The Importance of Placenta Measurements in Prenatal Care: *Here's the Research*

Research from leading peer-reviewed journals (including Obstetrics & Gynecology, American Journal of Perinatology, and Journal of Fetal Medicine) has found:

Abnormal placenta size is associated with increased likelihood of stillbirth and other adverse pregnancy outcomes. Measurement of placental size during pregnancy might help identify patients at increased risk of poor outcomes. Estimated Placental Volume (EPV) is an effective tool to estimate placenta size in utero and could be a useful screen during pregnancy to stratify risk. (See research findings #9-11)

(See research findings #1-8)

RESEARCH FINDINGS AT A GLANCE

- 1 Extremes of placental weight are associated with stillbirth and other adverse perinatal outcomes, independent of birth weight.
- 2 Assessing birth weight:placental weight ratios and RFM during pregnancy may help identify seemingly low-risk fetuses at increased risk of stillbirth in late pregnancy.
- **3** Placentas from adverse outcome pregnancies were significantly smaller than placentas from normal outcome pregnancies.
- 4 High fetal:placental weight ratios are associated with adverse birth outcomes due to fetuses outgrowing their placentas.
- **5** Abnormal placental weight and birth weight:placental weight ratio are significantly associated with adverse pregnancy outcomes.
- 6 Disproportionate birth weight:placental weight ratios are associated with stillbirth.
- **7** Abnormal birth weight:placental weight ratios are associated with poor perinatal outcomes.
- 8 Abnormal placental size may help identify infants at increased risk of neonatal death.
- 9 Placental weight can be accurately predicted by two-dimensional ultrasound using Estimated Placental Volume (EPV) calculations.
- 10 EPV is valid in different populations, at various gestational ages and matches the placental parabolic growth curve described in other publications.
- **11** Establishing EPV growth curves (similar to fetal and pediatric growth charts to detect outliers and concerning trends) allows providers to risk-stratify prenatal patients.





RESEARCH FINDING #1 Extremes of placental weight are associated with stillbirth and other adverse perinatal outcomes, independent of birth weight.

Hutcheon, J.A., et al., 2012. Placental weight for gestational age and adverse perinatal outcomes. Obstetrics & Gynecology, 119(6), pp.1251-1258.

- "After controlling for birth weight, fetuses with a low placental weight z-score were at significantly increased risk of stillbirth (...percent population attributable risk 17.8%). In contrast, adverse neonatal outcomes were significantly more likely among those with high placental weight z scores (...percent population attributable risk 5% for any serious neonatal morbidity)."
- "Placental weight for gestational age is an independent risk factor for adverse perinatal outcomes, above and beyond the known association with birth weight."
- "After adjusting for birth weight, placental weight remained an independent predictor of perinatal mortality and serious neonatal morbidity in our study. We conclude that placental weight is not merely a reflection of fetal growth, but has independent effects on fetal and neonatal outcomes."
- "Obstetricians may wish to include subjective assessments of placental size on ultrasound scans when forming an overall clinical impression, with the recognition that both small and large placentas are associated with increased risks."

RESEARCH FINDING #2

Assessing birth weight:placental weight ratios and RFM during pregnancy may help identify seemingly low-risk fetuses at increased risk of stillbirth in late pregnancy.

Campbell, J., et al., 2020. Normally Grown Non-dysmorphic Stillbirth Post 38 Weeks Gestation and Reduced Fetal Movements: A Matter of Reserve? A Retrospective Study. Journal of Fetal Medicine, 7(2), pp.111-117.

