Original Paper

Maternal Lipid Profile as Predictor for Mother and Fetus Outcome-an Artificial Neural Network Approach

MANUELA STOENESCU[1], MIRCEA-SEBASTIAN ȘERBĂNESCU[2], ANDA LORENA DIJMARESCU[4], MARIA MAGDALENA MANOLEA[4], SIDONIA SANDULESCU[4], SIDONIA VRABIE[4], IOANA CAMEN[1], MARIA CARMEN TABACU[1], NOVAC MARIUS BOGDAN[3]

[1]*PhD, University of Medicine and Pharmacy of Craiova, Romania*

[2]*Medical Informatics and Biostatistics Department, University of Medicine and Pharmacy of Craiova, Romania*

[3]*Anesthesiology and Intensive Care Department, University of Medicine and Pharmacy of Craiova, Romania*

[4]*Obstetrics and Gynecology Department, University of Medicine and Pharmacy of Craiova, Romania*

ABSTRACT: Purpose. The study aims to predict mother and fetus outcome based on the mother's lipid profile in the second and third trimester of pregnancy. Material and method. Blood and urinary samples were taken from 135 mothers that were prospectively monitored during the hole pregnancy. Total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), together with other parameters, were used as predictors in a multilayer perceptron (MLP) artificial neural network (ANN). Small for gestational age (SGA) was used to assess the fetal outcome, while Gestational diabetes mellitus (GDM) and, Hypertensive disorders in pregnancy (HDP) to assess the mother's outcome. Results. SGA prediction rate was 0.637±0.022 for the second trimester and 0.632±0.017 for the third trimester. GDM prediction rate was 0.897±0.006 for the second trimester and 0.632±0.017 for the third trimester. HDP prediction rate was 0.620±0.046 for the second trimester and 0.775±0.030 for the third trimester. When used with other parameters (hemoglobin, thrombocytes, uric acid, GOT, GPT, the presence of proteinuria, urea, and creatinine) the prediction rates raised, going over 90% for the GDM. Conclusions. Though individual lipid parameters do not statistically correlate with the output variables the use of ANN generated prediction rates raging from 60% to 90%. The lipid profile from the third trimesters seems to be a better prediction for both fetus and mother outcome.

KEYWORDS: *Lipid profile, fetus outcome, mother outcome.*

Introduction

Studies have shown that maternal dyslipidemia can predict pregnancy and neonatal outcome.

In normal pregnancy, the lipid parameters represented by total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C) show a gradual increase from 12 week of gestation and continues to increase in the second and third trimesters [1-3].

In the second half of pregnancy, maternal lipid metabolism is focused on lipolysis, which leads to an increase in fatty acid levels.

These changes show that for good fetal development, the maternal body undergoes a physiological adaptation by transforming carbohydrate metabolism to lipid metabolism [4,5].

But, it is quite difficult to determine what are the plasma lipid levels that differentiate their physiological or pathological growth.

In early pregnancy, the mother is in an anabolic status, and lipids are used as a source of calories for the mother and the growing fetus [6].

Maternal lipid profile abnormalities increase with increasing gestational age and so it seems that dyslipidemia may play certain roles in the pathogenesis of adverse pregnancy outcomes [7].

Artificial neural networks (ANN) are a collection of connected computing units called artificial neurons, which mimic the behavior of neurons in a biological system.

Each neuron is connected, forming synapses like in a biological system, and can transmit a signal to other neurons.

Neurons receive signals then processes them and can signal other neurons connected to them.

Each neuron receives signals as real numbers from other neurons, processes the values with the use of a non-linear function and creates an output value which will be passed to its connected neurons from the next layer.

Attached to each neuron, typically there is a variable called weight that adjusts during the learning process.

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Details about the mechanisms behind ANN can be found in [8].

A multilayer perceptron (MLP) is a class of feedforward artificial neural network (ANN) composed of at least three layers of neurons: an input layer, a hidden layer and an output layer.

