

Utility of Non-Invasive Prenatal Test (NIPT) as a Screening Tool for Fetal Aneuploidy in a Family Medicine Setting in Saudi Arabia

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Background: Chromosome aneuploidy is the most common type of fetal chromosome disorder. This study aims to determine the utility of Non-Invasive Prenatal Test (NIPT) in detecting chromosomal aneuploidy among high-risk Saudi pregnant women.

Methods: This retrospective cohort study examined the charts of all pregnant women who attended the antenatal clinics of the Ministry of National Guard-Health Affairs, King Abdulaziz Medical City, Riyadh, Saudi Arabia, from January 2012 to July 2022, and underwent NIPT testing. Data were collected on obstetric history, NIPT testing, confirmatory invasive testing (amniocentesis/chorionic villus sampling, "CVS"), and pregnancy outcomes.

Results: Of all the studied pregnant women (n=958), 46 women had positive NIPT (40 trisomy 21, 4 trisomy 18, and 2 trisomy 13), giving an incidence of 4.8% (95% CI 3.6–6.3%), and a positive predictive value of 100%. Pregnant women >40 years of age showed an 8-fold increased risk of any aneuploidy compared to younger women <30 years of age (OR=8.07, 95% CI 2.35–27.73). Those with fetal ultrasound (US) results of more than 30 weeks of gestation had a 2-fold increased risk compared to those with results of less than 20 weeks of gestation (OR = 2.15, 95% CI 0.93–4.98), and those with abnormal US fetal anatomy had an 88-fold increased risk compared to those with normal US (OR=88.33, 95% CI 36.10–216.16). Both advanced maternal age (OR = 1.14, p < 0.001) and abnormal ultrasound fetal anatomy (OR = 92.45, p < 0.001) were significant predictors of chromosomal aneuploidy. None of the counseled women opted for pregnancy termination.

Conclusion: The study's finding is a powerful clinical message that strengthens confidence in positive NIPT results at similar referral centers and provides a strong local evidence base for counseling high-risk Saudi women about the implications of positive NIPT results. It provides confirmation that local risk factors align with global patterns.

Keywords: chromosome aneuploidy, prenatal screening, genetic counselling, chromosome disorders, trisomies, genetic disorders

Introduction

To make the most informed decision when evaluating pregnancy outcomes, it is crucial to select the most accurate, safe, precise, and practical screening tests and diagnostic techniques throughout early pregnancy. Approximately 2.5% of infants are born with congenital anomalies, accounting for 8–15% of perinatal deaths and 13–16% of neonatal mortality.¹ Chromosomal abnormalities occur in 0.1% to 0.2% of live births.^{2,3} Trisomy 21 (Down syndrome) is the most common karyotypic abnormality in live-born infants (1 per 800 live births), and is a leading cause of intellectual disability.⁴ In Saudi Arabia, 6.7% of recurrent pregnancy loss is caused by chromosomal abnormalities,⁵ and Down syndrome is considered the most common chromosomal anomaly with a prevalence of 6.6 per 10,000 children.⁶ The rate of point mutations was slightly higher in the sperm of older fathers.⁷ The risk of trisomy increases significantly with the mother's age.⁸

Noninvasive prenatal testing (NIPT) is a screening method for early detection of genetic mutations in developing fetuses, including Down Syndrome, Edwards Syndrome, and Patau Syndrome. NIPT has been widely used in recent years for antenatal testing. Regarding women's knowledge of NIPT, a study done in Riyadh, Saudi Arabia, showed that over half of the population involved had no previous knowledge of NIPT, as they had not had adequate counseling regarding prenatal screening.⁹ A systematic review done in 2017 in the United Kingdom has reported that the rate of termination of pregnancy (TOP) remains unchanged from the rate before introducing NIPT.¹⁰

A recent study was conducted at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia, in 2021. This study is considered the first to investigate NIPT after its implementation at KAMC. It involved 200 pregnant women and concluded that although NIPT is accurate and highly specific, it can still produce false-positive and negative results.¹¹ This signifies that other prenatal testing methods, such as amniocentesis and obstetric ultrasound, are still used to confirm the diagnosis if a woman has a positive or false-positive NIPT result. To our knowledge, no sufficient data or guidelines are available regarding the utility of NIPT testing for the KAMC situation, its accuracy, and the acceptance rate of abortion following positive results of confirmatory tests. Thus, this study aims to evaluate the utility of NIPT for predicting chromosomal aneuploidy, specifically trisomies 13, 18, and 21, among high-risk pregnant women.

