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Research Article

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A Comparison of the performance of Invasive Tests for Genetic Congenital Defects in Response of the First- Trimester Screening with High and High Moderate Risks

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ABSTRACT

To evaluate the pregnancy outcomes in women with high and high moderate risks in first trimester screening.Among pregnant women in gestational age within 11 to 13 weeks and 6 days who were screened in the first-trimester from January of 2013 to January of 2014 (NT sonography and simultaneous tests of PAPP A, FREE BHCG) and classified in high risk and high moderate risk groups, 99 persons were selected randomely. High- risk involves women with a risk below 1/50 and high moderate risk involves women with a risk between 1/50- 1/300. 21 women were at high-risk and 78 women were at high-moderate risk. After informing women from the benefits and complications of diagnostic invasive tests, informed consents were taken from the patients, amniocentesis or CVS was carried out and the sample was examined for karyotype.Other women who didn't consent to do the invasive tests were under the control until the birth of their children and were examined for their phenotype. 21 women with high-risk and 65 women with high-moderate risk were subjected to amniocentesis or CVS.The mean age of women with high-risk included 15 (%71.5) women below 35Yand 6(%28.5) women above 35Y.The mean age of women who have shown high modrate-risk in first-trimester screening included 57(%73.5) women with an age below 35y and 21(%26.5) women with an age above 35y. Finally, they found two fetuses with trisomy 21 who were at high-risk group. The age of the first mother was above 35y and NT was in the range between %50-%95, papp A was 1.162 mom and FREE BHCG was equal to 4.875 mom, the age of the latter was below 35y with NT in a range above %95, papp A was 0.364 mom and Free BHCG was equal to 0/695 mom. Among the fetuses who had normal karyotype but faced with some complications, one case led to the death of a seven-month-old fetus due to kidney problem who was at high modrate-risk and the age of his/her mother was above 35y with NT between %50 and %95, papp A equals to 0.799 mom and Free BHCG equals to 0/950 mom, the other fetus was aborted in fourth month was at high risk and him/her mother age was less than 35y, her NT was in a range above 0/95, pappA = 0/909 MOM and free BHCG = 0.566 mom.In women who did not consent to invasive testing, all infants had normal phenotype but there was one case with the problem of hearth VSD who was at high-moderate risk and his/her mother age was below 35, NT was between %50-%95, pappA was 0/803 mom and free BHCG was equal to 0/582 mom.The first-trimester screening has significantly contributed to diagnosing the chromosomal abnormalities and mother age is not a reason for not doing the screening. Mothers with high and high-moderate risks in first-trimester screening were recommended to do the diagnostic invasive testes. Despite, the women are at high and high-moderate risk groups and their karyotype results are normal, they are still at risk of pregnancy problems, so they need more cares during their pregnancy.

Keywords: First-trimester screening; High risk; High-moderate risk; Aminocentesis; cvs

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INTRODUCTION

Chromosomal abnormalities is one of the serious problems in pregnancy. Down syndrome was first described by John Langdon in 1866 with the incidence of 1/700 in live borns(1).Children with Down syndrome are faced with the increase of congenital defect risk and infectious morbidity and all have different levels of decreasing the IQ with an average of 24 and a decrease in lifetime up to 10-20 years (2).

Among the different screening strategies for Down syndrome, the first-trimester screening including a combined evaluation of serumal markers FREE BHCG and PAPP A and nuchal translucency screening (NT) within 11-14 weeks of pregnancy that its detection rate was %90 with a false-positive %5 was used in screening, this method is effective and acceptable in many countries(3, 4). The effectiveness of first-trimester combined test can be increased when more serum markers are assessed،either sequentially in all pregnancy(integrated test)(5)،in the vast majority of pregnancy (stepwise sequential test)(6) or only in intermediate-risk pregnancies (contingent screening)(7).A contingent screening strategy was proposed by Nicoladies, et.al for the first time in 2005. In contingent screening, individuals are classified into three groups: High-risk, moderate-risk and low-risk. Women with high risk are invited to consultation sessions in order to perform the invasive tests. Only women with moderate risk are subjected to second- trimester screening, and no more test is carried out on women who are in low- risk group(8). The validity of diagnosis by karyotyping cells obtained from the invasive testes is between %97.5 and %99/8 (9-13), although, the invasive tests are associated with the abortion risk(14, 15). The purpose of the present study is to compare the results from detective invasive tests in women with a risk below 1/50 and women with a risk between 1/50 to 1/300.

