then 20 feature subsets were created, including 1, 2, ...,10, 15, 20, 25, 30, 35, 40, 45, 50, 55, and 60 important variables, respectively. In other words, the first group included the most important feature, the second one included the two most important features and so on. According to these subsets, 20 data subsets were created, and ML algorithms were implemented on these data subsets. Each time, one type of CPR was considered as the outcome. Figures 4 and 5 reveal the results of the ML algorithms with the 20 data subsets obtained from FS.

According to Figures 4 and 5, J48 using the four first important variables with an accuracy of 90.89% and an F-measure of 90.9% produced the best results. GA, delivery type, presentation, and maternal addiction were the most important features in general CPR prediction. J48 also achieved the best results in predicting basic CPR on the basis of the 10 most significant variables: GA, delivery type, prenatal care, decollement, addiction, amniotic fluid, other chronic diseases, macrosomia, infant rank, and fetal hydrops. To predict the need for advanced CPR, J48 achieved the best accuracy of 90.97% using the six most important variables: GA, infertility, gestational diabetes, kidney diseases, HIV, and PRoM. However, according to F-measure, the NB method with the three variables of GA, infertility, and gestational diabetes had the best performance. Given that only 510 infants received advanced resuscitation, the data subsets were unbalanced. Therefore, the SVM method can categorize all items in the majority group (non-CPR), and the value of the F-measure could not be calculated (Figure 5C).

The best results of every algorithm are shown in Table 4. Comparing the results shown in Figure 3 and Table 4, we found that use of the FS algorithms in general CPR prediction caused 4.88% increased accuracy and 5.12% increased F-measure on average. Further, the use of the FS method in basic and advanced CPR prediction models increased mean accuracy by 3.05% and 3.34%, respectively, and mean F-measure by 1.49% and 1.26%.

Graphical user interface of the proposed CDSS for CPR prediction was designed in Visual Studio 2015, based on the three best models which were developed on the basis of J48 (Figure 6). After entering the data, all three prediction models (general/basic/advanced CPR prediction models) were executed, and the final output was calculated by OR combination of the output of each model.

DISCUSSION

This paper dealt with a prediction system for the need for neonatal CPR immediately after birth in the delivery room. To achieve a system with proper performance, various ML algorithms were compared with different sets of risk factors to identify the best system and the most effective factors for predicting type of CPR. According to the obtained results, to predict the need for at-birth CPR in general, SVM using all risk factors reached an accuracy of 88.43% and an F-measure of 88.4%, while J48 using the first four most important variables reached an accuracy of 90.89% and an F- measure of 90.9%. For basic CPR prediction, the highest accuracy and F-measure were achieved for the SVM model at 87.64% and 87.4%, respectively. After applying the FS methods and selecting the 10 most important features, the best fit model was J48, with an accuracy of 88.92% and an F-measure of 88.9%. Among the

Table 2. Descriptive statistics of risk factors

Variable	Total (n=3,882)	CPR (n=2,011)	Non-CPR (n=1,871)	P-value (CPR vs. non-CPR group)
Gestational risk factor				
Prenatal care	3,426 (88.25)	1,837	1,589	<0.001
Chorioamnionitis	71 (1.83)	37	34	0.958
Steroid administration	933 (24.03)	647	286	<0.001
Magnesium sulfate administration	333 (8.58)	238	95	<0.001
Maternal risk factor				
Hypertension	184 (4.74)	113	71	0.008
Gestational hypertension	654 (16.85)	379	275	0.001
Diabetes	105 (2.71)	53	52	0.783
Gestational diabetes	600 (15.46)	317	283	0.583
Mother addiction	63 (1.62)	22	41	0.007
Mother HIV	28 (0.72)	14	14	0.848
Cardiac disease	304 (7.83)	142	162	0.064
Blood disease	187 (4.82)	98	89	0.866
Kidney disease	63 (1.62)	33	30	0.926
Thyroid disorders				0.274
Hyperthyroidism	15 (0.39)	8	7	
Hypothyroidism	694 (17.88)	344	350	
Thyroidectomy	2 (0.05)	0	2	
Respiratory disease	28 (0.72)	15	13	0.851
Mental disease	21 (0.54)	11	10	0.958
Infectious disease	16 (0.41)	8	8	0.885
Brain diseases	62 (1.6)	37	25	0.211
Cancer disease	33 (0.85)	19	14	0.505
Skin disease	7 (0.18)	3	4	0.635
Liver disease	63 (1.62)	32	31	0.872
Autoimmune disease	64 (1.65)	32	32	0.771
Uterus disease	41 (1.06)	23	18	0.580
Digestive disease	34 (0.88)	15	19	0.368
Eye disease	4 (0.10)	2	2	0.942
Other chronic disease	12 (0.31)	9	3	0.107
Pre-eclampsia				0.192
Eclampsia	8 (0.21)	4	4	
Preeclampsia	198 (5.10)	115	83	
Abortion history	17 (0.44)	9	8	0.925
Intrauterine fetal death Infertility	10 (0.26)	3	7	0.167
Female infertility	214 (5.51)	146	68	<0.001
ART	144 (3.71)	94	50	0.001
Drug	26 (0.67)	23	3	<0.001
IUI	18 (0.46)	9	9	
IVF	100 (2.58)	62	38	
Accreta status				
Decollement/placenta abruption	41 (1.06)	28	13	0.034
Vasa previa	1 (0.03)	1	0	0.335
Previa	113 (2.91)	62	51	0.508
Placenta accreta	163 (4.2)	94	69	0.126
Fetal data				
Number of infants				<0.001
1	3,407 (87.76)	1,678	1,729	
2	419 (10.79)	293	126	
3	55 (1.42)	39	16	
4	1 (0.03)	1	0	
Sex				0.396
Female	1,730 (44.57)	881	849	

