

Pregnant Women's Attitudes to and Knowledge of Non-invasive Prenatal Testing in Down Syndrome Screening in Hong Kong

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Objectives: To evaluate pregnant women's attitudes to and knowledge of non-invasive prenatal testing in Down syndrome screening.

Methods: From 1 November 2012 to 31 December 2012, all pregnant Chinese women who attended for Down syndrome screening were invited to complete a self-administered questionnaire, which enquired about their knowledge and attitudes regarding non-invasive prenatal testing. Those who subsequently screened positive for Down syndrome were given the same questionnaire again.

Results: A total of 651 pregnant women were included, of whom 439 (67.4%) returned their questionnaires after Down syndrome screening (group 1). Among 29 patients who screened positive for Down syndrome, 16 (55.2%) completed the questionnaire for the second time (group 2). Most of the women in group 1 were aware of first-trimester combined Down syndrome screening (78.1%), second-trimester biochemical screening (66.7%), and invasive tests (78.4%). However, only 96 (21.9%) were aware of non-invasive prenatal testing. The mean overall knowledge score on non-invasive prenatal testing in group 1 patients was 2.55 of 9, with a significantly higher score in women who were of higher education level, higher family income, undergoing antenatal care in both the public and private sectors, and those with positive Down syndrome screening (group 2). Overall, 328 (74.7%) would consider having non-invasive prenatal testing. However, about one-third would still proceed to diagnostic tests even when non-invasive prenatal testing was negative. Over 80% would like the public sector to provide non-invasive prenatal testing, of whom 52.8% considered that this should be free of charge.

Conclusion: Non-invasive prenatal testing is relatively new. It is not surprising that this study showed an overall low level of knowledge. Although most pregnant women preferred the test to be provided free of charge by the public sector, adequate counselling and information should still be provided.

Hong Kong J Gynaecol Obstet Midwifery 2014; 14(1):43-50

Keywords: Attitude; Down syndrome; Knowledge; Pregnant women; Prenatal diagnosis

Introduction

In 2010, a universal Down syndrome screening programme was launched by the Hong Kong Hospital Authority in the public sector. Pregnant women were offered either the first-trimester combined test (which includes measurements of nuchal translucency, free beta-human chorionic gonadotropin, and pregnancy-associated plasma protein-A) or the second-trimester dual test (alpha-fetoprotein and total human chorionic gonadotropin) irrespective of their age. Conventionally, those women who are screened positive are offered diagnostic tests (chorionic villus sampling or amniocentesis).

A recently published local research¹ summarising the first-year experience showed that the detection rate for the first-trimester combined screening test for Down syndrome was 91.2%, with a screen-positive rate of 5.1%, and a

false-positive rate of 4.9%. There were seven miscarriages after subsequent invasive diagnostic tests (0.9%). As one of the main concerns of pregnant women about prenatal diagnosis is the safety and non-invasiveness of the tests², the introduction of non-invasive prenatal testing (NIPT) into clinical services should be able to address this concern.

The discovery of cell-free fetal DNA in the maternal circulation has driven developments in non-invasive prenatal diagnosis in the past decade³. Cell-free fetal DNA has been used successfully as a non-invasive screening test for fetal sex and fetal Rhesus D genotype since the 1990s^{4,5}.

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Further studies suggested that this NIPT technique can also be used for Down syndrome screening, by identifying the presence of an elevated amount of chromosome 21 sequences in maternal blood⁶. The NIPT is advantageous in that the number of invasive procedures with the inherent risk of procedure-related miscarriage can be reduced, and the test can also be performed much earlier in the pregnancy, with some studies showing its feasibility at 7 weeks of gestation⁷. A recent systematic review of seven large-scale cohort studies on NIPT showed a high sensitivity of 98.5-100% with a low false-positive rate of 0-2%⁸.

