# Prenatal Loss at Term: The Role of Uteroplacental and Fetal Doppler Assessment

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**Short Title:** Uterine and Fetal Dopplers in Perinatal Death

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**ABSTRACT**

**Objective:** To examine the association of uterine artery (UtA) Doppler indices and cerebroplacental ratio (CPR) on perinatal outcome at term.

**Methods:** This retrospective cohort study conducted in a single tertiary referral centre included all singleton pregnancies undergoing ultrasound assessment in the third trimester, which subsequently delivered at term. Fetal biometry and Dopplers including the umbilical artery (UA), middle cerebral artery (MCA) and uterine artery were recorded. Data was corrected for gestational age and CPR was calculated as a ratio between the MCA pulsatility index (PI) and UA PI. Logistic regression analysis was conducted to examine for independent predictors of adverse perinatal outcome.

**Results:** The study included 7013 pregnancies; 12 were complicated by perinatal death. When compared to pregnancies resulting in live birth, pregnancies complicated by perinatal death had significantly more small for gestational age (SGA) infants (27.3% vs 5%, p=0.001) and a higher incidence of low CPR (16.7% vs 4.5%, p= 0.041). A subgroup analysis comparing 1527 low risk pregnancies demonstrated that the UtA PI MoM, CPR <5$^{th}$ centile and estimated fetal weight (EFW) centile were all significantly associated with the risk of perinatal death at term (all p<0.05). After adjusting for confounding variables, only EFW (OR 0.96, 95% CI 0.93-0.99; p=0.003) and UtA PI MoM (OR 13.10, 95%CI 1.95-87.89; p=0.008) remained independent predictors of perinatal death in the low risk cohort.

**Conclusion:** High uterine artery PI at term is independently associated with increased risk of adverse perinatal outcome regardless of fetal size. These results suggest that perinatal mortality at term is related, not only to EFW and fetal redistribution (CPR), but also on indices of uterine perfusion.

## INTRODUCTION

Growth restricted fetuses are at increased risk of perinatal mortality, as well as immediate and long-term morbidity.[1] In cases of early onset fetal growth restriction (FGR), the TRUFFLE study has set the standard for monitoring and determining timing of delivery for these fetuses in order to optimise the perinatal outcome.[2] However, the identification and management of growth restricted fetuses at term remains a major challenge.

Previous efforts focused almost exclusively on estimated fetal weight (EFW) and the identification of small-for-gestational age (SGA) birth as a determinant of outcome, however, recent literature has challenged the idea of fetal size defining those at high risk. Firstly, the majority of perinatal losses at term occur in babies born appropriately sized for gestational age. More recently, Sebire *et al.* investigated the effect of post-mortem interval on the interpretation of bodyweight in cases of stillbirth. They reported more than 10% reduction in fetal weight between delivery and the post mortem examination, and concluded that this phenomenon is likely to result in an overestimation of unexplained stillbirths subsequently being classified as being small for gestational age.[3] Markers for placental dysfunction such as uterine perfusion (uterine artery Doppler) and fetal redistribution (cerebroplacental ratio) could arguably play a larger role in the identification of term pregnancies at high risk of adverse outcome.

The cerebroplacental ratio (CPR), calculated as a simple ratio between the middle cerebral artery pulsatility index (MCA-PI) and the umbilical artery pulsatility index (UA-PI) has been suggested as a marker of fetal compromise secondary to placental insufficiency. In a high-risk population, a lower CPR was independently associated with the admission to the neonatal intensive care unit at term.[4] In gestations greater than 26 weeks, the CPR has been shown to be an independent predictor of stillbirth and perinatal mortality.[5] The application of the uterine artery (UtA) Doppler in the third trimester as a predictor of adverse neonatal outcome has been explored by some investigators, particularly with respect to suspected growth restricted fetuses.[6-8] The aim of this study was to examine the importance of uterine perfusion (UtA Doppler) and fetal redistribution (CPR) with regards to perinatal outcome specifically at term.