(Continued to the next page)

Table 2. Continued

Variable	Total (n=3,882)	CPR (n=2,011)	Non-CPR (n=1,871)	P-value (CPR vs. non-CPR group)
Male	2,146 (55.28)	1,128	1,018	
Ambiguous genitalia	6 (0.15)	2	4	
Rank of infant				<0.001
1	3,628 (93.46)	1,838	1,790	
2	235 (6.05)	160	75	
3	19 (0.49)	13	6	
IUGR	223 (5.75)	134	89	0.011
Tumor	14 (0.36)	8	6	0.689
Genetic problems/anomaly	18 (0.46)	13	5	0.082
Macrosomia	19 (0.49)	3	16	0.002
Cardiac problem	31 (0.8)	16	15	0.983
Surgery (defect of the abdominal)	54[a] (1.39)	24	30	0.276
Blood problem	4 (0.10)	2	2	0.942
Pulmonary problem	12 (0.31)	9	3	0.107
Brain problem	25 (0.64)	13	12	0.984
Fetal hydrops	12 (0.31)	10	2	0.029
Other problem (fetus)	6 (0.15)	3	3	0.930
Delivery risk factor				
Delivery type				<0.001
Cesarean	3,617 (93.17)	1,923	1,694	
Vaginal	265 (6.83)	88	177	
PRoM	549 (14.14)	304	245	0.071
Presentation				0.073
Breech	106 (2.73)	42	64	
Transverse	6 (0.15)	2	4	
Hand	1 (0.03)	1	0	
Normal	3,769 (97.09)	1,966	1,803	
Cord				0.240
Absent Doppler	27 (0.69)	18	9	
Cord prolapse	4 (0.10)	3	1	
Reverse	1 (0.03)	1	0	
No	3,850 (99.18)	1,989	1,861	
Thick meconium	24 (0.62)	16	8	0.144
Amniotic fluid				0.041
Oligohydramnios	43 (1.11)	18	25	
Polyhydramnios	26 (0.67)	8	18	
Normal	3,813 (98.22)	1,985	1,828	
Fetal heart condition				0.395
Arrhythmia	1 (0.03)	0	1	
BPP	2 (0.05)	1	1	
Bradycardia	6 (0.15)	5	1	
Tachycardia	10 (0.26)	5	5	
Decreased FHR	269 (6.93)	148	121	
Fetal distress	8 (0.21)	6	2	
Sinusoidal	1 (0.03)	1	0	
PVC	1 (0.03)	1	0	
No	3,584 (92.31)	1,844	1,740	
Continuous risk factor				
Maternal age (yr)	30.89±5.9	30.85±3.81	30.94±3.68	0.474
Gestational age (day)	247.15±25.17	237.19 ±26.35	257.85 ±18.38	<0.001
PRoM (hr)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	<0.001

Values are presented as number (%), mean±standard deviation (range), or median (interquartile range).

CPR: cardiopulmonary resuscitation; HIV: human immunodeficiency virus; ART: assisted reproductive technique; IUI: intrauterine insemination; IVF: *in vitro* fertilization; IUGR: intrauterine growth restriction; PRoM: prelabor rupture of membranes; BPP: biophysical profile; FHR: fetal heart rate; PVC: premature ventricular contraction.

[a]Including colonic atresia, diaphragmatic hernia, duodenal atresia, esophageal atresia, gastroschisis, internal hernia, intestinal atresia, jejunal atresia, omphalocele.

