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Original Article

The predictors of poor outcome in early onset fetal growth restriction

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Abstract: The aim of this study was to evaluate the obstetric and sonographic parameters associated with perinatal mortality and neonatal intensive care unit admission (NICU) in pregnancies affected by small for gestational age before 34 weeks gestation. Study recruited 313 singleton pregnancies who were referred if small fetal size was suspected due to clinical evaluation in the antenatal setting. The primary outcomes for this study were perinatal mortality and NICU admission. The outcomes were analyzed based on predictors including gestational age at enrollment, gestational age at delivery, abnormal umbilical artery Doppler, preeclampsia, oligohydramnios, birthweight, birthweight percentile, gender and cesarean delivery. Neonatal intensive care unit admission rate was 64%. Gestational at delivery was detected to be the significant independent predictors for NICU admission. The presence of preeclampsia, oligohydroamnios and abnormal umbilical artery Doppler were detected to be non-independent predictors. Perinatal mortality rate was 4.5%. GA at delivery was detected to be the significant independent predictor for perinatal mortality. The presence of preeclampsia and abnormal umbilical artery Doppler were detected to be non-independent predictors. The predictive accuracy of GA at delivery as a marker for NICU admission and perinatal mortality were determined by receiver-operating curves (ROC) analysis with area under curve (AUC): 0.97 (95% CI: 0.95-0.99) and AUC: 0.93 (95% CI: 0.87-0.99), respectively.

Keywords: Fetal growth restriction, small for gestational age, perinatal mortality

Introduction

One of the major focus of prenatal care is to determine whether a fetus is at risk for growth restriction (FGR) and to identify the growth restricted fetus. This is important because these fetuses are at increased risk of adverse perinatal outcome. The most common sonography-based definition of FGR is a weight below the 10th percentile for gestational age [1-3]. When a small fetus is detected, it can be difficult to distinguish between the fetus that is constitutionally small versus growth restricted. Correct diagnosis is not always possible, but is important prognostically and for estimating the risk for recurrence.

The aim of this study was to evaluate the obstetric and sonographic parameters associated with perinatal mortality and neonatal intensive care unit (NICU) admission in pregnancies affected by small for gestational age (SGA) before 34 weeks gestation.

Material and methods

This retrospective study was performed between May 2011 and May 2015 at Zeynep Kamil Research Hospital, Istanbul, Turkey. The study was approved by the local ethics committee. Study recruited 313 singleton pregnancies who were referred if small fetal size was suspected due to clinical evaluation in the antenatal setting. Fetuses met the inclusion criteria: gestational age between 24 0/7 and 34 weeks confirmed by first trimester ultrasonography, absence of structural or chromosomal abnormality, estimated fetal weight below 10th centile based on sonographic measurements of fetal biparietal diameter, head circumference, abdominal circumference, and femur length [4]. The diagnosis of SGA was made by convention-

Table 1. Maternal demographics and fetal characteristics (n=313)

Characteristics	Value
Age, y	29±6
GA at enrollment, wk	29.1±2.9
GA at delivery, wk	33.9±4.2
Preeclampsia	80 (25.6%)
Birthweight, g	1529.2±684.6
NICU admission	202 (64.5%)
Apgar score <7	12 (3.8%)
Stillbirths	11 (3.6%)
Neonatal deaths	3 (0.9%)
Perinatal mortality	14 (4.5%)
Mode of delivery	
Cesarean	219 (70%)
Vaginal	94 (30%)

Continuous variables are summarized with mean ± SD and categorical variables with n (%). GA, gestational age; NICU, neonatal intensive care unit.

al population-based growth standards [5]. Baseline demographic data were recorded. All pregnants underwent evaluation of multivessel Doppler of umbilical artery (UA), middle cerebral artery, ductus venosus; amniotic fluid volume; biophysical profile scoring at every subsequent visit. Umbilical artery Doppler recordings were performed on a free floating cord loop in the absence of fetal breathing or movements. Abnormal UA Doppler was defined as a pulsatility index (PI) above the 95th percentile [6], absent and reversed end-diastolic blood flow. All prenatal data were recorded. In the absence of umblical artery Doppler abnormalities pregnants underwent serial sonographic evaluation at intervals of every 2 weeks. Weekly assesment was performed when there was UA pulsality index >95th centile or oligohydramniosis. Delivery was indicated in the presence of absent diastolic flow in UA after 34 weeks, reverse end diastolic flow in UA after 32 weeks and abnormalities of ductus venosus (PI>95th centile, absent-negative a wave), non-reassuring fetal testing (continuous late decelerations) and maternal/fetal indications necessitate delivery such as severe preeclampsia, placental abruption at any gestational age. Preeclampsia is defined by the presence of elevated blood pressure (140/90 mmHg) and significant proteinuria (300 mg per 24 h) after the 20th week of gestation in normotensive women. Maternal steroid was applied before timed delivery when indicated.