MATERIALS AND METHODS

Among pregnant women in gestational age within 11 to 13 weeks and 6 days who were screened in first-trimester from January of 2013 to January of 2014 (NT sonography and simultaneous tests of PAPP A, FREE BHCG) and classified in high-risk and high-moderate risk groups, 99 persons were selected randomly.Women with high risk were those with a risk below 1/50 and women at high-moderate risk were those with a risk between 1/50 and 1/300. some explainations were given to all patients about pre-birth diagnostic methods such as CVS or amniocentesis. After informing them from the benefits and shortcomings of detective invasive tests, informed consents were taken from the patients, aminocentesis or CVS was carried out and the sample was examined for karyotype. Other women who didn't consent to do the invasive tests were under the control until the birth of their children and a study of phenotype was carried out on them. In the study, a trained person is employed to do sonography and desired studies. The trained person puts aminocentesis or CVS into the amnion sack with needles NO.20-22 under the sonography guidance, he must be careful that the needle doen't touch with the umbilical cord. Then, a sample of placenta (CVS) or about 20cc of amnion liquid (aminocentesis) is drawn out by a needle in order to evaluate the karyotype. By sonography, the bore site of uterus was examined for bleeding and at the end, the fetus hearth movement was checked and recorded.

RESULTS

In present study, pregnancy consequences were evaluated in 99 pergnant women who were selected randomly and subjected to first-trimester screening (nuchal translucency sonography, Free BHCG, PAPP A) between January of 2013 to January of 2014 and were at high- risk (below 1/50) and high-moderate risk (1/50-1/300) groups. From this, a number of 21 women (%21,2) were at high- risk and 78 women (%78.8) were at high-moderate risk (Table 1).