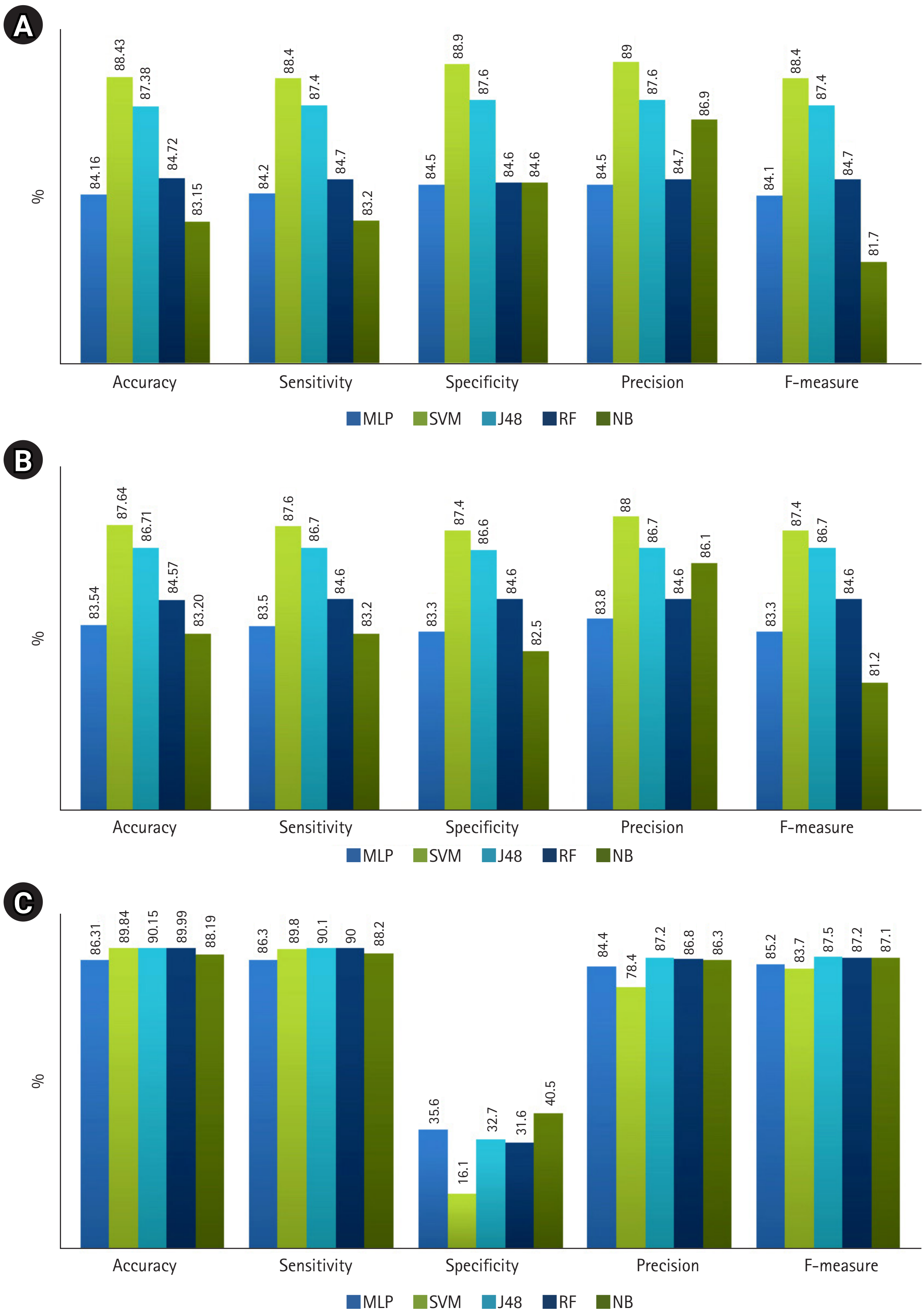

Figure 3. Performance metrics of Machine Learning algorithms for original dataset. (A) At-birth cardiopulmonary resuscitation (CPR) prediction in general, (B) at-birth basic CPR prediction, (C) at-birth advanced CPR prediction. MLP: multilayer perceptron; SVM: support vector machine; RF: random forest; NB: Naïve Bayesian.

