First trimester biochemistry and Low birth weight babies: Screening beyond aneuploidies

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Objective

Low birth weight (LBW) is an important adverse neonatal outcome in terms of morbidity and mortality. The aim of our study was to investigate the effectiveness of first-trimester biochemical screening i. e. , Pregnancy-Associated Plasma Protein A (PAPP-A) and free beta Human Chorionic Gonadotrophin (fbeta-hCG) in prediction of Low Birth Weight (LBW) babies.

Methods

This is a single center retrospective study of prospectively collected data at a tertiary fetal care center in South India. We examined 5,494 singleton pregnancies that had undergone first trimester screening by a combination of fetal Nuchal Translucency (NT) thickness and maternal serum free beta-human Chorionic Gonadotropin (fbeta-hCG) and Pregnancy-Associated Plasma Protein-A (PAPP-A) at 11^{+0} - 13^{+6} weeks' gestation from January 2014 to October 2021. The biochemical markers were analyzed on either Roche Elecsys or PerkinElmer Auto Delfia analytical platforms, both approved for first trimester screening by FMF. The values were converted to Multiples of Median (MoM) for that gestational age and corrected for ethnicity. All examinations were recorded on Astraia fetal database software. Outcome of the pregnancy was obtained by telephonic conversation with the parents and examination of the delivery details in the hospital records. After exclusion of aneuploidies, structural malformations and cases lost to follow-up, 3,660 pregnancies were further analyzed. All pregnancies were followed up for recording the birthweight and gestational age at delivery. Low birth weight was defined as birthweight less than the 5th centile for the gender and gestational age at delivery. The effect of high free beta-hCG (> 2.5 MoMs), low free beta-hCG (< 0.5 MoMs) and low PAPP-A (< 0.5 MoMs) were studied. The Odd ratios (OR) of LBW babies were analyzed for each parameter (low and high free beta-hCG and low PAPP-A).

Results

Amongst the 3,660 pregnancies, 248 (6.8%) had high free beta-hCG MoMs, 519 (14.2%) had low free beta-hCG MoMs and 383 (10.4%) had low PAPP-A MoMs. In total cohort, there were 216 (5.9%) babies with LBW. 22 (8.9%) with high free beta-hCG, 46 (8.8%) with low free beta-hCG and 40 (10.4%) with low PAPP-A had LBW babies. All the three parameters i. e. , high free beta-hCG (p – 0.0417, OR – 1.61), low free beta-hCG (p – 0.007, OR – 1.59) and low PAPP-A (p - < 0.0001, OR – 2.18) levels significantly increased the risk for LBW babies.

Conclusion

Abnormal serum biochemistry in the first trimester plays an important role in prediction of low-birth-weight babies. Pregnancies with low PAPP-A, low free beta-hCG and high free beta-hCG levels should be serially followed up with growth scans in the third trimester. On suspicion of fetal growth restriction, early referral to tertiary care center for fetal surveillance and close monitoring is likely to optimize the outcome of these pregnancies by timely intervention. The strength of our study is a good sample size where all fetuses underwent standardized combined first trimester screening. The limitations of the study are non-consideration of confounding factors like history of maternal hypertension, effect of maternal Body Mass Index (BMI) and Uterine artery Doppler.

	High free beta-hCG	Low free beta-hCG	Low PAPP-A
LBW babies	22 (8.9%)	46 (8.8%)	40 (10.4%)
Odds Ratio (p value)	1.61 (0.0417)	1.59 (0.007)	2.18 (<0.0001)