Table 1. Number of women in high-risk and high-moderaterisk groups

Percentage	Number	
21.2	21	High Risk
78.8	78	High modrate Risk
100	99	Total

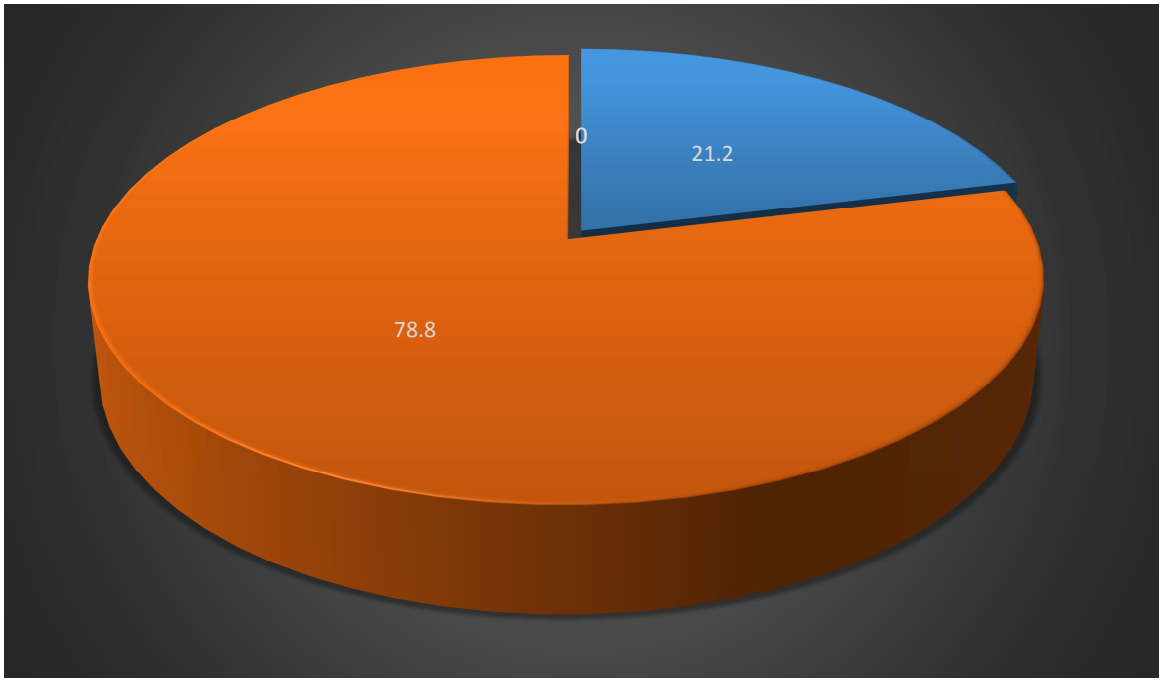

Figure 1. Percentage of people in the study
Blue: High-risk
Red: High-moderate risk

Mean age of women at high- risk was as follow: 15(%71.5) women below 35Yand 6(28.5%) women above 35Y. The mean age of women who were at high modrate-risk in first-trimester screening included 57(%73.5) persons below 35y and 21(%26.5) persons above 35y (Tables 2 and 3).

Table 2. Mean age of pregnant women at high- risk

Percentage	Number	
71.5	15	below 35
28.5	6	above 35
100	21	Total

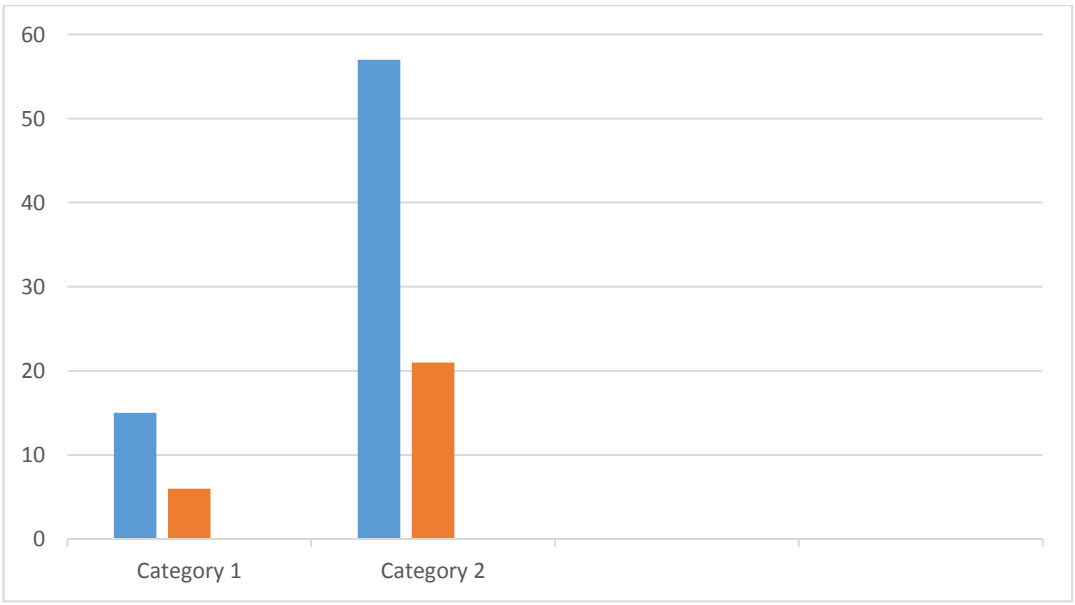

Figure 2. Mean age of pregnant women
Blue: below 35, Red: above 35
Category$_1$: High Risk, Category$_2$: High-moderate Risk

Table 3. Mean age of pregnant women at high modrate- risk

Percentage	Number	
73.5	57	below 35
26.5	21	above 35
100	78	Total

Aminocentesis or CVS was recommended to all women at high and high-moderate risks. Finally 86 women consented to do aminocentesis or CVS. 21(%100) women were at high- risk and 65(%83.3) women were at high-moderate risk (Table 4).