**MATERIALS AND METHODS**

This retrospective cohort study was conducted in the Fetal Medicine Unit at St George's Hospital, London, a tertiary referral centre. Cases were identified by performing an electronic database search (Viewpoint 5.6.8.428, Wessling, Germany) between January 2008 to October 2015 and June 2016.

The inclusion criteria consisted of singleton pregnancies that had an ultrasound assessment performed in the third trimester during which the UtA, UA and MCA Dopplers were measured and subsequently delivered after 36 weeks' gestation. A single ultrasound assessment was recorded per pregnancy and where serial scanning was conducted, the examination findings prior to delivery were recorded. This cohort constituted a mixed population of low and high-risk pregnancies. The indications for ultrasound scan included reduced fetal movements, suspected or past history of fetal growth disorders, follow up for high mid-trimester UtA Doppler indices, maternal hypertension and metabolic disorders in pregnancy. Low risk pregnancies were defined as those that underwent an ultrasound assessment after 36 weeks' gestation for indications such as routine post dates assessment, confirmation of fetal presentation or placental localisation. Multiple pregnancies, pregnancies complicated by fetal abnormality, aneuploidy or genetic syndromes or those with missing pregnancy outcome data were excluded from the analysis.

Gestational age (GA) was determined according to the crown-rump length (CRL) measurement in the first trimester.[9] Pregnancies were dated according to the head circumference measurement when the first ultrasound examination was performed after 14 weeks' gestation.[10] In all ultrasound examinations, routine fetal biometry and Doppler assessment were performed by experienced operators. The EFW was calculated from the biparietal diameter, head and abdominal circumference, and femur length using the Hadlock formula.[11] Doppler recordings were performed during periods of fetal quiescence. All Doppler parameters were recorded automatically from consecutive waveforms with the angle of insonation below 30°. The UA Doppler waveform was produced by sampling a free-floating portion of the umbilical cord using colour Doppler. The UA-PI was calculated according to a standard protocol.[12] A transverse section of the fetal head was obtained and the MCA was identified at the level of its origin from the circle of Willis using colour Doppler. The MCA was sampled using Pulsed Doppler where the vessel passes the sphenoid wing and the PI was calculated according to standard protocol.[13] The CPR was calculated as the ratio MCA-PI/UA-PI.[14] Colour Doppler was also used to visualize the left and right uterine arteries at the level of cross over with the external iliac artery. Pulsed-wave Doppler was applied to assess impendence to flow and the PI was measured over three consecutive waveforms.[15] The mean value of the right and left UtA-PI was subsequently calculated. All Doppler indices were converted into multiples of the median (MoM), correcting for gestational age in weeks.[16] EFW and birthweight (BW) values were converted into centiles.[17]

Maternal characteristics including maternal age, ethnicity (Asian, Black, Caucasian, Mixed and Other), body mass index (BMI), method of conception, cigarette smoking during pregnancy and parity (parous/nulliparous if no previous pregnancy >24 weeks' gestation) were recorded. Data on pregnancy outcome was collected from hospital obstetric and neonatal records. This included labour onset, mode of delivery, outcome (live birth/stillbirth/neonatal death less than and greater than 1 week from delivery), gestational age at delivery, gender, birth weight and admission to the neonatal intensive care unit. Perinatal mortality included stillbirth and neonatal death within the first 28 days after delivery. A stillbirth was defined as fetal demise after 24 completed weeks of pregnancy. Small for gestational age (SGA) was defined as an estimated fetal weight < $10^{th}$ centile after correcting for gestational age.

*Statistical Analysis*

The Kolmogorov- Smirnov test was used to assess the normal distribution of the data. Continuous variables were presented as median (interquartile range (IQR)) and as n (%) for categorical variables. Maternal baseline characteristics were compared using the chi-square test. Comparison between the two outcome groups (live birth and perinatal death) was performed using the Mann-Whitney U-test for non-normally distributed values. Correlation between continuous variables was described using Pearson coefficient or Spearman rho.

