Is prenatal genetic testing essential in fetuses with structural anomalies and / or soft markers?

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Objective
To assess the prevalence of aneuploidies in fetuses with structural defects and compare to those with only soft markers and neither.

Methods
This is a single centre retrospective study conducted at a tertiary care centre in South India. The study period was from January 2010 till December 2020. Singleton pregnancies scanned at 16<sup>th</sup> – 24<sup>th</sup> weeks with known outcomes and karyotype were included in the study. All scans were performed by FMF certified operators for the 18-24 weeks’ scan. Eight established 2<sup>nd</sup> trimester markers [aberrant right subclavian artery (ARSA), Echogenic Intracardiac Foci (EIF), Hypoplastic /Absent nasal bone (HANB), Hyperechogenic bowel (HEB), Increased nuchal fold (NF), Renal Pelvic Dilatation (RPD), Short femur length /short humerus Length (SFL/SHL) and ventriculomegaly (VM)] were considered. All examinations were retrieved from the Astraia fetal database software. Outcome of the pregnancy was obtained by telephonic conversation with the parents and/or examination of the delivery details in the hospital records. The karyotype of was confirmed antenatally by invasive testing postnatally by neonatal examination and postnatal karyotype where available as per the information given by parents. The positive and negative likelihood ratios (LR) were calculated for all 3 groups.

Results
Of the 14872 singleton pregnancies with known outcomes, 753 (5.1%) fetuses had structural defects, 2473 (16.6%) had soft markers and 11646 (78.3%) had neither markers nor defects. The prevalence of fetal aneuploidies was 32 (4.3%), 20 (0.8%) and 11(0.1%) in the fetal structural defects, soft markers and no markers’ groups respectively. The negative LR were 0.27 in fetuses with structural defects, 0.42 in fetuses which were structurally normal but had soft markers and 3.46 in structurally normal fetuses with no markers. The positive LR were 15.31 in fetuses with structural defects, 3.7 in fetus which were structurally normal fetuses with soft markers and 0.33 in structurally normal fetuses with no markers.

Conclusion
The prevalence of fetal soft markers is significantly higher as compared to that of fetal structural defects in our study. However, fetal aneuploidies are more frequently seen in fetuses with defects. Our study shows that in the absence of any soft markers or defects, 1: 1000 fetuses have an aneuploidy. In the presence of soft marker(s), 1: 125 fetuses is likely to have an aneuploidy. If there is a fetal defect, this is significantly increased 5 times to 1: 25 fetuses. The strength of our study is a good sample size where all fetuses were examined systematically for the presence of defects and markers. India is a country with limited resources in the healthcare system and prenatal diagnosis and tests are largely available only in the private healthcare system. Hence, decisions regarding performing diagnostic tests is largely driven by financial constraints. The limitation of our study is the exclusion of fetuses with structural defects and markers that did not have karyotyping done and the pregnancy was interrupted either by a termination miscarriage or intra uterine demise. To the best of our knowledge this is the first such study that has objectively assessed the importance of fetal karyotyping in the presence and absence of fetal defects and soft markers.