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Original Article

Trisomy 21 screening based on first and second trimester in a Taiwanese population

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ABSTRACT

Objective: This study investigates the performance of first- and second-trimester screening tests for detecting fetal trisomy 21 in a Taiwanese population.
Materials and methods: This multicenter study 29,137 cases enrolled the chromosomal abnormality screening between 2013 and 2014 two years period from Taipei city. There were 23,990 was done the first trimester screening using a combination of fetal nuchal translucency, maternal serum β-human chorionic gonadotropin, and pregnancy-associated plasma protein-A between 11^{+0} and 13^{+6} weeks of gestation age. Second-trimester screening was done for 5149 cases using a double test (β-human chorionic gonadotropin and serum alpha fetoprotein) between 15 and 20 weeks of gestation. The cut-off risk for both is 1:270 or higher.
Results: This multicenter study 29,137 cases that completed first- and second-trimester screening, and the outcome was available in 28,726 cases. The mean maternal age of the screen-positive group was 34.6 ± 4.2 years. The first-trimester had 891 cases screening positive with a detection rate of 97.5% for fetal trisomy 21, and false positive rate of 3.5%. In the second-trimester had 334 cases screening positive, the detection rate and false positive rate were 33.3% and 6.4% for trisomy 21, respectively.
Conclusion: The first-trimester screening had higher performance with a lower false positive rate than the second-trimester screening. First-trimester screening could reduce the rate of unnecessary invasive testing for all pregnant women.

Introduction

Trisomy 21 is the most common prenatal chromosomal abnormality, with prevalence of about 1/600–800 pregnancies [1]. This genetic disorder is caused by the presence of a complete or partial third copy of chromosome 21. The incidence of trisomy 21 increases with maternal age. Infants with trisomy 21 could have multiple defects, including mental retardation, congenital heart disease, and facial defects. Hence, prenatal screening and diagnosis of trisomy 21 for a fetus are an important issue for pregnant women aged 35 years or older.

At 11^{+0} to 13^{+6} gestational weeks, first-trimester screening using ultrasound is done to scan the fetal neck for enlarged nuchal translucency (NT). Increased NT is associated with not only trisomy 21 but also other chromosomal abnormalities [2–7]. First-trimester aneuploidy screening considers a combination of maternal age, NT, and maternal serum (i.e., pregnancy associated plasma protein A (PAPP-A) and free β-human chorionic gonadotropin (free β-hCG)). This method can identify about 90% of fetuses with Down

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syndrome with a false positive rate of 5% [8–10]. The second trimester maternal serum double test considers a combination maternal age and maternal serum markers such as β-hCG and serum alpha fetoprotein (AFP), and it has an estimated detection rate of 56% for fetal trisomy 21 with a false positive rate of 5% [11,12].

Chorionic villus sampling (CVS) or amniocentesis is the most accurate method for prenatal diagnosis of fetal trisomy 21 and other chromosomal abnormalities. However, it may result in miscarriage at a rate of 1–3% [13,14], which leads to psychological stress, especially for older pregnant women. Therefore, the American College of Obstetricians and Gynecologists (ACOG) recommends that all pregnant women be screened first to determine the individual risk. Women who have high risk can further receive genetic counseling or invasive tests [15,16]. In this study, we compared the performance of screening for fetal trisomy 21 and other chromosomal abnormalities using first- and second-trimester screening in an unselected pregnant population in Taipei.

Methods

This multicenter study was done in Taipei to screen for trisomy 21 using first- and second-trimester screening between 2013 and 2014. The first-trimester combined screening test examined a combination of fetal NT, maternal age, and maternal serum markers (free β-hCG and PAPP-A) at 11 + 0 to 13 + 6 weeks of gestation age. For fetal NT measurements, fetal crown-rump length should be 45–84 mm, and a true sagittal view was obtained. The fetus posture was a neutral position that is not hyperextended or hyperflexion, and the fetal head, neck, and upper chest should be obtained. The fetal NT thickness was measured from the inner to inner borders of the two echogenic lines at the widest part of the NT [17,18]. All sonographers were certified by The Fetal Medicine Foundation (FMF) or the Taiwan Maternal Fetal Medicine Society (TMFMS). The Institutional Review Board of the institution approved this study.