Table 3. Rank of attributes based on five feature selection methods

No.	Variable name	General CPR						Basic CPR						Advanced CPR					
		Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank	Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank	Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank
1	Abortion	30	43	48	13	10	28.8	48	48	50	36	19	40.2	55	45	53	17	11	36.2
2	Addiction	12	12	7	14	19	12.8	10	16	26	17	20	17.8	27	53	2	15	24	24.2
3	Amniotic fluid	17	10	8	42	27	20.8	15	11	47	18	3	18.8	30	24	38	31	31	30.8
4	ART name	23	22	49	50	47	38.2	16	30	13	44	34	27.4	18	23	4	55	52	30.4
5	ART use	37	59	16	56	30	39.6	33	59	10	56	26	36.8	17	56	6	56	42	35.4
6	Autoimmune	60	55	51	35	29	46	59	52	58	40	23	46.4	38	39	39	33	48	39.4
7	Blood diseases	18	47	38	36	34	34.6	57	46	53	19	29	40.8	23	37	5	8	54	25.4
8	Blood problems	43	37	45	22	12	31.8	46	26	39	26	11	29.6	48	14	46	16	20	28.8
9	Brain diseases	56	33	12	9	43	30.6	20	51	49	24	32	35.2	28	46	11	28	34	29.4
10	Brain problem	46	42	56	23	40	41.4	42	28	42	7	33	30.4	43	26	42	47	36	38.8
11	Cancer	35	38	23	38	49	36.6	34	41	29	37	53	38.8	33	17	30	3	25	21.6
12	Cardiac diseases	14	24	11	52	51	30.4	17	23	25	43	41	29.8	4	7	7	53	49	24.0
13	Cardiac problems	36	54	52	24	37	40.6	35	47	41	28	44	39	41	50	36	30	17	34.8
14	Chorioamnionitis	15	58	53	27	26	35.8	12	45	28	9	17	22.2	29	10	24	24	35	24.4
15	Cord	39	19	28	51	16	30.6	32	14	18	51	24	27.8	35	6	47	37	29	30.8
16	Decollement/placenta abruption	27	11	31	4	14	17.4	28	21	17	4	14	16.8	45	42	60	44	45	47.2
17	Delivery type	5	4	4	2	2	3.4	3	4	12	2	2	4.6	10	44	58	27	51	38.0
18	Diabetes	55	56	57	15	18	40.2	18	50	51	16	42	35.4	22	51	29	5	53	32.0
19	Digestive diseases	38	41	24	29	33	33	29	36	45	15	30	31	54	43	51	20	19	37.4
20	Pre-eclampsia	54	29	42	16	58	39.8	54	34	19	35	57	39.8	12	8	50	19	56	29.0
21	Eye diseases	33	32	37	12	7	24.2	38	38	44	21	8	29.8	53	16	48	11	6	26.8
22	FHR	44	8	54	54	54	42.8	44	10	23	50	36	32.6	11	12	44	29	33	25.8
23	GA	1	1	1	1	1	1	1	1	1	1	1	1	1	1	19	1	1	4.6
24	Gestational diabetes	7	51	18	44	56	35.2	7	58	59	32	48	40.8	2	5	28	35	28	19.6
25	Genetic problems/ anomaly	26	36	33	11	25	26.2	24	20	20	27	35	25.2	36	47	34	34	13	32.8
26	Gestational hyperten- sion	9	14	25	10	59	23.4	13	17	6	54	58	29.6	7	31	26	21	60	29.0
27	HIV	58	45	50	20	28	40.2	55	49	57	13	21	39	34	38	3	23	7	21.0
28	Hydrops Fetal	32	16	21	6	15	18	36	15	21	10	27	21.8	56	33	9	41	38	35.4
29	Hypertension	16	17	17	40	57	29.4	49	22	9	48	51	35.8	16	52	25	26	44	32.6
30	Infant number	8	3	5	58	45	23.8	5	3	3	58	46	23	15	58	22	60	32	37.4
31	Infant rank	11	15	15	59	31	26.2	9	12	5	59	22	21.4	25	59	18	58	37	39.4
32	Infectious diseases	47	35	40	19	5	29.2	25	37	27	20	12	24.2	58	28	10	13	21	26.0
33	Infertility	13	13	19	57	48	30	14	6	7	57	37	24.2	21	3	15	2	2	8.6
34	IUFD	48	21	10	30	9	23.6	50	24	37	38	10	31.8	50	11	55	14	8	27.6
35	IUGR	20	30	14	41	38	28.6	22	35	11	47	49	32.8	19	22	1	52	47	28.2

(Continued to the next page)

