Analysis of Prenatal Diagnosis Results and Pregnancy Outcome of Non-invasive Prenatal Screening High-risk Fetuses

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Abstract

Background

With the development of whole-genome sequencing, small chromosomal deletions and duplications could be found by NIPT. This study is to evaluate the clinical significance of fetal chromosomal karyotype analysis and chromosomal microarray analysis (CMA) to clarify the clinical significance of 528 cases of high-throughput sequencing noninvasive prenatal screening suggesting high-risk cases.

Methods

Non-invasive prenatal screening showed that the fetus 21, 18, 13, sex chromosomes, and other chromosomes are at high risk of aneuploidy and fetal chromosome copy number variations (CNVs) are at high risk, requiring prenatal diagnosis Pregnant women are the research objects. After obtaining informed consent, fetal cells were obtained by amniocentesis or umbilical vein puncture for chromosomal karyotype and CMA analysis. All cases of childbirth were followed up by telephone over a period of 1 year.

Results

Among 528 fetuses, 447 were at high risk of aneuploidy. The positive predictive value (PPV) for trisomy 21(T21), trisomy 18 (T18), trisomy 13 (T13), sex chromosome aneuploidies (SCAs), and other chromosome aneuploidy was 85.24%, 51.52%, 12.5%, 50.82%, and 5.88% respectively. Another 81 cases of non-invasive prenatal screening suggest CNVs High risk. The PPV for CNVs was 34.57% .Among them, CNVs has a clear pathogenic significance can reach 24.69% .

Follow-up of childbirth cases: Of the 62 pregnant women diagnosed with fetal SCA, 13 chose to continue their pregnancy, and the overall continued pregnancy rate was 20.97% (13/62); CNVs has no clear significance/no disease reported in 8 cases, 1 case After being lost to follow-up, all 7 cases chose to continue their pregnancy. One of the children was not informed about the specific situation; one girl had six fingers on both hands, and the rest had no abnormal growth; the remaining five children developed normally.

Conclusion

This study has obtained relatively reliable PPV data for NIPT screening for chromosomal aneuploidy, which provides a reliable basis for clinical genetic counseling and treatment; it is recommended to perform prenatal diagnosis and perform chromosomal nucleus when non-invasive and high-risk prompts suspicious chromosomal abnormalities (over/under/microdeletion/microduplication). Type and CMA inspection, so that the inspection is more comprehensive and not easy to miss the diagnosis.

Introduction

Chromosome disease is a disease caused by abnormal number and structure of chromosomes. It is one of the common causes of fetal birth defects in clinic. Among them, Trisomy 21 (T21), Trisomy 18 (T18),

Trisomy 13 (T13) and sex chromosomal aneuploidy (SCA) are fetal chromosomes of the main types of aneuploidy account for 80%-90% of all chromosomal diseases [1]. Although traditional prenatal screening has certain screening value, there are a certain proportion of false positives and false negatives. Non-invasive prenatal testing (NIPT) is a rapid development in recent years with the development of high-throughput sequencing technology that uses cfDNA in the peripheral blood of pregnant women to screen for common chromosomal aneuploidies in the fetus. The new method of prenatal screening that is safe, efficient and easy to promote has greatly improved the sensitivity and specificity of prenatal screening for chromosomal diseases [2, 3]. A large number of studies have shown that the efficiency of screening for fetal aneuploidy is much higher than that of traditional serological screening [4, 5], but there are still some false positives and false negatives, so it can only be used as Prenatal screening methods are not yet available as methods for prenatal diagnosis.

This study retrospectively analyzed cases of prenatal diagnosis in our department due to the high risk of NIPT, analyzed the test results and pregnancy selection, and calculated NIPT to screen fetal chromosomal aneuploidy and microdeletion and micro duplication PPV in our department, And preliminarily explore the pregnancy selection of pregnant women for SCA, chromosome microdeletion, microduplication fetus, and hope to provide more reference for clinical genetic counseling and management.