Using a supervised learning technique called back-propagation for training [9,10], the MLP network can distinguish data that is not linearly separable [11] making it superior to its predecessor-the linear perceptron and suitable for medical decision-making.

The objective of the current paper is to predict mother and fetus outcome based on the mother's lipid profile in the second and third trimester of pregnancy by using the MLP accuracy (ACC) as a performance parameter.

Material and Method

A prospective study was conducted in 135 pregnant women who attended prenatal care at Obstetrics and Gynecology Department, in Municipal Clinical Hospital "Filantropia", Craiova, between October 2016-May 2020.

Inclusion criteria were:

1) singleton pregnancy;

2) ultrasound examinations performed in all three trimesters.

Exclusion criteria were:

1) twin/multiple pregnancy;

2) women with pre-pregnancy cardio vascular disease, diabetes mellitus,

2) maternal age <18 years;

3) fetuses diagnosed with congenital malformation.

Venous blood samples for lipid assessment were taken in the second trimester (21-24 gestational weeks) and the third trimester (33-37 gestational weeks), the blood being assayed for CT, TG, HDL-C concentrations.

Other parameters that were collected were: hemoglobin, platelets, GOT, GPT, proteinuria, serum urea, uric acid and creatinine.

We defined Small for gestational age (SGA) fetuses or newborns as those who are smaller than their gestational age, the weight being less than 10 percentile for the gestational age.

This classification was developed by the World Health Organization (WHO) in 1995, based on the measurement of birth weight by gestational age compared to a specific reference population [12].

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance of variable degree that begins or is first recognized during pregnancy [13].

Hypertensive disorders in pregnancy (HDP) includes gestational hypertension, chronic hypertension, preeclampsia, and eclampsia, remaining as a leading cause of maternal and fetal morbidity and mortality.

The study was approved by the Ethics Commission of the University of Medicine and Pharmacy of Craiova and the participants signed an informed consent regarding their participation in this study, after a complete information.

A MLP having 20 neurons in the hidden layer was trained independently for each of the prediction task.

The same network architecture was kept for all prediction tasks.

The design of the network for the first dataset can be seen in Figure 1.

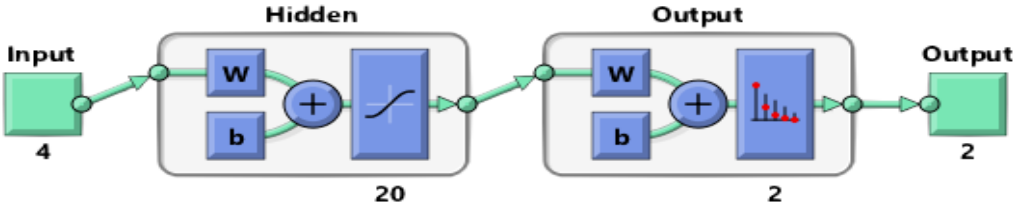

Figure1. ANN architecture: MLP with one hidden layer and 20 neurons.

For each prediction tasks the algorithm was independently run 100 times in a complete 10-fold cross-validation cycle.

ACC was saved at each step and considered as the performance parameter.

85% of the data was used for training and the remaining 15% for testing.

The first set of predictions was done taking in consideration only the lipidic profile, while the second set of predictions was done including the other collected parameters.

The statistical assessment of the variables taken in consideration was done using Student t-Test.

The programs and the statistical assessment were done using Matlab (Mathworks, USA).

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Results

The ACCs of the first set of predictions are presented in Table 1 and are computed using only the lipidic profile.

Results for the second set of predictions that combine the variables used in set 1 together with the other variables described in the previous section are presented in Table 2

Table 1. ACC of the lipidic profile on the output variables.

	SGA	GDM	HDP
ACC on second drimester	0.63±0.02	0.89±0.00	0.62±0.04
ACC on third drimester	0.63±0.01	0.89±0.01	0.77±0.03

As noted, SGA prediction rate was 0.637±0.022 for the second trimester and 0.632±0.017 for the third trimester.