Table 3. Continued

No.	Variable name	General CPR						Basic CPR						Advanced CPR					
		Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank	Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank	Relief	CFS	Wrapper (SVM)	Wrapper (NB)	Wrapper (J48)	Averaged rank
36	Kidney diseases	52	50	58	39	50	49.8	40	54	56	41	28	43.8	37	35	8	12	12	20.8
37	Liver diseases	45	46	59	32	17	39.8	27	33	43	39	25	33.4	44	29	32	32	40	35.4
38	Macrosomia	22	18	9	3	24	15.2	19	13	32	3	31	19.6	39	21	33	4	18	23.0
39	Magnesium sulfate	3	5	60	55	46	33.8	21	5	4	55	56	28.2	26	2	21	59	58	33.2
40	Maternal age	21	60	22	53	22	35.6	11	60	33	53	38	39	13	57	56	9	30	33.0
41	Mental diseases	57	52	43	8	29	37.8	56	43	40	6	18	32.6	60	32	12	40	3	29.4
42	Other chronic diseases (mother)	29	23	32	5	6	19	31	19	24	8	13	19	49	19	57	6	15	29.2
43	Other problems (fetus)	49	48	47	34	11	37.8	51	57	46	31	9	38.8	57	25	45	18	10	31.0
44	Placenta accreta	51	31	26	28	36	34.4	58	29	15	30	47	35.8	14	54	49	46	57	44.0
45	Prenatal care	6	6	3	47	39	20.2	4	8	8	11	45	15.2	3	15	23	43	46	26.0
46	Presentation	10	7	6	17	8	9.6	6	9	52	42	4	22.6	20	9	41	25	41	27.2
47	Previa	25	53	39	45	32	38.8	26	56	31	46	50	41.8	24	41	54	48	50	43.4
48	PRoM	24	57	20	49	52	40.4	23	55	14	45	54	38.2	5	55	17	7	23	21.4
49	PRoM (hr)	50	9	30	60	44	38.6	45	7	16	60	40	33.6	52	60	16	54	4	37.2
50	Pulmonary problems	34	26	35	31	35	32.2	39	27	22	29	43	32	42	40	43	42	26	38.6
51	Respiratory diseases	42	44	41	21	41	37.8	52	44	48	23	39	41.2	40	20	14	36	14	24.8
52	Sex	4	28	46	43	55	35.2	8	31	60	33	59	38.2	6	30	20	39	43	27.6
53	Skin diseases	53	49	36	25	3	33.2	53	53	35	34	6	36.2	59	48	31	10	5	30.6
54	Steroids administration	2	2	2	46	60	22.4	2	2	2	52	55	22.6	8	13	27	57	55	32.0
55	Surgery	28	34	13	18	23	23.2	30	32	38	5	7	22.4	32	4	37	51	39	32.6
56	Thick meconium	31	25	29	37	21	28.6	37	40	34	14	16	28.2	47	36	40	45	27	39.0
57	Thyroid disorders	19	20	55	48	53	39	60	18	54	49	60	48.2	9	18	13	50	59	29.8
58	Tumors	40	40	44	26	13	32.6	41	39	55	22	15	34.4	46	34	35	49	16	36.0
59	Uterus diseases	59	39	34	33	42	41.4	43	42	30	25	52	38.4	31	49	52	22	22	35.2
60	Vasa previa	41	27	27	7	4	21.2	47	25	36	12	5	25	51	27	59	38	9	36.8

CPR: cardiopulmonary resuscitation; CFS: correlation-based feature selection; SVM: support vector machine; NB: Naïve Bayesian; ART: assisted reproductive techniques; FHR: fetal heart rate; GA: gestational age; HIV: human immunodeficiency virus; IUFD: intrauterine fetal death; IUGR: intrauterine growth restriction; PRoM: prelabor rupture of membranes.