The primary outcomes for this study were perinatal mortality and NICU admission. For the neonatal outcomes, need for NICU and neonatal death were obtained from the records of our Neonatology Department. Perinatal mortality was defined as the sum of fetal deaths (≥20 weeks gestation) plus neonatal deaths (ie, deaths within the first 28 days of birth) [7]. Fetal death (stillbirth) is also defined as death of the fetus occuring after 20th week of gestation.

Statistical analyses were performed using the Statistical Package of Social Sciences and Problem Solutions (SPSS, version 15; SPSS, Inc. Chicago, IL). Data were expressed as numeric (%) or mean ± standard deviation (SD) values, as appropriate. The primary outcome variables of interest were perinatal mortality and NICU admission. Kolmogorov-Smirnov test was performed to identify whether or not parameters are normally distributed. Student's t-test and Mann-Whitney test were applied to compare parameters among the groups. Categorical variables were analysed by χ^2 test. The multiple logistic regression was performed to identify the independent markers for NICU admission and perinatal mortality. Hosmer-Lemeshow goodness of fit statistics were performed to assess model fit. The area under the curve (AUC) for independent variables determination of NICU admission and perinatal mortality were calculated by receiver-operator curve (ROC) analysis. Results were evaluated with 95% confidence intervals, and $P \leq 0.05$ was considered to be statistically significant.

Results

A total of 313 pregnancies were recruited into the study. Maternal demographics and fetal characteristics are summarized in **Table 1**. The mean age of the patients was 29.6±6.1. The mean gestational age (GA) at enrollment and delivery were 29.1±2.9 and 33.9±4.2, respectively. Median birth weight was 1529±864.6 g and the median interval between birth and last Doppler study was 5 days. Preeclampsia occured in 80 of 313 (25.6%) cases. In cases with perinatal mortality; 10 of 14 (71%) cases had preeclampsia and 70 of 243 (23.4%) cases without perinatal mortality had preeclamsia.

Sixty four percent (n=202) of the cohort required admission to the NICU with a median length of stay of 25 days. Comparison of de-

Table 2. Comparison of demographic and fetal characteristics in cases with and without NICU admission

Characteristics	NICU (+) N=202	NICU (-) N=99	P
Gestational age at enrollment, wk	28.4±2.6	31±2.8	<0.001
Gestational age at delivery, wk	32.1±4.2	38.4±1.5	<0.001
Preeclampsia	62 (30.7%)	9 (9.1%)	<0.001
Oligohydramniosis	92 (45.5%)	21 (21.2%)	<0.001
Abnormal umblical artery Doppler	154 (76.2%)	21 (21.2%)	<0.001
Birthweight, gram	1199±468	2311±302	<0.001
Estimated fetal weight percentile (%)	1.4±1.8	3.2±2.6	<0.001
Gender (male)	96 (49.2%)	45 (45.9%)	0.592
Cesarean section	182 (90.1%)	36 (36.4%)	<0.001

Table 3. Comparison of demographic and fetal characteristics in cases with and without perinatal mortality

