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EDITORIAL

Changing paradigm in prenatal management

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Screening during pregnancy has evolved significantly over the last decade from being an optional investigation into an integral part of a wider program of maternal care. Earlier, screening was directed towards diseases in the mother. The only screening test for fetal abnormality was maternal age and a previous abnormal pregnancy. These have been recognized as poor markers for a community based screening approach.[1] More sophisticated methods of screening based on biochemical markers and measurements made on ultrasound scan are now evolving and becoming a part of antenatal care. There has been considerable focus on methods that detect majority of fetal disorders in the first trimester. The purpose behind this is to allow sufficient time for more detailed investigations, making measured decisions and safe terminations of pregnancy if required.

It has been well established that the success of an individual marker can be considerably improved upon by measuring a combination of different markers. This has been demonstrated especially in the detection of Down syndrome. Various strategies for Down syndrome screening exist. The screening can take place in the first trimester at 11 to 13 weeks 6 days (Combined Screening, Contingent Screening), the second trimester at 15 to 20 weeks (Triple, Quadruple, Penta screens) or in both trimesters (Integrated, Sequential, Contingent screening), and might involve from one to six markers in addition to maternal age. In general, Combined First Trimester Screening seems to have gained wide popularity and acceptability because it offers good efficacy as well as allows for early intervention. A combination of ultrasound measurement of fetal nuchal translucency (NT) and biochemical markers (PAPP-A and free b-HCG) in the first trimester is emerging as the screening protocol of choice. [1] Results of screening are critically dependent upon the accuracy of NT and biochemistry measurements and hence it is pertinent that NT is measured with the same approach to quality control as is used in biochemical assays.[2]

Nuchal translucency has also been found to be a marker for other fetal problems such as chromosomal anomalies, genetic syndromes and cardiac and other systemic malformations.[3] Increased interest in early screening with ultrasound has resulted in development of other markers for Down syndrome such as nasal bone, ductus venosus flow, tricuspid regurgitation and FMF (fronto maxillary facial) angle. These could further improve the efficiency of Down syndrome screening.[4] The early scan also provides reliable identification of chorionicity, which is the main determinant of multiple pregnancy outcomes.

Since the 1970s karyotyping has been the gold standard for diagnosing aneuploidies. Recently, Fluorescence in situ hybridization (FISH) and quantitative fluorescence polymerase chain reaction (QF-PCR) has contributed rapidity of results especially in investigations requiring targeted approach. Molecular karyotyping, also known as array comparative genomic hybridization (aCGH), combines the advantages of conventional karyotyping with the targeted approaches such as FISH and QF-PCR. aCGH examines the whole genome simultaneously with higher resolution than traditional karyotyping and as no cell culture is needed, results are available within a few days. In the near horizon, a promising development in molecular chromosomal analysis is prenatal BOBs (BACs-on-Beads). BACs is an acronym for bacterial artificial chromosomes. This technology has the potential to exponentially increase the number of PCR assays on a minute sample and also allows for a more indepth analysis of the chromosomes and diagnosis of microdeletions. Results are possible within 24 hours.[5]

The drawback of diagnostic tests is the need for fetal tissue sample. As of now, this can be obtained only by an invasive procedure which carries a risk (albeit small) of miscarriage and preterm delivery. Safety and efficacy are the two main issues that will guide the future development of maternal health monitoring. Increased safety means less use of potentially dangerous, invasive diagnostic tests. Increased efficacy means detecting a higher proportion of affected fetuses at a lower cost. If simple, non-invasive diagnostic tests can be developed, screening as such will become redundant. Interesting possibilities in this direction may arise through the isolation of fetal cells from maternal serum. However, the challenges involved in developing testing are substantial for aneuploidy, autosomal dominant mutations inherited from the mother, and recessive disorders with homozygocity for

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identical mutations. This is because free fetal DNA (ff-DNA) or RNA (ff-RNA) generally constitutes a small proportion of the nucleic acids present in maternal plasma. Nevertheless, a number of approaches have already been proposed.[6]

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