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ORIGINAL RESEARCH

Chromosomal Microarray Analysis in Fetuses with Ultrasound Abnormalities

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Objective: To explore and evaluate the value of chromosomal microarray analysis (CMA) in prenatal diagnosis of fetuses with ultrasound abnormalities.

Methods: A retrospective analysis was performed on 370 fetuses with ultrasound abnormalities received invasive prenatal diagnosis at Meizhou People's Hospital from October 2022 to December 2023. Fetal specimens were analyzed by CMA, and the detection rates of aneuploidy and pathogenic (P)/likely pathogenic (LP) copy number variations (CNVs) in ultrasound structural abnormalities (malformations of fetal anatomy) and non-structural abnormalities (abnormalities of fetal nonanatomical structure) were analyzed.

Results: There were 114 (30.8%) cases with isolated ultrasound structural abnormalities, 226 (61.1%) cases with isolated non-structural abnormalities (182 isolated ultrasound soft markers abnormalities, 30 isolated fetal growth restriction (FGR), and 8 isolated abnormalities of amniotic fluid volume), and 30 (8.1%) cases with both structural and non-structural abnormalities. The overall detection rate of aneuploidy and P/LP CNVs in isolated ultrasonic structural abnormalities was 5.3%, among which cardiovascular system abnormalities were the highest. In addition, the largest number of fetuses with non-structural abnormalities was nuchal translucency (NT) thickening (n = 81), followed by ventriculomegaly (n = 29), and nasal bone dysplasia (n = 24). The detection rate of chromosomal abnormalities of fetuses with abnormal ultrasound soft markers was 9.9%, and the detection rate in single abnormal ultrasound soft marker, and multiple ultrasound soft markers abnormalities was 9.7% (16/165) and 11.8% (2/17), respectively. Moreover, the detection rate of chromosomal abnormalities of fetuses with FGR and structural abnormalities combined with non-structural abnormalities was 6.7% (2/30), and 13.3% (4/30), respectively.

Conclusion: The incidence of chromosomal abnormalities (aneuploidy and P/LP CNVs) varies among different fetal ultrasound abnormalities.

Keywords: chromosomal microarray analysis, copy number variation, abnormal ultrasound fetus, prenatal diagnosis

Introduction

Birth defect is the main cause of infant death and an important factor of child disability and affecting the quality of the population.[1] Birth defect refers to congenital abnormalities caused by genetic factors, environmental factors, or the interaction between genetic factors and environmental factors, usually including congenital malformation, chromosomal abnormalities, genetic metabolic diseases, and functional abnormalities.[2,3] The overall incidence of birth defect in China is about 5.6%,[4] it brings a huge burden to both the family and the society. Prenatal ultrasound examination is widely used as a routine technique for screening fetal malformations. It can detect different fetal abnormalities, including structural abnormalities, minor abnormalities (also known as abnormal ultrasound soft markers), fetal growth restriction (FGR), and abnormalities of amniotic fluid volume.[5] And ultrasound shows significant fetal abnormalities in about 2–3% of the pregnancies.[6] Prenatal ultrasonography can detect some abnormalities or related signs caused by chromosomal abnormalities in the prenatal period to assist in screening high-risk cases.[7,8] It is an important method for prenatal screening of fetal malformations and plays an important role in the prevention and treatment of birth defects.[9–11]

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Timely and accurate diagnosis and appropriate intervention are essential for congenital abnormalities. Fetal ultrasound abnormalities are the primary indicators for invasive prenatal genetic testing, and their genetic etiology can be explored by chromosomal microarray analysis (CMA).[12,13] CMA is based on microarray comparative genomic hybridization and single nucleotide polymorphism microarray techniques to detect copy number variation (CNV) larger than 1 kilobase (kb) in the genome.[14] CMA can detect complementary sequences on chromosomes by using high-density DNA probes fixed to the matrix, and scanning at the genome-wide level to reveal chromosomal microduplications and microdeletions.[12] Compared with chromosomal karyotype analysis, CMA has the advantages of convenience, speed, high throughput, and accuracy.[15] In 2009, American College of Obstetrics and Gynecology (ACOG) recommended CMA technology for fetuses with ultrasound structural abnormalities and normal karyotype for the first time, opening the application of CMA in prenatal diagnosis.[16] Chromosomal abnormality was detected 3% to 6% more often in fetuses with abnormal ultrasound and normal karyotype by CMA.[17–20]

The incidence and characteristics of birth defects and genetic diseases vary from population to region.[21,22] As far as we know, there are little data on the use of CMA in the genetic diagnosis of fetal ultrasound abnormalities in this region. In this study, a retrospective analysis was performed on fetuses with ultrasound abnormalities in the Department of Prenatal Diagnostic Center at Meizhou People's Hospital. The differences of the detection rate of chromosomal abnormalities in fetuses with ultrasound structural abnormalities, abnormal ultrasound soft markers, FGR, and abnormalities of amniotic fluid volume by CMA were analyzed. The purpose of this study was to evaluate the clinical value of CMA in different ultrasound abnormalities and provided valuable information for pregnancy management of fetuses with abnormal ultrasound.

