

# Factors Associated with Macrosomia among Singleton Live-births: A Comparison between Logistic Regression, Random Forest and Artificial Neural Network Methods

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**DOI:** 10.2427/11985

Accepted on October 10, 2016

## ABSTRACT

**Background:** Macrosomia is caused by several risk factors with adverse outcomes for mothers and infants. Classification methods used to determine high-risk groups for macrosomia include logistic regression (LR), random forest (RF) and an artificial neural network (ANN).

**Methods:** We conducted this cross-sectional study on 4342 pregnant women with singleton live-births in Tehran, Iran, during July 6-21, 2015. The above mentioned methods were compared in terms of sensitivity (SE), specificity (SP) and accuracy (ACC). Cochran-Q and McNemar's tests checked for differences in proportion among the methods. We calculated the kappa statistic to assess the association between observed and predicted values.

**Results:** Body mass index (BMI), socioeconomic status (SES), education, parity, age, gestational age and occupation of the mothers were the most important variables that affected macrosomia as identified by the RF method which had the highest ACC (0.89). The association of RF predictions and observed values were: 0.43 ( $\phi$  coefficient), 0.39 (contingency coefficient), 0.43 (Kendall tau-b), and 0.31 (kappa).

**Conclusions:** The RF method had the best performance that classified macrosomia compared to the ANN and LR methods. The RF method might be used as an appropriate method for such data.

*Key words:* Macrosomia, Artificial Neural Network, Random Forest, Logistic Regression, Classification

## INTRODUCTION

Macrosomia is a term used to describe excessive birth weight in a new-born [1]. Although there is no

absolute consensus on the definition of macrosomia, it is widely accepted that macrosomia is defined as a birth weight of more than 4000 grams [1, 2]. This disorder has potentially serious outcomes for the mother and infant.

Common maternal consequences include an increased risk of caesarean delivery, prolonged labour, perineal trauma and postpartum haemorrhage [1, 2]. Short-term consequences for the infant include shoulder dystocia, birth injury or death. Long-term effects for the infant include higher risks for diabetes and obesity later in life [1-4]. The often-cited risk factors for macrosomia are maternal diabetes and obesity, excessive weight gain, male infant sex, prolonged gestation, high maternal age and multiparity [5].

In the USA, the macrosomia rate is 8.0% [6]; in Europe and other developed countries, reported rates range between 5% and 20% [1]. A study of data collected in 23 developing countries throughout Asia, Africa and Latin America reported a prevalence of macrosomia that ranged from 0.5% (India) to 14.9% (Algeria) [5]. The rate of macrosomia has risen in most developed countries in the past two decades, despite advancing knowledge of risk factors and mechanisms related to macrosomia. This trend may be due to an increase in the prevalence of diabetes and obesity in women of reproductive age [1, 5].

Macrosomia is associated with adverse maternal and infant outcomes, therefore it is important to predict this condition according to its risk factors. Determining a class of binary response variables for a new subject can be performed by classification methods. Several methods have been used, including data mining (machine learning) techniques [7]. There are two main steps in a classification process. First, determination of the best model by fitting the methods on a training dataset. The second step tests the resultant model from the previous step [8]. Several criteria such as sensitivity (SE), specificity (SP) and accuracy (ACC) can be used to compare classification methods [9].

Logistic regression (LR) is the most popular method to classify discrete response variables based on a number of factors and covariates. However, random forest (RF) is preferable when there are huge numbers of predictors and the response is discrete [10]. Artificial neural network (ANN), as a non-linear, flexible, and general tool, is capable of dealing with most arbitrary functions [11].

This study aims to determine risk factors and covariates that affect macrosomia as a binary response variable by using three different classification methods - LR, RF and ANN. We compare these methods using different evaluation tools in terms of SE, SP and ACC.