- "There was a significant difference (p = 0.0117) in the mean ratio of birth weight to placental weight (BW:PW) between the stillbirth group (8.17) and control group (7.33). Cases of stillbirths where the mother had reported reduced fetal movements (RFM) had a higher BW:PW compared to controls (p = 0.024). Within the RFM stillbirth group, 5/6 (83%) cases showed significant changes of maternal vascular malperfusion (MVM) and/or fetal vascular malperfusion (FVM)... Reduced fetal movements may indicate diminished placental reserve. We propose that the ability to predict a high BW:PW within pregnancies where the mothers report RFM may help to prevent late stillbirth in non-IUGR infants."
- "Our supposition is that physiological changes reduce the functional reserve of the placenta as it progresses to term and beyond and when the placenta is disproportionately small for the size of the fetus may lead to critical compromise and hypoxic episodes in utero."
- "The implication of this study would be to consider induction of labour in women reporting multiple episodes of RFM where the baby is large in relation to the placental size. The use and identification of biomarkers associated with falling placental reserve at ≥ 38 weeks and assessment of placental and fetal weight by MRI or USS might provide further insight into this phenomenon and allow us to identify this 'at risk' group."

RESEARCH FINDING #3 Placentas from adverse outcome pregnancies were significantly smaller than placentas from normal outcome pregnancies.

Higgins, L.E., et al., 2015. Placental features of late-onset adverse pregnancy outcome. PloS One, 10(6), p.e0129117.

- "Placentas from pregnancies ending in adverse outcome (N = 23) were ~25% smaller in weight, volume, length, width and disc area (all p<0.0001) compared with those from normal outcome pregnancies."
- "The data reported here support our hypothesis that there is an altered placental phenotype in pregnancies reporting RFM when there is an adverse pregnancy outcome versus those with RFM and a normal pregnancy outcome. In any case, such changes merit exploration as they could form the basis of future tests of placental health to assist the identification of the 'at-risk' fetus, for example by measurement of placental size and vascularity by placental ultrasound..."
- "In late pregnancy a treatment (delivery) to prevent stillbirth is available; what is required now to make progress is an accurate test. This study highlights areas of placental health that could form the basis for the development of such tests, for example by measurement of placental size using ultrasound..."

RESEARCH FINDING #4

High fetal:placental weight ratios are associated with adverse birth outcomes due to fetuses outgrowing their placentas.

Bonds, D.R., et al., 1984. Fetal weight/placental weight ratio and perinatal outcome. American Journal of Obstetrics and Gynecology, 149(2), pp.195-200.

- "The incidence of perinatal problems was increased in those infants whose fetal weight/placental weight ratio was greater than 11: intrapartum fetal distress, 20% (p = 0.0046); meconium-stained amniotic fluid, 28.9% (p = 0.0017); Apgar score less than 7, 11.1% (p = 0.04); and hyperbilirubinemia, 24.4% (p = 0.0008). On the basis of these data, the conclusion drawn was that there is a population of presumably low-risk infants who are at increased risk because they have outgrown their placentas."
- "If placental and fetal size could be accurately determined in utero, the subgroup of infants who were originally thought to be low risk, but who are at increased risk because of small placenta size, could be identified."

RESEARCH FINDING #5

Abnormal placental weight and birth weight:placental weight ratio are significantly associated with adverse pregnancy outcomes.

Janthanaphan, M., et al., 2006. Placental weight and its ratio to birth weight in normal pregnancy at Songkhlanagarind Hospital. Journal – Medical Association of Thailand, 89(2), p.130.

- "There was an association between placental weight below the 10th percentile and fetal distress (p = 0.003). Placental weight to birth weight ratio below the 10th percentile was also associated with fetal distress (p = 0.02). Placental weight above the 90th percentile was associated with newborns requiring neonatal intensive care admission (p = 0.016)."
- "Overall, it seems that abnormal placental weight or the abnormal placental weight ratio may predict adverse outcomes even in a low risk population."
- "The advent of ultrasonic techniques that may permit the assessment of PWR (placental weight ratio) prior to term raises the possibility of the prenatal recognition of a high-risk group of newborns even in a low-risk population."

RESEARCH FINDING #6 Disproportionate birth weight:placental weight ratios are associated with stillbirth.