GDM prediction rate was 0.897±0.006 for the second trimester and 0.632±0.017 for the third trimester.

HDP prediction rate was 0.620±0.046 for the second trimester and 0.775±0.030 for the third trimester.

Table 2. ACC of the lipidic profile together with the other collected variables on the output variables.

	SGA	GDM	HDP
ACC on second drimester	0.66±0.01	0.92±0.01	0.82±0.06
ACC on third drimester	0.72±0.07	0.94±0.01	0.91±0.01

In our study, the SGA prediction rates did not show statistical differences between the second and third trimesters, if we refer to the maternal lipid profile (Student's t-test, p=0.110), but showed significant differences (Student's t-test, p <0.001) between trimesters, when we added the data obtained from the second set of parameters, and also between sets.

It should be noted that the SGA prediction rate by lipid profile was only about 63% but, taking into account all variables, the prediction rate increased to about 66% for the second trimester and to about 72% for the third trimester.

The same behavior is present at the GDM statistical differential between the second and third trimesters on the first date set (Student's t-test, p=0.120).

Statistical differences are not present, but are present (Student's t-test, p <0.001) between the second set and inter-sets.

When used with other parameters (hemoglobin, platelets, GOT, GPT, proteinuria, serum urea, uric acid and creatinine) the prediction rates raised, going over 90% for the GDM.

HDP predictions generate statistical differences (Student's t-test, p <0.001) between the second and third semester on both lipid profile set and in the hole variable profile.

It should be noted that HDP prediction rates on the lipid profile were about 62% in the second trimesterr and increased to 77% in the third.

When all available variables are taken into account (second set), the average accuracy increased to 82% in the second trimester and to 91% for the third trimester.

Because only in the case of HDP predictions did we met statistical differences between the second and third trimester on both the lipid profile set and in the all variables set, we extracted a sample of the confusion matrix from a network run on the first set of data on HDP prediction, which is shown in Figure 2 and from the second set of data on the third trimester, which is shown in Figure 3.

Comparing the two confusion matrices (Figure 2 and 3) we can clearly see a data aggregation on the first diagonal (green background) with a major improvement when all the variables were taking into consideration (Figure 3).

Statistical analysis showed significant differences between most of the prediction rates.

The only insignificant differences in prediction ACC rates were between the first set of data, between the two trimesters, and only for SGA and GDM.

Figure 2. Confusion matrix of 78th run on the first set of data on the second trimester on HDP prediction, 1-yes, 2-no, green-correct, red-incorrect.

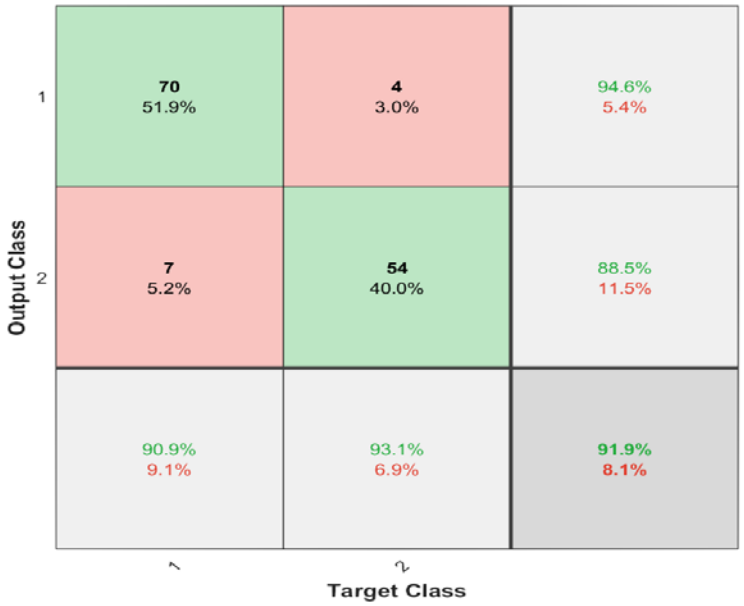

Figure 3. Confusion matrix of 78th run on the second set of data on the third trimester on HDP prediction, 1-yes, 2-no, green-correct, red-incorrect.