Table 4. The mean number of people who were subjected to aminocentesis or CVS in high and high-moderate risk groups

Percentage	Number	
100	21	High- risk
83.3	65	High-moderate risk

Finally, two Fetuses had abnormal karyotype, both were trisomy 21 and at high- risk group. Among the fetuses with normal karyotype, two fetuses faced with some problems, one of them died in seven- month age due to kidney problem at high-moderate risk group and the other was aborted at high- risk group. The pregnant mothers who didn't consent to perform the invasive test, all had infants with normal phenotype, but one case was seen with heart VSD who was at high-moderate risk (Table5 and6).

Table 5. Specifications of women having a fetus with chromosomal abnormalities

Person (2)	Person (1)	
31	42	mother age
zero	2	Parity
61kg	70kg	mother weight
unwanted	unwanted	Pregnancy way
12weeks and 3 days	11 weeks and 5 days	pregnancy week
0.364MOM	1.162MOM	PAPP A
0.695MOM	4.875MOM	FREE BHCG
%95 above	Between%50 and %95	NT
1/8	1/65	Final risk
Trisomy 21	Trisomy 21	chromosomal abnormalities

Table 6. Specifications of women having a fetus with complication with normal karyotype

Person (2)	Person (1)	
38	33	mother age
1	1	Parity
73kg	84kg	mother weight
unwanted	unwanted	Pregnancy way
12weeks and 6 days	11 weeks and 3 days	pregnancy week
0.799 MOM	0.909 MOM	PAPP A
0.950 MOM	0.566 MOM	FREE BHCG
Between%50 and %95	%95 above	NT
1/150	1/45	Final risk
Fetus death due to Kidney problem	abortion in 4 weeks	Type of complication

The specifications of a pregnant mother who didn't consent to do invasive test and faced with the heart VSD complication in her fetus are as follow: mother age was 33 years old with parity1, mother weight was 83 kg and her way for pregnancy was unwanted way and pregnancy age was 11 weeks and 3 days, NT was between %50 and %95, Papp A equals to 0/803 MOM, free BHCG equals to 0/582 MOM and final risk was 1.171.

Both cases had trisomy 21 and were at high- risk group but the age of one of them was above 35Y and here NT was between %50 and %95, papp A equals to 1.162 MOM and FREE BHCG equals to 4.875 MOM, the age of another was below 35Y with NT in a range above %95, PAPP A equals to 0.364 MOM and free BHCG equals to 0.695 MOM. Among the fetuses who had normal karyotype, two of them faced with complication. One led to fetus death in seven months due to kidney problem who was at high-moderate risk and the mother age was above 35Y with NT between %50 and %95, Papp A equals to 0.779 mom and free BHCG equals to 0.950 mom, the other led to fetus abortion in fourth month who was at high risk and the mother age was below 35, NT was at a range above %95, papp A equals to 0/909 MOM and free BHCG equals to 0.566. There was no trace of trisomy 18 and 13 and turner.

DISCUSSION

In this study, among 99 pregnant women with a risk below 1/300 in first- trimester screening, a total of 86 women consented to do the amniocentesis or CVS . Finally, two cases of Down syndrome were observed. In first case, the age of mother was above 35Y, NT was in a range between %50 and %95, papp a equals to 1.162 MOM and FREE BHCG equals to 4.875 MOM, and in second case, the age of mother was below 35Y, NT was in a range above %95, PAPP a equals to 0.364 MOM and FREE BHCG equals to 0.695 MOM. Among the fetuses who had normal karyotype, two of them were faced with complication, one with death in seventh month because of the kidney problem who was at high-moderate risk group and mother age was above 35Y with NT between %50 and %95, papp a=0.779 and free BHCG=0.950 MOM, and the other with abortion in fourth month who was at high risk and mother age was below 35Y, NT in a range above %95, papp a=0.909 MOM, free BHCG=0.566 MOM.

In pregnant mothers who didn't consent to do invasive test, all infants had normal phenotype, but in one case, the infant was suffering from the heart VSD who was at high-moderate risk and mother age was below 35, NT was in a range between %50 and %95, papp a=0.803 MOM and free BHCG=0.582 MOM.

