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Original Article

Evaluation the Application of Karyotype Analysis and Chromosome Microarray in Prenatal Diagnosis

Huafeng Li, *Yongli Li, Yanli Zhang, Jinping Zhu, Yuqiang Huang

Medical Genetics Department, Linyi Women and Children's Health Care Hospital, Linyi 276000, China

***Corresponding Author:** Email: liyonglilinyi@126.com

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Abstract

Background: We aimed to compare the difference of the chromosomal abnormalities using karyotype analysis and chromosomal microarray (CMA) as well as to evaluate their application in different prenatal diagnosis indications.

Methods: Overall, 3007 pregnant women with prenatal diagnosis indications from Medical Genetics Department of Linyi Women and Children's Health Care Hospital, who underwent standard G-banded karyotype analysis and CMA, were enrolled from 2018-2022. G-banded karyotype analysis and CMA were undergone simultaneously. All fetuses with genetic variants were enrolled for further analyzing. The frequency and differences of chromosomal abnormalities of the two methods were compared in different prenatal diagnosis indications groups.

Results: CMA improved 4.09% (123/3007) of genetic changes compared karyotype analysis. CMA is on par with karyotyping for detection of aneuploidies and gross unbalanced rearrangements. Serological screening and ultrasound abnormalities were the main indications of prenatal diagnosis. The detection rate of chromosomal abnormalities was highest in non-invasive prenatal testing (NIPT) abnormal group. In the ultrasound abnormality group, the detection rate of genetic variants in nuchal translucency (NT) increased group was higher than other subgroups and there was statistically significant difference in the detection rate of pCNVs. CMA can detect 5.57% (40/718) more genetic abnormalities in ultrasound abnormality group on the normal karyotype. CMA improved 0.67% (20/3007) of genetic changes with clinically significant compared karyotype, brought 3.42% (103/3007) of variants with uncertain significance (VOUS).

Conclusion: CMA identified additional, clinically significant genetic variants on the basis of normal karyotype analysis, brought a proportion of unclear significant variants. All the pregnant women accepted amniocentesis should be informed about their characteristics of karyotype analysis and CMA by genetic counselors.

Keywords: Prenatal diagnosis; Chromosome microarray analysis; Karyotype analysis; Genetic variant

Introduction

Prenatal diagnosis is widely recognized as the basic measure to prevent birth defects in fetus, and the traditional karyotype analysis is used as the "gold standard" for cytogenetic diagnosis for detecting fetal chromosomal disorders. Compared with the defects of karyotype analysis with time-consuming and low resolution, chromosomal microarray analysis (CMA) shows

the advantages with high resolution, high throughput, and high sensitivity, which can detect chromosomal microdeletions and microduplications that cannot be found by karyotype analysis (1). Moreover, CMA also can detect triploidy, uniparental disomy (UPD) and loss of heterozygosity (LOH). With the advancements of technology, CMA is becoming more and more widely used in the field of prenatal diagnosis especially for the fetuses with ultrasonographic structural abnormalities (2).

Despite all the advantages, CMA also had the drawbacks that CMA can detect genetic changes of unclear significance. We analyzed the results of 3007 pregnant women underwent karyotype analysis and CMA with different reasons, assessed the frequency of the chromosomal disorders as well as evaluated their application in different prenatal diagnosis indications.

Subjects

Overall, 3007 pregnant women with prenatal diagnosis indications from Medical Genetics Department of Linyi Women and Children's Health Care Hospital, who underwent standard G-banded karyotype analysis and CMA, were selected as the research subjects from January 2018 to December 2022. All pregnant women were accepted detailed genetic counselling and signed informed consent before amniocentesis. All cases which detected chromosomal abnormalities were enrolled for further analyzing.

Indications for prenatal diagnosis include: high risk of serological screening, advanced age, ultrasound abnormality, non-invasive prenatal testing (NIPT) abnormality, abnormal karyotype of couples, a history of adverse pregnancy outcomes and the others. Ultrasound abnormality group was divided into 4 subgroups, including structural variation, soft index abnormal, increased NT and others.

This study was verified and approved by the Ethics Committee of Linyi Maternal and Child Health Care Hospital (KYL-YXLL-2023002). The maternal age was range from 17 to 45 years and the gestational week was range from 17 to 32 weeks.