Haavaldsen, C., et al., 2013. Fetal death and placental weight/birthweight ratio: a population study. Acta Obstetricia et Gynecologica Scandinavica, 92(5), pp.583-590.

- "Both small and large placentas relative to birthweight were associated with fetal death in preterm births. At term, only small placentas relative to birthweight were associated with fetal death. Understanding the mechanisms behind the increased risk of adverse pregnancy outcomes in pregnancies with disproportionate placental weight/birthweight ratio may be important for prevention of fetal deaths."
- "Small placentas may have a reduced capacity to supply the fetus with sufficient oxygen and nutrition. Thus, if the fetus is programmed to be large, a small placenta, for instance due to insufficient implantation, may be increasingly unable to provide oxygen and nutrition to the growing fetus. The increased risk for fetal death in pregnancies with low placental weight/birthweight ratio supports such hypothesis."

RESEARCH FINDING #7 Abnormal birth weight:placental weight ratios are associated with poor perinatal outcomes.

Olaleye, A.A., et al., 2019. The Relationship between the Weight of the Placenta and Birth Weight of Term Neonate Delivered in Alex Ekwueme Federal University Teaching Hospital Abakaliki, Nigeria. Advances in Reproductive Sciences, 7(4), pp.82-93.

- "A placenta weight to birth weight ratio (PBWR) range of 15.0% to 24.9% is optimal for foetal survival according to this study. Conversely, an abnormally low PBWR (<15.0%) indicates foetuses with presumed reduced placental reserves and carries poor perinatal outcome. Such foetuses tend to show asymmetric growth restriction, suggesting that the small placenta limits optimal foetal growth with poor immediate neonatal outcome and this was in accordance with previous studies. From this study, PBWR of lower than 15% and higher than 24% are associated with poor neonatal outcome."
- "One thousand, nine hundred and five (90.5%) patients had PBWR that ranged between 15 and 24. Twenty five percent (25%) of babies delivered with PBWR of less than 15 were admitted into NICU for moderate to severe birth asphyxia and 40% of them suffered perinatal death. Also, 30.9% of babies with PBWR that ranged between 25 and 29 were admitted into NICU and 11.1% of them suffered perinatal death. For babies with PBWR of 30 - 34, 54.45% of them were admitted into NICU whereas [the] remaining 45.45% suffered perinatal mortality. All the babies with PBWR of greater than 35 suffered early perinatal mortality. The correlation coefficient (r) between the PBWR and immediate neonatal outcome was 0.7104 (reflecting a positive correlation)."

RESEARCH FINDING #8 Abnormal placenta size may help identify infants at increased risk of neonatal death.

Dypvik, J., et al., 2020. Placental weight and risk of neonatal death. JAMA Pediatrics, 174(2), pp.197-199.

• "We found that preterm born infants with either high or low placental weight had an increased risk of neonatal death. In term-born infants, low placental weight was associated with an increase in the risk of neonatal death among infants with congenital malformations. These findings may help to identify infants at increased risk of neonatal death."



RESEARCH FINDING #9 Placental weight can be accurately predicted by two-dimensional ultrasound using Estimated Placental Volume (EPV) calculations.

Azpurua, H., et al., 2010. Determination of placental weight using two-dimensional sonography and volumetric mathematic modeling. American Journal of Perinatology, 27(02), pp.151-155.