Materials And Methods

Clinical data

Pregnant women went to the Department of Reproductive Genetics, Hebei Provincial People's Hospital from January 1, 2014 to December 31, 2018. Non-invasive prenatal screening revealed that the fetus 21, 18, 13, sex chromosomes, and other chromosomal trisomy imperfections Pregnant women who are at high risk of ploidy and fetal chromosome copy number variations (CNVs) are subject to prenatal diagnosis. The pregnancy gestations were 18^{+0}~28^{+3}, the years of age were 18–47.

All the subjects had no contraindications to puncture for prenatal diagnosis, and all signed an informed consent form for prenatal diagnosis. Amniotic fluid or cord blood was drawn for fetal chromosome karyotype analysis and CMA testing according to different gestational weeks, and followed up after delivery (after induction of labor).

Chromosome analysis and Statistical analysis

Chromosome detection techniques include chromosome karyotype analysis and chromosome microarray analysis (CMA). The pros and cons of the test plan and the technical pros and cons are informed in detail by the consulting physician, and pregnant women make informed choices. Statistical method Collect data with Excel table, and express count data with rate and composition ratio.

Results

The abnormal types of fetal chromosomal aneuploidy

Non-invasive prenatal screening revealed 447 cases of high risk of chromosomal aneuploidy, 210 cases of high risk of trisomy 21, 66 cases of high risk of trisomy 18, 32 cases of high risk of trisomy 13, 122 cases of high risk of sex chromosome aneuploidy, and other chromosomes 17 cases of trisomy; 174 cases of trisomy 21 (PPV 85.24%), 34 cases of trisomy 18 (PPV 51.52%), 4 cases of trisomy 13 (PPV 12.5%), sex chromosome aneuploidy were confirmed by karyotype analysis 62 cases (PPV 50.82%) and 1 case of other chromosomal trisomy (PPV 5.88%). (Table 1)

Table 1

The abnormal types and composition ratio of fetal chromosomal aneuploidy

Exception type	NIPT high risk (Number of cases)	Karyotype positive(Number of cases)	Positive detection rate(%)
T21	210	174	85.24
T18	66	34	51.52
T13	32	4	12.5
SCA	122	62	50.82
Other types of trisomy	17	1	5.88
total	447	275	61.52

Types of sex chromosome aneuploidy abnormalities

62 cases of sex chromosome aneuploidy were confirmed by karyotype analysis, of which 45, X 1 case (1.56%), 47, XXX 11 cases (17.74%), 47, XXY 32 cases (51.62%), 47, XYY 10 cases (16.13%), 8 cases of mosaic type (12.9%). (Table 2).Among the 122 cases with high risk of non-invasive chromosomal aneuploidy, 1 case had a chromosome 46, XN, ? del(X)q(11), induced labor,1 case with chromosome 46, XN, add(X8), lost to follow-up.

Table 2

Types of sex chromosome aneuploidy abnormalities

Karyotype	Number of cases (ratio %)	Pregnancy options
45,X	1(1.61%)	Induction of labor
47,XXX	11(17.74%)	2 cases gave birth to a baby girl respectively, which were well developed; 2 cases were lost to follow-up; 7 cases of labor induction
47,XXY	32(51.62%)	4 cases gave birth to a baby boy respectively, which were well-developed; 1 case was lost to follow-up; 27 cases of labor induction
47,XYY	10(16.13%)	3 cases gave birth to a baby boy respectively, 2 cases were developed well. One pregnant woman was delivered by cesarean section at 7 months' gestation, and the child died of lung dysplasia and lung infection; one case was lost to follow-up; 4 cases of labor induction
Other abnormalities	8(12.9%)	gave birth to a baby girl, which was well developed
45,X□[9]/47□XXX□4□/46□XX□[72]	1	Induction of labor
45,X[13]/46□XX[37]	1	gave birth to a baby girl, which was well developed
45,X[4]/46□XX[65]	1	Induction of labor
45,X[42]/46□XX[8]	1	Induction of labor
45,X[46]/47□XXX[4]	1	Induction of labor
45,X[7]/46□XX□[93]	1	gave birth to a baby girl, which was well developed
47,XXX□[46]/46□XX[4]	1	
Amniotic fluid-, FISH turner (43/57); cord blood-, FISH turner (25/75) normal?		