Methods

Karyotype Analysis

Amniocentesis was performed with ultrasound-guided localization. Two 10 ml of amniotic fluid was collected and used for karyotype analysis simultaneously. Conventional G banding karyotype analysis was performed according to the standard cytogenic procedures and then scanned by Leica GLS120 Automated Nuclear Scanning System.

Chromosomal Microarray Analysis

Ten mL amniotic fluid was used for CMA detection. Genomic DNA was extracted according to the manufacturer's protocol from amniotic fluid using DNA Extraction Kit (Tiangen Biotech Co.). DNA samples were concentrated using a NanoDrop 2000 spectrophotometer (Thermo Fisher Scientific Inc.). CytoScan 750 K Array chip (Affymetrix, USA) was used for whole-genome scanning which contains 200,000 SNP probes and 550,000 CNV probes. All procedures were performed according to the manufacturer's instructions. The chip was scanned using the Affymetrix GeneChip3000 Scanner 7G. Chromosome Analysis Suite ChAS 3.2 software was used for array images analysis.

Date Interpretation

Karyotypes were analyzed by two doctors according to the International System for Human Cytogenomic Nomenclature (2020).

All CNVs were described refer to the National Center for Biotechnology Information human genome build 37 (hg 19). Quality control was conducted by using the Median Absolute Pairwise Diference (MAPD<0.25) and SNP-QC score (QC >15) for CNV and SNP probes respectively.

CNVs were analyzed at the resolution of gains≥500 kb, losses≥200 kb, regions of homozygosity (ROH)≥10 Mb and compared with assistance of in-house and national online databases as follows: Humans Using Ensemble Resources (DECIPHER), Online Mendelian Inheritance in

Man (OMIM), Database of Genomic Variants (DGV), Clinical Genome Resource (ClinGene), University of California Santa Cruz Genomic Browser (UCSC) and PubMed. According to the American College of Medical Genetics (ACMG) for CNV interpretation, the CNVs were classified into five categories: pathogenic, likely pathogenic, variants of uncertain significance, benign and likely benign.

Statistical method

SPSS 26.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The count data was expressed as both a frequency and a percentage. Comparisons between groups were performed using a $\chi 2$ test, and $P < 0.05$ was considered statistically significant.

Results

The results of karyotype analysis

A total of 236 chromosomal abnormalities were detected in 3007 fetuses and the detection rate was 7.84% (236/3007). Aneuploidies were the most common pattern and the detected rate was 4.86% (146/3007), which including 53 cases of autosomal aneuploidies and 93 cases of sex chromosomal aneuploidies. The structural variations in karyotyping were detected in 1.80% (55/3007) patients, including 26 cases of balanced structural rearrangements which failed by CMA and 29 cases of unbalanced structural variants which detected by CMA synchronously. Others included mosaics (29/3007, 0.96%) and marker chromosomes (6/3007, 0.20%) (Table 1).

Table 1: The detected number and frequency of abnormal results on Karyotype and CMA

Types	***Karyotype results n(n/3007) (%)***	***CMA results***			
		pCNVs n(n/3007) (%)	VOUS n(n/3007) (%)	LpCNVs n(n/3007) (%)	Benign and likely benign n(n/3007) (%)
Aneuploidy	146(4.86)	146(4.86)			
47,XN,+21	39(1.30)	39(1.30)			
47,XN,+18	13(0.43)	13(0.43)			
47,XN,+13	1(0.03)	1(0.03)			
45，X	10(0.33)	10(0.33)			
47，XXX	28(0.93)	28(0.93)			
47，XXY	36(1.20)	36 (1.20)			
47，XYY	19(0.63)	19(0.63)			
Structural variation	55(1.83)	28(0.93)	1(0.03)		26(0.86)
Balance translocation	19(0.63)	1(0.03)			18(0.60)
Robertson translocation	6(0.63)		1(0.03)		5(0.17)
Inversion	3(0.20)				3(0.10)
Deletion	12(0.10)	12(0.40)			
Duplication	3(0.40)	3(0.10)			
Derivative chromosome	12(0.10)	12 (0.40)			
Mosaic	29(0.96)	22(0.73)	2(0.06)	1(0.03)	4(0.17)
Marker chromosome	6(0.20)	1(0.03)	2(0.06)	2(0.07)	3(0.10)
Normal	2771(92.15)	51(1.70)	98(3.26)	5(0.17)	2618 (87.03)
Sum	3007(100.00)	248(8.25)	103(3.42)	8(0.27)	2651(88.16)