Methodology

This retrospective cohort study examined the charts of all pregnant women who attended the antenatal clinics of the Ministry of National Guard Health Affairs at King Abdulaziz Medical City, MNGHA, Saudi Arabia, from January 2012 to July 2022, and who underwent NIPT testing. Those include pregnant women at higher risk of having a child with aneuploidy who agreed to be tested for chromosomal aneuploidy and undergo NIPT procedures.

Those without NIPT were excluded from the review.

Chart review and using the BestCare electronic records to collect data on the following:

Obstetric History

1. Maternal age in years
2. Gravidity and Parity: Parity was classified as nulliparous (no previous viable pregnancy), multiparous (given birth to 1–4 children), and grand-multiparous (given birth to 5 or more children).¹²
3. Comorbidities such as hypertension, diabetes mellitus, gestational diabetes, bronchial asthma, Liver disease, Connective Tissue disease, Epilepsy, Hypothyroidism, etc.
4. Personal or family history of a genetic disorder.
5. First Trimester Obstetric ultrasound (US) Report; date and age of pregnancy, fetal anatomy, gestational age (weeks +days), expected date of delivery, Fetal viability, gender, and appearance.
6. Pregnancy outcomes: These include term delivery (baby gender and whether the baby was phenotypically normal or abnormal), abortion, Intrauterine fetal death (IUFD), and termination of pregnancy (TOP). A stillborn baby was defined as a baby born after the 24th week of pregnancy who did not show any signs of life. Intra-uterine stillbirth was considered if the baby died in the womb. Intra-partum stillbirth was considered if the baby died during labor, and miscarriage was considered if the baby died before 24 weeks.¹³ Pieces of Advice for TOP by the obstetrician were retrieved from the records.

NIPT Testing

Operational definition of high-risk for aneuploidy: (1) Pregnant women at higher risk of having a child with family-specific autosomal recessive (AR) disease; (2) those above 30 years of age, (3) those with a personal or family history of chromosomal anomaly, and (4) those with a detected ultrasound fetal abnormality during pregnancy, who agree to be tested for chromosomal aneuploidy, undergo NIPT procedures. However, most pregnant women decline undergoing NIPT, possibly due to their worry about effects like routinization, pressure to test, and less acceptance of people with disabilities.¹⁴

Confirmatory Invasive Testing

Amniocentesis was performed on all women with positive NIPT results at an average gestational age of 20 weeks. For women with negative NIPT, pregnancy outcomes were verified through routine postnatal assessment. Prenatal invasive diagnosis is conducted utilizing both chromosomal karyotyping and CNV-seq. Chromosomal karyotyping is used to confirm CNV-seq-identified whole-chromosomal aneuploidies and sub-chromosomal deletions and duplications. Samples were processed according to established karyotyping protocols, which included harvesting, colchicine treatment, digestion, fixation, preparation of spreads, and chromosome banding. We analyzed at least 20 metaphases; up to 50 were analyzed when mosaicism was detected. The sequencing reads are aligned to the human reference genome. CNV-seq is performed using NGS, which involves randomly interrupting genomic fragments with a restriction enzyme, end-filling, adding AMPs, linking to the primer, and ultimately sequencing and analyzing the fragments.