NIPT results for CNVs (Table 3).

Another 81 cases of non-invasive prenatal screening suggest CNVs High risk. After chromosome karyotype and CMA verification, chromosome karyotype was normal, CMA found copy number variation in 17 cases, chromosome abnormal karyotype, CMA found copy number variation in 11 cases, The PPV for CNVs was 34.57% (28/81). Among them, CNVs has a clear pathogenic significance can reach 24.69% (20/81).

Table 3

Non-invasive results	Karyotype	CMA	Pregnancy outcome	Couple karyotype
Fewer sex chromosomes	45，X[23]/46，X，X[67]	Xp22.33×3 1.2Mb duplicate	Induction of labor	
chr18 Microdeletion	45，XN，-18[42]/46，Xn，i，18，p10[4]/46，Xn，i，18，q10[1]	18p11.32p11.21×1 14.2Kb deletion	Induction of labor	
chr 4 Microduplication	46，XN，add，18，，p11，	4p16.3p11×3 49Mb duplicate，18p11.32p11.31×1 3.2Mb deletion	Induction of labor	
chr 2 Microduplication	46，XN，add，2，，p25.3，	2p25.3×1 1.9Mb deletion，2p25.3p23.1×3 28.4Mb duplicate	Induction of labor	No abnormalities in the couple Fish
chr 10 Microduplication	46，XN，add，21，，p10，	10p15.3-p12.1×3 26.62Mb duplicate	Induction of labor	Woman 's is 46，XX，t，10，21，，p10;q10，
chr 2 Microdeletion	46，XN，del，2，，p25p24，，del，2，，p22p21，，inv9，q12q13，	2p25.1-p24.3×1 5Mb deletion， 2p22.3p21 ×1 8Mb deletion	Induction of labor	
chr 21 core area Microduplication	47，XN，+21	21q11.2q22.3×3	Induction of labor	
chr 3 too much	47，XN，+3[8]/46，XN[69]	2p22.3p16.1×2,3p26.3q29×2-3	Induction of labor	
chr 5 abnormal	46，XN，del，5，，p13.2p15.3，	5p15.33p13.2×1 35.7Mb deletion，5q34q35.3×3 15.2Mb duplicate	Induction of labor	The woman's karyotype is normal，men's is 46，XY，inv，5，，p13.2q34，
chr]15 Microduplication	46,XN,dup，15，，q21.2q22.2，	15q21.2q22.2×3, 12Mb duplicate	1 baby girl with normal development	
Sex chromosome abnormalities	46，XN，dup，X，，q27q28，	Xq27.1q28×2, 13.7Mb duplicate	Induction of labor	
chr 16 Microdeletion	Normal	16p13.11p12.3×1 2.8Mb deletion	1 baby boy with no other information	
chr 11	Normal	11q24.1q25×2	1 baby girl	

