

Assessment of the Sensitivity and Specificity of Screening Tests Performed in the First and Second Trimester in the Pregnant Women

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ABSTRACT

Background & Objective: Diagnosing fetal disorders and abnormalities in the early stages of pregnancy can prevent future adverse conditions for the infant and his/her family. This study aimed to evaluate the sensitivity and specificity of the first- and second-trimester screening tests for identifying fetal chromosomal disorders in pregnant women.

Materials & Methods: A total of 960 pregnant women participated in this retrospective cohort study that was performed at Yas Hospital. The participants' mean age was 31.07±0.17 years. In the present study, all pregnant women, who referred to Yas Hospital for their first- and second-trimester screening tests, were studied from 2015 to 2017.

Results: Most of the participants (43.4%) were primigravida. The sensitivity of the first-trimester screening test was 70%, and its specificity was 80.3%. The sensitivity and specificity of the second-trimester screening test were 45% and 94.5%, respectively.

Conclusion: Despite recent advances in the prenatal field, the accuracy of screening tests may still vary depending on maternal age and other existing characteristics. Consequently, in parents consulting, the possibility of false positives and negatives should be considered in the tests.

Keywords: Screening, Aneuploidy, Pregnancy, Sensitivity, Specificity



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Introduction

Infant health is one of the main goals of the health system, which ultimately creates a healthy and successful society. In advanced countries, pregnancy screening tests are commonly carried out to diagnose chromosomal disorders. Screening tests are also being conducted in Iran, and there are ongoing programs to make such tests pervasive (1).

For every pregnant woman, without any positive medical history, having a child with chromosomal disorders is probable. Although this is not very likely, screening tests can greatly discern the true extent of the possibility (2).

Pregnant women should refer to an obstetrician for prenatal care and early pregnancy screening tests. After performing an ultrasound scan and a double, triple, and/or quadruple test, the fetus's health status can be largely determined. If these tests are done accurately, their accuracy will be up to 85% (3).

Deficiencies found in prenatal screening tests include chromosomal disorders (trisomy 13, 18, 21) and neural

tube defects, which trisomy 21 is the most common of them (formerly referred to as Down's syndrome) (4).

Down's syndrome may randomly occur in any pregnancy. Therefore, even if there is no family history or history of giving birth to a child with Down's syndrome, the risk of this complication remains in the current pregnancy. The prevalence of Down's syndrome is about 1 in every 800 pregnancies. It is reported that increasing maternal age enhances the risk of Down's syndrome (5).

The results of screening tests for fetal abnormalities only show the risk level. If the screening result indicates a low risk, no invasive diagnostic procedures will be needed. If the screening results are positive and indicate a high risk, invasive chorionic villus sampling (CVS) and amniocentesis (amniotic fluid sampling) may be required to have a definitive diagnosis and decide on pregnancy termination (6).

However, CVS or amniocentesis is associated with complications such as fetal death, rupture of the membranes, vaginal bleeding, and chorioamnionitis. Other risk factors, which increase the probability of CVS

or amniocentesis complications, are maternal age, gestational age, placental position, twin pregnancy, fibroma, the number of needling, and bloody amniotic fluid (7).

Given that the diagnosis of fetal disorders and abnormalities in the early stages of pregnancy can prevent future adverse conditions for the infant and his/her family, and regarding the fact that the early diagnosis of fetal abnormalities will be imposed fewer costs on the country's healthcare system, this study aimed to assess the sensitivity and specificity of screening tests performed in pregnant women.

Materials and Methods

This retrospective cohort study was carried out at Yas Hospital. In this study, a total of 960 pregnant women, who referred to a prenatal clinic in Yas Hospital for their first-trimester screening test, were studied from 2015 to 2017.

Inclusion criteria included all mothers who referred to Yas Hospital for their first-trimester screening test. Of those who had positive screening results, only those, with impaired biochemical tests, were included in the study regardless of Nuchal Translucency (NT) examination results.

Exclusion criteria included patients who were unwilling to participate in the study and failed to respond to the researcher's phone calls.

In the first-trimester screening, the levels of Human chorionic gonadotropin (HCG) and Pregnancy-associated plasma protein A (PAPP-A) analyses in the mothers' blood were tested, and ultrasound was performed for examining NT at 11 to 14 weeks of gestation.

Among those who referred for their first-trimester screening, about 47% (448 women) did not go back to the hospital for the second-trimester screening test. At 15 to 21 weeks of gestation, all the 511 women, who referred for their second-trimester screening, were tested for 4 markers, including HCG, alpha-fetoprotein (AFP), unconjugated estradiol, and inhibin.

Yas Hospital's laboratory used ROCHE kits and a COBAS E411 device (GERMANY, ROCHE Company) to perform the screening tests.

All the participants in the study were followed up maximally to two years after their babies were born, and they were asked about their infants' health status over the phone. Finally, the infants' health status was considered as the gold standard, and the sensitivity and specificity of the first- and second-trimester screening tests were measured.

This research was conducted in compliance with the Helsinki Declaration and approved by the ethics committee of Tehran University of Medical Sciences. (IR.TUMS.MEDICINE.REC.1398.253)

Finally, the data were analyzed by SPSS 24 (SPSS Inc., Chicago, Illinois, USA). The Crosstabs procedure was used to measure the sensitivity and specificity of the first- and second-trimester screening tests. The significance level was set at 0.05.