Materials and Methods

Study Cohort

This study was approved by the Medical Ethics Committee of Meizhou People's Hospital (Clearance No.: 2023-C-30), and the written informed consent of pregnant couples for invasive prenatal diagnosis was obtained. The study cohort was recruited between October 2022 and December 2023. The patients involved were from the Genetic Counseling Clinic of Department of Prenatal Diagnostic Center at Meizhou People's Hospital.

Inclusion criteria: (1) abnormal ultrasound fetus with invasive prenatal diagnostic indications; (2) all receive detailed genetic counseling and informed consent from pregnant women and their families; (3) no contraindications for invasive prenatal diagnosis; (4) the possibility of maternal cell contamination (MCC) of fetal sample has been ruled out, and the quantity and quality of fetal DNA sample meet the requirements of CMA testing.

Fetal ultrasound abnormalities included:

(1) Fetal ultrasound structural abnormalities:[23] ultrasound indicated the abnormality of fetal anatomical structure, including cardiovascular system, urinary system, thoracic, cephalic facial, nervous system, digestive system, skeletal system, abdominal wall, and other malformations.

(2) Abnormal ultrasound soft markers:[24,25] nonspecific and minor abnormalities in fetal structure detected on ultrasound, including nuchal translucency (NT) thickening, ventriculomegaly, nasal bone dysplasia, choroid plexus cyst, short long bones, pyelic separation, echogenic bowel, single umbilical artery, tricuspid regurgitation, and pyelectasis.

(3) Fetal growth restriction (FGR): fetal ultrasound estimates of body weight or abdominal circumference are less than the 10th percentile for the corresponding gestational age, or two standard deviations below their average weight;[26]

(4) Abnormalities of amniotic fluid volume: deepest vertical pocket (DVP) $\geq$ 8 cm and (or) amniotic fluid index $\geq$ 24 cm, polyhydramnios is considered; if DVP $\leq$ 2 cm and/or amniotic fluid index $<$ 8 cm, oligohydramnios is considered.[27,28]

Abnormal ultrasound soft markers, FGR, and abnormalities of amniotic fluid volume are collectively referred to as fetal ultrasound non-structural abnormalities.[29,30]

A total of 370 fetuses (chorionic villus samples, n = 55; amniotic fluid samples, n = 314; and umbilical cord blood samples, n = 1) were successfully analyzed for CMA.

CMA Detection and Data Analysis

DNA extraction of fetal sample was performed in accordance with the operating instructions (Qiagen, Valencia, CA, USA). The extracted DNA samples were cleaved, ligated, amplified, pure, quantified, fragmented, labeled, hybridized, washed, stained, scanned, and analyzed according to Affymetrix standard procedures. The chip used for CMA detection is Affymetrix Cytoscan 750K Array chip (Affymetrix, USA). Finally, the obtained original data is analyzed by the corresponding software.

The CMA test results were analyzed and interpreted in combination with public databases commonly used internationally, such as the University of California Santa Cruz Database (UCSC) (https://genome.ucsc.edu), Database of Genomic Variation and Phenotype in Humans using Ensembl Resources (DECIPHER) (http://decipher.sanger.ac.uk), Clinical Genome Resource (ClinGen) (https://www.clinicalgenome.org/), Database of Genomic Variants (DGV) (http://dgv.tcag.ca/dgv/app/homr), and Online Mendelian Inheritance Database in Man (OMIM) (https://www.omim.org). According to the American College of Medical Genetics and Genomics (ACMG) guidelines, the clinical significance of CNVs is divided into 5 grades: pathogenic (P), likely pathogenic (LP), variants of uncertain significance (VUS), likely benign (LB), and benign (B).[31,32]