Microdeletion			with normal development	
chr 9 Microduplication chr 14 Microdeletion	Normal	14q32.32q32.33×1 3.2Mb deletion	1 baby boy with normal development	
chr 15 Microduplication	Normal	15q11.2-q13.1×3 4.9Mb duplicate	1 baby boy with normal development	Woman 's is 46□XX□□dup □15□ □q11.2q13□
chr 17 Microdeletion	Normal	17p12×1 1.3Mb deletion	1 baby girl with normal development	Woman 's is 17p12×1 1.3mb□□
chr 3 Microduplication	Normal	17P13.3×1 3.1Mb deletion	Induction of labor	
chr 18 Microduplication	Normal	18q22.1×3 866.4Kb duplicate	1 baby girl with six fingers on both hands, no other abnormalities	
chr 5 Microdeletion	Normal	3q13.12q13.13×3 1.5Mb duplicate	1 baby boy with normal development	
chr 4 Microduplication	Normal	4q13.1q13.2 ×3 2.3Mb duplicate	1 baby boy with normal development	
chr 15 Microduplication□ Sex chromosome reduction	Normal	5q21.2q21.3×3 2.5Mb duplicate□ 10q11.22q11.23×3 2.3Mb duplicate	1 baby girl with normal development	
chr 15 Microdeletion	Normal	7p15.3×3 1.0Mb duplicate□ 15q11.2q13.1×1 5.4Mb deletion	Induction of labor	
chr 15 Microduplication	Normal	7p21.3×3 1.0Mb duplicate□ 15q11.2q13.1 ×3 5.7Mb duplicate	Induction of labor	
chr 5 Microdeletion and Microduplication	Normal	5p15.33p13.3×1 31.16Mb deletion□5q11.1q35.3×3 130.31Mb duplicate	lost to follow-up	
chr 4 Microdeletion	Normal	Xp22.11×1 464.5Kb deletion	1 baby girl with normal	

			development
chr 15 Microdeletion	Normal	15q11.12q13.1×1 5.6Mb deletion	Induction of labor
chr 7 abnormal	normal	15q13.3×3 422.4Kb duplicate	lost to follow-up
chr 14 too much	Normal	Xp22.31×2 1.6Mb duplicate	1 baby boy with normal development

Follow-up

Non-invasive fetal chromosome 21-trisomy high-risk follow-up

1 family member whose fetus was diagnosed as 21-trisomy refused to follow-up; 1 case died in utero 3 days after the amniotic fluid was drawn, and the karyotype was diagnosed as 21-trisomy; 2 cases of nuclear Type 46, XN, + 21 (der) (21; 21) (q10; q10), induced labor; 1 case of karyotype 47, XN, inv(9) (p12; q13), + 21, induced labor; 1 case The karyotype was 46, XN, der(4; 21) (p10; q10), + 21, induced labor; 8 cases of karyotype were 21-trisomy, all induced labor; 1 case was 46, XN, 15ps+, del(21)(q22.3), induced labor; 1 case of karyotype was 45, XN,? der(18t)(18;21)(p11;q10), -21, girl, well-developed; 1 case of normal karyotype, girl, microtia in the right ear, no ear canal, and no abnormalities in development.

Non-invasive fetal chromosome 18-trisomy high-risk follow-up

4 cases with karyotype 47, XN, + 18, check appearance after induction of labor, 1 case with right foot varus, thick back of neck, 1 case with six fingers, 1 case with bruising appearance, 1 exception Ear morphology was abnormal; 1 case of 18-trisomy mosaicism induced labor.

Non-invasive fetal chromosome 13-trisomy high-risk follow-up

1 case with karyotype 47, Xn, + 13, 1 girl with induced labor, cleft lip; 1 case with karyotype 47, XN, + 13[7]/46, XN [93], girl, normal development.

Non-invasive follow-up of high risk of chromosomal aneuploidy and high risk of chromosome copy number variation is shown in Table 2-Table 3.

