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Retrospective Analysis of Prenatal Diagnosis Results and Exploration of Screening Strategies for 137 Fetuses with Down Syndrome

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ABSTRACT

Objective: To analyze the detection of fetuses with Down syndrome in the Prenatal Diagnosis Center of Guigang Maternal and Child Health Care Hospital, Guangxi, evaluate the efficacy of different prenatal screening methods, and provide data support for optimizing regional prenatal screening and diagnostic strategies. Methods: A retrospective analysis was conducted on the chromosome karyotype analysis results of 6799 pregnant women who underwent invasive prenatal diagnosis in our hospital from January 2020 to July 2025. Clinical data of fetuses diagnosed with trisomy 21 (Down syndrome) were collected, and their pregnancy outcomes were tracked. Results: Among the 6799 pregnant women, a total of 137 fetuses with Down syndrome were detected. Karyotype analysis showed 131 cases of standard type (95.6%), 2 cases of Robertsonian translocation type (1.5%), and 4 cases of mosaic type (2.9%). All diagnosed fetuses underwent termination of pregnancy. The primary indications for prenatal diagnosis included high-risk non-invasive prenatal testing (NIPT) (highest proportion), abnormal ultrasound soft markers (such as increased nuchal translucency (NT) or absent/hypoplastic nasal bone), advanced maternal age, and high-risk serum screening. NIPT showed the highest positive predictive value for trisomy 21 (97.4%), significantly higher than serum screening (1.05%). The detection rate of trisomy 21 in advanced-age pregnant women (≥35 years) (3.30%) was higher than that in non-advanced-age women (1.45%), and the detection rate increased with maternal age. Conclusion: Actively performing invasive prenatal diagnosis for pregnant women with indications such as high-risk NIPT, advanced age, abnormal ultrasound soft markers, or high-

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risk serum screening can effectively improve the prenatal detection rate of Down syndrome, enabling early intervention and reducing the birth rate of affected children. The combined use of multiple screening methods (such as first-trimester ultrasound soft marker screening combined with NIPT or serum screening) and standardizing the prenatal diagnostic process for high-risk populations are key measures for preventing birth defects.

1. INTRODUCTION

Down syndrome, also known as trisomy 21 syndrome, is the most common chromosomal aneuploidy disorder, with an incidence of approximately 1/1100 in live births [1]. Affected children present with characteristic facial features, intellectual disability, multiple malformations, and other issues. As there is currently no cure, it imposes a heavy burden on families and society [2]. Therefore, timely detection and intervention through prenatal screening and diagnosis are central to reducing its birth rate. This study retrospectively analyzed data from 137 fetuses with trisomy 21 diagnosed via prenatal diagnosis in our hospital from January 2020 to July 2025, aiming to summarize their karyotype characteristics, distribution of prenatal indications, and the efficacy of different screening methods, thereby providing clinical evidence for optimizing regional prenatal screening protocols.

2. MATERIALS AND METHODS

2.1. Study Subjects

A total of 6799 pregnant women who underwent invasive prenatal diagnosis at the Prenatal Diagnosis Center of Guigang Maternal and Child Health Care Hospital, Guangxi, from January 2020 to July 2025 were selected. Among them, 137 fetuses were diagnosed with trisomy 21. Maternal age ranged from 18 to 52 years, and gestational age ranged from 12 to 29 weeks. Indications for prenatal diagnosis included: high-risk NIPT (risk value ≥ 1/270), abnormal ultrasound soft markers (e.g., increased NT, absent/hypoplastic nasal bone) or structural anomalies, advanced maternal age (delivery age ≥ 35 years), high-risk second-trimester serum screening (risk value ≥ 1/270), etc. This study was approved by the Hospital Medical Ethics Committee (Approval No.: GGFYYXLL-20240306-07), and all participants provided written informed consent.

2.2. Instruments and Reagents

Main instruments included an inverted microscope (Olympus CK41), a CO_2 incubator (Thermo, USA), and a fully automated chromosome scanning system (ZEISS, Germany). Main reagents included amniotic fluid cell culture medium (Baidy Biotech, Heneng Biotech), colchicine (Dahui Biotech), Giemsa stain (Heneng Biotech), and trypsin powder (Gibco, USA).