The International Society for Prenatal Diagnosis (ISPD) accepts that, with suitable genetic counselling, NIPT can be helpful for women who may have been determined to be at high risk by one of the previous recommended screening strategies⁹. The ISPD does not endorse the ad-hoc use of NIPT in women at low risk, outside a formal protocol that considers the overall best combination of tests, their impact on screening performance, and patient acceptability.

NIPT has been available in local private practice for about 1 year, with charges ranging from HK\$6,000-8,000. This study was conducted to evaluate pregnant women's attitudes to and knowledge of this relatively new screening test for Down syndrome.

Methods

Participants and Recruitment

From 1 November 2012 to 31 December 2012, all pregnant Chinese women who attended the United Christian Hospital and the Tseung Kwan O Hospital in Hong Kong for Down syndrome screening were invited to complete a self-administered questionnaire (group 1). Pregnant women who were not Chinese or who were unable to give consent were excluded. Women with a positive screening result (group 2) were contacted by a specialist nurse by telephone, informed of the positive Down syndrome screening results, and invited to attend the Prenatal Diagnosis Counselling Clinic for further counselling and plan of management. The same questionnaire was completed when the women attended the clinic. The study protocol was approved by the Research Ethics Committee of the Kowloon Central / East Clusters.

Questionnaire

The questionnaire was designed to evaluate the women's knowledge of and attitudes to NIPT. Knowledge was assessed by asking if the women knew the cause of Down syndrome, different methods of Down syndrome

screening (including first-trimester combined Down syndrome screening, second-trimester biochemical screening, amniocentesis, chorionic villus sampling, and NIPT), the detection rates, and the details of NIPT (including the methods, detection rate, and the abnormalities that could be detected). Each correct answer scored 1 and incorrect answer scored 0 for a total score of 9.

In the second part, attitude was assessed, including the women's acceptance of NIPT, and whether they would still proceed to an invasive diagnostic test if NIPT screened negative. Questions were asked about the cost and turnaround time for the results, and whether the women would like provision of the test in the public sector.

In the last part, basic demographic data were collected, including age, marital status, education level, occupation, family income, obstetric history, and any family history of chromosomal abnormality.

Statistical Analyses

Data were analysed using the Statistical Package for the Social Sciences, Windows version 16.0 (SPSS Inc., Chicago [IL], US). Descriptive statistics of responses to the survey questions were calculated. Chi-square test was used to calculate the difference in knowledge and attitudes between group 1 and group 2. Independent sample *t* test was used to compare the mean overall knowledge score between the two groups based on their demographic data.

Results

During the study period, a total of 651 eligible pregnant women attended for Down syndrome screening. Among them, 439 (67.4%) returned their questionnaires (group 1). Among 29 (4.5%) women who screened positive during the study period, 16 (55.2%) returned their questionnaires (group 2). A total of 455 questionnaires were received. Demographic data of the two groups are shown in Table 1. The proportion of women aged ≥ 35 years in group 2 was significantly higher than that in group 1 (62.5% vs. 20.5%; $p < 0.001$).

Details of women's knowledge of NIPT are shown in Table 2. In group 1, 394 (89.7%) were aware of Down syndrome, and 367 (83.6%) could correctly identify the cause as being a chromosomal abnormality. However, 34 (7.7%) did not know the cause of Down syndrome and there were 25 (5.7%), 11 (2.5%), and 2 (0.5%) who believed that the disorder was related to drugs, radiation, and birth asphyxia, respectively.