Results

Baseline Characteristics of Study Cohort

Of the 370 fetuses, there were 316 pregnant women aged less than <35 years old, 54 pregnant women aged ≥35 years old. There were 93 (25.1%), 229 (61.9%), and 48 (13.0%) cases of fetal gestation age ≤ 13 weeks, 14–28 weeks, and > 28 weeks, respectively. Among the fetuses with abnormal ultrasound, 114 (30.8%) cases with isolated ultrasound structural abnormalities, 226 (61.1%) cases had isolated non-structural abnormalities, and 30 (8.1%) cases had both structural abnormalities and non-structural abnormalities. In fetuses with non-structural abnormalities, the proportion of isolated ultrasound soft markers abnormalities, isolated fetal growth restriction, and isolated abnormalities of amniotic fluid volume was 49.2%, 8.1%, and 2.2%, respectively (Table 1).

Table 1 Demographic Characteristics of Pregnant Women and General Characteristics of Fetuses

Characteristics	All cases (n=370)
Age of mothers who had abortions (years)	
<35, n(%)	316(85.4%)
≥35, n(%)	54(14.6%)
Gestational week at the time of discovery of fetal abnormalities (weeks)	
≤13, n(%)	93(25.1%)
14–28, n(%)	229(61.9%)
>28, n(%)	48(13.0%)
Type of samples tested by CMA	
Villus, n(%)	55(14.9%)
Amniotic fluid, n(%)	314(84.9%)
Cord blood, n(%)	1(0.3%)
Abnormal fetal ultrasound types	
Structural abnormalities, n(%)	114(30.8%)
Non-structural abnormalities, n(%)	226(61.1%)
Isolated ultrasound soft markers abnormalities, n(%)	182(49.2%)
Isolated fetal growth restriction, n(%)	30(8.1%)
Isolated abnormalities of amniotic fluid volume, n(%)	8(2.2%)
Structural abnormalities + non-structural abnormalities, n(%)	30(8.1%)

Abbreviation: CMA, Chromosome microarray analysis.

Distribution of Different System Malformations in Fetuses with Structural Abnormalities and the Corresponding CMA results

In the fetuses with isolated ultrasound structural abnormalities, the number of abnormal cases of cardiovascular system was the largest (n = 38), accounting for 33.3% of the total number of cases with isolated ultrasound structural abnormalities, followed by urinary system abnormality (n = 22, 19.3%), thoracic abnormalities (n = 11, 9.6%), cephalic facial abnormalities (n = 10, 8.8%), nervous system abnormalities (n = 9, 7.9%), digestive system abnormalities (n = 6, 5.3%), skeletal system abnormalities (n = 6, 5.3%), and abdominal wall abnormalities (n = 2, 1.8%).

In the fetuses with isolated ultrasonic structural abnormalities, 2 cases with chromosomal aneuploidy and 4 cases with P/LP CNVs were detected, with the overall detection rate was 5.3%. In the single structural abnormality group, 5 cases were detected with aneuploidy or P/LP CNVs, and the detection rate was 4.5% (5/110). Among them, the detection rate of aneuploidy and P/LP CNVs of fetal cardiovascular system abnormalities was the highest (7.9%). In addition, one case was detected in the fetuses with multiple structural malformations, with a detection rate of 25.0% (1/4) (Table 2).

Distribution of Different Abnormalities in Fetuses with Abnormal Ultrasound Soft Markers and the Corresponding CMA Results

In this study, the largest number of fetuses with abnormal ultrasound soft markers was NT thickening (n = 81, 44.5%), followed by ventriculomegaly (n = 29, 15.9%), and nasal bone dysplasia (n = 24, 13.2%). Chromosomal aneuploidy was detected in 4 fetuses and P/LP CNVs were detected in 14 cases, the overall detection rate was 9.9%. Among them, the detection rate of aneuploidy and P/LP CNVs of NT thickening was the highest (12.3%), followed by choroid plexus cyst (11.1%), ventriculomegaly (6.9%), and nasal bone dysplasia (4.2%). And the detection rate in fetuses with single abnormal ultrasound soft marker, and multiple ultrasound soft markers abnormalities was 9.7% (16/165) and 11.8% (2/17), respectively (Table 3).

Distribution of Different Abnormalities in Fetuses with Fetal Growth Restriction, and Abnormalities of Amniotic Fluid Volume, and the Corresponding CMA Results

There were 30 fetuses with FGR and 8 cases with abnormalities of amniotic fluid volume. P/LP CNVs were detected in 2 FGR cases, with the detection rate was 6.7%. Chromosomal aneuploidy and P/LP CNVs were not detected in fetuses with abnormal amniotic fluid volume. In addition, one pathogenic CNV was detected in one fetus with FGR and abnormal ultrasound soft marker (NT thickening) (Table 4).

