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Detecting fetuses with major Trisomies – can we rely on ultrasound only?

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Objective

The importance of screening and diagnosis of chromosomal abnormalities antenatally has increased significantly. Early identification of aneuploid fetuses helps in better management of current and subsequent pregnancies. The aim of our study was to assess the pattern of ultrasound scan and biochemical abnormalities in fetuses established to have a major aneuploidy, i. e. , Trisomy 21, 18 or 13.

Methods

This is a single center retrospective study of prospectively collected data at a tertiary fetal care center in South India. The study period was from January 2006 to December 2021. We included 202 pregnancies that were confirmed to have a major and common aneuploidy, i. e. , Trisomy 21, 18 or 13 either antenatally or postnatally. Pregnant women undergoing first trimester and second trimester scans were screened for major aneuploidies based on ultrasound findings, biochemical screening, and/or cell free DNA testing. If found to be at increased risk of aneuploidies, invasive testing was offered. All scans were performed by FMF certified operators for the 11^{+0} to 13^{+6} weeks and 18 – 24 weeks' scan. All examinations were recorded on Astraia fetal database software. Biochemical screening in the first and second trimester was performed on FMF certified analytical platforms (PerkinElmer Manual Delfia, Auto Delfia, Delfia Express or Roche Elecsys). Outcome of the pregnancy was obtained by telephonic conversation with the parents and examination of the delivery details in the hospital records. The incidence of ultrasound defects, markers, abnormal biochemical screening, and cell free DNA testing were calculated for each trisomy.

Results

During the study period, 3,958 women underwent invasive testing, of which 251 (6.3%) were detected to have chromosomal anomalies. 202 (80.4%) fetuses had major trisomies, i. e. , Trisomy 21, 18 or 13. 197/ 202 (97.5%) of these were detected antenatally and 5 (2.5%) were detected postnatally. 157 (77.7%) had Trisomy 21 (152 detected antenatally and 5 postnatally), 38 (18.8%) had Trisomy 18 and 7 (3.5%) had Trisomy 13. In the Trisomy 21 group, 30 (19.7%) had major structural defects, 99 (65.1%) had ultrasound markers, 15 (9.8%) had abnormal biochemistry only, 5 (3.3%) had high risk on cell free DNA only and 3 (2%) had history of T21 only. Amongst the five neonates detected to have Trisomy 21 postnatally, 4 had ultrasound markers and were offered antenatal testing that was declined. One baby was reported "normal" on all antenatal scans and had a "low risk" first trimester combined screening. In the Trisomy 18 group, 24 (63.1%) had major structural defects, 13 (34.2%) had ultrasound markers (increased NT, hypoplastic nasal bone, hydrops, polydactyly and rocker bottom feet) and 1 (2.6%) was an intra-uterine demise at the time of testing. In the Trisomy 13 group, 5 (71.4%) had major structural defects and 2 (28.6%) had ultrasound markers (hydrops). All fetuses with trisomy 13 and 18 were detected antenatally.

Conclusion

Our study confirms that fetuses with Trisomy 18 and 13 are very likely to be detected antenatally due to the presence of major structural anomalies and/ or distinct soft markers. However, 15% of fetuses with Trisomy 21 can appear structurally normal on the scan. Hence, combining with biochemical screening, including NIPT especially in "normal appearing fetuses" on scan can further improve the detection of Trisomy 21. India is a country with limited resources and skewed healthcare services with private sector being largely responsible for standardized scans and prenatal diagnostic tests. Hence, financial constraints largely affect the decision making of parents. As per our analyses, 15% of Trisomy 21 fetuses were detected only based on either serum biochemistry, cell free DNA or history of Trisomy 21 in family. Hence, it is paramount to offer standardized combined screening. With this study, we would like to propose universal combined screening for aneuploidies through government aided programs across all socio-economic strata. The strength of our study is a good sample size where all fetuses underwent systematic examination for the presence of defects and markers. The limitation of our study is the exclusion of those pregnancies which had ultrasound anomalies but were terminated without any investigations, thus leading to a possible bias.

Aneuploidies (n = 202)	Defects	Markers	No defects/markers
T21 – 157 (77.7%)	30 (19.7%)	99 (65.1%) Postnatal – 4	Abnormal Biochemistry – 15 (9.8%), NIPT-5 (3.3%), History-3 (2%); 1 – Postnatal
T18 – 38 (18.8%)	24 (63.1%)	13 (34.2%)	1 (2.6%) - Miscarriage
T13 – 7 (3.5%)	5 (71.4%)	2 (28.6%)	0