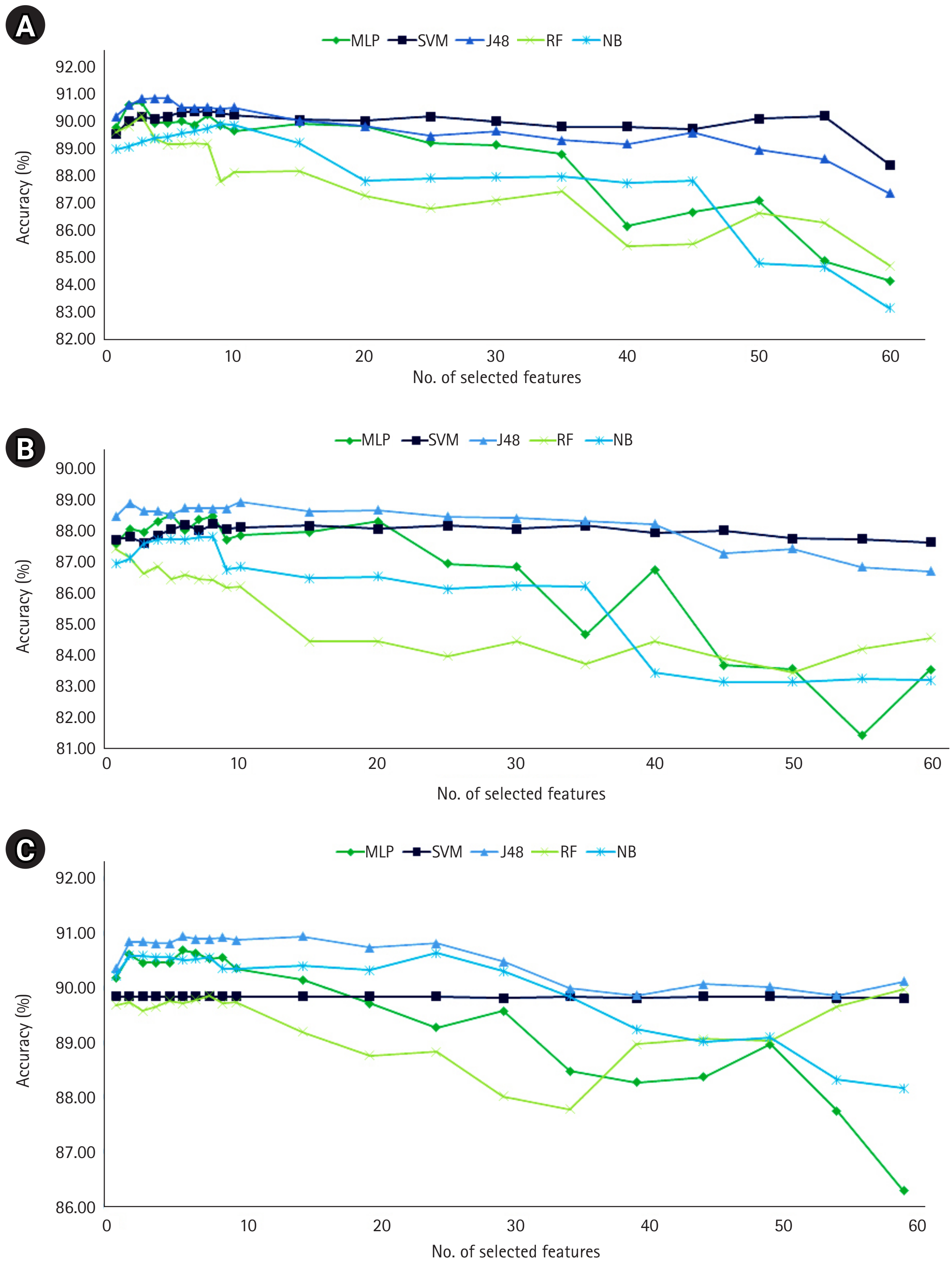

Figure 4. Accuracy of Machine Learning algorithms for 20 feature subsets. (A) At-birth cardiopulmonary resuscitation (CPR) prediction in general, (B) at-birth basic CPR prediction, (C) at-birth advanced CPR prediction. MLP: multilayer perceptron; SVM: support vector machine; RF: random forest; NB: Naïve Bayesian.