## MATERIALS AND METHODS

### Participants and study design

We conducted this cross-sectional study on 4342 pregnant females who referred to maternity hospitals in Tehran, the capital city of Iran. We collected the data from July 6<sup>th</sup> to July 21<sup>st</sup>, 2015. A checklist was provided to collect the data on demographic characteristics of

each mother, the midwife, and new-born information. A trained nurse completed the checklists by an interview with the mother and by abstraction of her records in the hospital delivery room. We recorded variables such as mother's age, education, occupation, socioeconomic status (SES), body mass index (BMI), type of pregnancy, preeclampsia, history of abortion and history of stillbirth. Macrosomia and preeclampsia were determined by a weight over 4000 grams and blood pressure over 140/90 mmHg, respectively. A principle component analysis was performed on questionnaires that pertained to home appliances, digital goods, and to determine the SES of each family. The Ethics Committee of Royan Institute, Tehran, Iran approved this study. Nurses and midwives verbally explained the aims and objective of this study and data confidentiality to the women prior to their participation. All participants gave written informed consent before completing the measures.

### Statistical analysis

The response variable was the occurrence of macrosomia as a binary outcome. The independent variables were mother's age, mother's education (academic/non-academic), mother's occupation (housewife, employed), SES, mother's BMI, parity, gestational age, unwanted pregnancy (yes/no), history of abortion (yes/no), history of stillbirth (yes/no), male infant sex (yes/no), preterm birth (yes/no), preeclampsia (yes/no), and use of assisted reproductive technology (ART).

The train and test sets were composed randomly among cases. The train set (70% of cases) was used for model fitting. The resultant models were then evaluated by the test sample (30% of cases). Tools used to compare the methods included SE, SP, positive predictive value (PPV), negative predictive value (NPV) and ACC.

#### Logistic regression (LR):

The most common parametric tool to model binary outcomes is LR. The model can be written as:

$$\log\left(\frac{\pi}{1-\pi}\right) = \alpha + \sum_{i=1}^k \beta_i x_i$$

In this model,  $x_i$ 's are the covariates or factors.  $\alpha$  and the  $\beta_i$ 's are "k+1" regression coefficients that state the measure of effect size. The odds,  $\frac{\pi}{1-\pi}$ , indicate the odds ratio of classifying the response in category one (success) than zero (failure) [12]. The results include the odds ratio of macrosomia occurrence in one group compared to another group. We used the Hosmer-Lemeshow test to check the adequacy of the model.

#### Artificial neural network (ANN):

This method is an information processing tool based on human brain performance. The multilayer perceptron (MLP) is the most common method used among the different ANN

models. ANN includes layers as input, output and hidden with nodes in each layer. An activation function transforms the data in each layer to the latter by introducing a degree of non-linearity. The input layer consists of all risk factors that affect macrosomia, including six variables. The response variable is shown in the output layer with two nodes as the possible outcomes for macrosomia. In order to determine the best performance of the network, a complicated non-linear mapping is found between the input and output layers using the number of nodes which have been empirically determined in the hidden layer [13]. The results of this method reveal the importance of the variables according to a scale of zero to one. We have chosen the best model among the different ANN models by using the percentage of correct predictions.

#### *Random forest (RF):*

RF models have been proposed by Breiman [10]. The RF model is a collection of classification and regression trees. The trees in this method are built by a replacement sampling of the main dataset. An "out-of-bag" sample consists of the rest of data and evaluates the performance of the trees. The trees create nodes using variables that assess the response variable and a random subset of covariates is chosen at the nodes. Selection of a covariate to split the node into subsequent nodes is determined by a covariate which causes the largest decrease in the Gini impurity criterion. If splitting a variable provides the process with the purity of classification in a certain class, the mean decrease Gini index will tend to be low. Therefore, the mean decrease Gini will be high as well as mean decrease ACC. After an iteration history, the final nodes contain only cases assigned to the same classes. Averaging predictions made by numerous trees allows for the prediction of a case at RF [10]. The importance of variables is determined based on comparing mean decrease Gini and ACC. An out-of-bag error, as an unbiased estimate of the true prediction error, has been used to determine the best RF.

In order to check the adequacy of the models, we calculated indices such as SE, SP, ACC, PPV, NPV, and area under curve (AUC) by using the observed data as the gold standard. The Cochran-Q test was used to check differences in proportion among the three methods. After checking for normality of the data, we used the independent samples t-test to locate any mean differences in continuous variables between the two groups. The chi-square independence test was applied to compare the proportions in two groups. We used the McNemar's test to check multiple comparisons. In order to assess the association between observed and predicted values, we calculated the  $\phi$  coefficient, contingency coefficient and Kendall's tau-b. Kappa statistic was calculated to find the agreement between the results and observed values for macrosomia. All statistical analyses were performed using statistical programming R software version 3.2.3 (<http://www.r-project.org>). All statistical tests were two-tailed and a p-value of less than 0.05 was considered statistically significant.