Logistic regression analysis was performed in order to assess the relationship between the BW centile, UtA-PI MoM and CPR MoM on adverse perinatal outcome. Odds ratios (OR) and confidence intervals (CI) were calculated. $P < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS 24.0 (SPSS Inc., Chicago IL, USA).

**RESULTS**

We identified 7100 singleton pregnancies that had an ultrasound assessment performed after 36 weeks' gestation where the UtA and fetal Doppler assessments were undertaken and pregnancy outcome data were available. We excluded 87 (1.2%) pregnancies that were complicated by either fetal structural abnormalities or aneuploidy. A final cohort of 7013 pregnancies was available for analysis, with a SGA birth prevalence of 4.4% and 12 perinatal deaths. The latter comprised of 9 cases of stillbirth (1.3 per 1000 pregnancies) and 3 neonatal deaths (0.4 per 1000 pregnancies). The median GA at the time of the ultrasound assessment and delivery were 36.43 weeks and 40.14 weeks.

A comparison of maternal and pregnancy characteristics between pregnancies resulting in live birth and those complicated by perinatal death are shown in Table 1. There were no significant differences in maternal age, BMI, ethnicity or median GA at the time of the ultrasound assessment between the two study groups. We also performed a subgroup analysis of 1527 low risk pregnancies that showed similar findings (Table 2).

The correlations between the UtA-PI MoM, CPR MoM and BW centile are displayed as scatterplots (Figures 1 and 2). Table 3 demonstrates a comparison of the ultrasound assessment and pregnancy outcome between cases resulting in live birth and those complicated by perinatal death. When compared to pregnancies resulting in live birth, pregnancies complicated by perinatal death had a significantly higher proportion of SGA (27.3% vs. 5%, $p=0.001$) and a significantly higher incidence of CPR < $5^{th}$ centile (16.7% vs. 4.5%, $p= 0.041$). When compared to low risk ultrasound assessments, pregnancies complicated by perinatal death had lower EFW (EFW centile 59.6 vs. 29.1, $p=0.020$), higher UtA-PI MoMs ($p=0.019$), higher proportion of SGA ($p<0.001$) and CPR <$5^{th}$ centile ($p=0.025$). There was a 30% difference between the median EFW centile and the actual BW centile in the perinatal death group compared to 7% difference of EFW to BW in the live birth cohort.

Logistic regression analysis revealed that EFW and UtA PI MoM are independent predictors of perinatal death (Table 4: OR 0.957 95% CI 0.93-0.99 and OR 13.10 95%CI 1.95-87.89, respectively).

## DISCUSSION

The findings of this study demonstrate that the UtA PI MoM, CPR <5$^{th}$ centile, EFW and BW centile were all significantly associated with perinatal death at term. After adjusting for interdependence of variables, only UtA PI MoM and EFW centile remained significantly and independently associated with adverse perinatal outcome. Furthermore, when comparing the perinatal deaths with the low risk cohort, there was a 30% difference between the median EFW centile and the actual BW centile compared to only 7% difference of EFW to BW in the live birth cohort.

UtA Doppler indices have conventionally been the focus of studies in early pregnancy. Low resistances in the uterine artery is felt to represent effective trophoblast invasion with adequate spiral artery remodelling, and therefore, normal placentation and placental function.[18] Conversely, in the presence of inadequate trophoblast invasion leading to placental dysfunction, high uterine artery Doppler pulsatility indices have been associated with an increased risk of preeclampsia, FGR, placental abruption and stillbirth.[19-23] More recent evaluation of this ultrasound parameter in the third trimester has suggested that the finding of abnormal uterine artery Doppler indices are also associated with an increased risk of adverse pregnancy outcome.[24,25] In keeping with previous work by Khalil *et al.,* the findings in our study confirm that a significantly higher uterine artery resistances in the third trimester are associated with increased risk of perinatal death.[5] By performing regression analysis to determine the factors affecting the risk of perinatal death, we confirmed that uterine artery PI was significantly and independently associated with increased perinatal mortality along with estimated fetal weight. In this work, we assessed ultrasound parameters in the third trimester - it would be important to determine if high third trimester uterine artery resistances are persistently elevated since the second trimester or a de novo finding.