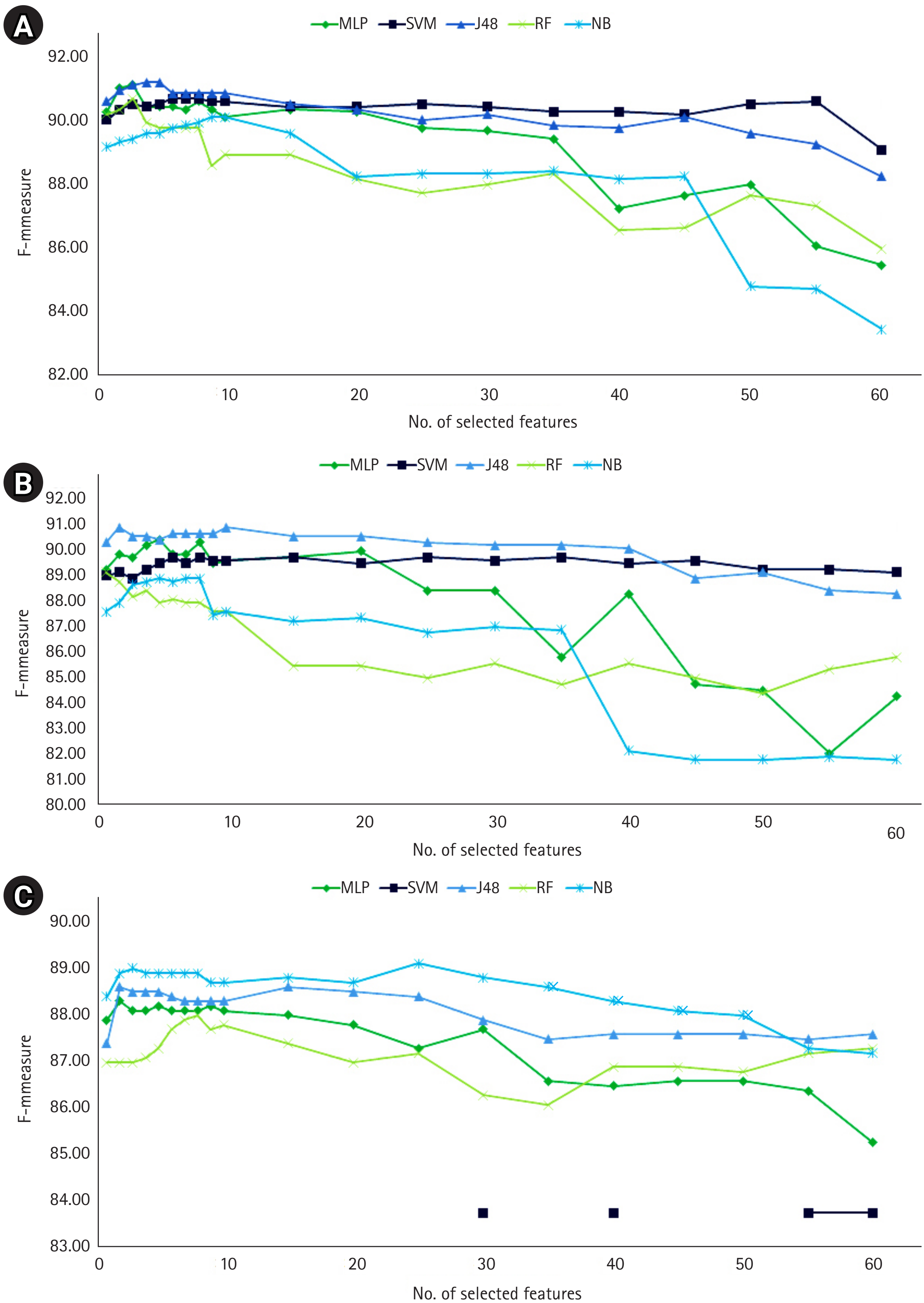

Figure 5. F-measure of Machine Learning algorithms for 20 feature subsets. (A) At-birth cardiopulmonary resuscitation (CPR) prediction in general, (B) at-birth basic CPR prediction, (C) at-birth advanced CPR prediction. MLP: multilayer perceptron; SVM: support vector machine; RF: random forest; NB: Naïve Bayesian.

Table 4. The best performance of each ML methods on various feature subsets

ML method	General CPR			Basic CPR			Advanced CPR		
	Accuracy	F-measure	Number of selected features	Accuracy	F-measure	Number of selected features	Accuracy	F-measure	Number of selected features
MLP	90.76	90.8	3	88.51	88.5	5	90.71	88.2	6, 2[a]
J48	90.89	90.9	4	88.92	88.9	10	90.97	88.5	6, 2[a]
RF	90.24	90.3	3	87.43	87.4	1	89.76	87.7	10
SVM	90.42	90.3	8	88.23	87.9	8	89.86	83.7	1, 30[a]
NB	89.93	89.6	9	87.82	87.2	7	90.61	88.9	3

ML: Machine Learning; CPR: cardiopulmonary resuscitation; MLP: multilayer perceptron; RF: random forest; SVM: support vector machine; NB: Naïve Bayesian.
[a]Number of selected features to obtain the best F-measure value.

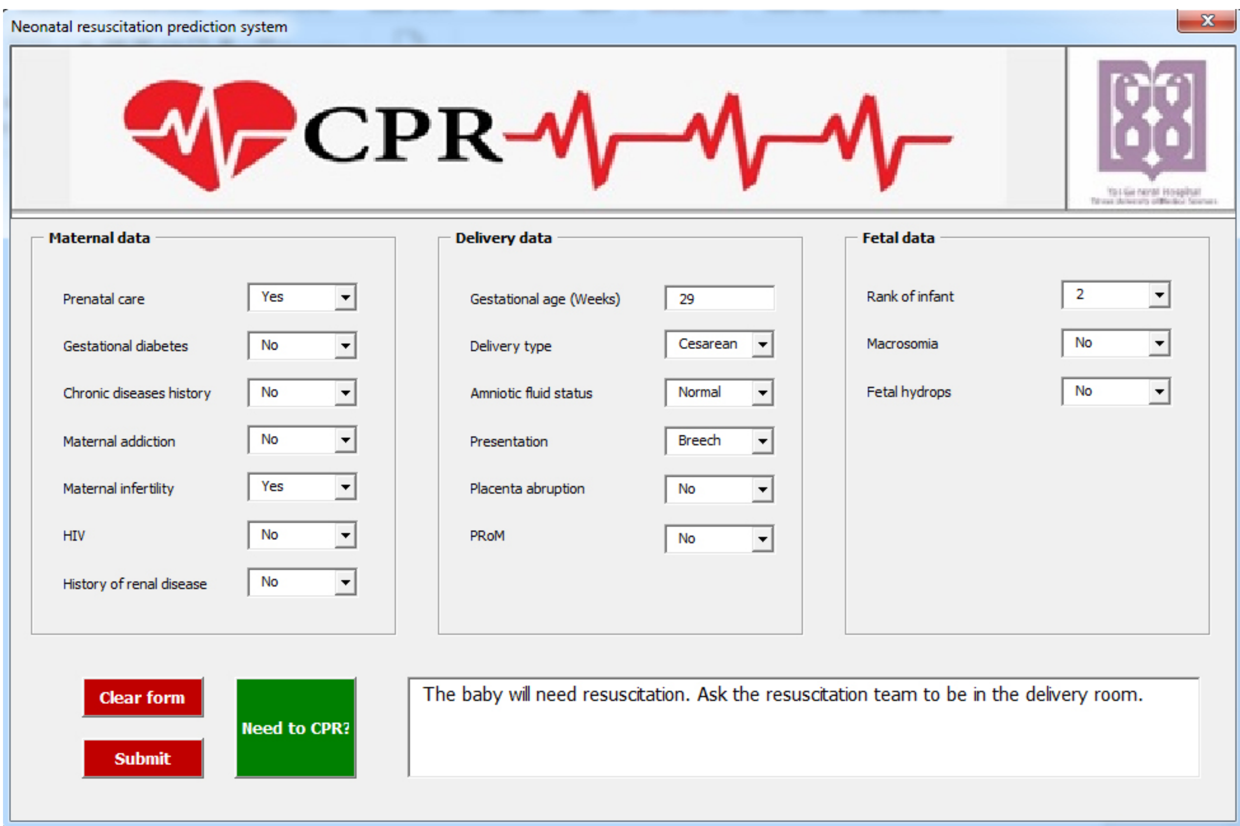

Figure 6. User interface of the proposed system. CPR: cardiopulmonary resuscitation.