Data Management

Data entry and statistical analysis were conducted utilising the Statistical Package for the Social Sciences (SPSS) software for Windows (version 28.0.1.1, © Copyright IBM Corporation, Armonk, NY, USA). Descriptive statistics, such as percentages, means, and standard deviations, were computed. The Pearson chi-square test, Fisher's exact test, and the Chi-square test for linear trend were utilised for the analysis of categorical data. The Student's *t*-test and the Mann-Whitney test were used to analyze continuous data. Logistic regression analysis was conducted to determine the significant predictors of aneuploidy, utilising maternal age in years, abnormalities identified during foetal ultrasound (a nominal variable), and a history of previous pregnancy with any genetic disease (a nominal variable) as independent variables. Loss to follow-up for 2 women with negative and two women with positive NIPT precluded assessment of the outcome, possibly because of their delivery outside the study's hospital, and they were not considered in data analysis.

Statistical significance was defined as $p < 0.05$ for all analyses.

Results

Of all the studied pregnant women ($n=958$), 46 women had positive NIPT; all of these were confirmed by invasive testing, including chromosomal aneuploidies, yielding an incidence of 4.8% (95% CI 3.6%-6.3%) and a positive predictive value (PPV) of 100%. Term delivery constituted 94.2% of all pregnancy outcomes, and the rest ended with abortion (3.4%), IUFD (2%), TOP (0.2%), and unknown (0.2%). Of all pregnancies with aneuploidy, one third (34.8%) ended with abortion (19.6%), IUFD (10.9%), or unknown outcome (4.3%) (Figure 1). Figure 2 shows the types of aneuploidy among 958 pregnant women (40 trisomy 21, 4 trisomy 18, and 2 trisomy 13).

In comparison to women with negative NIPTs, those with positive NIPT had significantly higher mean maternal age (38.7 yr versus 34.7, $t=4.10$, $p<0.001$), higher median gravidity (6 versus 4 gravida, $Z=2.62$, $p<0.001$), higher median US GA (23 weeks versus 19 weeks, $Z=2.477$, $p=0.013$), higher rate of abnormal fetal anatomy (87.0% versus 6.6%, $X^2=309.56$, $p<0.001$), and higher rate of abnormal pregnancy outcome (33.3% versus 4.5, FET, $p<0.001$), Table 1.

All term-delivered infants of women with negative NIPT tests were normal and free of any chromosomal aneuploidy. The incidence of chromosomal aneuploidy was significantly associated with advanced maternal age ($X^2_{LT}=16.30$, $p<0.001$), advanced US gestational age ($X^2_{LT}=4.16$, $p=0.041$), and abnormal ultrasound fetal anatomy (FET, $p<0.001$), as shown in Table 1 and Figure 1. Of all 46 pregnant women with fetal aneuploidy, 27 (58.7%) were provided the choice to have their pregnancy terminated. Pregnant women above 40 years of age showed an 8-fold increased risk of any aneuploidy compared to younger women less than 30 years of age (OR=8.07, 95% CI 2.35–27.73, $p<0.001$). Ultrasound in those with gestational age greater than 30 weeks was associated with a 2-fold increase in risk compared with less than 20 weeks of gestation (OR=2.15, 95% CI 0.93–4.98, $p=0.041$). Those with sonographically abnormal fetal anatomy had an 88-fold increased risk compared to those with normal ultrasound (OR=88.33, 95% CI 36.10–216.16, $p<0.001$), Table 2.

Both advanced maternal age (OR = 1.14, $p < 0.001$) and abnormal ultrasound fetal anatomy (OR = 92.45, $p < 0.001$) were significant predictors of chromosomal aneuploidy, Table 3.