Table 2 The Distribution of Different System Malformations in Fetuses with Structural Abnormalities and the Corresponding CMA Results

Structural Abnormalities	n (%)*	CMA			
		Aneuploidy	P/LP CNV	VUS	Detection Rate of Aneuploidy and P/LP CNV
Cardiovascular system	38(33.3%)	1	2	3	7.9%
Urinary system	22(19.3%)	0	1	1	4.6%
Thoracic	11(9.6%)	0	0	1	–
Craniofacial malformation	10(8.8%)	0	0	1	–
Nervous system	9(7.9%)	0	0	2	–
Digestive system	6(5.3%)	0	0	0	–
Skeletal system	6(5.3%)	0	0	2	–
Abdominal wall	2(1.8%)	0	1	0	–
Other malformations	6(5.3%)	0	0	0	–
Multiple structural malformations	4(3.5%)	1	0	0	25.0%
Total	114(100.0%)	2	4	10	5.3%

Abbreviations: CMA, chromosome microarray analysis; CNV, copy number variant; P/LP CNV, Pathogenic/Likely pathogenic CNV; VUS, variants of uncertain significance.

Table 3 The Distribution of Different Abnormalities in Fetuses with Abnormal Ultrasound Soft Markers and the Corresponding CMA Results

Abnormal Ultrasound Soft Markers	n (%)*	CMA			
		Aneuploidy	P/LP CNV	VUS	Detection Rate of Aneuploidy and P/LP CNV
NT thickening	81(44.5%)	3	7	10	12.3%
Ventriculomegaly	29(15.9%)	0	2	2	6.9%
Nasal bone dysplasia	24(13.2%)	1	0	2	4.2%
Choroid plexus cyst	9(4.9%)	0	1	0	11.1%
Short long bones	6(3.3%)	0	0	1	–
Pyelic separation	5(2.7%)	0	0	2	–
Echogenic bowel	4(2.2%)	0	0	0	–
Single umbilical artery	3(1.6%)	0	0	0	–
Tricuspid regurgitation	2(1.1%)	0	1	0	50.0%
Pyelectasis	2(1.1%)	0	1	0	50.0%
Multiple ultrasound soft markers abnormalities	17(9.3%)	0	2	0	11.8%
Total	182(100.0%)	4	14	17	9.9%

Note: *, Constituent ratio.
Abbreviations: CMA, chromosome microarray analysis; CNV, copy number variant; VUS, variants of uncertain significance.

Table 4 The Distribution of Different Abnormalities in Fetuses with Fetal Growth Restriction, and Abnormalities of Amniotic Fluid Volume, and the Corresponding CMA Results

Types of Non-Structural Abnormalities	n (%)*	CMA			
		Aneuploidy	P/LP CNV	VUS	Detection Rate of Aneuploidy and P/LP CNV
Fetal growth restriction	30(68.2%)	0	2	3	6.7%
Abnormalities of amniotic fluid volume	8(18.2%)	0	0	1	-
Fetal growth restriction + abnormal ultrasound soft markers	3(6.8%)	0	1	1	33.3%
Abnormalities of amniotic fluid volume + abnormal ultrasound soft markers	2(4.5%)	0	0	0	-
Fetal growth restriction + abnormalities of amniotic fluid volume + abnormal ultrasound soft markers	1(2.3%)	0	0	0	-
Total	44(100.0%)	0	3	5	6.8%

Note: *, Constituent ratio.
Abbreviations: CMA, chromosome microarray analysis; CNV, copy number variant; VUS, variants of uncertain significance.

Distribution of Different Abnormalities in Fetuses with Structural Abnormalities Combined with Non-Structural Abnormalities and the Corresponding CMA Results

There were 30 fetuses with structural abnormalities combined with non-structural abnormalities, and the largest number was structural abnormalities combined with abnormal ultrasound soft markers (n = 25). In these fetuses, 2 cases with chromosomal aneuploidy and 2 cases with P/LP CNVs were detected, and the overall detection rate in this group was 13.3% (4/30) (Table 5).