Table 1. Demographic data of pregnant women undergoing Down syndrome screening*

Characteristic	No. (%) of patients		p Value
	Group 1 (n=439)	Group 2 (n=16)	
Age (years)			<0.001
<35	349 (79.5)	6 (37.5)	
≥35	90 (20.5)	10 (62.5)	
Marital status			0.446
Married	395 (90.0)	16 (100)	
Single	37 (8.4)	0	
Widowed / divorced	3 (0.7)	0	
Gravida			0.854
First pregnancy	179	7	
Gravida ≥2	253	9	
Parity			0.371
0	229 (52.2)	9 (56.3)	
1	163 (37.1)	4 (25.0)	
2	34 (7.7)	3 (18.8)	
3	6 (1.4)	0	
Current pregnancy			0.594
Planned	296 (67.4)	12 (75)	
Unplanned	140 (31.9)	4 (25.0)	
Antenatal care			0.565
Public	246 (56.0)	7 (43.8)	
Public and private	174 (39.6)	8 (50.0)	
Education			0.858
No formal education	2 (0.5)	0	
Primary	10 (2.3)	0	
Secondary	276 (62.9)	9 (56.3)	
Tertiary	136 (31.0)	6 (37.5)	
Occupation			0.590
Housewife	162 (36.9)	4 (25.0)	
Health care worker	4 (0.9)	0	
Professional	44 (10.0)	1 (6.3)	
Clerk	139 (31.7)	8 (50.0)	
Other	74 (16.9)	2 (12.5)	
Husband's occupation			0.678
Health care worker	2 (0.5)	0	
Professional	83 (18.9)	3 (18.8)	
Clerk	109 (24.8)	6 (37.5)	
Other	218 (49.7)	6 (37.5)	
Family income (HK\$)			0.493
<10,000	78 (17.8)	1 (6.3)	
10,000-30,000	219 (49.9)	9 (56.3)	
>30,000	119 (27.1)	5 (31.3)	

* Some of the items do not total 100% because of missing data. Group 1 denotes all pregnant women attending for Down syndrome screening; group 2 denotes pregnant women who screened positive for Down syndrome and completed the questionnaire for the second time

Table 2. Comparison of knowledge of non-invasive prenatal testing (NIPT) between the two groups*

Item	No. (%) of patients		p Value
	Group 1 (n=439)	Group 2 (n=16)	
Cause of Down syndrome being a chromosomal abnormality	367 (83.6)	16 (100)	0.172
Awareness of NIPT	96 (21.9)	8 (50.0)	0.014
Accuracy of tests in correct order: invasive test > NIPT > first-trimester combined screening > second trimester biochemical screening	34 (7.7)	6 (37.5)	<0.001
Method of NIPT (maternal blood alone)	289 (65.8)	14 (87.5)	0.103
NIPT cannot achieve a diagnosis of Down syndrome	54 (12.3) [†]	1 (6.3)	0.735
NIPT cannot identify all chromosomal abnormalities	66 (15.0) [‡]	4 (25.0)	0.464
NIPT cannot identify structural abnormalities	166 (37.8)	7 (43.8)	0.827
NIPT can identify the fetal sex	27 (6.2)	1 (6.3)	1.000
Sensitivity >95%	69 (15.7)	5 (31.3)	0.191
False-positive rate <1%	47 (10.7)	1 (6.3)	0.876
Overall mean score (maximum score: 9)	2.55	3.44	0.022

* Group 1 denotes all pregnant women attending for Down syndrome screening; group 2 denotes pregnant women who screened positive for Down syndrome and completed the questionnaire for the second time

[†] 120 Women in group 1 did not answer the question

[‡] 143 Women in group 1 did not answer the question

Most of the pregnant women in group 1 were aware of first-trimester combined Down syndrome screening (n=343; 78.1%), second-trimester biochemical screening (n=293; 66.7%), and invasive tests such as chorionic villus sampling and amniocentesis (n=344; 78.4%). However, only 96 (21.9%) were aware of NIPT. The women had acquired their knowledge of NIPT from different sources, including public sector doctors (n=20; 20.8%), relatives and friends (n=21; 21.9%), the internet (n=32; 33.3%), magazines and newspapers (n=9; 9.4%), and private obstetricians (n=11, 11.5%); the remaining three women did not give an answer.

