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Non-Invasive Prenatal Testing (NIPT) - We Need a National Programme

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Abstract

Aims

The provision of non-invasive prenatal testing (NIPT), a blood test screening for aneuploidy during pregnancy, varies widely internationally. In Ireland, NIPT is available privately, costing over €400. Gobal research on the patient perspective on NIPT shows a strong desire for the test to be provided for free. Attitudes towards NIPT amongst pregnant women in Ireland have not previously been studied. We assessed this in women attending maternity services in our unit.

Methods

This was a cross-sectional observational study involving a telephone survey. Women were asked about their prior knowledge of NIPT. Women with no prior knowledge were given information about NIPT and asked about their opinion of the test.

Results

One hundred and twelve (n=112) women participated. Of these, 60% (n=67) had not heard of NIPT, 86% (n=96) believe it should be freely available, and 80% (n=90) said they would avail of the test if it were free. Cost was the main prohibitive factor for those choosing not to have the test. All women wished to be more informed about NIPT.

Conclusion

Awareness of NIPT amongst women attending maternity services in Ireland may be low, but there is a desire for more information and a more equitable provision of the test.

Introduction

Non-invasive prenatal testing (NIPT) is a screening test which involves testing of cell free fetal DNA (cffDNA) in maternal serum to screen for aneuploidy [1]. The approximate fraction of cffDNA in maternal circulation is 10%, with a minimum fraction of 4% required for NIPT [2, 3].

The accuracy of the test depends on several factors including number of fetuses and the prevalence of the condition being tested for [4]. NIPT has a high sensitivity and specificity for Down syndrome (99%) but lower accuracy for the detection of Edward and Patau syndrome [5]. In addition to screening for aneuploidy, fetal sex and rhesus status can be determined diagnostically [4]. NIPT is more accurate than maternal serum markers and ultrasound which has been traditionally used to screen for fetal anomaly, but it is not diagnostic and thus, invasive diagnostic testing in the form of an amniocentesis or chorionic villus sampling (CVS) is needed to confirm suspected aneuploidy [6]. Many women are not comfortable undergoing invasive testing as both amniocentesis and CVS carry a small risk of miscarriage, often quoted at 1-2% [7]. Proper counselling of patients is essential so that they fully understand the implications of a 'positive' or 'high risk' test prior to undergoing NIPT [1].

Many professional bodies endorse the use of NIPT, but equitable provision of the test presents ethical challenges [6]. A recent practice bulletin from the American College of Obstetricians and Gynaecologists (ACOG) recommend NIPT be offered to all pregnant women regardless of maternal age or other risk factors for aneuploidy [8]. A new guideline on NIPT is currently under development from the Royal College of Obstetricians and Gynaecologists (RCOG) in the UK. In the UK the Fetal Anomaly Screening Programme (FASP) offers screening for fetal anomaly in the form of the combined test in the first trimester or quadruple test in the second trimester, using a combination of ultrasound findings and serum biomarkers [9]. NIPT is offered to women who get a result from either test indicating a higher chance of aneuploidy [9]. Belgium and the Netherlands offer the test free of charge to all pregnant women, irrespective of risk factors for aneuploidy. In Ireland antenatal screening for anomalies is not standardised across the country and not all maternity units provide a second trimester 'anomaly scan'. NIPT was first released commercially in Hong Kong in 2011 and has been available in Ireland since 2013 [6, 10]. There are three different types of test currently available privately- *Panorama*, *Harmony* and *Verifi* at a cost of approximately €400-450. This means that currently, NIPT is only available in Ireland to those who can afford to pay for it.

Several studies have looked at the patient perspective on NIPT. Knowledge of NIPT and the aneuploidies which may be detected as a result of the test amongst patients varies with most patients having an awareness of Down syndrome but not as much knowledge of less common aneuploidies [11]. Prenatal testing has been found to increase stress and anxiety in some women [12]. However, attitudes towards NIPT amongst women are largely positive [13]. In a Canadian study 66.9% of women surveyed felt that NIPT should be made available to all pregnant women free of charge, regardless of pre-existing risk factors for aneuploidy [14].