Discussion

With the rapid development of prenatal diagnosis technology, imaging examination can detect more and more fetal abnormalities.[33] Fetal ultrasound abnormalities are congenital birth defects characterized by anatomical abnormalities,

Table 5 The Distribution of Different Abnormalities in Fetuses with Structural Abnormalities Combined with Non-Structural Abnormalities and the Corresponding CMA Results

Fetal Ultrasound Structural Abnormalities Combined with Non-structural Abnormalities	n (%)*	CMA			
		Aneuploidy	P/LP CNV	VUS	Detection Rate of Aneuploidy and P/LP CNV
Structural abnormalities + abnormal ultrasound soft markers	25(83.3%)	2	2	2	16.0%
Structural abnormalities + abnormalities of amniotic fluid volume	2(6.7%)	0	0	1	-
Structural abnormalities + fetal growth restriction	1(3.3%)	0	0	0	-
Structural abnormalities + abnormal ultrasound soft markers + fetal growth restriction	1(3.3%)	0	0	0	-
Structural abnormalities + abnormal ultrasound soft markers +abnormalities of amniotic fluid volume	1(3.3%)	0	0	0	-
Total	30(100.0%)	2	2	3	13.3%

Note: *, Constituent ratio.
Abbreviations: CMA, chromosome microarray analysis; CNV, copy number variant; VUS, variants of uncertain significance.

minor variations, or abnormal growth and development of the fetus, often accompanied by changes in genetic material, some of which are genetic material of germ cells such as chromosomal abnormalities, gene mutations, and transmitted to offspring, and can also be caused by environmental factors and other unknown causes.[34–36] This study analyzed the detection rate of chromosomal abnormalities by CMA in different fetal ultrasound abnormalities, and the results showed that the incidence of aneuploidy and P/LP CNVs varies among different fetal ultrasound abnormalities.

In this study, in the group of isolated ultrasonic structural abnormalities, the number of cardiovascular system abnormalities was the largest (38 cases, 33.3%), which was consistent with the main types of fetal congenital structural abnormalities.[37] In 2022, Mastromoro G et al[38] proposed that CMA could be used as a first-line detection method in fetal structural abnormalities, with the detection rate of pathogenic CNVs was 19.47% in isolated structural abnormality and 27.47% in multiple structure abnormalities. In a smaller cohort reported by Lee et al,[39] the detection rate of pathogenic CNVs was 10.5% in fetuses with isolated ultrasound structural abnormality and 15.4% in fetuses with multiple ultrasound structural abnormalities. Another study has shown that among fetuses with abnormal urinary system, the chromosomal abnormalities rate was 11.04% and the detection rate of pathogenic CNVs was 6.31%, and the detection rate in fetuses with non-isolated urinary system abnormalities is significantly higher than that in isolated fetuses.[40] Israeli scholars performed CMA tests on fetuses with corpus callosum absence and concluded that fetuses with isolated corpus callosum absence combined with central nervous system abnormalities had a higher risk of pathogenic CNVs than fetuses with isolated corpus callosum absence.[41] In this study, the overall detection rate was 5.3% in the fetuses with isolated ultrasonic structural abnormalities and 4.5% in the fetuses with single structural abnormality, however, the CMA results of fetuses with single structural abnormality and multiple structural abnormalities were not compared owing to the number of fetal multiple structural abnormalities was small.

In this study, the largest number of abnormal ultrasound soft markers was NT thickening, followed by ventriculomegaly and nasal bone dysplasia. NT thickening is 11 to 13^{+6} weeks of gestation, NT $\geq$ 95th percentile, usually resolves by the middle of pregnancy, but in a small number of cases, this hyaline layer may become neck edema or hystoma.[42] NT thickening is an independent marker of fetal chromosomal aneuploidy and a marker for further invasive prenatal diagnosis and genetic analysis.[43] Nasal bone dysplasia refers to undetectable ossification of the nasal bone or short length of the nasal bone, which is closely related to trisomy 21 syndrome, trisomy 18 syndrome, and trisomy 13 syndrome[44] and is an indicator of invasive prenatal diagnosis. Ventriculomegaly refers to measuring the width of the anterior or posterior foot of the lateral ventricle between 10 and 15mm at any gestational week. More than 50% of the non-isolated mild ventriculomegaly is often associated with central nervous system abnormalities.[45] In a study conducted genetic analysis on four ultrasound soft markers (NT measurement, nasal bone observation, tricuspid valve regurgitation, and abnormal venous catheter Doppler