For detection rates, only about half of the women (n=217; 49.4%) believed that invasive tests were the most accurate, while 49 (11.2%) believed that NIPT was the most accurate test. Only 34 (7.7%) women could rank the tests in the correct order of detection rates.

Two-thirds (n=289; 65.8%) of pregnant women in group 1 could correctly state that NIPT was performed by maternal blood collection alone, 265 (60.4%) believed that NIPT could achieve a diagnosis of Down syndrome, and 230 (52.4%) believed that NIPT could screen for all chromosomal abnormalities. Less than half (n=166; 37.8%) were aware of the limitation that NIPT could not identify structural abnormalities, whereas 27 (6.2%) understood

that NIPT could detect fetal sex. Also, 69 (15.7%) women correctly stated that the test had a sensitivity of >95%, while 254 (57.9%) believed it being between 50% and 95%. One-third of the women (n=141; 32.1%) understood that NIPT was more specific than first-trimester combined Down syndrome screening.

Details of women's attitude of NIPT are shown in Table 3. Overall, 328 (74.7%) would consider having NIPT. In group 1, 316 (72.0%) would consider having the test, 345 (78.6%) would proceed to diagnostic tests if NIPT was positive, and 141 (32.1%) would still proceed to diagnostic tests even when NIPT was negative. Most of the women expected the test results to be available in less than 1 week, of whom 177 (40.3%) and 111 (25.3%) expected results to be available on the same day and within a few days, respectively. Most women (n=380; 86.6%) preferred NIPT to be available in the public sector, and 232 (52.8%) considered that this test should be free of charge. For those who were willing to pay, the proposed amounts were <HK\$500 in 21.4%, HK\$500-2000 in 13.9%, HK\$2001-5000 in 1.8%, HK\$5001-10,000 in 0.5%, and >HK\$10,000 in 0.2% of women.

When comparing the knowledge of women attending the Down syndrome screening clinic (group 1) with those who screened positive for Down syndrome (group 2), there

Table 3. Comparison of attitudes towards non-invasive prenatal testing (NIPT) between the two groups*

Item	No. (%) of patients		p Value
	Group 1 (n=439)	Group 2 (n=16)	
Will consider having NIPT	316 (72.0)	12 (75.0)	0.792
Will proceed to have diagnostic test if NIPT is positive	345 (78.6)	14 (87.5)	0.585
Will proceed to have diagnostic test if NIPT is negative	141 (32.1)	6 (37.5)	0.857
Expected turnaround time			
Same day	177 (40.3)	5 (31.3)	0.640
Few days	111 (25.3)	6 (37.5)	0.420
1 week	102 (23.2)	4 (25.0)	0.870
Few weeks	9 (2.1)	0	0.563
Proposed fee for NIPT (HK\$)			
Free	232 (52.8)	8 (50.0)	0.823
<500	94 (21.4)	3 (18.8)	0.798
500-2000	61 (13.9)	3 (18.8)	0.855
2001-5000	8 (1.8)	1 (6.3)	0.737
5001-10,000	2 (0.5)	0	0.787
>10,000	1 (0.2)	0	0.848
Public sector should offer this test	380 (86.6)	15 (93.8)	0.646

* Some of the items do not total 100% because of missing data. Group 1 denotes all pregnant women attending for Down syndrome screening; group 2 denotes pregnant women who screened positive for Down syndrome and completed the questionnaire for the second time

were significant differences in the awareness of NIPT ($p=0.014$) and the mean overall knowledge score (2.55 vs. 3.44; $p=0.022$). For the detection rates of different tests, significantly more women in group 2 ranked the tests in the correct order than in group 1 (37.5% vs. 7.7%; $p<0.001$).