2.3. Methods

Under ultrasound guidance, experienced physicians performed amniocentesis, chorionic villus sampling, or umbilical vein puncture to obtain fetal samples. Samples were sent to the laboratory, and the flask culture method was used for cell culture (amniotic fluid/villus cultured for 7-15 days, umbilical cord blood for 72 hours). After harvest, cells were treated with colchicine, subjected to hypotonic treatment and fixation to prepare chromosome slides, followed by G-banding. Karyotype images were acquired using the fully automated scanning system and independently analyzed by two technicians. For each sample, at least 20 metaphase spreads were analyzed (10 each by two technicians), and well-dispersed, clearly banded karyotypes (resolution ≥440 bands) were selected for counting and interpretation. Chromosome karyotype nomenclature followed the ISCN (2020) standard [3]. For suspected mosaicism, the number of counted cells was increased, and CNV-seq technology was used for verification [4].

2.4. Follow-Up of Pregnancy Outcomes

Pregnancy outcomes of the 137 diagnosed fetuses were confirmed via the "Gui Women and Children" Health Management System or telephone follow-up.

2.5. Statistical Analysis

A database was established using Excel. Data analysis was performed using SPSS 30.0 software. Categorical data are presented as counts (n) and percentages (%).

3. RESULTS

3.1. Karyotype Types and Composition Ratio of Trisomy 21 Fetuses

Among the 137 trisomy 21 fetuses, the standard type (47, XN, +21) accounted for 131 cases (95.6%), Robertsonian translocation type for 2 cases (1.5%), and mosaic type for 4 cases (2.9%). All cases resulted in termination of pregnancy (Table 1).

Table 1. Karyotype types and composition ratio of 137 trisomy 21 fetuses.

Karyotype Type	Karyotype Description	Number (n)	Percentage (%)	Pregnancy Outcome
Standard Type	47, XN, +21	131	95.6	Termination of Pregnancy
Translocation Type	46,XN, der(14;21)(q10;q10),+21 46,XN,+21, der(21;21)(q12;q10)	2	1.5	Termination of Pregnancy
Mosaic Type	47,XN,+2155/46, XN140140 47,XN,+219797/46, XN33 47,XN,+2155/46, XN4545 47,XN,+2166/46, XN175175	4	2.9	Termination of Pregnancy
Total	-	137	100.0	-

3.2. Distribution of Prenatal Diagnosis Indications

Among the 137 confirmed cases, the highest proportion of prenatal diagnosis indications was high-risk NIPT (81 cases, 59.1%), followed by abnormal ultrasound soft markers (increased NT or absent/hypoplastic nasal bone, 26 cases, 19.0%) and high-risk serum screening (11 cases, 8.0%). There were 68 advanced-age pregnant women (≥35 years) (49.6%) and 69 non-advanced-age women (50.4%). The specific distribution is shown in Table 2.

3.3. Detection Rate of Trisomy 21 in Pregnant Women of Different Age Groups

Among the 6799 pregnant women who underwent prenatal diagnosis, the detection rate was 1.45% in the <35 years group and 3.30% in the ≥35 years group. The detection rate increased significantly with maternal age, reaching as high as 12.8% in the ≥45 years group (Table 3), consistent with previous research findings [5].

Table 2. Distribution of prenatal diagnosis indications for 137 pregnant women with trisomy 21 fetuses.

Prenatal Diagnosis Indication	Number (n)	Percentage (%)
Advanced Maternal Age Group (≥35 years)		
Age alone	9	6.6
Age + High-risk NIPT	45	32.8
Age + Increased NT/Absent Nasal Bone	12	8.8
Age + B-ultrasound Structural Anomaly	3	2.2
Non-Advanced Age Group (<35 years)		
High-risk serum screening alone	11	8.0
Non-advanced age + High-risk NIPT	36	26.3
Non-advanced age + Increased NT/Absent Nasal Bone	14	10.2
Pregnant woman has Down syndrome	3	2.2
Non-advanced age + B-ultrasound Structural Anomaly	3	2.2
Both parents are thalassemia carriers	1	0.7
Total	137	100.0

Table 3. Comparison of trisomy 21 detection rates in pregnant women of different age groups.