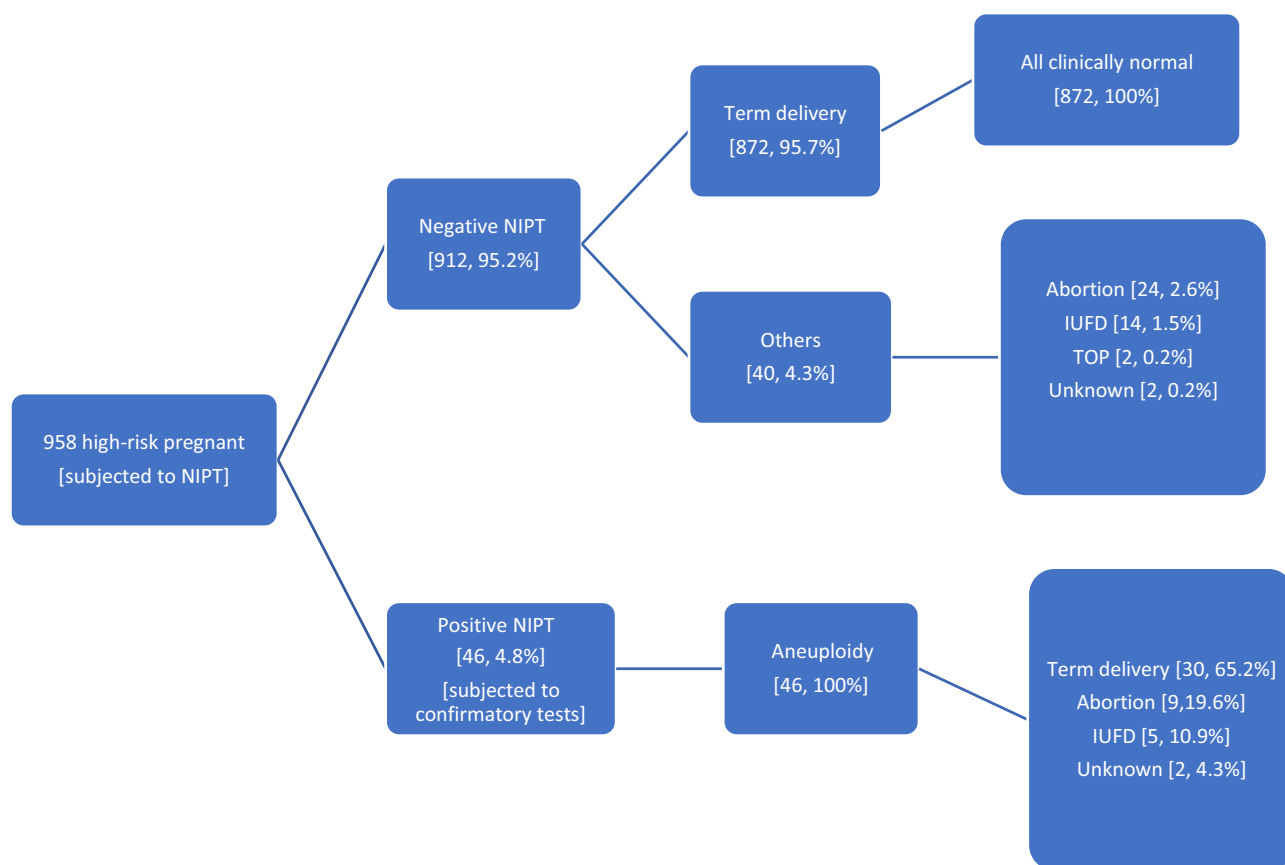


Figure 1 Flow chart of the Screening of 958 high-risk pregnant women by NIPT.
Abbreviations: IUFD, intrauterine fetal death; TOP, termination of pregnancy.