The results of CMA

Abnormal results were found in a total of 359 cases (11.94%, 359/3007) by CMA, which can be broken down into 248 (8.25%, 248/3007) cases of pathogenic copy number variants (pCNVs), 103(3.43%, 103/3007) cases of variants of uncertain significance (VOUS) and 8(0.27%,8/3007) cases of likely pCNVs. In 8.25% of cases, observed genomic abnormalities were classified as pCNVs and deletions were more common as pathogenic than duplications. The common patterns of pCNVs detected in CMA were 22q11.2 microdeletion, 5p15.33-p15.1 microdeletion, 8p23.3-23.1 microdeletion and 1q21.1q21.2 microdeletion. There were totally 103 genetic variants classified as VOUS, since there was no sufficient evidence to predicate the variant was either benign or pathogenic because of the uncertain of phenotype. Among the cases of VOUS, 22q11.22 microduplication, 16p13.11 duplication, 15q11.2 microdeletion and heterozygosity deletion (LOH) had a higher detection rate (Table 2).

Table 2: The common patterns of pCNVs and VOUS detected by CMA

Region of variants	*Approximate coordinates(hg19)*	*Size*	*OMIM genes*	*n(n/3007) (%)*
pCNVs				
22q11.2 del	Chr22:18,648,856-21,800,471	2.88-3.16 Mb	44-49	4(0.13)
5p15.33-p15.1 del	Chr5:113,576-17,373,382	6.73-11.26 Mb	32-49	4(0.13)
8p23.3-23.1 del	Chr8:158,048-7,044,046	6.77-6.88 Mb	17	4(0.13)
1q21.1q21.2(BP3-BP4) del	Chr1:146,023,922-147,830,830	1.72-1.90 Mb	13	4(0.13)
VOUS				
22q11.2 dup	Chr22:16,888,899-25,0002659	1.35-4.91 Mb	22-55	12（0.39）
16p13.11 dup	Chr16:15,058,821- 18,242,713	0.827-2.91 Mb	7-11	8（0.26）
15q11.2 del	Chr15:22,770,421-23,288,350	0.312-0.518 Mb	4	7（0.23）
LOH	Chr2、4、5、8、13、15、16、X			9（0.30）

The disorders of the chromosomal abnormalities detected by karyotype analysis and CMA

CMA improved 4.09% (123/3007) of genetic changes compared karyotype analysis. CMA is on par with chromosome karyotyping for detection of aneuploidy and unbalanced structural rearrangements. In additional, CMA detected 154 microdeletions and duplications that were not identified by karyotype analysis, including 51cases of pCNVs, 5 cases of likely pathogenic CNVs and 98 cases of VOUS. CMA detected 0.67% (20/3007) of genetic changes with pathogenic and likely pathogenic compared karyotype, but also brought 3.42% (103/3007) of variants with uncertain significance (VOUS) (Table 1).

However, CMA failed to identify 4 cases of low proportion mosaics, 3 cases of marker chromosomes and 26 cases of balanced chromosomal rearrangements (balance translocation 18 cases, robertson translocation 5 cases, inversion 3 cases) and that were detected by karyotype analysis (Table 3).

Table 3: The abnormal chromosomes detected by karyotype analysis but failed by CMA