Discussion

NIPT screens the ppv of fetal chromosomal aneuploidy and pregnancy follow-up

This study found that the positive predictive values of further prenatal diagnosis for pregnant women with high NIPT risk were 85.24% (174/210) of 21-trisomy, 51.52% (34/66) of 18-trisomy, and 12.5% (4/32) of 13-

trisomy, other types of trisomy 5.88% (1/17). Petersen et al. [6] In the test of 712 samples, the PPV of NIPT for 21-trisomy, 18-trisomy, and 13-trisomy were 84%, 76%, and 45%, respectively. Chen et al. [7] found that the PPV of NIPT for trisomy 21, trisomy 18, and trisomy 13 were 79.24%, 54.84% and 13.79%, respectively. Hu et al. [8] found that the PPV of NIPT for trisomy 21, 18, and 13 was 80%, 60% and 14.28%, respectively. Some previous studies reported that the PPV range of trisomy 21 was 65–94%, trisomy 18 was 47–85%, and trisomy 13 was 12–62% [9–11]. There is no difference between this study and the literature reports. Big. The number of trisomy 13 and other types of chromosomes is relatively small, and the differences in various literature reports are slightly larger. In this study, the positive predictive values of trisomy 13 and other types of chromosome trisomy were only 12.5% and 5.88%.

The karyotype of a fetus was 45, XN, ? der(18t)(18;21)(p11;q10), -21, the parents chose to continue the pregnancy and gave birth to a girl. There is no abnormality in the current development. 4 cases of fetus with karyotype 47, XN, + 18, check the appearance after induction of labor, 1 case of right foot varus, thick back of the neck, 1 case of six fingers, 1 case of appearance of bruising, 1 case of abnormal ear morphology, more frequently in children with trisomy 18 The external phenotype is abnormal. The karyotype of one fetus was 47, XN, + 13[7]/46, XN[93]. The parents decided to continue the pregnancy and gave birth to a girl with normal development.

NIPT to screen the ppv of fetal sex chromosome aneuploidy and follow-up of pregnancy

The incidence of sex chromosomal aneuploidy (SCA) in newborns is 1/1200 ~ 1/400, and the incidence in the fetal period is as high as 1/435 [12]. The common type of SCA has a single sex chromosome. Sex chromosome (45, X), sex chromosome trisomy (47, XXX, 47, XXY and 47, XYY), other aneuploidies and various forms of mosaic sex chromosome abnormalities [13]. However, NIPT has been controversial about the accuracy of SCA testing. Petersen et al. [6] In the test of 712 samples, the PPV of NIPT for 45, X, 47, XXX and 47, XXY was 26%, 50% and 87%, respectively. Wang et al. [14] found that the PPV of NIPT for SCA was only 38% (6/16) in the study of 109 samples tested. Xiong et al. [15] confirmed from the study of 35827 patients that the PPV of NIPT for SCA was 48.5% (32/66). Zhang et al. [16] studied 10 275 samples and found that the PPV of NIPT for SCA was 54.54% (18/33). Porreco et al. [17] confirmed that the PPV of NIPT for SCA was 48.4%. In this study, 528 cases of NIPT positive samples were studied. The results showed that the PPV of NIPT for SCA was 50.86% (64/122), which was closer to the results of Xiong, Zhang, Porreco, etc. [15–17], and 47, XXY was better than others. Chromosome karyotypes are more common, accounting for 51.62% (32/62). The study of Xiong [15] also confirmed that 47, XXY in SCA can account for 46.9% (15/32).

The phenotypes of SCA patients are diverse, and patients may have no abnormal phenotypes throughout their lives, such as 47, XXX and 47, XYY [14]. Some phenotypes are very mild, and the clinical prognosis is relatively good, which can be manifested as abnormal height development, abnormal organ structure, abnormal behavior, underdevelopment, and hypoplastic secondary sexual characteristics [6]. Of the 62 pregnant women diagnosed with fetal SCA in this study, 2 cases had karyotypes of 47, XXX, 4 cases of 47, XXY, 4 cases of 47, XYY (1 case was born prematurely at 7 months of pregnancy, and died due to pulmonary dysplasia), low proportion of mosaic 3 cases all chose to continue pregnancy, 49 cases chose

