

Predictors of intrauterine growth restriction

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Abstract

IUGR is pathologic inhibition of intrauterine fetal growth. Risk factors for IUGR comprise maternal factors, fetal factors, adnexal factors & Placental or umbilical cord factors. For predicting IUGR a combined approach using clinical data, serum markers, biophysical parameters has higher predictive value. Maternal BMI, Symphysis–fundal height have been used to predict IUGR. Biochemical markers are recently being evaluated for predicting IUGR including angiogenesis-related biomarkers, endothelial function/oxidative stress-related biomarkers, placental proteins/ hormone-related biomarkers metabolomics & genetic biomarkers. Sonography is a noninvasive technique for predicting IUGR early. Sonographically measured fetal femur length- abdominal circumference ratio, Foetal Ponderal Index, Umbilical artery systolic/ diastolic (S/D) ratio, resistance index, pulsatility index, MCA-PSV, TCD/AC ratio, Placental Quotient, increased pulsatility index in uterine artery are used in predicting IUGR. Biometry & amniotic fluid volume also show promising value in predicting IUGR early.

Keywords: IUGR, Biomarkers, Biometry.

Intrauterine growth restriction (IUGR) is defined as pathologic inhibition of intrauterine fetal growth & failure of fetus to achieve its growth potential. It occurs in about 10% of pregnancies. Risk factors for IUGR comprise **maternal factors** like socioeconomic status, weight, smoking, use of recreational drugs, advanced maternal age, nulliparity, history of gestational hypertension, family history of IUGR/ previous IUGR pregnancy, previous pregnancy with preeclampsia, inherited/acquired thrombophilia, anemia, high altitude living, autoimmune disorders, antepartum diabetes mellitus, chronic diseases; **fetal factors** like multiple gestation, congenital infections, aneuploidies, genetic syndromes; **adnexal factors** like uterine malformations, subchorionic haematoma, extensive villous infarction, marginal/ velamentous cord insertion, placental mosaicism; **Placental or umbilical cord factors** like twin-to-twin transfusion syndrome, placental abnormalities, chorionic abruption, placenta previa, abnormal cord insertion, cord anomalies. There are various factors associated with IUGR which help in predicting growth restriction early & hence help in prompt management to prevent stillbirths & morbidities.

For predicting IUGR a combined approach using clinical data, serum markers, biophysical parameters has higher predictive value. Maternal Body mass index (BMI) screening has been used as an effective method for predicting fetal growth [1]. Symphysis–fundal height

customized for maternal weight, height & ethnicity has nearly 50% detection rate for IUGR screening. A lag in fundal height of 4 cm or more suggests IUGR. **Biochemical markers** studied in association with IUGR include pregnancy associated plasma protein A (PAPP-A), alpha fetoprotein, β -hCG, unconjugated estriol, inhibin-A, A-disintegrin and metalloprotease 12 (ADAM-12), placental protein 13 (PP-13) [2]. However sensitivity of PAPP-A & β -hCG as isolated screening tools is low. Integrated assessment of PP-13, PAPP-A & uterine artery doppler at 11-13 weeks of gestation has a 20% detection rate of IUGR [3]. **Newer biomarkers** recently being evaluated for predicting IUGR include **angiogenesis-related biomarkers** like placental growth factor (plgf), soluble fms-like tyrosine kinase-1(sflt-1), soluble endoglin, vascular endothelial growth factor; **endothelial function/oxidative stress-related biomarkers** like homocysteine, leptin, asymmetric dimethyl-arginine, soluble vascular cell adhesion molecule-1, interferon-C, C-reactive protein, folate; **placental proteins/ hormone-related biomarkers** like Insulin-like growth factor binding protein-1 & -3, Activin A, placental growth hormone; **metabolomics & genetic biomarkers**.

Sonography is a noninvasive technique for predicting IUGR early. Sonographically measured fetal femur length- abdominal circumference ratio is a date independent predictor of IUGR helpful in evaluating high-

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risk patients presenting late with no dates. Foetal Ponderal Index (PI) is a predictor of IUGR with sensitivity around 75% & specificity around 80% [4]. Umbilical artery systolic/diastolic (S/D) ratio, resistance index (RI) & pulsatility index (PI) are used commonly to detect IUGR. An average S/D ratio >3 at 30 or more weeks of gestation has a sensitivity of 78% & specificity of 85% in predicting IUGR. However Umbilical artery doppler early between 10-14 weeks of gestation has a low positive predictive values for IUGR but better prediction for IUGR secondary to preeclampsia or IUGR alone with delivery < 32 weeks. Middle cerebral artery –peak systolic velocity (MCA-PSV) is a better predictor of IUGR. Transverse cerebellar diameter/ Abdominal circumference (TCD/AC) ratio exceeding 2 SD above mean is predictive of growth restriction with both sensitivity & specificity around 70%. Placental Quotient (PQ) [placental volume / crown rump length] assessed with uterine artery doppler has low sensitivity in diagnosis of IUGR. During 2nd trimester IUGR in low-risk patients is best predicted by an increased pulsatility index in uterine artery with notching (positive likelihood ratio 9.1)[5]. Recently virtual organ computer-aided analysis software (VOCAL) using vascularization index (VI), flow index (FI) & vascularization flow index (VFI) detect changes in vascularisation earlier than umbilical artery doppler abnormalities.

Biometry & amniotic fluid volume have been used to predict IUGR. Low abdominal circumference (AC) percentile has highest sensitivity (98%) for diagnosing IUGR [6]. Amniotic fluid maximum vertical pocket (MVP) value < 2 cm was associated with IUGR rate of 20% whereas MVP < 1 cm with an IUGR rate around 40% [7]. Using oligohydramnios definition of largest vertical fluid pocket < 1 cm, Manning reported sensitivity & specificity for prediction of IUGR around 84% & 97% respectively [8]. Total intrauterine volume (TIUV) has also been used for predicting IUGR. 3-Dimensional ultrasonography has been used to measure fetal femur or fetal humerus volume as a predictor of IUGR. Measurement of fetal soft tissue like subcutaneous tissue thickness at level of fetal midcalf, midthigh or abdominal wall & cheek-to-cheek diameter is probably predictive of IUGR with sensitivity & specificity around 76 & 67% respectively [9]. Maternal plasma fibronectin at a cut point of 475 mg/L & serum ferritin are recently being used as predictors of IUGR [10]. With advances of medical field & rise of newer biochemical markers &

imaging techniques it is possible to predict IUGR early & thereby prevent stillbirths & neonatal morbidities.

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