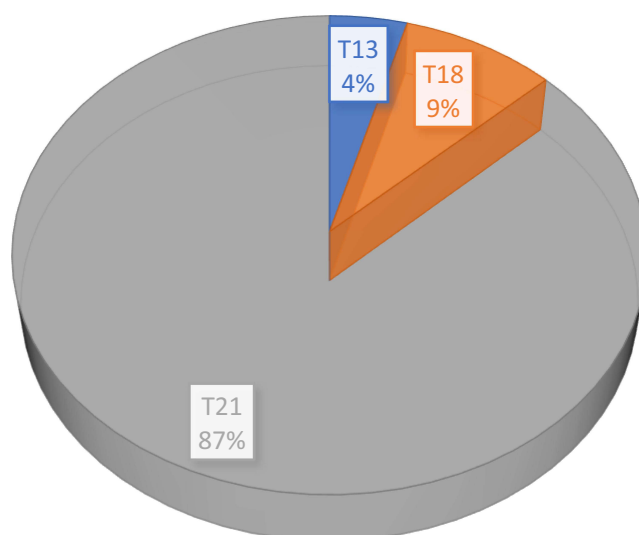


Figure 2 Types of Aneuploidy Among 958 Pregnant Women.
Abbreviations: T13, trisomy 13; T18, trisomy 18; T21, trisomy 21.

Table 1 Comparison Between NIPT-Positive and NIPT-Negative Pregnant Females According to Some Obstetric Characteristics

	Positive NIPT (n=46)	Negative NIPT (n=912)	Significance
Maternal age in years (X ± SD)	38.7 ± 5.9	34.7 ± 6.2	t=4.10, p<0.001*
Gravidity (M, IQR)	6 (3,9)	4 (2,7)	Z=2.62, p<0.001*
Parity (M, IQR)	4 (2,7)	4 (2,5)	Z=1.66, p=0.10
Ultrasound GA in weeks (M, IQR)	23 (15.5, 28.5)	19 (14, 26)	Z=2.477, p=0.013*
Past/family history of genetic disease (n,%)	4 (8.7)	59 (6.5)	FET, p=0.62
Abnormal fetal anatomy (n,%)	40 (87.0)	60 (6.6)	X ² =309.56, p<0.001*
Fetal gender (M/F)	27/19 (1.42)	480/432 (1.11)	X ² =1.13, p=0.29
Twin pregnancy (n,%)	1 (2.2)	44 (4.8)	FET, p=0.26
Abnormal pregnancy outcome (n,%)	15 (33.3)	41 (4.5)	FET, p<0.001*

Note: *Statistically significant.

Abbreviations: NIPT, non-invasive prenatal test; GA, gestational age; (X ± SD), mean ± standard deviation; (M, IQR), median ± interquartile range; t, Student's t-test; Z, Mann-Whitney test; X², Pearson Chi-square test; FET, Fisher's exact test.

Table 2 Incidence of Fetal Aneuploidy and Associated Factors Among 958 Pregnant Women

	Aneuploidy (n=46, 4.8%)	OR (95% CI)	Statistical Significance
Maternal age (years)			
<30 (n=221)	3 (1.4)	1	
30-40 (n=547)	24 (4.4)	3.34 (0.99–11.19)	
>40 (n=190)	19 (10.0)	8.07 (2.35–27.73)*	X ² LT=16.30, p<0.001*
Gravidity			
One (n=9)	0 (0.0)	1	
Two (n=131)	2 (1.5)	1.02 (0.99–1.04)	
Three (n=111)	8 (7.2)	1.08 (1.02–1.14)*	
Four or more (n=599)	32 (5.3)	1.06 (1.04–1.08)*	X ² LT=2.48, p=0.12
Parity			
Nullipara (n=111)	5 (4.5)	1	
Multipara (n=511)	20 (3.9)	0.86 (0.32–2.35)	
Grand multipara (n=336)	21 (6.2)	1.41 (0.52–3.84)	X ² Lt=1.78, p=0.18
Ultrasound GA (weeks)			
9-19 (n=482)	16 (3.3)	1	
20-29 (n=344)	20 (5.8)	1.80 (0.92–3.52)	
30+ (n=131)	9 (6.9)	2.15 (0.93–4.98)	X ² Lt=4.16, p=0.041*

(Continued)

Table 2 (Continued).