Case	*Age*	*Week*	*Prenatal diagnostic indication*	*CMA results*	*Karyotype results*	*Inheritance*
1	32	21+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(11;18)(p11.2;p11.2)	Maternal
2	31	17+2	History of adverse pregnancy	Arr(1-22)×2,(XN)×1	46,XY,inv(8)(p23q13)	Unknown
3	34	20	History of adverse pregnancy	Arr(1-22)×2,(XN)×1	46,XX,t(5;8)(p13;q11.2)	Paternal
4	29	18+4	Others	Arr(1-22)×2,(XN)×1	46,XX,t(2;12)(p25.3;q24.1)	Unknown
5	32	25	Ultrasound abnormality	Arr(1-22)×2,(XN)×1	45,XY,der(13;14)(q10:q10)	Unknown
6	26	19	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	45,XY,der(13;14)(q10:q10)	Maternal
7	35	18	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(13;15)(p12;q13)	Maternal
8	35	17	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(11;15)(q23;q11.2)	Maternal
9	33	20+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	45,XX,der(13;14)(q10;q10)	Maternal
10	31	18+1	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(4;14)(p10;q10)	Maternal
11	25	19	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,inv(Y)(p11.2q11.23)	Paternal
12	31	17+3	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(14;18)(q13;p11.32)	Maternal
13	32	19+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(2;5)(q31;p15.3)	Maternal
14	32	17	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(3;10)(q29;q21)	Maternal
15	27	17+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(3;5)(p13;q35)	Maternal
16	31	18+3	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	45,XY,der(13;14)(q10;q10)	Maternal
17	31	19	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XX,t(5:9)(q31;p24)	Paternal
18	32	20	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(5;7)(p14;q21)	Maternal
19	28	18+1	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XX,t(2;8)(q13.1;q22)	Paternal
20	26	19+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,der(13;15)(q10;q10)	Paternal
21	32	18+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,inv(7)(p14q11)	Maternal
22	33	17+6	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(12;13)(p13;q22)	Maternal
23	28	16+5	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XX,t(5;8)(p14;p22)	Maternal
24	36	18+5	History of adverse pregnancy	Arr(1-22)×2,(XN)×1	46,XX,t(6;7)(q23;q32)	Unknown
25	29	19+2	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	46,XY,t(3;4)(p21;33)	Paternal
26	36	20+4	Others	Arr(1-22)×2,(XN)×1	46,XX,t(10;21)(p11.2;q21)	Unknown
27	39	18	NIPT abnormality	Arr(1-22)×2,(XN)×1	45,X[7]/46,XY[27]	Unknown
28	30	19	NIPT abnormality	Arr(1-22)×2,(XN)×1	45,X[7]/46,XX[84]	Unknown
29	38	17+3	NT increased	Arr(1-22)×2,(XN)×1	45,X[3]/46,XX[64]	Unknown
30	34	18	Ultrasound abnormality	Arr(1-22)×2,(XN)×1	47,XXX[8]/46,XX[167]	Unknown
31	34	22+4	NIPT abnormality	Arr(1-22)×2,(XN)×1	47,XX,+mar	Unknown
32	29	17	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	47,XY,+mar	Maternal
33	32	19	Abnormal karyotype of couple	Arr(1-22)×2,(XN)×1	47,XY,+mar	Paternal

Comparison of the abnormal results on karyotyping and CMA in different prenatal diagnostic indications groups

Serological screening and ultrasound abnormalities were the main indications of prenatal diagnosis of high-risk pregnant women who received amniocentesis. The pregnant women with high risk of serological screening reached 25.37% (763/3007), and the detection rate of pCNVs and karyotype were 3.93% (30/763) and 2.88% (22/763) respectively.

Ultrasound abnormalities (747 cases) were consisted of 395 cases of structural malformation, 173 cases of soft index abnormal, 165 cases of increased nuchal translucency (NT) and the others. The total detection rate of abnormal CNV in ultrasound abnormalities group was 9.64% (72/747). But there were only 5.62% (42/747) of abnormal CNV regards as pCNVs, 3.61% (27/747) of cases were classified as VOUS. The detection rate of chromosomal abnormalities in NT increased group was higher than other two subgroups and there was statistically significant difference in the detection rates of pCNVs in ultrasound abnormality subgroups. The abnormal results of karyotype were 29 (3.88%,29/747), in which the detection rate of abnormalities was 7.88% (13/165) in NT increased group, followed by soft index abnormal (2.89%,5/173). CMA detected 5.57% (40/718) more genetic abnormalities in ultrasound abnormality group when fetuses with normal karyotype. But there was no significant difference in the detection rates of pCNVs and abnormal karyotype (> 0.05) by CMA and karyotyping.

