An Intelligent Prenatal Screening System for the Prediction of Trisomy-21 Using Triple Test Variables: The Hacettepe System

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ABSTRACT

OBJECTIVE: To introduce an intelligent prenatal screening system, using triple test variables.

STUDY DESIGN: In this study, we have used a backpropagation learning algorithm (a supervised artificial neural network) to develop an intelligent antenatal screening system (heretofore referred as Hacettepe System). Triple test variables were used as input variables, while "Down syndrome" and "non-Down syndrome" fetuses were the output of the algorithm. Unconjugated estriol (E3), beta-human chorionic gonadotropin, and α-feto protein with gestational week and maternal age (triple test) were used as input variables in the training and testing. Multiples of median values of the E3, α-feto protein, and beta-human chorionic gonadotropin were used in this study.

The testing group of Hacettepe system consisted of 97 patients who were found to be high-risk (>1/250) during the routine antenatal screening (triple test) and underwent amniocentesis for fetal karyotyping.

RESULTS: Amniocentesis was performed in 97 pregnancies with "high-risk" triple test results (>1/250). Fetal karyotyping revealed trisomy 21 in about 9.3% (9/97) of the pregnancies. Our algorithm (Hacettepe System) detected 77.8% (7/9) of Down syndrome cases. Moreover, all of the normal fetal karyotypes were assigned as normal in the Hacettepe System.

CONCLUSION: We have developed an intelligent system using the backpropagation learning algorithm (using triple test variables) to predict trisomy 21.

Keywords: Antenatal screening, Artificial intelligent system, Neural networks, Prenatal diagnosis, Triple test

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Introduction

Prenatal screening (PS) is an essential part of the antenatal care programs worldwide (1,2). There are various types of screening policies and tests with different statistical measure capabilities (1-3). Double test (DT), combined test (CT), triple test (TT), quadruple test (QT), and noninvasive prenatal test (NIPT) using the cell-free fetal DNA are the widely used PS tests (1-3).

Some institutions are still using PS tests based on maternal serum biochemical markers because of their cost-effectiveness (4,5). Different probability algorithms (such as the tri-variate Gaussian algorithm) with various cut-off values are used in routine clinical practice (6). However, some questions remain in the patients' minds regarding the cut-off values and probability concepts in daily applications. They expect easier and better explanations about screening mentality and test results.

Recent technological improvements enable physicians to use artificial intelligent systems (AIS) in clinical decision making (7-9). We have previously reported an artificial intelligent diagnostic system with neural networks to determine genetic disorders and fetal health using the TT biochemical markers (10). Unconjugated estriol (E3), beta-human chorionic gonadotropin (β-hCG), and α-feto protein (AFP) with gestational week and maternal age were used in the TT (6). The advantage of supervised, unsupervised and hybrid intelligent systems is the flexibility in choosing input variables and goals. Various versions may be created to detect different fetal

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health problems, such as genetic disorders in general, aneuploidies, certain trisomies, or trisomy 21 only.

In this version of supervised AIS (backpropagation learning algorithm), we have used TT variables as input variables to detect "only trisomy 21" fetuses. This study aimed to introduce an alternative approach (methodology) in the clinical application of TT.

Material and Method

In this study, we have used a backpropagation learning algorithm (a supervised artificial neural network) to develop an intelligent antenatal screening system (heretofore referred as Hacettepe System) (10). TT variables were used as input variables, while "Down syndrome" (DS) and "non-DS" fetuses were the output of the algorithm. Unconjugated estriol (E3), beta-human chorionic gonadotropin (β-hCG), and α-feto protein (AFP) with gestational week and maternal age (TT) were used as input variables in training and testing. Multiples of median (MoM) values of the E3, AFP, and β-hCG were used in this study.

The testing group of Hacettepe system consisted of 97 patients who were found to be high-risk (>1/250) in the antenatal screening (TT) and underwent amniocentesis (AC) for fetal karyotyping. The institutional ethics committee of the Hacettepe University (GO 16/690) has approved the study protocol.

Result

Amniocentesis was performed in 97 pregnancies with "high-risk" TT results (>1/250). Fetal karyotyping revealed trisomy 21 in about 9.3% (9/97) of the pregnancies.

Then, the TT variables in our study subjects (97 pregnancies) were used for testing our algorithm. Our algorithm detected 77.8% (7/9) DS cases. Moreover, all of the normal fetal karyotypes were assigned as normal in the Hacettepe System.

Discussion

PS is an essential component of antenatal care programs, and different types of tests are used for this purpose (11,12). Maternal blood biochemical markers and "maternal blood cell free fetal DNA" are still used in PS due to their cost-effectiveness (4,5). Classical statistical methods (probability algorithms) are used in DT, CT, and TT, which make patients uncomfortable in terms of understanding their purpose.

The association between low maternal serum unconjugated E3 and AFP concentrations and increased hCG blood levels were already known for a long time (6). TT is still used in some institutions under certain conditions, especially when AFP measurements are necessary. However, the predictive value of TT is not as satisfactory as that of CT and NIPT (13,14).

AIS are widely used in medical applications and decision making in our routine medical practices (7-9). Neural network and learning algorithms broaden our perspectives in the utilization of various test results (7-9). The advantage of learning algorithms is the flexibility in creating various versions using the same input variables of the different patient groups. The limitation of this study is testing the algorithm. The algorithm is only tested using the TT data of high-risk patients detected by the classic TT.

In conclusion, we have developed an intelligent system using the backpropagation learning algorithm (using TT variables) to predict trisomy 21. Therefore, this study aimed to introduce an alternative, patient-friendly PS test using input variables same as those of TT.

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