	Aneuploidy (n=46, 4.8%)	OR (95% CI)	Statistical Significance
Comorbidities (HBP/DM, etc.)			
Yes (n=341)	18 (5.3)	1.17 (0.64–2.15)	
No (n=617)	28 (4.5)	1	$\chi^2=0.26$, $p=0.61$
Past history of genetic disease			
Yes (n=63)	4 (6.3)	1.38 (0.48–3.79)	
No (n=895)	42 (4.7)		$\chi^2=0.35$, $p=0.55$
Ultrasound fetal anatomy			
Normal (n=854)	6 (0.7)		
Abnormal (n=104)	40 (38.5)	88.33 (36.10–216.16)*	FET, $p<0.001$ *
Fetal gender			
Male (n=507, 52.9%)	27 (5.3)		
Female (n=451, 47.1%)	19 (4.2)	1.28 (0.70–2.33)	$\chi^2=0.65$, $p=0.42$
Singleton			
Single (n=913, 95.3%)	45 (4.9)		
Twin (n=45, 4.7%)	1 (2.3)	0.97 (0.93–1.02)	FET, $p=0.72$

Note: *Statistically significant.

Abbreviations: χ^2 , Chi square test; χ^2 Lt, Chi square for linear trend; FET, Fisher's exact test.

Table 3 Predictors of Aneuploidy Among Pregnant Females

	B	SE	p-value	OR	95% C.I	
					Lower	Upper
Maternal Age in years	0.131	0.036	<0.001	1.14	1.06	1.22
Abnormalities of fetal ultrasound (yes [#] versus no)	4.53	0.47	<0.001	92.45	36.73	232.71
Previous pregnancy with genetic diseases (yes versus no)	0.72	1.26	0.57	2.06	0.18	24.12
Constant	−9.84	1.445	0.000	0.000		

Note: [#]Reference category.

Abbreviations: B, coefficient of determination; SE, standard error; OR, odds ratio; CI, confidence interval.

Discussion

In this study, of all the studied pregnant women (n=958), 46 women had positive NIPT (40 trisomy 21, 4 trisomy 18, and 2 trisomy 13), and all of these were confirmed by confirmatory invasive testing, as chromosomal aneuploidies, giving an incidence of 4.8%, (95% CI 3.6%–6.3%), and a positive predictive value (PPV) of 100%. The incidence of chromosomal aneuploidy was significantly associated with advanced maternal age, advanced US gestational age, and abnormal US fetal anatomy. Both advanced maternal age and abnormal ultrasound fetal anatomy were significant predictors of chromosomal aneuploidy.

Chromosomal aneuploidy is the most prevalent category of foetal chromosome disorders, with trisomies 21, 18, and 13 being the most common. The incidence of these trisomies is notably high, comprising approximately 0.2% of all full-

term pregnancies.¹⁵ In our study, an incidence of 4.8% was detected among 958 pregnant women who agreed to undergo NIPT testing and were at high risk. This figure is too high when compared with figures in previous studies. However, our study targeted the high-risk pregnant females for whom the incidence is expected to be high. When NIPT was offered to high-risk women, it resulted in fewer women declining follow-up testing.¹⁶ In our study, all pregnant women whose NIPT results were positive were followed up by confirmatory tests.

Aneuploidy accounts for approximately 1 in 150 live births; however, the incidence across all pregnancies is significantly higher.¹⁷ A substantial percentage of the 10–15% of clinically acknowledged pregnancies that culminate in miscarriages are linked to aneuploidy. Moreover, approximately 50% of early pregnancy losses exhibit chromosomal abnormalities.¹⁸ In our study, there might be an underestimate of the actual incidence of aneuploidy, simply because 40 women (4.3%) of all 912 pregnant women with negative NIPT for which no confirmatory test was done, ended up with abortion (2.6%), IUFD (1.5%), or TOP (0.2%). There is a possibility of NIPT false-negative results among these cases, with some of those who tested negative having had any aneuploidy. NIPT results require confirmation by invasive testing due to the risk of false positives.¹⁹ However, in our study, all positive NIPT results were positive for invasive testing, with no false-positive results, which reflects the high performance of NIPT for the detection of aneuploidy in high-risk pregnant females. While high PPV for NIPT is known, reporting a perfect 100% PPV over a decade and 46 confirmed cases in a real-world clinical setting is striking and noteworthy. This level of certainty, while specific to this highly selected population, is a powerful clinical message that strengthens confidence in positive NIPT results for similar referral centers.