In a study carried out by peuhkurinen et al. (16), they found that Down syndrome can be diagnosed by using the biochemical markers and nuchal translucency and a combination of them with %64.2 , %64.5, %72.4 respectively, thus, the false-positive rate will reach 7.8، 4.4، 4 respectively. In similar study, Sieroszewski (17) also reached to the same result that using the nuchal translucency sonography and serumal markers such as "ESTRADIOL", "BHCG", "AFP" in second- trimester have high sensivity and safety in diagnosing genetic anomaly with false- positive rate of 0.6% and decrease in invasive tests. Nicolaides, et.al in their study suggested that depending on mother age and NT sonography and the measurement by serumal marker in first-trimester screening with moderate risk between 1/50-1/1000, detective rate of chromosomal anomaly is %90(18).

In a study by D.S.SAHOTA, et al.(19), it was found that with the moderate risk 1/50-1/1000, detective rate of Down syndrome by using the biochemical marker and NT is %87.5 which considering the lack of nasal bone, the rate of false- positive will be decreased from %2.5 to %2.3. Dr. YEO GS et al.(20)studied the effect of nasal bone in first-trimester screening and found that with the threshold of 1/300, the rate of Down syndrome detection is increased from %87.1 to %96.8 and the false- positive rate is decreased from %5.1 to %3.7.

MAIZ N, et al. (21) studied the Ductus venosus blood flow in patients having a risk between 1/51 and 1/1000 in order to discover the aneuploidy. Finally they suggested that by determining ductus venosus flow %96 with the false- positive rate of 3%, we can detect Down syndrome. In a similar study, M. Munoz et al. evaluated pregnant women with moderate risk between 1/101 to 1/1000 for down syndrome،women were referred for risk reassessment that include the use of secondrey ultrasound markers(nasal bone،ductus venosus and tricuspid flows). Moderate risk was divided into two typs: High (1/101-1/250) and low (1/251-1/1000). They concluded that the false- positive rate will be decreased from 3% to 1.3-1.8%(22).In our study, the mean age of women with high risk were 15 (%71.5) women below 35Yand 6 (28.5%) women above 35Y. The mean age of women who were at high-moderate risk in first- trimester screening were 57(73.5%) women below 35Y and 21(26.5%) women above 35Y. It indicates the incrcase in pregnant women numbers below 35Y and it is in consistent with other studies. Ranta JK, et al. (23) in their work evaluated the detective rate of genetic abnormality by using the serumal markers and concluded that using the biochemical markers in an age above 35Y, has the most effectiveness in diagnosing genetic diseases and combined screening is recommended for the age below 35Y. The mean age of women having the fetus with Down syndrome was 37Y. We also used the combined screening (biochemeical marker and NT sonography) in our work, and the mean age of mothers having the fetus with Down syndrome is consistent with Ranta.

Simpson LL, et al.(24)in their work studied the incidence of major heart congenital disease with the increase of nuchal translucency. They found that with the increase of NT from 2 to 3, the incidence rate of heart disease reached to 14.1/1000 from 49.5 /1000. They concluded that NT≥2/5 is as indication for echocardiography. It was in consistent with our findings.

Rossi A, et al.(25) in their work found that CUT OFF: 1.25 for PAPP A had the necessory feature and sensivity for detecting the LGA. HUNG, et al. in other work found that women with low PAPP A and non- conjugated estrogen and high AFP, HCG are subjected to the risk of fetus abortion and birth before 32weeks (26). A case of fetus abortion with high risk was also seen in our study.

In study by Mohammad jafariet al. (27) low PAPP A of≤0.4 MOM occurred in 29.7% of women with screen positive pregnancies and normal karyotype and in women with low PAPP A of ≤0.4 MOM preeclampsia،spontaeous abortion preterm labor and birth weight were higher than normal PAPP A(> 0.4 mom).

Considering the results, the first- trimester screening (biochemeical markers and NT sonography) has significantly contributed to detecting the chromosomal abnormalities. Doing the detective invasive test is an appropriate method for detecting genetic abnormalities before approaching to second- trimester of pregnancy in women at high-risk and high-moderate risk and here the age of mother is not reason for not doing screening. Although women are at high-risk and high-moderate risk groups and the result of their karyiotype are normal, they are subjected to the risk of pregnancy complications and need more care during their pregnancy. It is strictly recommended that all pregnant women do scan anomaly sonography in second-trimester and women with increased NT are subjected to echocardiography.

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