When comparing women's attitudes towards NIPT between the two groups, such as whether they would consider having NIPT, proceed to having a diagnostic test if the NIPT results were positive, proceed to having a diagnostic test if the NIPT results were negative, whether the public sector should offer this test, the expected turnaround time for the results, and the proposed fee for NIPT, no statistically significant difference was found. For group 2, 12 (75.0%) would consider NIPT, two (12.5%) would not consider NIPT, and another two (12.5%) did not answer the question. Among those 12 women who would consider NIPT, four had NIPT done in the private sector, and the results were all negative.

The mean knowledge scores in group 1 were compared according to the women's demographic characteristics (Table 4). The scores were significantly higher for those with a higher education level ($p=0.020$),

higher family income ($p<0.001$), and antenatal care in both the public and private sectors (vs. public sector alone; $p=0.002$). The mean knowledge scores were also higher among women who had heard about NIPT (3.35) than those who never heard of NIPT (2.41) [$p<0.001$].

Discussion

As NIPT was introduced into clinical practice in Hong Kong approximately 1 year ago, it is timely to evaluate the basic understanding of NIPT among pregnant women and their attitudes towards the test. This prospective questionnaire study aimed to identify any knowledge gaps so that appropriate information and counselling can be provided prior to the test. In addition, there has been worldwide discussion of how NIPT can be integrated into the current Down syndrome screening programmes. This study also provided important information on the attitudes of pregnant women towards the test.

About 65-80% of the women were aware of first-trimester combined Down syndrome screening, second-trimester biochemical screening, and invasive tests for Down syndrome. This awareness is unexpectedly low given that the screening provided in the public sector in

Table 4. Mean knowledge score for group 1*

Item	Mean overall score	p Value
Age (years)		
<35	2.49	0.139
≥35	2.79	
Marital status		
Married	2.55	0.907
Single / divorced	2.52	
Gravida		
First pregnancy	2.62	0.558
Gravida ≥2	2.53	
Parity		
Nulliparous	2.60	0.628
≥1	2.53	
Current pregnancy		
Planned	2.65	0.070
Unplanned	2.37	
Family history		
Chromosomal abnormality	2.70	0.850
Nil	2.61	
Education level		
Primary school level or below	1.58	0.020
Secondary school level or above	2.61	
Family income (HK\$)		
<10,000	1.92	<0.001
10,000-30,000	2.48	
>30,000	3.25	
Antenatal care		
Public	2.41	0.002
Public and private	2.87	

* Group 1 denotes all pregnant women attending for Down syndrome screening

the past 2 to 3 years is universal, meaning that all pregnant women should have received adequate information in the form of videos, pamphlets, or individual counselling prior to the test. This result may also reflect that some pregnant women would accept whatever procedure was provided without really understanding the process, and is supported by the overall poor knowledge of the various screening methods in this survey. Only half of the women believed that invasive tests were the most accurate, and almost one-third misunderstood that first-trimester combined screening was the most accurate test. This result is in accordance

with previous studies¹⁰⁻¹² showing that, in general, pregnant women had limited knowledge of prenatal testing.

NIPT is a recent introduction to the various Down syndrome screening methods. Therefore, it is not unexpected that the overall knowledge of NIPT was poorer than that of other tests. Two-thirds of the women understood that NIPT was performed on maternal blood alone. However, only 16% and 11% could provide correct answers for the sensitivity and false-positive rates, respectively. Around one-third of the women wrongly stated that the sensitivity of NIPT was between 75% and 95%, with a false-positive rate of 5%. The awareness of the limitations of NIPT was also low, as less than half of the women correctly stated that NIPT could not identify all chromosomal and structural abnormalities. The women had relatively better knowledge of the procedural and practical aspects of the test. This was similarly reported in a study from Denmark¹³ which provided large-scale documentation of pregnant women's knowledge of first-trimester combined Down syndrome screening in a setting of required informed consent. In our study, it was also possible that some women mixed up the details of the first-trimester combined Down syndrome screening test with NIPT.