The literature is deficient in examining how translocations and mosaicisms influence the relationship between aneuploidy and advanced maternal age, as well as the age-related correlation with rarer fetal aneuploidies.^{20–27} In our study, a significantly increased incidence of aneuploidy was shown with increased maternal age. Pregnant women above 40 years of age showed an 8-fold increased risk of any aneuploidy compared to younger women less than 30 years of age. A woman is born with all the eggs she will ever have, and these oocytes age with her. Over time, the chromosomes in these older eggs are less likely to separate correctly during cell division (meiosis), leading to a higher probability of aneuploidy. A nationwide cohort study involving over 500,000 singleton pregnancies in Denmark from 2008 to 2017 identified established associations between advanced maternal age and an increased risk of trisomy 21, 18, and 13, particularly in women aged 35 years and older.⁸ Gravity itself is not a direct risk factor for fetal aneuploidy, but maternal age, which is often associated with higher gravity, is a significant risk factor for aneuploidy. In our study, no linear trend was shown between the gravity and the incidence of fetal aneuploidy.

A second-trimester ultrasound scan identifies two categories of sonographic markers indicative of aneuploidy: the first category includes markers for significant foetal structural abnormalities, while the second category, referred to as “soft markers,” also indicates potential aneuploidy.^{4,28} Prenatal ultrasonography in the second trimester serves as a “genetic sonogram” for identifying morphological characteristics indicative of foetal Down syndrome.²⁹ Our study identified a positive correlation between US GA and the incidence of aneuploidy. Data indicate that sonographic findings are not influenced by maternal age or biochemical markers;³⁰ thus, sonographic assessment may be relevant for low-risk patients.⁴ Our study found that abnormal fetal ultrasound serves as an independent predictor of fetal aneuploidy. The importance of ultrasound in fetal anomaly screening is well established, and positive ultrasound findings are the primary indications for amniocentesis.³¹ For this reason, before amniocentesis, we advise a detailed ultrasound examination by an experienced specialist.

The NIPT technique enables the detection of foetal trisomies 21, 13, and 18 as early as 9 weeks into pregnancy, with the potential for earlier identification, ensuring both earlier and safer prenatal testing.³² Our study indicates that individuals with a gestational age exceeding 30 weeks exhibit a twofold increased risk relative to those at 9–19 weeks of gestation.

Indications for prenatal genetic testing include follow-up of anomalies detected by routine ultrasound or maternal aneuploidy screening, a family history of genetic disorders, advanced maternal or paternal age, and assessment of low-risk pregnancies prompted by parental concerns.²⁸ In our study, personal or family history of genetic diseases was not found to be an independent predictor of fetal aneuploidy. However, this might be because the targeted pregnant females in our study were not representative of all pregnant females.

Research indicates that twin pregnancies exhibit a higher incidence of fetal structural abnormalities compared to singleton pregnancies, and they are associated with distinct complications during gestation.³³ Twin pregnancies represented 4.6% of the total pregnancies in our study. NIPT is a safe option for women with twin pregnancies, as the risk of abnormal results and the likelihood of complications from invasive testing are greater compared to those in singleton pregnancies.³⁴ However, ACOG guidelines acknowledge the limitations in non-singleton pregnancy.³⁵ In our study, the incidence of aneuploidy was not different between single and twin pregnancies.