The highest detection rate of an abnormal CNVs and karyotype was detected in the NIPT abnormality group, at 39.28% (163/415) and 31.81% (132/415) respectively. The capability of detecting chromosomal aneuploidies by CMA and karyotyping were comparable in NIPT abnormality group. The 24 cases of structural rearrangements and 2 cases of marker chromosomes were detected by karyotype analysis in the group of the couples with abnormal karyotype. All of these were inherited from their parents. However, only 2 cases of pCNVs were detected by CMA in this group. The lowest proportion of detected pCNVs and abnormal karyotypes were concentrated in history of adverse pregnancy group. CMA increased the detection of genetic changes with clinically significance, but there was no statistically significance in the detection rate of pCNVs and abnormal karyotypes (P>0.05) by CMA and karyotyping in the pregnant women with different indications except the couples with abnormal karyotype (Table 4).

Table 4: The number and frequency of abnormal results on CMA and karyotype for pregnant women with different prenatal diagnostic indications

Prenatal diagnostic indication		***N***	***CMA***			***Abnormal karyotypes n (n/N) (%)***	***P value****
			pCNVs n (n/N) (%)	VOUS n (n/N) (%)	LpCNVs n (n/N) (%)		
Abnormal serological screening		763	30(3.93)	15(1.97)	1(0.13)	22(2.88)	>0.05
Advanced age		358	18(5.03)	10(2.79)	1(0.28)	11(3.07)	>0.05
Ultrasound abnormality	Structural variation	395	17(4.30)	12(3.04)	2(0.51)	11(2.78)	>0.05
	Soft index abnormal	173	8(4.62)	3(1.73)		5(2.89)	>0.05
	Increased NT	165	16(9.70)	12(7.27)	1(0.61)	13(7.88)	>0.05
	others	14	1(7.14)				
NIPT abnormality		415	133(32.05)	27(6.51)	3(0.72)	132(31.81)	>0.05
Abnormal karyotype of couple		94	2(2.13)	5(5.32)		26(27.66)	<0.05
History of adverse pregnancy outcome		449	16(3.56)	14(3.12)		12(2.67)	>0.05
Others		181	7(4.97)	5(2.76)		4(2.21)	>0.05
Total		3007	248(8.25)	103(3.42)	8(0.27)	236(7.84)	>0.05

* Pearson Chi-Square significance for comparison of pCNVs and abnormal karyotypes

Discussion

Karyotype analysis is the mainly technology for detecting chromosomal abnormalities in the field of prenatal diagnosis but it has several limitations with time consuming, low resolution and long turnaround time. CMA, as an emerging molecular diagnosis technology, can provide extensive information on an individual's genetic makeup. In 2013, the American College of Obstetrics and Gynecology (ACOG) published guidelines recommending CMA as a substitute for traditional karyotyping when fetus with structural anomalies observed by ultrasound required invasive prenatal diagnosis (4). CMA is capable of detecting not only clinically significant submicroscopic aberrations, but also identify mosaic and heterozygous deletions (LOH), making this technology more and more widely used in the field of prenatal diagnosis with different indications (5,6).

In this study, we used CMA (CNV and SNP array platform) and karyotype analysis for 3007 cases of pregnant women with various prenatal diagnostic indications. We compared the difference of the results between CMA and karyotyping. The positive rate of copy number variants (CNVs) and chromosomal karyotype abnormalities was 11.94% and 7.84% on CMA and karyotyping. CMA detected 4.09% more genetic changes than karyotyping, which is lower than the previous report (7). CMA was equivalent to traditional karyotype analysis for the aneuploidies. 53(1.76%)cases of autosomal aneuploidies and 93 (3.09%) cases of sex-chromosome aneuploidies were identified by karyotyping and CMA. CMA have the limitations on low-proportion mosaic and balanced chromosomal rearrangement. Four of these cases were low-proportion mosaics on karyotyping but failed on CMA. All of the balanced rearrangements were identified by karyotyping that undetected by CMA, suggesting that these structural deviations were truly balanced. CMA is comparable to karyotyping on detecting gross unbalanced structural rearrangements. 27 cases of gross chromosomal variants were identified by karyotyping and CMA simultaneously. Of the six marker chromosomes detected on karyotyping, we detected three on CMA. Karyotype analysis combined with CMA were recommended to be performed on detecting variants in prenatal diagnosis.