About 60% of the women believed that NIPT could diagnose Down syndrome. This carries important implications. Currently, although some studies report a 100% detection rate for Down syndrome for NIPT¹⁴⁻¹⁶, 100% is not universally attained in a clinical situation⁸. Pregnant women should be reminded of the existence of false-negative results to reduce any possible disappointment, and even litigation, in the future. Additionally, there is a reported 0-2% false-positive rate for NIPT⁸. Therefore, when NIPT is positive, meaning that a diagnosis is very likely, it is still generally believed that an invasive procedure should be performed for confirmation, especially before considering termination of pregnancy.

Less than 10% of pregnant women knew that NIPT could identify fetal sex. Although the technology enables detection of fetal sex in maternal plasma, currently this is not reported by the NIPT test providers in Hong Kong¹⁷. There is some concern that reporting fetal sex accurately in early pregnancy may allow its misuse for sex selection¹⁸, which could further worsen the sex imbalance seen in countries such as China and India¹⁹. However, about 80% of pregnant women in a previous local study²⁰ expected fetal sex to be identified at a late first-trimester ultrasonography examination. For most women, the demand for this information is simply for early preparation

for the arrival of their baby, rather than controversial sex selection. Although it is not easy to identify those who may opt for sex selection, clinicians or sonographers can choose to withhold the sex information when ultrasonography is performed in suspicious circumstances. For NIPT, once the sex information is routinely reported, it will no longer be easy to withhold this information. Therefore, thorough discussion among stakeholders is important to achieve a consensus for this sensitive ethical issue.

As expected, a significantly higher overall knowledge score was shown for those women with a higher education level and higher family income, and who screened positive with other Down syndrome screening tests. This was similarly reported in previous studies^{12,13,21-24}, which also identified associations between knowledge and years of education, age, and parity. Therefore, in addition to supplementing information for those who may have better access to this knowledge, counselling should also be provided for those who may be at risk of misunderstanding the implications of undergoing screening for Down syndrome.

Although only 21.9% of the women had heard about NIPT, 72% of group 1 women would opt to have the test. A similar observation was noted in a questionnaire study from Japan², which showed that respondents with inadequate knowledge of NIPT tended to appreciate NIPT testing. It was suggested that pregnant women might accept NIPT more easily because of an “unquestioned acceptance of anything new”². Therefore, it is even more important for accurate education of the public (including pregnant women) on this new technological advancement to be disseminated for informed consent to participate in NIPT, which is currently available only in the private sector. In addition, most of the women would like the public sector to offer NIPT and over half expect it to be free of charge. This information is vital for health care administrations when considering the probable future integration of NIPT in the

current Down syndrome screening algorithm.

Large-scale studies⁶ have suggested that 98% of invasive diagnostic procedures might be avoided with the use of NIPT. Surprisingly, one-third of the women in this study would choose to proceed to an invasive diagnostic test even if NIPT was negative. This may be related to the low knowledge level or the need for extra reassurance for some women that the fetus does not have any chromosomal abnormalities. It would be interesting to further investigate this psychology in the local setting.

Pregnant women rely on multiple sources of information to learn about prenatal screening, including prenatal health care workers, the internet, and other mothers²⁵. This was also found in this study whereby one-third of the women acquired their knowledge from doctors. It is important for health care providers to supply adequate and accurate information to pregnant women, as it was shown that knowledge gained would influence the pregnant women’s attitudes towards further diagnostic investigations²⁶.

One limitation of this study was that the number of returned questionnaires in group 2 was too small to enable meaningful comparison of the results for the women before screening and after they were informed of a positive screening result. In addition, pre- and post-counselling evaluation in this group may have been beneficial to assess the effects of counselling.

Conclusion

This study showed a generally poor knowledge of NIPT among the included pregnant women. Adequate counselling should be provided to allow informed consent to undergo this new screening test. Health care providers need to equip themselves with the accuracy, limitations, and drawbacks of each screening method, rather than just the procedural and practical aspects of the tests.

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