After the fetal dating was determined, first-trimester serum markers of PAPP-A and free β-hCG were measured at 9 to 13^{+6} weeks of gestation at an outpatient clinic. Maternal blood serum was isolated for analysis at less than 20 °C within 24 h after collection using a Kryptor analyzer (Brahms Diagnostics GmbH, Berlin, and Germany). The laboratory that performed the testing is a part of the quality control program of the United Kingdom National External Quality Assessment Service. Maternal age, weight, height, method used for conception, and smoking status were recorded at the time of blood sampling. The ultrasound measurements and biochemical results were recorded, and the risk for trisomy 21 was calculated using the FMF or the first trimester screening of TMFMS algorithm [19].

The second-trimester serum test was done using maternal serum markers including β-hCG and AFP. The test was carried out between 15 and 20 weeks of pregnancy. The risk of trisomy 21 was calculated using a combination of maternal age and maternal serum markers. A risk above 1:270 was considered screen-positive, and an invasive test such as CVS or amniocentesis was offered. Karyotypes and outcomes of the pregnancy were added to the database. Statistical analysis was done using Microsoft Excel (2007) and SPSS v. 19.0. Both of the detection rate and the false-positive rate were calculated.

Results

The characteristics of the high-risk population of the first- and second-trimester screening test shows in Table 1. In the screen-positive group, there were mostly singleton and spontaneous conceptions. The mean times of performing the screening test in the first- and second-trimester screening tests were 12 ± 0.7 and 16 ± 1.08 weeks of gestation age. The mean maternal age of the screen-positive group was 34.6 ± 4.16 years, and 48.1% of the study sample had advanced maternal age (35 years or older).

Table 1
Characteristics of the screen-positive population.

	Value (n (%))			
	First-trimester screening		Second-trimester test	
Number of fetuses				
Singleton	871 (97.8)		331 (99.1)	
Twins	20 (2.2)		3 (0.9)	
Method of conception				
Spontaneous conception	853 (95.7)		324 (97.0)	
Ovulation induction drugs	11 (1.2)		6 (1.8)	
In vitro fertilization	27 (3.0)		4 (1.2)	
Maternal age				
≥35 years	462 (51.9)		136 (40.7)	
<35 years	429 (48.1)		198 (59.3)	
Gestation age				
	11 weeks	194 (21.8)	15 weeks	115 (34.4)
	12 weeks	460 (51.6)	16 weeks	151 (45.2)
	13 weeks	237 (26.6)	17 weeks	43 (12.9)
			18 weeks	11 (3.3)
			19 weeks	8 (2.4)
			20 weeks	6 (1.8)
Total	891 (100)		334 (100)	

Among the first trimester screening group, 778 pregnant women (87.3%, 778/891) were screen-positive and underwent an invasive diagnosis, of which 93.8% (730/778) underwent amniocentesis and 6.2% (48/778) underwent CVS. Maternal age distribution of the screen-positive group in two screening group and general population of Taipei shows in Fig. 1. There were 92 women (10.3%, 92/891) accepted non-invasive prenatal testing (NIPT) as a second option. Of the 21 screen-positive cases that did not accept advanced diagnosis, three spontaneous abortions occurred before the diagnostic test (14.3%, 3/21). In the second-trimester screening group, 89.8% screen-positive pregnant women underwent amniocentesis to confirm the fetal karyotype, and 5.7% screen-positive pregnant women accepted NIPT as a second option. There were 17 pregnant women who did not receive any invasive diagnosis, and one of them had a spontaneous miscarriage before amniocentesis.

Screening was carried out in 29,137 cases (23,990 first trimester and 5147 s trimester). Outcomes were obtained in 28,726 cases

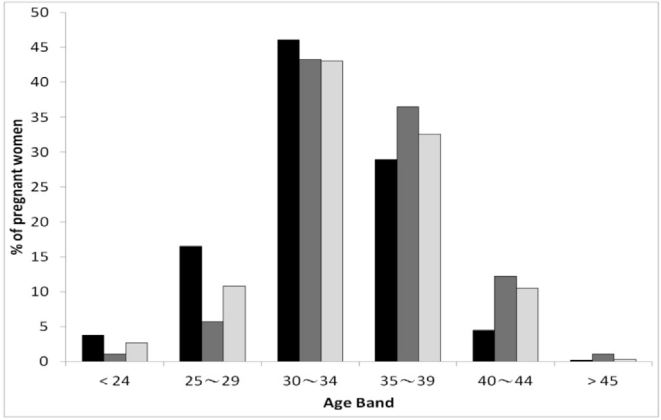

Fig. 1. Maternal age distribution of the screen-positive group in first-trimester screening group (□), second-trimester screening group (▒), and general population of Taipei (■).