Discussion

In our study, SGA prediction rates did not show statistical differences between the second and third trimesters in the case of maternal lipid profile (Student's t test, p=0.110), as other studies have shown. In the study of Kandimalla et al. [14] it was found that in preeclampsia and in newborn small for gestational age (SGA), HDL-C values were low and LDL-C values were increased, as has been found in other studies [15,16].

A recent study by Chen Q et al. [2] showed in the third trimester a positive association between HDL-C and SGA, a negative association between TG and SGA and no significant association between TC or LDL-C with SGA.

In the second trimester, a negative association was found between lipids in the

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second trimester (TC, TG, LDL-C and HDL-C) and SGA [2].

But, we noticed that if we introduce the second set of parameters, significant statistical differences appear (Student's t-test, $p < 0.001$) between trimesters, and also between sets.

Hyperlipidemia, especially hypertriglyceridemia, is an important risk factor for metabolic syndromes.

We noticed that GDM prediction rate on the lipid profile was about 89% (regardless of the trimester) and when taking in consideration all the variables rose to about 92% for the second trimester and about 94% for the third trimester, which is consistent with other studies.

Detection and treatment of GDM is important because it increases the risk of perinatal complications in the short term, but in the long term it increases the risk of subsequent onset of type 2 diabetes (T2DM) and cardiovascular disease [17].

In a prospective case-control study, higher TG levels at 11-14 weeks of gestation were present in women with GDM, TG levels being a significant predictor of subsequent GDM [18].

Triglyceride levels are significantly elevated in women with gestational diabetes mellitus and hypertensive disorders in pregnancy (HDP), and although such increases are lower in the first trimester, they become significant in the second and third trimesters of pregnancy [22].

The study by Niromanesh et al. [19] concluded a positive relationship between hypertriglyceridemia and preeclampsia, preterm delivery.

Other studies that have focused on TC have found that hypercholesterolemia can lead to complications such as preeclampsia and preterm delivery [20,21].

Maternal dyslipidemia in animal studies has shown that the long-term health of offspring can be affected [23].

And what has been shown to be very important is that maternal dyslipidemia in the perinatal period causes changes that cannot be adjusted after birth.

Note that HDP prediction rates on the lipid profile was about 62% on the second trimester and rose to 77% on the third.

When taking in consideration all the available variables (second set) the average accuracy rose to 82% in the second semester and to 91% for the third semester.

The use of linear neural networks and of MLP for prediction tasks in medicine has been previously used [24,25].

Though there are other possible techniques [26,27] we expect that through the development of the high-performance graphical processing boards a new technique will emerge in the medical-deep neural networks.

With good results in other medical prediction tasks [28,29] this approach should have good results in maternal and fetal outcome when used with ultrasound Doppler images.

The proposed method has limitations.

The first limitation comes from the relative small input dataset (n=135) that was used for the study.

The second limitation, is related, again, to the input data, where the prediction classes were unbalanced.

Nevertheless, by using multiple runs of the algorithms we achieved statistical significance.

Conclusion

SGA had the smallest prediction rate on the lipid profile and when using the other available variables showing that the fetus output is multifactorial and the lipid profile of its mother is just part of it.

GDM showed the best prediction performance showing that the lipid profile is somehow directly related to the GDM, and the fact that when using the other parameters we obtain only 5% increase on the prediction rate underlays the importance of the lipid profile in GDM.

HDP shows much better prediction rates on both sets in the third semester when compared to the second one.

Though individual lipid profile parameters do stratify on the output variables the use of ANN generated prediction rates raging from 60% to 90%.

The lipid profile from the third trimesters seems to be a better prediction for both fetus and mother outcome.

Conflict of interests

None to declare.

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Corresponding Author: Mircea-Sebastian Şerbănescu, Medical Informatics and Biostatistics Department, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Romania, e-mail: mircea_serbanescu@yahoo.com