ML algorithms, the best model to predict advanced CPR was J48, with an accuracy of 90.15% and an F-measure of 87.5%. According to the experiment performed on the six most important features, J48 had the highest accuracy of 90.89%, while NB using the three most significant features achieved the best performance with an F-measure of 88.9%.

Feature ranking was performed using five FS algorithms, and the most effective risk factors were identified for the general/basic/advanced CPR prediction. Among all variables, only GA was significant in all types of CPR prediction models. Delivery type, presentation, and addiction are other important factors in general CPR prediction. Also, the most significant risk factors of basic CPR prediction were GA, delivery type, prenatal care, placental abruption, mother's addiction, amniotic fluid status, maternal chronic disease history, macrosomia, rank of infant, and fetal hydrops. Moreover, GA, infertility, gestational diabetes, history of kidney disease, HIV, and PRoM were the most important risk factors for predicting the need for advanced CPR.

According to the sixth edition of the *Textbook of neonatal resuscitation* [21] and the ILCOR guidelines [22], the risk factors of GA, delivery type, presentation, macrosomia, prenatal care, PRoM, history of kidney disease, multiple gestation, fetal hydrops, amniotic fluid status, diabetes, placental abruption, and maternal chronic disease history all can contribute to an increased need for at-birth CPR in neonates. In a study by Afjeh et al. [18], risk factors affecting CPR in neonates were examined, whereby placental abruption, multiple gestation, delivery type, and infertility were identified as the risk factors that contribute to increasing the need for delivery room CPR. Also, a study by Jiang et al. found that diabetes, hypertension, and delivery type affect the need for CPR in neonates [19]. In our study, HIV was identified as an effective risk factor in predicting advanced CPR. To the best of our knowledge, the association between maternal HIV infection and need for neonatal CPR has not previously been reported. However, many previous studies have shown that maternal HIV infection is associated with small for gestational age, preterm birth, low birth weight, and stillbirth [34-37]. Our results revealed that macrosomia is one of the most important risk factors for predicting the need for basic resuscitation. However, while association between macrosomia and CPR was not found in the literature, previous studies showed that macrosomia is associated with shoulder dystocia, perinatal asphyxia, diabetes or gestational diabetes, and prolonged labor [38,39], factors that all play vital roles in increasing the need for at-birth resuscitation risk.

The prevalence of mortality, neurodevelopmental impairment, respiratory support at 28 days, days to full oral feeds, and length of stay are very high among neonates who have undergone at-birth CPR [9,40]. Even the National Institute of Child Health and Developmental Neonatal Research reported that CPR in the delivery room is a prognostic factor for morbidity and later complications up to 18 months of age [41]. Thus, the healthcare system should be able to better predict which neonates require CPR before delivery, so that the neonatal resuscitation team is present in time [42]. Previous studies have shown that antenatal transfer of high-risk mothers reduces pre-discharge neonatal mortality [43,44]. Thus, predicting the need for at-birth CPR can be very effective, as it increases the preparation of the neonatal resuscitation team and provides the possibility of consultation with the family before delivery [42]. Therefore, according to the results obtained from this study, use of the proposed system for predicting the need for at-birth CPR in neonates will greatly reduce the adverse outcomes in childbirth with more preparation time for the CPR team.

In addition, coordination between the CPR team and obstetricians can lead to reduced adverse events in the delivery room and improve overall care [42]. A study by Draper et al. [45] examined intrapartum deaths in the UK and found that around 25% of mortalities were due to lack of suitable communication between the multidisciplinary team members during delivery. Thus, the proposed system can be used as an infant pre-resuscitation guide to ensure coordination between the CPR team and obstetricians.

Despite the importance of CPR prediction, very few studies have dealt with neonatal CPR, most of which have addressed CPR in the NICU [13-16], which have small numbers of samples and few risk factors because of challenges in data collection [13-17]. However, in this study, in addition to considering a sample of suitable size, attempts were made to capture all fetal and maternal risk factors mentioned in credible guidelines, which also had demonstrated their importance in previous studies.

The main limitation of this study, like most previous studies, was that the data related to only one center were examined. Thus, it is suggested to conduct studies with a more diverse sample extracted from multiple centers with different grades of NICU. Comparison of the results can be useful in identifying significant risk factors affecting the need for CPR and its prediction. Also, the included population was all neonates hospitalized in the NICU, which is a very selective high-risk group of neonates who had a very high incidence of resuscitation. This limited the generalizability of this dataset to the usual situation in the delivery room.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

This study was supported by Tehran University of Medical Sciences (TUMS) and Maternal, Fetal and Neonatal Research Center. We acknowledge their kind supports in this study.

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