## RESULTS

Of 4342 births included in this study, 147 (3.4%) had macrosomia. There were 67.4% non-academic mothers, 87.9% housewives, 80.7% wanted pregnancies, 80.7% with no history of abortion, 98.2% with no history of stillbirth, 50.8% male infants, 94.8% with no preeclampsia history, and 92.7% of participants did not undergo ART. The mothers had a mean (standard deviation) age of 29.15 (5.32) years (range: 15 to 57). Table 1 shows the descriptive characteristics of patients in the groups of macrosomia and non-macrosomia. The macrosomia group had significantly higher mothers' age, BMI, and gestational age ( $p < 0.05$ ). Female infants had less macrosomia compared to male infants. Women with histories of stillbirth were more prone to experience macrosomia.

In order to identify the risk factors that affected macrosomia, we analysed the data according to the LR, ANN and RF methods. There were 1316 (30%) cases for the test samples and 3026 (70%) cases comprised the train samples. The test sample evaluated the results from the training sample. We considered mother's age, SES, mother's BMI, parity, gestational age, mother's education, mother's occupation, type of pregnancy, history of abortion and stillbirth, infant sex, preeclampsia and ART as the explanatory variables for the performed methods. The demographic and clinical characteristics of the training and test sets are shown in Table 2. With the exception of preeclampsia ( $p = 0.024$ ), there were no statistical differences observed between the test and training sets.

We tested several ANN models and determined the best model based on the least prediction error. The ANN was carried out using 21 nodes for the input layer and seven units in the hidden layer. Hyperbolic tangent was used as the activation function for the hidden layer. The occurrence of macrosomia was considered as the event for the binary response variable. The output layer included two units. Hyperbolic tangent and softmax were the activation functions for the hidden and output layers, respectively. The importance of the variables is shown in Figure 1. The importance of the variables is presented by scores using SE analysis. The higher the variable scores, the more effective the risk factor is.

The LR model fitted the training data at the first step. After a stepwise variable selection, we determined that mother's BMI, parity, gestational age and male infant sex were significant variables which affected macrosomia. In order to test the resultant variables, the LR model was then fitted to the test dataset (Table 3). The odds of macrosomia in mothers with higher BMI values was not significantly higher ( $p = 0.109$ ). The odds of macrosomia were 1.54 for a one unit increase in parity and 1.305 for a one unit increase in gestational age. Although the results showed that male infants had less association with macrosomia after adjusting for other variables in the model, the result

**TABLE 1. Demographic and clinical characteristics of the participants.**

VARIABLES	MACROSOMIA	NON-MACROSOMIA	P-VALUE
	MEAN ± SD <sup>4</sup>	MEAN ± SD <sup>4</sup>	
Mother's age (years)	30.05 ± 4.71	29.11 ± 5.34	0.037
SES <sup>1</sup>	0.05 ± 1.90	0.02 ± 2.04	0.863
Mother's BMI <sup>2</sup> (kg/m <sup>2</sup> )	26.60 ± 3.88	24.93 ± 5.60	<0.001
Parity	1.85 ± 0.96	1.64 ± 0.75	0.001
Gestational age (weeks)	39.07 ± 1.19	38.59 ± 1.52	<0.001
	N (%)	N (%)	
Mother's education			0.986
Non-academic	99 (67.4)	2828 (67.4)	
Academic	48 (32.7)	1367 (32.6)	
Mother's occupation			0.331
Housewife	133 (90.5)	3684 (87.8)	
Employed	14 (9.5)	511 (12.2)	
Type of pregnancy			0.905
Wanted	118 (80.3)	3384 (80.7)	
Unwanted	29 (19.7)	811 (19.3)	
History of abortion			0.765
No	120 (81.6)	3383 (80.6)	
Yes	27 (18.4)	812 (19.4)	
History of stillbirth			0.031
No	141 (95.9)	4124 (98.3)	
Yes	6 (4.1)	71 (1.7)	
Infant sex			0.002
Male	93 (63.3)	2113 (50.4)	
Female	54 (36.7)	2082 (49.6)	
Preeclampsia			0.359
No	137 (93.2)	3981 (94.9)	
Yes	10 (6.8)	214 (5.1)	
ART <sup>3</sup>			0.591
No	138 (93.9)	3889 (92.7)	
Yes	9 (6.1)	306 (7.3)	