Counseling for women with positive NIPT is recommended for her to decide whether she wishes to terminate the pregnancy or not. A systematic review conducted in 2017 in the United Kingdom reported that the rate of termination of pregnancy (TOP) remained unchanged from the rate before the introduction of NIPT.^{10,11} In our study, advice to terminate pregnancy was given to nearly one-half of all women with aneuploidy. This advice should have been given to all women whose NIPT was positive, yet because of the cultural issues regarding termination of pregnancy in the Saudi community, physicians are possibly not motivated to provide the necessary counselling to all women. Yet, none of these women who were provided the advice to terminate their pregnancy accepted termination, and they decided to continue their pregnancy even if this test identified a disorder. This was in agreement with other studies.⁵ According to the resolution No. 240 of the Council of Senior Scholars, dated 5th May 2011 in Saudi Arabia, regarding the issue of abortion, it is permissible to abort a fetus before the soul is breathed into it - ie before 120 days have passed - if the fetus is afflicted with a hereditary or non-hereditary disease that may render life impossible after birth, or if life is possible in the future, but this causes severe harm to the fetus, such that the fetus is afflicted with a severe, permanent disability for which there is no hope of recovery.

This Zero Uptake of Pregnancy Termination is arguably the most novel and socioculturally significant finding. Despite clear medical advice and the existence of a religious-legal framework (Resolution No. 240) permitting early termination for severe fetal anomalies, 0% of counseled women (n=27) opted for termination. This quantitative documentation of a uniform decision against termination in the face of a serious diagnosis is a major contribution to the bioethical and sociocultural literature on prenatal screening in conservative religious settings. It moves beyond anecdote to data.

Limitations

The study is likely adequately powered for its primary aim of estimating PPV and identifying strong risk factors (eg, abnormal ultrasound with an OR >80), given the large effect sizes and the cohort of 958 with 46 positive cases. However, it may be underpowered for subgroup analyses. The study targeted the high-risk pregnant females for fetal aneuploidy who underwent NIPT, and only one hospital's patient data was included in this study; most pregnant women decline undergoing NIPT, possibly due to their worry about effects like routinization, pressure to test, and less acceptance of people with disabilities. Thus, the study results could not be generalized. However, the ten-year timeframe (2012–2022) is sufficient to observe meaningful outcomes and achieve a robust sample size, particularly for a single-center study targeting a high-risk population. It appropriately covers the period of NIPT's clinical introduction and maturation. Only NIPT-positive cases received the gold-standard verification (invasive testing). NIPT-negative cases did not undergo systematic invasive confirmation. Therefore, while PPV can be calculated accurately, the study cannot validly calculate the sensitivity, specificity, or Negative Predictive Value (NPV) of NIPT. This is a critical limitation that must be explicitly acknowledged and discussed, as it defines the scope of the “performance” that can be evaluated. Moreover, data loss due to pregnancy termination and loss to follow-up cannot be avoided; hence, the validity of NIPT in detecting aneuploidy among the target group of the study was not calculated. Larger-scale, multicenter studies in real-world settings are needed to provide a more comprehensive exploration of NIPT performance. While this observation is important, it is based on a small cohort, and more data are required to confirm these findings.

Conclusion

This study summarizes local NIPT practice, recommendations for a single center in Saudi Arabia. It yielded a total of 46 true positive NIPT results, all of which were true cases after confirmatory testing (100% PPV), with an incidence of 4.8%

fetal aneuploidy among the high-risk pregnant females. This finding is a powerful clinical message that strengthens confidence in positive NIPT results for similar referral centers. It provides a strong local evidence base for counseling high-risk patients about the implications of a positive NIPT result. The finding of association of fetal aneuploidy with advanced maternal age and abnormal ultrasound is well-established in global literature, providing a confirmation that local risk factors align with global patterns.

Data Sharing Statement

Most of the data supporting our findings are contained in the manuscript, and all other data, excluding identifying/confidential patient data, will be shared upon request from the corresponding author.

Ethics Approval and Consent to Participate

The Institutional Review Board (IRB) of the Ministry of National Guard- Health Affairs (MNG-HA) approved the study under study number NRC23R/514/08. The MNG-HA IRB waived the informed consent requirement due to the study's retrospective design. All methods were conducted in accordance with applicable guidelines and regulations to maintain data confidentiality. This research adhered to the principles outlined in the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests in this work.

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