to terminate the pregnancy, the overall continued pregnancy rate was 20.97% (13/62). In a study of 399 fetal SCA cases in Hong Kong, So et al. [18] found that more than half of pregnant women chose to terminate their pregnancy (the overall pregnancy termination rate was 55.6%). A study by Xiong [15] showed that 50% of pregnant women whose fetuses were SCA screened by NIPT can accept this result (the overall continued pregnancy rate is 50%). Among the pregnant women diagnosed with SCA in this study, 20.97% chose to continue their pregnancy, which was significantly lower than the 40–50% overall continued pregnancy rate of Xiong and So[15, 18]. So is located in Hong Kong and bear is located in Shanghai, Hong Kong and Shanghai are both economically developed areas, families have higher education levels, pregnant women and their families have higher awareness and acceptance of diseases, so the overall continued pregnancy rate is also higher.

CMA detects the advantages and disadvantages of fetal chromosome copy number variation and follow-up of pregnancy

Chromosomal microdeletion and microduplication are a chromosomal disease that causes normal gene imbalance due to submicroscopic chromosome deletion or duplication. It is another important genetic factor for fetal birth defects [19], accounting for about 15% of all genetic diseases [20]. Its clinical manifestations are complex and changeable, which can cause clinical symptoms such as fetal developmental delay, mental retardation, multiple malformations of internal organs and external phenotypes, and because less fatal genes are involved, the mortality rate after birth is not high, and it can survive long-term disability, giving society and families the burden of weight-bearing is worthy of the attention of birth defect prevention and control workers. Traditional karyotype analysis is the gold standard for diagnosing large fragments and abnormal numbers of chromosomes, but it is difficult to distinguish chromosomal mutations below 5Mbp, and karyotype analysis is also affected by the subjective judgment ability of technicians. When diagnosing small fragments of CNVs Often powerless. CMA technology is a newly developed molecular detection technology that can scan at the whole genome level and has outstanding advantages in detecting chromosomal imbalance abnormalities. It has become the main technology platform for detecting CNVs at this stage. In this study, NIPT showed that 81 fetuses at high risk of CNVs were tested for karyotype and CMA. Among them, 17 cases had abnormal karyotype and CMA, and 11 cases had normal karyotype and abnormal CMA. The positive rate of CMA test could reach 34.57% (28/81), of which CMA has a clear pathogenic significance in 20 cases, which can reach 24.69% (20/81). Jiang et al. [20] performed CMA on 52 pregnant women with a high risk of CNV s in the NIPT sample, and detected 15 cases of copy number variation that were more consistent with the NIPT results, with a positive rate of 28.85%. Hu et al. [8] verified the pregnant women whose NIPT indicated a high risk of CNVs, and the PPV was 36.11%. Chen et al. [7] verified that pregnant women whose NIPT indicated a high risk of CNVs had a PPV of 28.99%. The results of this study are consistent with those of Chen, Hu, and Jiang [7, 8, 21]. In this study, 11 cases of fetal karyotype and CMA were abnormal, of which 1 case was born with karyotype 46, XN, dup (15) (q21.2q22.2), chip 15q21.2q22.2 12 Mb duplication, There are reports of cases where the repetition of less than this fragment is associated with clinical phenotypes such as hydrocephalus, microcephaly, and overall developmental delay. The child is currently well-developed. Among the 10 cases of labor induction, 1 case had a karyotype of 46, XN, add (2) (p25.3), a chip of 2p25.3 × 1 1.9 Mb deletion,