<sup>1</sup>Socioeconomic status; <sup>2</sup>Body mass index; <sup>3</sup>Assisted reproductive technology; <sup>4</sup>Standard deviation

was not statistically significant ( $p=0.075$ ). The Hosmer-Lemeshow test showed a significant good fitting of the data by the test sample (chi-square: 9.122, df: 8,  $p=0.332$ ).

According to mean decreases in the Gini and ACC indices, the results from RF indicated that the mother's BMI, SES, education, parity, age, gestational age and occupation were the seven most important variables that classified macrosomia (Fig. 2). The out of bag estimate of error rate was 3.39%.

Table 4 shows the comparisons of SE, SP, positive probability value, negative probability value and ACC for the training and testing sets of the classification methods. The

ROC curve is shown in Figure 3. The 0.89 ACC of RF for classifying macrosomia significantly differed compared to the other two methods. Table 4 also shows the association of results from the performed methods with observed macrosomia. The Cochran-Q test resulted in differences between proportions in the different methods (Cochran-Q: 281.88, df: 2,  $p<0.001$ ). Multiple comparisons adjusted for significance were performed using the McNemar test. The results showed a significant difference in proportions of LR versus RF (chi-square: 196,  $p<0.001$ ) and ANN versus RF (chi-square: 249.59,  $p<0.001$ ), whereas there was no statistical difference observed between the performances of

TABLE 2. Distribution of variables in training and testing samples.

VARIABLES	TESTING SAMPLE (N=1316)	TRAINING SAMPLE (N=3026)	P-VALUE
	MEAN ± SD <sup>4</sup>	MEAN ± SD <sup>4</sup>	
Mother's age (years)	29.25 ± 5.23	29.10 ± 5.36	0.374
SES <sup>1</sup>	0.02 ± 1.99	0.02 ± 2.05	0.932
Mother's BMI <sup>2</sup> (kg/m <sup>2</sup> )	25.08 ± 6.02	24.94 ± 5.33	0.451
Parity	1.66 ± 0.77	1.64 ± 0.75	0.339
Gestational age (weeks)	38.57 ± 1.62	38.62 ± 1.45	0.359
	N (%)	N (%)	
<b>Macrosomia</b>			0.231
Positive	38 (2.9)	109 (3.6)	
Negative	1278 (97.1)	2917 (96.4)	
<b>Mother's education</b>			0.093
Non-academic	911 (69.2)	2016 (66.6)	
Academic	405 (30.8)	1010 (33.4)	
<b>Mother's occupation</b>			0.368
Housewife	1148 (87.2)	2669 (88.2)	
Employed	168 (12.8)	357 (11.8)	
<b>Type of pregnancy</b>			0.713
Wanted	1057 (80.3)	2445 (80.8)	
Unwanted	259 (19.7)	581 (19.2)	
<b>History of abortion</b>			0.914
No	1063 (80.8)	2440 (80.6)	
Yes	253 (19.2)	586 (19.4)	
<b>History of stillbirth</b>			0.933
No	1293 (98.3)	2972 (98.2)	
Yes	23 (1.7)	54 (1.8)	
<b>Infant sex</b>			0.104
Male	644 (48.9)	1562 (51.6)	
Female	672 (51.1)	1464 (48.4)	
<b>Preeclampsia</b>			0.024
No	1233 (93.7)	2885 (95.3)	
Yes	83 (6.3)	141 (4.7)	
<b>ART<sup>3</sup></b>			0.846
No	1219 (92.6)	2808 (92.8)	
Yes	97 (7.4)	218 (7.2)	