To our knowledge, awareness, and attitudes towards NIPT has not yet been studied amongst pregnant women in Ireland. The purpose of our study was to investigate awareness of and explore attitudes towards NIPT amongst women booking in early pregnancy in our unit and to determine whether there is a desire for this test to be provided free of charge.

Methods

Wexford Hospital is a general hospital with a co-located maternity unit with approximately 1800 deliveries annually. We carried out a cross-sectional observational study involving a telephone survey of women who were booked to attended maternity care in our unit over a three month period. Our aim was to contact 150 patients and have responses to analyse for 100-150 patients. All women were in their first or second trimester at the time of the telephone survey. Women who had conceived spontaneously or by assisted reproductive technologies (ART) were included. Women with singleton or multiple pregnancies and those who did not yet know the number of fetuses they were carrying were included. Women who had miscarried the index pregnancy or who were unable to complete the consent process or survey in English were excluded. Investigators made at least two attempts to contact each patient before recording 'no response'. All participants were sent information about the study by email and all participants gave informed consent to participate. Ethical approval for the study was granted by the Ethics Board from University Hospital Waterford.

Women were asked to provide details of their socio-demographic information. They were asked about their prior knowledge of NIPT. If they had heard of NIPT they were asked further questions about the details of the test as well as about their attitudes towards the test. Women who had no prior knowledge of the test were given information about NIPT by the investigators, then asked about their opinion on provision of the test. Self-reported responses were recorded by the investigators.

Results

We attempted to contact 154 patients by telephone. There was no response from 36 women, four women were excluded as they had miscarried their pregnancy when contacted, two women declined to participate. One hundred and twelve (n=112) women consented to participate and completed our survey, 73% of the total number contacted.

The median age of our participants was 32, 89% (n=100) were Irish, and English was the first language of 90% (n=101). The median gestation of participants was 9 weeks' gestation (range 5-15 weeks). Eighty five percent (n=95) of women surveyed were in the first trimester of their pregnancy. Fiver percent of women (n=6) had conceived using ART and 19% (n=21) had experienced previous pregnancy loss. Eighty eight percent (n=99) of patients were attending as public patients and 12% (n=13) were attending as private patients. Demographic details of patients are shown in table 1.

Table 1: Demographic details of patients.

Maternal demographics (n=112)	
Age in years, median (range)	32 (18-43)
Gestation, mean (range)	9 (5-15)
Nulliparous, n (%)	57/112 (50.8)
Multiparous, n (%)	55/112 (49.2)
ART, n (%)	6 (5.6)
Ethnicity, n (%)	
White Irish	100 (89.3)
White non-Irish	5 (4.5)
Non- White	7 (6.3)
Educational attainment, n (%)	
Junior certificate	5 (4.5)
Leaving certificate	27 (24.1)
Third level or higher	80 (71.4)
First language, n (%)	
English	101 (90)
Other language	11 (10)
Relationship status, n (%)	
Single	7 (6.25)
In a relationship, not married	53 (47.3)
Married	52 (46.4)
Religion, n (%)	
Roman Catholic	64 (57.1)
Not religious	43 (38.4)
Other Christian	4 (3.6)
Muslim	1 (0.9)
Maternity care, n (%)	
Public patient	99 (88.4)
Private patient	13 (11.6)

Sixty percent of respondents (n=67) had never heard of NIPT. Of the 40% (n=45) who had prior knowledge of NIPT, 13% (n=6) of these had received information from a healthcare professional and 37% (n=17) had heard of NIPT from a friend or family member. 34% (n=34) of public patients and 46% (n=6) of private patients had heard of NIPT. 26% (n=7) of those who had completed second level education and 44% (n=35) of those who had completed third level education had heard of NIPT before.

Of the women who had heard of NIPT, 88% (n=40) knew that NIPT screened for chromosomal abnormalities, 12% (n=5) were unsure what it screens for, 15% (n=7) thought it screened for structural abnormalities in addition to genetic abnormalities.

Eighteen percent (n=8) of those who had heard of NIPT were aware of how the results are reported and 69% (n=31) were aware that further diagnostic testing would be offered in the case of an 'high probability' NIPT result. Nine percent of women who had heard of NIPT (n=4) answered all questions about NIPT correctly, all these women had had the test themselves prior to being contacted in relation to the study. Answers to questions in relation to NIPT are shown in table 2.