Results

In the current study, a total of 960 pregnant women participated. The participants' mean age was 31.07 ± 0.17 years. The youngest participant was 17 years, and the oldest participant was 45 years.

The number of pregnancies was assessed in the study, and it demonstrated that most of the participants (43.4%) were primigravida. About 36.4%, 14.4%, and 4.5% of them were pregnant with their second, third, and fourth child, respectively. Moreover, 0.8% and 0.2% of them were pregnant with their fifth and sixth child, respectively. Only one of them was pregnant with her seventh child.

The sensitivity of the first-trimester screening test was 70%, and its specificity was 80.3% (Table 1). Of those who participated in the study, about 47% (448 women) did not refer to the hospital for their second-trimester screening test. However, all the other 511 women referred to the hospital for their second-trimester screening test; of these, only 40 women had positive results, and the rest had negative results (Table 2).

The sensitivity and specificity of the second-trimester screening test were measured in this study. The results indicated that its sensitivity and specificity were 45% and 94.5%, respectively (Table 3).

Table 1. The sensitivity and specificity of the first-trimester screening test

Screening results	Outcome until two years old		Total
	Healthy	Abnormal	
Negative	754	6	760
	80.30%	30.00%	79.20%
Positive	185	14	199
	19.70%	70.00%	20.80%
Total	939	20	959
	100.00%	100.00%	100.00%

Table 2. Frequency of the second-trimester screening test results

Screening results	Frequency (N)	Percent (%)	Cumulative Percent (%)
Negative	471	49.1	49.1
Positive	40	4.2	53.3
Not done	448	46.7	100
Total	959	100	100

Table 3. The sensitivity and specificity of the second-trimester screening test

Screening Results	Outcome until two years		Total
	Healthy	Abnormal	
Negative	460	11	471
	94.50%	55.00%	92.90%
Positive	27	9	36
	5.50%	45.00%	7.10%
Total	487	20	507
	100.00%	100.00%	100.00%

Discussion

Chromosomal abnormalities can occur in the developing fetus in any pregnancy. These abnormalities lead to death before or shortly after birth and/or lifelong disabilities. On the other hand, early diagnosis of fetal abnormalities, helps parents decide whether to hold or terminate current pregnancy (8). This study aimed to diagnose fetal abnormalities in the early stages of pregnancy and hence, to prevent future adverse conditions for the infant and his/her family.

In the past few decades, very few prepartum fetal disorders were diagnosable. Now, after many years, the process of prenatal diagnosis has changed. The purpose of prenatal diagnosis is to provide accurate information on the short- and long-term prognosis, risk of recurrence, and potential treatments for the affected fetus (9).

On the other hand, screening tests are not always accurate and can be problematic, and the accuracy of the tests may vary depending on the maternal age and other existing characteristics. Hence, in parents consulting, the sensitivity and specificity of the tests should be taken into account by considering the possibility of false positives and negatives in the test results. Evidence showed that the sensitivity of the first-trimester screening test is between 80% and 84%, and the second-trimester screening test's sensitivity ranges from 80% to 82% (10,11).

The sensitivity of the first- and second-trimester screening tests were evaluated in the present study, which was estimated to be 70% and 45%, respectively. These sensitivities are lower than the actual level. This might be due to the participants who had positive biochemical results in this study; and those whose fetuses had an NT

defect were not included. This is while fetal NT is crucial in the first-trimester screening test and is effective in raising test sensitivity. Another reason could be the lower accuracy of the laboratory tools and kits used.

Previous studies showed that the specificity of the first-trimester screening test was about 95%, and the specificity of the second-trimester screening test was about 95%. In the current study, the specificity of the first-trimester screening test was 80.3%, which was lower; however, the specificity of the second-trimester screening test was 94.5%, which was in accordance with previous studies (10,11).

There were many false positives in this study, and this is due to that our studied population was young, 72% of them were under 35 years old. Therefore, the screening tests were performed on a low-risk population, and this result could be justifiable.

Given the importance of the first trimester of pregnancy in the process of fetus development and the prevalence of anxiety in pregnant women during this period, it is recommended that stress coping strategies should be taught to pregnant women, especially mothers with positive screening results. There is a statistically significant relationship between anxiety scores and second-trimester markers, including gonadotropin, β -hCG, α -fetoprotein, and unconjugated estriol (12,13).

Amniocentesis and CVS are two invasive and high-risk diagnostic methods used to diagnose chromosomal, genetic, and metabolic diseases in the embryonic period. Because of that, these invasive tests are associated with several complications, such as fetal death, rupture of the

membranes, vaginal bleeding, and chorioamnionitis, they are usually used if needed and after the positive screening tests (14,15).

On the other hand, invasive tests for assessing fetal health, such as amniocentesis and CVS, should not be abandoned just because of the complications. Finally, the appropriate screening and diagnostic tests should be selected based on each patient's characteristics and without being afraid of their complications (16,17).

Conclusion

Despite recent advances in the prenatal field, the accuracy of screening tests may still vary depending on maternal age and other existing characteristics. Consequently, in parents consulting, the possibility of false positives and negatives should be considered in the tests.

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Conflict of Interest

Authors declared no conflict of interests.

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