- "Placental volume was calculated in 29 third-trimester pregnancies using linear measurements of placental width, height, and thickness to calculate the convex-concave shell volume within 24 hours of birth...There was a significant positive correlation between EPV [Estimated Placental Volume] and APW [Actual Placental Weight] (rs = 0.80, p < 0.001) at all gestational ages examined (Fig. 2A). In the preterm pregnancies, the correlation between EPV and APW was even stronger (rs = 0.89, p < 0.001; Fig. 2B). There was also a significant positive correlation between EPV and APV (rs = 0.76, p < 0.001)."
- "An abnormally decreased placental weight has been linked to increased perinatal complications, including intrauterine fetal demise (IUFD) and fetal growth restriction (IUGR). Despite its promise, determining placental weight prenatally using three-dimensional systems is time-consuming and requires expensive technology and expertise. We propose a novel method using two-dimensional sonography that provides an immediate estimation of placental volume...This method is simple, rapid, and accurate, making it practical for routine prenatal care, as well as for high-risk cases with decreased fetal movement and IUGR. Routine EPV surveillance may decrease the rates of perinatal complications and unexpected IUFD."
- "Placental volume assessment is uncommon in routine obstetric practice, a lack that prevents obstetricians from identifying their patients with extremely small placentas. This is a population who are at risk of sudden intrauterine fetal demise."
- "Its normal development during gestation ensures the necessary support for the formation of a healthy fetus. Advances in prenatal surveillance have focused mainly on the fetus, with little attention paid to the placenta. It is apparent that a significant fraction of stillbirths are secondary to very small placentas."
- "Because EPV measurement is simple and rapid, we propose including this procedure to rule out the presence of a placenta that is small for gestational age whenever a patient is evaluated by ultrasound."

RESEARCH FINDING #10

EPV is valid in different populations, at various gestational ages and matches the placental parabolic growth curve described in other publications.

Isakov, K.M., et al., 2018. Estimated placental volume and gestational age. American Journal of Perinatology, 35(08), pp.748-757.

- "EPV could serve as a red flag to follow the mother and fetus more closely and to evaluate the placenta for underlying pathology... Proactive monitoring with EPV is crucial because the placenta growth restriction precedes fetal growth restriction. A fetus that appears to be growing well on routine ultrasound evaluation may in fact have a small placenta, which would not be imaged or measured based on current clinical practice."
- "As EPV is so easy to perform, we recommend routine EPV measurements whenever the fetus is examined by ultrasound. Although the scans in this study were performed by trained ultrasonographers, EPV measurements could possibly be performed by a clinician with minimal training."
- "Obtaining 2D ultrasound images of the placenta and calculating EPV is fast and requires minimal cost and training. It is a robust method with demonstrated validity across different populations. As such, it has the potential for clinical utility in a variety of settings."

RESEARCH FINDING #11 Establishing EPV growth curves (similar to fetal and pediatric growth charts to detect outliers and concerning trends) allows providers to risk-stratify prenatal patients.

Arleo, E.K., et al., 2014. Utilizing two-dimensional ultrasound to develop normative curves for estimated placental volume. American Journal of Perinatology, 31(08), pp.683-688.

- "The implications for patient care are important: just as the CDC recommends that pediatricians use growth charts to monitor growth for infants and children, such an EPV growth chart could be used by obstetricians to monitor the growth of the placenta in utero, in addition to the developing fetus, for risk stratification purposes."
- "As the growth of a fetus is dependent on the placenta, a small for GA placenta (defined as an EPV reading below the 10th percentile on an EPV growth chart) could be an earlier indication of a small for GA newborn than waiting until a fetus is noted to be in the 10th percentile or less on standard fetal growth charts. A small for GA fetus is at increased risk for adverse peri- and postnatal outcomes. Therefore, if there is an easily usable and accessible screening test to potentially identify such fetuses as early as possible, then earlier interventions to optimize outcome may be a possibility. EPV represents such a screening test: in our experience, sonographers can quickly be taught to measure the placental length, width, and height of routine 2D prenatal US images. The EPV can be easily calculated using a free iPhone [or Android] application, an Excel spread sheet, or even directly on US machines that have the EPV equation programmed into the user options. In short, an EPV reading can be achieved within a minute or two, thus quickly providing reassurance that a placenta is within normal limits (10th–90th percentile) or flagging it as an outlier (below the 10th percentile or above the 90th percentile)."

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