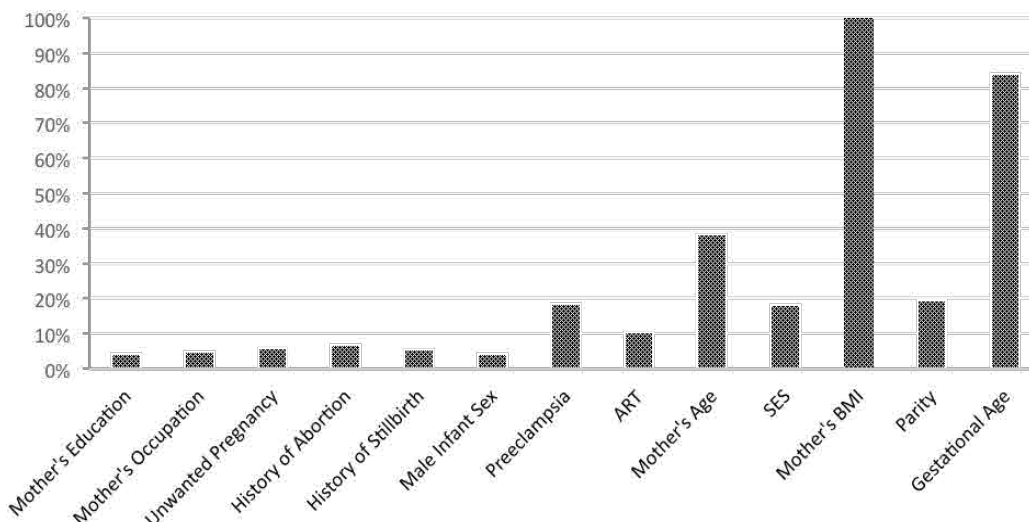
<sup>1</sup>Socioeconomic status; <sup>2</sup>Body mass index; <sup>3</sup>Assisted reproductive technology; <sup>4</sup>Standard deviation

LR and ANN (chi-square: 1.429, p=0.232). We calculated the  $\phi$  coefficient, contingency coefficient and Kendall tau-b in order to evaluate the associations of the methods' predictions with the observed value for macrosomia. The results demonstrated that RF had the best performance compared to the other methods. In addition, the kappa statistic showed a significantly higher agreement between RF results and observed macrosomia compared to LR and ANN.

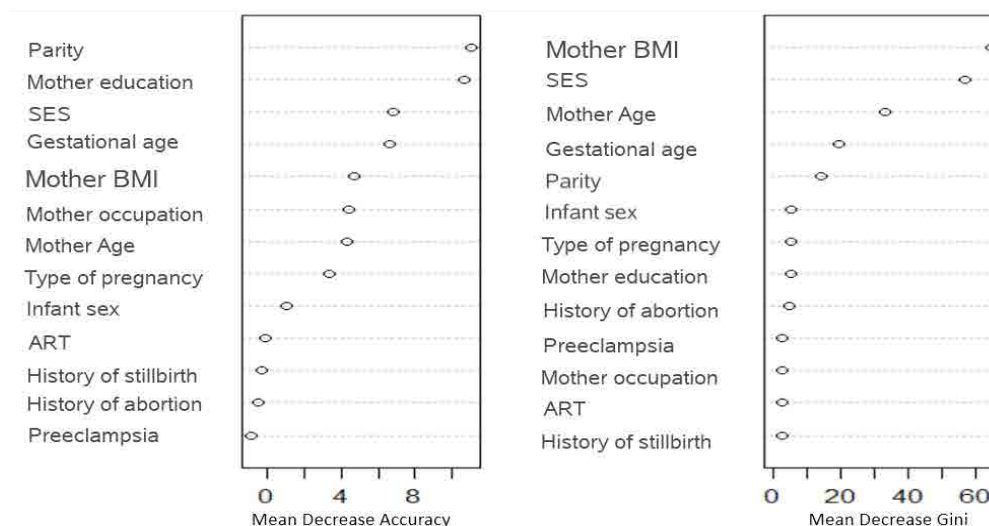
## DISCUSSION

This study assessed the impact of several variables on macrosomia. We compared three classification methods - LR, RF and ANN. RF was the best classifier method. According to the results, mother's BMI, SES, education, parity, age, gestational age, and occupation were the most important variables that affected macrosomia.