and 2p25.3p23.1 × 3 28.4 Mb duplication. No abnormalities in the couple Fish; 1 case of karyotype is 46, XN, add(21) (p10), chip is 10p15.3p12.1 × 3, 26.62 Mb duplication, pregnant woman karyotype is 46, XX, t(10; 21) (p10 ;q10); 1 case of karyotype 46, XN, del(5) (p13.2p15.3), chip 5p15.33p13.2 × 1 35.7 Mb deletion, 5q34q35.3 × 3 15.2 Mb duplication (Catscry Syndrome), the pregnant woman has a normal karyotype, and the man's karyotype is 46, XY, inv(5) (p13.2q34). The karyotype in 1 case is 45, XN, -18[42]/46, XN, i(18) p10[4]/46, XN, i(18)q10[1], chip 18p11.32p11.21 × 1 14.2 Kb is deletion. The karyotype of one case was 46, XN, del (2) (p25p24), del (2) (p22p21), inv9 (q12q13), the chip was 2p25.1p24.3 × 1 5 Mb deletion and 2p22.3p21 × 1 8 Mb deletion. From the above analysis, when a parent's chromosome has a balanced translocation or inter-arm inversion, the fetus's chromosomes are prone to deletion/duplication of large fragments and/or small fragments; there may be discrepancies between the karyotype results and the microarray results. 1 The karyotype is a duplication of chromosome 21, and the chip is a microduplication of chromosome 10; the chip cannot detect a low proportion of mosaicism. In this study, the karyotype is 45, XN, -18[42]/46, XN, i (18) p10 [4]/46, XN, i(18) q10[1], the chip only detects the microdeletion of chromosome 18, and there are literature reports [22] that CMA cannot detect the low proportion of chimeras < 10%. This study also can be confirmed; the chip cannot detect balanced translocations and inter-arm inversions of chromosomes with normal copy numbers. In this study, the karyotype is 46, XN, del (2) (p25p24), del (2) (p22p21), inv9 (q12q13), the chip only detects the microdeletion of chromosome 2.

In this study, there were 17 cases with normal fetal karyotype and abnormal chip. Among these 17 cases, the chip had no clear significance/no disease reported in 8 cases, which could reach 9.88% (8/81). Domestic scholar Jiang Yulin and others [23] The study found that CNVs of unknown clinical significance in CMA detection accounted for 15.3% of the total number of cases examined. Among these 8 cases, 1 case was lost to follow-up, and 7 cases chose to continue their pregnancy. 1 case had a 2.8 Mb deletion of chromosome 16 and gave birth to a boy, but the specific situation of the child was not informed; 1 case had a duplication of chromosome 18 of 866.4Kb, gave birth to a girl with six fingers on both hands, and no abnormal development was seen in the remaining 5 cases. Normal development. This study shows that: if the CMA results have no clear significance or no disease reports, those who choose to continue pregnancy, except for one child who was not informed about the specific situation, the other children have no obvious mental retardation, will there be other problems such as childbirth in the future, Long-term follow-up is required.

Conclusion

In conclusion, this study obtained more reliable PPV data for NIPT screening for chromosomal aneuploidy, followed up pregnancy outcomes, and obtained reliable follow-up data, which provided a reliable basis for clinical genetic counseling and management. The limitation of this study is that the number of cases collected by NIPT in screening for chromosomal microdeletion and microduplication is relatively small, and the conclusions drawn need to be further collected and confirmed to increase the credibility of the conclusions. In addition, although CMA has its advantages, there are also limitations. Therefore, it is recommended to perform prenatal diagnosis and perform chromosomal nucleus when non-invasive and

high-risk prompts suspicious chromosomal abnormalities (over/under/microdeletion/microduplication). Type and CMA inspection, so that the inspection is more comprehensive .

Abbreviations

cfDNA Cell-free DNA

CMA Chromosomal microarray analysis

CNVs Copy-number variants

NIPT Non-invasive prenatal testing

PPV Positive predictive value

Declarations

Acknowledgements

Not available.

Authors' contributions

All authors have materially participated in the study and manuscript preparation.LY, designed the work and drafted the manuscript.LY, SYand LH collected all clinical data. TH and YX carried out all the molecular genetic analyses. ML and ZY participated in the data analysis. GJ and LY designed the work and revised the manuscript. All authors have approved the final article.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Hebei General Hospital.

Consent for publication

The authors declare that they have no competing interests and the patients in this case report had provided their consent for publication.

Competing interests

The authors declare that they have no competing interests.

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