The association between low BW and perinatal mortality is also well established and presumed to be the consequence of placental insufficiency resulting in poor fetal growth and fetal hypoxia. The findings of our study confirm that fetal size (EFW centile) is a significant independent predictor of perinatal death. The ongoing debate of using fetal size exclusively as a screening tool to predict adverse perinatal outcome continues to be challenged.[1] Importantly, in our study, we noted a significant difference between EFW and BW centiles in the perinatal death group compared to the live born cohort. The reported accuracy of ultrasound estimation of fetal weight at term varies within the literature, however, a 30% difference cannot be explained by scan inaccuracy alone – especially when an EFW to BW discordance is not evident in the livebirths.[26,27] The most likely contributor to this weight discrepancy is the effect of the time interval between intrauterine demise and the determination of birth weight at the time of post mortem examination. Seibre *et al.*, recently demonstrated that following intrauterine death, fetuses lose weight in utero by maceration and continue to lose weight from dehydration after birth. Hence, it is likely that a significant proportion of stillbirths became SGA after their demise and that autopsy weight assessment may result in overestimation of the proportion of stillbirths defined as growth restricted.[3]

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*Clinical and research implications*

As the controversy regarding the reference standards for assessing fetal size endures[28] the evaluation of additional ultrasound parameters as predictors of adverse pregnancy outcome increases in relevance.[2,4,5] The umbilical artery Doppler resistance is invariably normal at term and fails to detect those appropriately grown fetuses with fetal hypoxaemia.[29] The oxygen requirements of the fetal brain increase with advancing gestation and one of the first haemodynamic alterations which occurs in the presence of fetal hypoxia is cerebral vasodilation and reduced MCA resistance – which has been associated with increased risk of adverse perinatal outcome and subsequent abnormal neurodevelopment.[30,31] The fetal CPR has also been proposed as a predictor of adverse perinatal outcome and has been shown to be more sensitive compared to umbilical or middle cerebral artery Doppler alone.[32,33] Fetal CPR measured in the third trimester is an independent and stronger predictor of stillbirth and perinatal mortality than EFW.[5] In our study CPR <5$^{th}$ centile was significantly associated with increased risk of perinatal mortality, however, we did not find CPR MoM to be a significant independent predictor of adverse outcome. These findings are consistent with the work by Nicolaides *et al.* who concluded that routine screening by CPR between 35 to 37 weeks' gestation provides poor prediction of indicators for adverse perinatal outcome.[34] One of the possible explanations for this finding may be related to the time interval between CPR measurement on ultrasound scan and the fetal demise. In the perinatal death group, the average interval between ultrasound assessment and gestation at delivery was 2.27 weeks (range 0.3-6.1 weeks). At term, the metabolic demands of the fetus increase exponentially such that the inability of the placenta to meet these needs may result in sudden unpredictable fetal demise. Rather than focusing our attention on finding a sole ultrasound parameter to reliably predict adverse outcome, perhaps a combination of biophysical and biometric parameters such as EFW, CPR, MCA and UtA together with maternal characteristics could be combined may assist in the effective identification of pregnancies at risk.

*Strengths and Limitations*

The strengths of our study include the large number of pregnancies and respective outcomes examined within the cohort. When performing statistical analysis, we adjusted for confounding variables such as GA to ensure accurate analysis and interpretation of the data. In order to overcome the wide diversity of case mix within the live birth cohort we performed a subset analysis on what we considered a "low risk population" and the findings remained significant. The main limitation of this study is its retrospective design and therefore its risk of bias. In an attempt to ensure adequate numbers for comparison, we performed the search over a 10-year period. This may be a limitation as clinical practice and protocols will have been subject to change over this time period. There are also a relatively small number of cases in the perinatal death group (perinatal mortality rate of 6 per 1000 total births). The finding of significant relationships despite these numbers indicates the strength of the associations and the potential utility in a clinical setting.