**FIGURE 1. Variable importance affecting macrosomia using artificial neural network (ANN).**



**FIGURE 2. Random forest plot of mean decrease Gini and accuracy (ACC).**



The prevalence of macrosomia was 3.4% which differed from another study conducted in Iran and developed countries. Henriksen [1], Hamilton et al. [14], and Koyanagi et al. [5] reported decreased prevalences of macrosomia. This study showed a significant impact of mother's BMI on macrosomia. Jolly et al. studied the effects of pre-pregnancy BMI and gestational weight gain on fetal macrosomia. They found that mothers with high BMI values had higher rates of macrosomia. The current study results confirmed those reported by other studies [15].

Our study showed that mother's age could be considered an important risk factor for macrosomia. This result agreed with other studies [5, 16, 17]. Jolly et al. evaluated the risk factors for macrosomia and its clinical consequences in a study on 350,311 pregnancies. They

showed that mothers over 40 years of age were more prone to experience macrosomia [15].

Gestational age and parity played significant roles in the onset of macrosomia. More numbers of births indicated a higher risk of macrosomia. Stotland et al. studied the epidemiology of macrosomia and characterised related maternal complications. Gestational age over 41 weeks was introduced as an affective risk factor for macrosomia [18]. Koyanagi et al. and Chatfield confirmed these findings [5, 15, 16]. Although RF analysis showed that mother's occupation had a nonsignificant impact on macrosomia, studies by Mardani et al. [19] and Bian et al. [20] reported different conclusions. We determined that educated mothers and those with better SES scores could reduce the rate of macrosomia. Boulet et al. described

**TABLE 3. Results of logistic regression (LR) in the training and test sets.**

VARIABLES	TRAINING SET				TEST SET			
	ESTIMATE	SE <sup>3</sup>	OR <sup>2</sup> <sub>ADJUSTED</sub> (95% CI <sup>4</sup> )	P-VALUE	ESTIMATE	SE <sup>3</sup>	OR <sup>2</sup> <sub>ADJUSTED</sub> (95% CI <sup>4</sup> )	P-VALUE
<b>BMI<sup>1</sup></b>	0.024	0.011	1.024 (1.002, 1.046)	0.033	0.021	0.013	1.021 (0.995, 1.048)	0.109
<b>Parity</b>	0.249	0.115	1.283 (1.024, 1.608)	0.030	0.433	0.165	1.542 (1.115, 2.132)	0.009
<b>Gestational age</b>	0.269	0.080	1.308 (1.118, 1.531)	0.001	0.266	0.092	1.305 (1.090, 1.561)	0.004
<b>Male infant sex</b>	-0.541	0.204	0.582 (0.390, 0.868)	0.008	-0.614	0.345	0.541 (0.275, 1.063)	0.075

<sup>1</sup>Body mass index; <sup>2</sup>Odds ratio; <sup>3</sup>Standard error; <sup>4</sup>Confidence interval

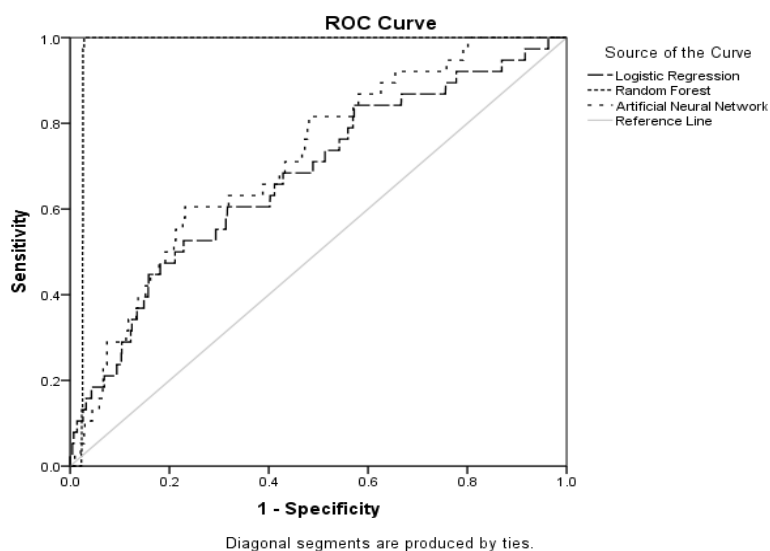
**TABLE 4. Comparison of LR, RF and ANN methods for the test sample using accuracy tools with 95% confidence interval (95% CI).**