waveform) in early pregnancy at 11 to 13^{+6} weeks of gestation by Thai scholars showed that NT thickening had the highest detection rate.[46] Pan L et al[47] conducted a CMA analysis on fetuses with nasal bone abnormalities and found that 17.7% of the fetuses had chromosomal abnormalities, and the detection rate was higher when nasal bone abnormalities combined with other soft markers or structural abnormalities. A number of domestic and foreign scholars have studied the incidence of chromosomal abnormalities in isolated and multiple ultrasonic soft markers, including echogenic bowel, pyelectasis, choroid plexus cyst, ventriculomegaly, and so on.[48–51] The results of this study suggest that the overall detection rate of aneuploidy and P/LP CNVs in fetuses with abnormal ultrasound soft markers was 9.9%, and the detection rate in fetuses with single abnormal ultrasound soft markers and multiple ultrasound soft markers abnormalities was 9.7% and 11.8%. Some of the abnormal ultrasound soft markers have a high rate of chromosomal abnormalities, so interventional prenatal diagnosis is recommended.[25,45] There are many kinds of fetal ultrasound soft markers, and the detection rate of different kinds of abnormal ultrasound soft markers is very different.

In terms of chromosomal abnormalities in fetuses with FGR, a study found that the most pathogenic CNVs in nonmalformed growth-restricted fetuses were 22q11.2 duplication, Xp22.3 deletion, and 7q11.23 deletion (Williams-Beuren syndrome), particularly in isolated fetal growth restriction.[52] A study from France found that in fetuses diagnosed with isolated FGR, the detection rate of genetic abnormalities detected by CMA was estimated to be 7.5% (11/146), with 10 pathogenic CNVs and 1 LP CNV.[53] The detection rate of chromosomal abnormalities by CMA in fetuses with FGR varied greatly in different studies, such as 13.42%,[54] 7.9%,[55] 6.6%,[35] and 4.5%.[56] FGR not only carries the risk of intrauterine stillbirth but also has long-term sequelaes such as postpartum metabolic diseases, diabetes, or hypertension.[57] Chromosomal abnormality is one of the important causes of FGR, especially when combined with other system abnormalities.[57,58] CMA can not only detect chromosomal aneuploidy detected by conventional karyotype analysis but also detect the microdeletion and microduplication of chromosomal fragments, prenatal diagnosis of FGR with CMA examination is recommended to evaluate the fetal prognosis.

In summary, although ultrasound cannot directly observe fetal chromosomal abnormalities, some ultrasound abnormalities and special signs related to genetic abnormalities can be found through prenatal ultrasound, which makes it possible to screen fetal genetic abnormalities with prenatal ultrasound. CMA can detect CNVs of chromosomal imbalances across the genome, revealing the exact size and gene content of chromosomal deletions or duplicates. Its providing appropriate genetic testing for fetuses with abnormal ultrasound can help to discover the genetic causes of fetal abnormalities, at the same time, to evaluate the prognosis of the fetuses, formulate appropriate delivery methods and neonatal management plans, and provide re-fertility risk assessment.[59] CMA should be used when fetal ultrasound is abnormal, and genetic counseling should be fully performed when CMA results are abnormal, especially when the test result is VUS.[60]

This study enriches the data on the genetic etiology of fetal ultrasound abnormalities in this region. However, there were some limitations in this study. First, although CMA has certain advantages in detecting chromosomal abnormalities, it cannot currently replace chromosomal karyotype analysis because CMA cannot detect chromosomal translocations and inversions. Differences in detection rates between CMA and karyotypes were not analyzed in this study. Second, due to the limited sample size, this study did not compare the chromosomal abnormalities of fetuses with single ultrasound structural abnormality and multiple structural malformations. Third, due to the limitation of sample size, this study did not summarize the CNV regions with significant directional characteristics for different fetal ultrasound abnormalities. Therefore, we need to conduct a larger sample size study to enrich the relevant data. The interpretation of CMA test results needs to refer to multiple databases, combined with relevant case reports, case-control analysis, and review. In the future, we need to establish and enrich the database of the population in the region to provide more valuable and direct data support for genetic counseling and clinical treatment.

Conclusions

The results of this study showed that the incidence of chromosomal abnormalities varies among different fetal ultrasound structural abnormalities and non-structural abnormalities. CMA is a first-line genetic test for fetal ultrasound abnormalities that helps to discover the genetic causes of fetal abnormalities. The establishment of a localized database will benefit the prevention and control of birth defects in the region.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval

All participants were informed on the study procedures and goals and the study obtained written informed consent from all the participants. We confirm that all methods were performed in accordance with relevant guidelines and regulations. The study was performed under the guidance of the Declaration of Helsinki and approved by the Ethics Committee of Medicine, Meizhou People's Hospital.

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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.

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Disclosure

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

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