*Conclusions*

The study findings demonstrate that high uterine artery resistances at term are independently associated with increased risk of severe adverse perinatal outcome regardless of fetal size. Small fetuses also continue to remain at increased risk of perinatal mortality. Further work to determine the optimum model of surveillance to identify those at increased risk of hypoxaemia is required. In order to explore the underlying mechanism associated with increased third trimester uterine artery Doppler indices and adverse perinatal outcome we would advocate performing a prospective study to examine the trends in uterine artery Doppler indices throughout the second and third trimesters and their relationship to pregnancy outcome.

**REFERENCES**


1. Gordjin SJ, Beune IM, Thilaganathan B et al. Consensus definition for placental fetal growth restriction: A Delphi procedure. Ultrasound Obstet Gynecol 2016;2016: 10.1002/uog.15884.
2. Lees C, Marlow N, Arabin B et al. Perinatal morbidity and mortality in early-onset fetal growth restriction: cohort outcomes of the trial of randomized umbilical and fetal flow in Europe (TRUFFLE). Ultrasound Obstet Gynecol 2013; 42:400-408.
3. Man J, Ashworth M, Levine S, Seibre N. Effects of Intrauterine Retention, Postmortem Interval and Other Factors on Bodyweight of Intrauterine Fetal Deaths: Implications for assessment of Fetal Growth Restriction at Autopsy. Ultrasound Obstet Gynecol In Press
4. The association between fetal Doppler and admission to the neonatal unit at term. Khalil A, Morales-Rosello J, Elsaddig M, Khan N, Papageorghiou A, Bhide A, Thilaganathan B. Am J Obstet Gynecol 2015;213: 57.e1-7.
5. Khalil A, Morales-Rosello J, Townsend R, Morlando M, Papageorghiou A, Bhide A and Thilaganathan B. Value of third-trimester cerebroplacental ratio and uterine artery Doppler indices as predictors of stillbirth and perinatal loss. Ultrasound Obstet Gynecol 2016; 47:74-80.
6. Vergani P, Roncaglia N, Andreotti C, Arreghini A, Teruzzi M, Pezzullo JC, Ghidini A. Prognostic value of uterine artery Doppler velocimetry in growth-restricted fetuses delivered near term. Am J Obstet Gynecol 2002**;** 187: 932–936.
7. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. BJOG 2009**;** 116: 424–430.
8. Oros D, Figueras F, Cruz-Martinez R et al. Longitudinal changes in uterine, umbilical and fetal cerebral Doppler indices in late-onset small-for-gestational age fetuses. Ultrasound Obstet Gynecol 2011;37(2):191-5.
9. Robinson HP, Fleming JE. A critical evaluation of sonar “crown-rump length” measurements. BJOG 1975; 82:702-710.
10. National Institute for Health and Care Excellence (2008). Antenatal care for uncomplicated pregnancies. Clinical Guideline 62. London: NICE.

11. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body and femur measurements, a prospective study. Am J Obstet Gynecol 1985; 151:333-337.
12. Acharya G, Wilsgaard T, Berntsen GK, Maltau JM, Kiserud T. Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy. Am J Obstet Gynecol 2005; 192:937-44.
13. Bahlmann F, Reinhard I, Krummenauer F, Neubert S Macchiella D, Wellek S. Blood flow velocity waveforms in the fetal middle cerebral artery in a normal population: reference values from 18 weeks to 42 weeks of gestation. J Perinat Med 2002; 30:490-501.
14. Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. Ultrasound Obstet Gynecol 2003; 21:124-127.
15. Gomez O, Figueras F, Fernadez S, Bennasar M, Martinez JM, Puerto B, Gratacos E. Reference ranges for uterine artery mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynaecol 2008; 32:128-132.
16. Morales-Rosello J, Khalil A, Salvi S, Townsend R, Premakumar Y, Perales-Marin A. Abnormal middle cerebral artery Doppler associates with spontaneous preterm birth in normally grown fetuses. Fetal Diagn Ther 2016; 40:41-7.
17. Yudkin PL, Aboualfa M, Eyre JA, Redman CW, Wilksinson AR. New birthweight and head circumference centiles for gestational ages 24 to 42 weeks. Early Hum Dev 1987; 15:45-52.
18. Verlohren S, Melchiorre K, Khalil A, Thilaganathan B. Uterine artery Doppler, birth weight and timing of onset of pre-eclampsia: providing insights into the dual etiology of late-onset pre-eclampsia. Ultrasound Obstet Gynaecol 2014;44(3):293-8.
19. Yu CK, Smith GC, Papageorghiou AT, Cacho AM, Nicolaides KH. Fetal Medicine Foundation Second Trimester Screening Group. An integrated model for the prediction of preeclampsia using maternal factors and uterine artery Doppler velocimetry in unselected low-risk women. Am J Obstet Gynecol 2005; 193: 429–436.
20. Khalil A, Garcia-Mandujano R, Maiz N, Elkhaouli M, Nicolaides KH. Longitudinal changes in uterine artery Doppler and blood pressure and risk of pre-eclampsia. Ultrasound Obstet Gynecol 2014; 43: 541–547.
21. Melchiorre K, Leslie K, Prefumo F, Bhide A, Thilaganathan B. First-trimester uterine artery Doppler indices in the prediction of small-for-gestational age pregnancy and intrauterine growth restriction. Ultrasound Obstet Gynecol 2009; 33: 524–529.
22. Melchiorre K, Wormald B, Leslie K, Bhide A, Thilaganathan B. First-trimester uterine artery Doppler indices in term and preterm pre-eclampsia. Ultrasound Obstet Gynecol 2008; 32: 133–137.
23. Singh T, Leslie K, Bhide A, D'Antonio F, Thilaganathan B. Role of second-trimester uterine artery Doppler in assessing stillbirth risk. Obstet Gynecol 2012; 119: 256–261.
24. Shwarzman P, Waintraub AY, Frieger M, Bashiri A, Mazor M, Hershkovitz R. Third-trimester abnormal uterine artery Doppler findings are associated with adverse pregnancy outcomes. J Ultrasound Med 2013; 32: 2107–2113.
25. Gaillard R, Arends LR, Steegers EA, Hofman A, Jaddoe VW. Second- and third-trimester placental hemodynamics and the risks of pregnancy complications: the Generation R Study. Am J Epidemiol 2013; 177: 743–754.

26. Lafont M, Dellinger P, Mutumba W, Bernanrd C, Hoyek T. Accuracy of ultrasound estimated fetal weight at term. Gynecol Obstet Fertil. 2016;44(7-8):391-5.
27. Paganelli S, Soncini E, Comitini G, La Sala GB. Sonographic fetal weight estimation in normal and overweight/obese healthy term pregnant women by gestation-adjusted projection (GAP) method. Arch Gynecol Obstet 2016;293(4):775-81.
28. Stirnemann JJ, Fries N, Bessis R, Fontanges M, Mangione R, Salomon LJ. Implementing INTERGROWTH fetal size references in France. Ultrasound Obstet Gynecol In Press.
29. Oros D, Figueras F, Cruz-Martinez R et al. Longitudinal changes in uterine, umbilical and fetal cerebral Doppler indices in late-onset small-for-gestational age fetuses. Ultrasound Obstet Gynecol. 2011;37(2):191-5.
30. Severi FM, Bocchi C, Visentin A et al. Uterine and fetal cerebral Doppler predict the outcome of third-trimester small-for-gestational age fetuses with normal umbilical artery Doppler. Ultrasound Obstet Gynecol. 2002; 19:225–228.
31. Eixarch E, Meler E, Iraola A et al. Neurodevelopmental outcome in 2-year-old infants who were small-for-gestational age term fetuses with cerebral blood flow redistribution. Ultrasound Obstet Gynecol. 2008; 32:894–899.
32. Murata S, Nakata M, Sumie M, Sugino N. The Doppler cerebroplacental ratio predicts risk of non-reassuring fetal status for fetal growth restriction in term pregnancy. J Obstet Gynecol Res 2011; 37: 1433–1437.
33. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral–umbilical Doppler ratio as a predictor of adverse perinatal outcome. Obstet Gynecol 1992; 79: 416–420.
34. Akolekar R, Syngelaki A, Gallo DM, Poon LC, Nicolaides KH. Umbilical and fetal middle cerebral artery Doppler at 35-37 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol. 2015;46(1):82-92.

