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Original Article

Noninvasive prenatal testing for fetal trisomy in a mixed risk factors pregnancy population

Wai-Hou Li [a, b], Peng-Hui Wang [a, b], Chi-Mu Chuang [a, b], Yi-Wen Chang [a, b], Ming-Jie Yang [a, b], Chih-Yao Chen [a, b, *], Kuan-Chong Chao [a, b], Ming-Shyen Yen [a, b, c]

[a] Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan
[b] National Yang-Ming University, School of Medicine, Taipei, Taiwan
[c] Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

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ABSTRACT

Objective: This study assesses the performance of noninvasive prenatal testing (NIPT) for fetal aneuploidies in a mixed risk factors pregnancy population.
Materials and methods: Data review of 169 pregnant women undergoing prenatal aneuploidy screening in a single tertiary medical center was conducted. Indications included maternal anxiety, advanced maternal age, abnormal nuchal translucency, and high/moderate risk of first trimester Down syndrome screening. Multifetal pregnancies and patients receiving *in vitro* fertilization were also enrolled for analysis.
Results: A total of 169 patients were enrolled in this study during a time period from July 2012 to June 2014. For patients' $\geq$ 34 years, anxiety about amniocentesis was the most common reason for patients selecting NIPT for fetal aneuploidy screening, with 107 (88.4%) patients choosing NIPT for this reason. Among the total patient population, two patients showed a positive result from NIPT. One patient displayed 47, XXY, which was confirmed to be a false-positive result. The other patient displayed trisomy 18, which was confirmed by an amniotic cell culture. The sensitivity for NIPT is 100% with the specificity 99.4%.
Conclusions: NIPT for fetal aneuploidy in a mixed risk factors pregnancy population showed high accuracy. NIPT applied to the low risk population might reassure the anxious family.

Introduction

Prenatal screening for fetal aneuploidy is a standard offering in most parts of the world. Fetal aneuploidies, such as trisomy 21 (T21, Down syndrome), trisomy 18 (T18, Edwards syndrome), and trisomy 13 (T13, Patau syndrome), as well as aneuploidies related to the X and Y chromosomes are the most common chromosomal abnormalities. Using the first trimester screening (FTS), consisting of maternal serum markers and nuchal translucency (NT) measurement, we were able to identify 85–95% of T21 and T18 cases, with a 5% rate of false positives. Invasive procedures, amniocentesis and chorionic villus sampling were taken as diagnostic tools [1,2]. The discovery of the presence of fetal cell-free DNA (cfDNA) and RNA in maternal plasma, combined with new DNA sequencing technology, has allowed noninvasive prenatal testing (NIPT) of common fetal trisomy with high sensitivity and specificity. From a multicenter prospective cohort study, NIPT provided detection rates > 99% for T21 and false-positive rates < 0.1% [3].

Due to the high accuracy of this new technology, the International Society for Prenatal Diagnosis, the National Society of Genetic Counselors, the American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal–Fetal Medicine (SMFM) have published committee opinions stating that cfDNA testing could be offered to pregnant women at high risk for fetal aneuploidy as a screening option after counseling [4–6]. Therefore, this technology might reduce the number of unnecessary invasive procedures, compared with conventional maternal serum

* Corresponding author. Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 11217, Taiwan.
E-mail address: zachary.joyce@gmail.com (C.-Y. Chen).

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Table 1
Maternal characteristics and gestational age of blood sampling.

Maternal age	
Median (y):	35.31
Advanced maternal age (≥ 34 y old):	121 (71.6%)
≤ 28 y old (*n*, %):	4 (2.5%)
29–33 y old (*n*, %):	44 (26.2%)
34–38 y old (*n*, %):	90 (53.3%)
39–42 y old (*n*, %):	27 (15.9%)
≥ 43 y old (*n*, %):	4 (2.5%)
Gestational age at blood sampling	
Median (wk)	13.45 wk
Range (wk)	7–31 wk
6–8 wk (*n*, %)	3 (1.8%)
9–12 wk (*n*, %)	64 (39.3%)
13–16 wk (*n*, %)	74 (45.5%)
17–20 wk (*n*, %)	17 (10.4%)
21–24 wk (*n*, %)	3 (1.8%)
25–28 wk (*n*, %)	1 (0.6%)
>28 wk (*n*, %)	1 (0.6%)
History or family history of aneuploidies (*n*, %)	**4 (2.4%)**

aneuploidy screening. Nevertheless, the power of this new technology in a mixed risk factors group has not yet been fully assessed. This study reports the finding from an observational study which was carried out to assess the performance of NIPT for fetal aneuploidy in a mixed risk factors pregnancy population.