The CMA technique can detect clinically significant micro-deletions or duplications, with a high sensitivity for submicroscopic aberrations of the whole genome compared with traditional karyotype analysis (8). In this study, CMA improved 4.09% (123/3007) of genetic changes compared karyotype analysis. And CMA revealed an additional 154 (5.12%) cases of genetic variants on the basic of normal karyotype. 33.12% (51/154) of these were pCNVs, mainly relevant to 22q11.2 microdeletion, 5p15.33-p15.32 microdeletion, 8p23.3-23.1 deletion, 1q21.1q21.2 deletion, which were the mutation sites of Digeorge syndrome, mi-du-chat syndrome, 8p23 deletion syndrome and 1q21 deletion syndrome. However, most of these CNVs were unclear significant, accounting for 63.64% (98/154). That uncertainty of VOUS adds complexity to prenatal genetic counselling and can result in harms and anxiety and adverse psychological effects to pregnant women (9). VOUS had a high detection rate of 22q11.22 microduplication, 16p13.11 microduplication and 15q11.2 microdeletion. Many VOUS affected pedigree members showed diverse clinical features or normal phenotype and the uncertainty of phenotype was related to incomplete penetrance and genetic heterogeneity and age of onset (10-13). Long-term follow-up as well as growth and development evaluation of related families are still needed in later stage.

CMA was gradually accepted as a prenatal invasive testing during pregnancy with all the indications (14-16). The detection rate of chromosome abnormalities were varied in different prenatal diagnostic indication groups. In this study, Serological screening was the main indications of prenatal diagnosis and the detection rate of pCNVs and karyotype were 3.93% (30/763) and 2.88% (22/763) respectively. NIPT group had the highest detection rate of abnormalities both CMA

and karyotyping. With the advantages of invasive and conveniency, NTPT for detection of aneuploidy has been recognized increasingly by doctors and pregnant women as a non-invasive prenatal test (17). CMA detected 133 cases of clinically pathogenic variants in NIPT abnormality group. 132 of these were chromosomal aneuploidies detected by CMA and karyotype analysis. The detection rate of total genetics variants was 9.64% in ultrasound abnormalities group by CMA, which was comprised of 5.62% (42/747) pCNVs, 3.61% (27/747) VOUS and 0.40% (3/747) likely pCNVs. The detection rate of pCNVs in NT increased group was higher than that in soft index abnormal group, followed by the structural variation group. There were statistically significant differences of pCNVs in three ultrasound abnormality subgroups. The abnormal karyotype rate was 3.88% in the ultrasound abnormalities. There was no significant difference in the detection rate of abnormal karyotype and pCNVs by karyotyping and CMA. Some studies shows that CMA can improve the detection rate of genetic abnormalities by 6 to 7% among fetuses with ultrasound abnormalities than karyotyping (18,19). Our study found that CMA could detect 5.57% (40/718) more genetic abnormalities in ultrasound abnormalities group when fetuses with normal karyotype.

Twenty three cases of balanced structural aberrations and 2 cases of marker chromosomes and 1cases of Cri-du-chat syndrome were identified by karyotyping in the couples with abnormal karyotype group, which were all inherited from their parents. However, only 2 cases of pCNVs were detected by CMA. These findings indicate that karyotype analysis also plays an important role in the detection of structural abnormalities. CMA cannot completely replace the traditional karyotype analysis in prenatal diagnosis. Several studies recommend CMA and karyotype analysis as an adjunct test in specific cases (20,21).

Overall, CMA could improve the detection rate of chromosomal abnormalities compared with karyotype analysis, but there was no statistically significance in pCNVs and abnormal karyotype in all the indications except the couples with abnormal karyotype.

Conclusion

CMA and traditional karyotype analysis have their own strengths and weaknesses. CMA can increase the detection rate of chromosome abnormalities and identify the source of genetic variants detected by karyotype analysis, which is of great significance for accurate prenatal diagnosis. But CMA can bring more genetic variants with unclear significance. It is therefore of necessary that genetic counselors were recommended that all the pregnant women performed karyotype analysis and CMA should be given information about their characteristics, and then they have the option of choosing.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Competing interest

The authors declare that they have no competing interest.

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