Maternal Age (years)	Number of Prenatal Diagnoses (n)	Number of Trisomy 21 Cases (n)	Detection Rate (%)
≤29	2844	33	1.16
30 - 34	1900	36	1.89
35 - 39	1474	42	2.85
40 - 44	542	21	3.87
≥45	39	5	12.82
Total	6799	137	2.01

3.4. Detection Efficacy of Different Prenatal Screening Methods for Trisomy 21

Comparing the positive predictive value of trisomy 21 for four common screening methods within their respective indicated populations: among high-risk NIPT cases (78), 76 were confirmed, with a positive predictive value of 97.4%; among cases with increased NT (≥2.5 mm) (257), 16 were confirmed, positive predictive value 6.55%; among cases with absent/hypoplastic nasal bone (151), 7 were confirmed, positive predictive value 4.63%; among high-risk serum screening cases (951), 10 were confirmed, positive predictive value 1.05%. The order of positive predictive value was: NIPT > Increased NT > Absent/Hypoplastic Nasal

Bone > Serum Screening, with NIPT demonstrating a highly significant advantage [6].

4. DISCUSSION

This study shows that standard trisomy 21 constitutes the vast majority (95.6%), consistent with most domestic reports [7]. Although translocation and mosaic types account for a low proportion, their genetic counseling and recurrence risk assessment are more complex. The four mosaic cases in this study were verified by both karyotype analysis and CNV-seq, emphasizing the necessity of this combined approach for quantifying the mosaicism level, comprehensively assessing the extent of fetal abnormalities, and excluding other cryptic genomic copy number variants (CNVs) [8].

Advanced maternal age is a well-established risk factor for trisomy 21. Our data confirm a positive correlation between maternal age and the detection rate of trisomy 21, with risk sharply increasing in women ≥45 years, consistent with the findings of Gu *et al.* [9]. Notably, non-advanced-age pregnant women accounted for 50.4% of cases in this group, indicating that prenatal screening for Down syndrome should not be limited to advanced-age pregnancies. This finding supports recommending high-efficiency screening methods like NIPT as a public health strategy for all pregnant women, regardless of age, to achieve more comprehensive prevention of fetal chromosomal abnormalities.

In the comparison of screening methods, NIPT demonstrated an extremely high positive predictive value (97.4%) and positive predictive value, significantly superior to traditional serum screening, aligning with conclusions from numerous global studies [6, 10]. Ultrasound soft markers, particularly increased NT and absent/hypoplastic nasal bone, hold significant value as independent screening indicators for suggesting chromosomal abnormalities [11]. However, all single screening methods have limitations. It is recommended to perform combined NT and nasal bone measurement in the first trimester, integrated with NIPT or serum screening for risk assessment, thereby constructing a more effective stratified screening system [12]. For pregnant women with high-risk screening results, adequate counseling and recommendation for invasive prenatal diagnosis for definitive diagnosis should be provided.

5. CONCLUSION

In summary, prenatal screening for Down syndrome should focus on populations with high-risk NIPT, abnormal ultrasound soft markers, advanced maternal age, and high-risk serum screening. Adopting a combined screening strategy and standardizing invasive prenatal diagnosis for screen-positive individuals are key pathways to improving detection rates, enabling early intervention, and effectively reducing the birth rate of children with Down syndrome.

6. STUDY LIMITATIONS

This study is a single-center retrospective analysis with a limited sample size; therefore, extrapolation of conclusions should be cautious. Systematic tracking of screening false-negative cases was not performed. Furthermore, the study population consisted only of women who underwent invasive prenatal diagnosis, which may introduce selection bias and may not be fully representative of the entire pregnant population or all individuals with positive screening results, thereby imposing some limitations on the evaluation of screening performance. Future multicenter, prospective studies are needed for further validation.

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CONFLICTS OF INTEREST

All authors declare no conflicts of interest.

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