Materials and methods

From July 2012 to June 2014, data were collected from a total of 169 pregnant women undergoing NIPT in a single tertiary medical center. Indications included maternal anxiety, advanced maternal age (≥ 34 years), abnormal NT, high/intermediate risk of maternal serum screening (2 and 4 markers), and high/intermediate risk result from first trimester screening. Twin pregnancies (total number 12), triplets (total number one), and patients receiving artificial reproductive technology (ART) to conceive, were also enrolled for analysis.

Result

A total of 169 pregnant women from a single tertiary medical center were recruited in this study. Maternal age ranged from 27 to 44 years. Median age was 35.31 years and 71.6% (121/169) were ≥ 34 years (Table 1). Thirty-one pregnant women had received ART, including six with intrauterine insemination, 24 with *in vitro* fertilization (IVF), and one with intracytoplasmic sperm injection (ICSI) (Table 2). Four women had a history or family history of aneuploidies.

Indication for NIPT

For patients < 34 years of age (48 patients) 27 (56.3%) asked for NIPT due to anxious feelings of possible fetal aneuploidies. Other indications included high risk of T13, T18, or T21, which accounted for 10 patients (20.8%), and intermediate risk of T13, T18, or T21, which accounted for another 10 patients (20.8%) (Fig. 1). For patients ≥ 34 years, anxiety about amniocentesis was the most common reason for the patient selecting NIPT for fetal aneuploidy screening, with 107 (88.4%) patients choosing NIPT for this reason. Other indications included 7 (5.8%) patients of high risk of T13, T18, or T21 and 7 (5.8%) patients of intermediate risk of T13, T18, or T21 (Fig. 2). For the 107 patients who were anxious about amniocentesis, 24 (22.4%) had taken NIPT as a primary test and had neither received FTS nor maternal serum screening (2 markers and 4 markers); 35 (32.7%) patients had taken NIPT before FTS; and 47 (43.9%) patients had taken NIPT and FTS on the same day.

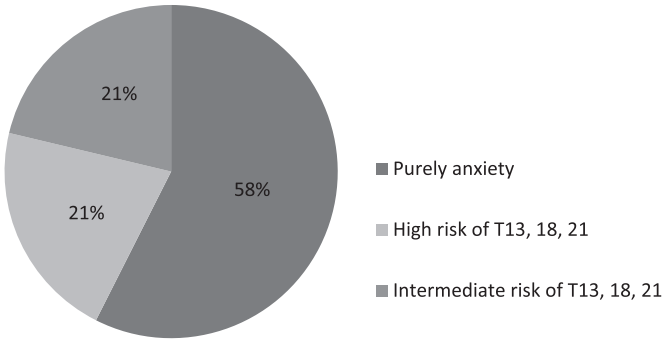

Fig. 1. Indication of NIPT—patients less than 34 years old.

Fetal aneuploidies

Among 169 patients, two patients showed positive results from NIPT. One showed positive for 47, XXY and the other showed positive for T18. Both later received amniocentesis for diagnostic confirmation. The patient who had the result of 47, XXY was later shown to have a false-positive result. The fetus was confirmed to be 46, XY using amniocentesis and was shown to be a healthy male baby after delivery. The other patient, who showed positive for T18 from NIPT, went on to have amniocentesis which confirmed the diagnosis of T18. After diagnosis, the patient decided to terminate the pregnancy.

The sensitivity for fetal aneuploidy screening in this study was 100% with a specificity of 99.4%.

Discussion

Since Lo et al [7] discovered the presence of fetal DNA fragments in maternal serum, a new technology for prenatal aneuploidy

Table 2
The ways of patients got conceived.

Method of conception	Number of patients	Percent (%)
IUI	6	3.6
IVF	24	14.2
IVF (ICSI)	1	0.6
Nature	138	81.7
Total	169	100.0

ICSI = intracytoplasmic sperm injection; IUI = intrauterine insemination; IVF = *in vitro* fertilization.

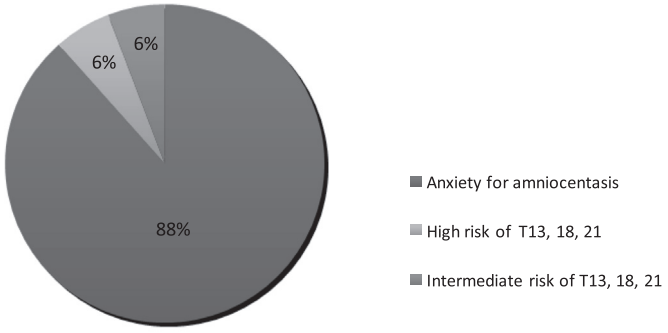

Fig. 2. Indication of NIPT—patients ≧ 34 years old.