Table 2: Answers to questions in relation to NIPT.

Knowledge tested in relation to NIPT	**Correct responses, n (%)**
Gestation at which test can be performed	22 (49)
Screens for chromosomal abnormalities	40 (89)
Does not screen for structural abnormalities	22 (49)
Results reported as a risk score	8 (18)
Invasive testing offered if high risk	31 (69)

Fifteen percent of those who had heard of NIPT (n=7) were planning to have the test or had already had the test. Fifty one percent (n=23) of those who had heard of NIPT were not planning to have the test, 83% (n=19) of these 23 women cited the cost of the test as the reason for not having it. Eighteen percent (n=8) stated that they were not going to have NIPT as the result would not influence to how they would manage their pregnancy. The remaining 33% (n=15) of women who had heard of NIPT were undecided as to whether they would have the test.

Eighty six percent (n=96) of the women we surveyed believe that NIPT should be made freely available to all pregnant women, and 14% (n=16) felt it should be subsidised or made available to high-risk patients, 93% (n=104) felt that if the test was offered it should be on an 'opt in' basis. Eighty percent (n=90) said they would avail of the test if it were free. One hundred percent of women surveyed (n=112) wished to be more informed about NIPT and 83% (n=93) felt they would like to receive this information from their general practitioner (GP), 82% (n=92) stated that they would prefer to receive information during a face-to-face consultation.

Discussion

At present, counselling about NIPT is not part of routine antenatal care in all units in Ireland. Awareness of NIPT in our study population was low, with the majority (60%) of women reporting they had never heard about the test. In our cohort, women who had reached a higher level of education and who were attending as a private patient were more likely to have heard of NIPT. Even amongst women who had heard of the test, knowledge of what exactly NIPT involves was low.

Only four of the 45 women who had heard of NIPT answered all questions in relation to the test correctly, all of these women had done the test themselves. All women we surveyed stated that they would like more information about NIPT, and the majority of these women would prefer the information to be delivered face-to-face by their GP, who is often the first healthcare provider that a pregnant woman comes into contact with.

Cost was the main prohibitive factor for those choosing not to have the test, 80% of women said that they would have NIPT if it were made freely available. This demonstrates a desire amongst pregnant women for a more equitable provision of the test in Ireland.

In the Netherlands, free NIPT testing has been offered to women since 2017 provided women are happy to participate in a nationwide study [15]. Prior to undertaking the test women receive counselling by trained professionals. In the first year of this study, NIPT was performed in 42% of all pregnancies and a 43.4% increase in the uptake of NIPT was observed [15, 16]. The benefits of increased detection of chromosomal abnormalities must be balanced against the risk of parental anxiety and the potential increase in invasive testing. In a Canadian study which looked at patient, partner, and physician attitudes towards NIPT, 66.9% of patients wished for NIPT to be provided for free to all women, compared to only 39.7% of physicians [14]. It would be interesting to look at the attitudes of physicians in Ireland around free provision of NIPT to see if this would differ from the patient perspective.

A strength of this study is that it is the first of its kind, exploring the attitudes of pregnant women towards NIPT in an Irish maternity service context. Limitations of our study were the small number of participants and the fact that it was restricted to English speaking patients. This was a study conducted in a single maternity unit over a three month period, during the Covid-19 pandemic. Surveys were conducted via telephone rather than face to face which may have impacted responses. Additionally, we carried out this study during the cyber-attack on the Irish Health Service Executive (HSE) during which time patient and staff contact details were leaked, leading to many people receiving ‘spam’ phone calls. This may have led to patients being reluctant to answer their phone and had an impact on the number of ‘no responses’.

Implementation of a national programme for NIPT in Ireland would be costly, not only in providing the test to those who want it but also ensuring proper counselling and follow up can be provided. The structure of a national programme in Ireland could be further informed by larger scale studies into the patient perspective of NIPT, as well as studies into the opinions of Obstetricians and Fetal Medicine specialists. Awareness of NIPT amongst some women attending maternity services in Ireland may be low, but there is a desire for more information and a more equitable provision of the test.

Declaration of Conflict of Interests:
All authors have no conflict of interest to declare.

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