**Table 1.** Comparison of the maternal and pregnancy characteristic between those resulting in live birth and those complicated by perinatal death

| | **Live birth (n=7001)** | **Perinatal Death (n=12)** | **P value** |
|---|---|---|---|
| Maternal age in years, median and IQR | 32.0 (27.0- 35.0) | 31.0 (28.5-33.0) | 0.672 |
| BMI in $kg/m^2$, median and IQR | 24.4 (21.7-28.5) | 26.5 (23.03-29.73) | 0.302 |
| Ethnicity | | | 0.147 |
| Caucasian, n (%) | 4023 (58.6) | 3 (25.0) | |
| Afro-Caribbean, n (%) | 1009 (14.7) | 4 (33.3) | |
| Asian, n (%) | 1561 (22.7) | 4 (33.3) | |
| Mixed, n (%) | 220 (3.2) | 1 (8.3) | |
| Other, n (%) | 55 (0.8) | 0 (0) | |
| GA at ultrasound in weeks, median and IQR | 36.43 (36.0-38.71) | 37.0 (35.89-38.64) | 0.932 |
| GA at delivery in weeks, median and IQR | 40.14 (39.0-41.0) | 39.00 (37.79-40.86) | 0.063 |
| Smokers, n (%) | 410 (6.4) | 0 (0) | 0.364 |
| Conception, n (%) | | | 0.790 |
| Spontaneous | 6398 (96.2) | 12 (100) | |
| IVF/ICSI/IUI | 184 (2.8) | 0 (0) | |
| Ovulation induction | 68 (1) | 0 (0) | |

IQR: interquartile range; BMI: body mass index; GA: gestational age; IVF: in vitro fertilization; ICSI: intracytoplasmatic sperm injection, IUI: intrauterine insemination

**Table 2.** Maternal characteristics in patients with third trimester ultrasound assessment comparing live births in low risk pregnancies and perinatal death

| | **Low risk live birth (n=1527)** | **Perinatal Death (n=12)** | **P value** |
|---|---|---|---|
| Maternal age in years, median and IQR | 32.0 (29.0-35.0) | 31.0 (28.5-33.0) | 0.274 |
| BMI in kg/$m^2$, median and IQR | 24.5 (22.0-28.78) | 26.45 (23.03-29.73) | 0.379 |
| Ethnicity | | | 0.041 |
| Caucasian, n (%) | 1001 (66.2) | 3 (25.0) | |
| Afro-Caribbean, n (%) | 213 (14.1) | 4 (33.3) | |
| Asian, n (%) | 249 (16.5) | 4 (33.3) | |
| Mixed, n (%) | 37 (2.4) | 1 (8.3) | |
| Other, n (%) | 11 (0.7) | 0 (0) | |
| GA at ultrasound in weeks, median and IQR | 37.86 (36.29-41.43) | 37.0 (35.89-38.64) | 0.023 |
| Interval US and delivery, weeks, median and IQR | 1.29 (0.43-3.57) | 1.64 (0.86-2.93) | 0.445 |
| GA at delivery in weeks, median, median and IQR | 41.14 (39.71-41.86) | 39.0 (37.79-40.86) | 0.001 |

Data are given as median (interquartile range) or n (%); BMI, body mass index; GA, gestational age