ACCURACY MEASURES	LR	RF	ANN
SE	0.60 (0.43, 0.75)	1.00 (0.90, 1.00)	0.64 (0.46, 0.78)
SP	0.64 (0.61, 0.67)	0.89 (0.86, 0.91)	0.63 (0.59, 0.64)
PPV	0.04 (0.03, 0.07)	0.21 (0.15, 0.27)	0.04 (0.03, 0.07)
NPV	0.98 (0.97, 0.99)	1.00 (0.99, 1.00)	0.98 (0.97, 0.99)
ACC	0.64 (0.61, 0.66)	0.89 (0.87, 0.90)	0.62 (0.59, 0.64)
AUC	0.67 (0.58, 0.76)	0.97 (0.96, 0.98)	0.71 (0.63, 0.79)
Ø coefficient	0.08* (0.03, 0.14)	0.43* (0.36, 0.49)	0.08* (0.03, 0.14)
Contingency coefficient	0.08* (0.03, 0.14)	0.39* (0.34, 0.44)	0.08* (0.03, 0.14)
Kendall tau-b	0.08* (0.03, 0.14)	0.43* (0.36, 0.49)	0.08* (0.03, 0.14)
Kappa	0.03* (0.01, 0.06)	0.31* (0.23, 0.38)	0.03* (0.01, 0.06)

SE: Sensitivity; SP: Specificity; ACC: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR: Logistic Regression; RF: Random Forest; ANN: Artificial Neural Network; AUC: Area Under Curve

\* P-value <0.05

**FIGURE 3. ROC curve comparing the three classification methods - logistic regression (LR), random forest (RF), and artificial neural network (ANN).**



maternal risk factors for macrosomia and assessed birthweight categories to determine predictive thresholds of adverse outcomes. They realised that higher numbers of mothers in the macrosomic groups had higher educational level, high parity for age and previous macrosomic births [3]. Park et al. reported that the socioeconomic situation influenced pregnancy outcomes such as macrosomia [21].

This study showed that out of the three different classification methods (RF, LR and ANN) for our data, the RF method significantly had the best performance. The RF outperformed among the mentioned methods and has shown both the highest association between RF predicted and observed values as well as the highest ACC. RF, as a non-parametric approach, can classify large amounts of data which handles a large number of input variables. In the case of missingness in the data, RF can provide effective approaches. In this method, each tree is built based on recursive partitioning and the prediction is made on the average of a set of trees rather than one tree. This method averages multiple trees from bootstrapped data sets [22].

ANN is non-parametric method without any distributional assumption. This non-linear approach requires a large number of data according to the number of independent variables. ANN can detect complex nonlinear relationships between dependent and all possible interactions among independent variables. This method requires complex computations [23].

The parametric LR uses a modeling approach. LR provides tools for understandable interpretations using odds ratios. A large number of input variables can cause collinearity. The number of input variables depends on the successes in the response variable. Semi or complete separation occurs when the outcome variable separates a predictor variable or a combination of predictor variables, resulting in complexities in the modeling process [12]. A number of studies have been performed with various medical, clinical and public health datasets in an attempt to compare classification methods [24-27].

Maroco et al. compared data mining methods to predict dementia. They assessed classification methods such as linear discriminant analysis, LR, neural networks, support vector machines, classification trees and RF. The researchers compared SE, SP, and overall classification ACC of these methods and concluded that RF and linear discriminant analysis ranked better than the other classification methods. They proposed that the RF classification method could improve ACC, SE and SP of dementia predictions from neuropsychological testing [24]. Mansiaux and Carrat suggested the use of data mining methods such as RF to be considered as credible alternatives to multivariate LR [28].

In addition to limitations such as low prevalence of binary macrosomia, the study sample might not represent the general population of patients. This study compared three different methods. The results suggested that RF was

the best classifier model, which might help policymakers to determine macrosomia risk factors. Based on our findings, the RF method had a better performance in classifying macrosomia compared to LR and ANN. The capability of this method in dealing with large numbers of variables could make it the first choice method for classification of this type of data.

## Acknowledgements

This study was funded by Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran. The authors would like to express their appreciation to those who participated in this study and to the staff at the hospitals of Tehran University of Medical Sciences, Shahid Beheshti University of Medical Sciences, Iran University of Medical Sciences and Islamic Azad University.

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