Characteristics	Mortalite (+) N=14	Mortalite (-) N=299	P
Gestational age at enrollment, wk	25.9±2	29.3±2.9	<0.001
Gestational age at delivery, wk	27.6±2.2	34.2±4	<0.001
Preeclampsia	10 (71.4%)	70 (23.4%)	<0.001
Oligohydramniosis	7 (50%)	112 (37.5%)	0.345
Abnormal umblical artery Doppler	13 (92.9%)	173 (57.9%)	<0.001
Birthweight, g	656±299	1570±670	<0.001
Estimated fetal weight percentile (%)	1±1.1	2±2.3	0.144
Gender (male)	5 (62.5%)	140 (48.1%)	0.422
Cesarean section	3 (21.4%)	216 (98.6%)	<0.001

mographics and fetal characteristics in cases with and without NICU admission were demonstrated in **Table 2**. GA at enrollment, GA at delivery, birthweight, EFW percentile were lower in cases with NICU admission. In addition preeclampsia, oligohydramniosis, UA Doppler abnormality and CS rates were significantly higher in cases with NICU admission. Logistic regression analysis was performed to examine the values of markers in predicting NICU admission for which a significant difference was found between groups with and without NICU admission. A significant correlation was found between GA at delivery and birthweight (0.88) as well as GA at delivery and EFW percentile (0.80). Thus, birthweight and EFW percentile were excluded from logistic regression analysis. Using GA at delivery, the presence of preeclampsia, oligohydramniosis and UA Doppler the variables for which a statistically significant difference was detected between the groups, independent predictors for NICU admission were examined via logistic regression analysis. GA at delivery was detected to be the significant independent predictor for NICU admission (P<0.001, RR: 0.28; 95% CI 0.19-0.41). The presence of preeclampsia, oligohydramniosis and abnormal UA Doppler were detected to be non-independent predictors (P= 0.74, P=0.36, P=0.93, respectively). Model fit was confirmed by Hosmer-Lemeshow test (P=0.079) (Nagelkerke R Square=0.80).

Perinatal mortality rate was 4.5%. Comparison of demographics and fetal characteristics were shown in cases with and without perinatal mortality in **Table 3**. GA at enrollment, GA at delivery, birthweight and CS rates were lower in cases with perinatal mortality. In addition preeclampsia, UA Doppler abnormality were significantly higher in cases with perinatal mortality. Logistic regression analysis was performed to examine the values of markers in predicting perinatal mortality. A significant correlation was found between GA at delivery and birthweight (0.94). Thus, birthweight was excluded from logistic regression analysis. Using GA at delivery, the presence of preeclampsia and abnormal UA Doppler, the variables for which a statistically significant difference was detected between the groups, independent predictors for perinatal mortality were examined via logistic regression analysis. GA at delivery was detected to be the significant independent predictors for perinatal mortality (P<0.001, RR: 0.50; 95% CI 0.35-0.72). The presence of preeclampsia and UA Doppler abnormality were detected to be non-independent predictors (P=0.186 and P=0.925, respectively). Model fit was confirmed by Hosmer-Lemeshow test (P=0.99) (Nagelkerke R Square=0. 45).

There were 11 stillbirths and 3 neonatal deaths in this cohort. There were 2 cases who presented with unexpected inutero fetal death at 26

Table 4. Characteristics of cases with perinatal mortality

Case	GA at entry	Group and Doppler findings before delivery	GA at delivery	Mode and endication of delivery	Birthweight	Prognosis
Case 1	30 w 1 d	Group 6 Doppler: UA PI>95th centile DV normal MCA<5th centile	33 w	Vaginal IUD	1400 g	Unexpected IUD
Case 2	30 w	Group 2 Doppler: UA PI>95th centile DV normal MCA<5th centile	31 w 2 d	CS Severe preeclamsia and worsening maternal symptoms	1195 g	Neonatal death at 3. day due to neonatal sepsis
Case 3	24 w 4 d	Group 6 Doppler: UA PI>95th centile DV absent a wave MCA<5th centile	26 w	Vaginal IUD	505 g	IUD*
Case 4	26 w	Group 8 Doppler: UA PI>95th centile DV normal MCA<5th centile	28 w 1 d	CS Recurrent late decelerations	510 g	Neonatal death at 3. day
Case 5	25 w 1 d	Group 6 Doppler: UA AEDF DV PI>95th centile MCA PI<5th centile	26 w	Vaginal IUD	560 g	IUD*
Case 6	24 w 2 d	Group 8 Doppler: UA REDF DV>95th centile MCA PI<5th centile	26 w	Vaginal IUD	502 g	IUD*
Case 7	25 w	Group 8 Doppler: UA REDF DV>95th centile MCA PI<5th centile	26 w 5 d	Vaginal IUD	510 g	IUD*
Case 8	25 w	Group 7 Doppler: Normal UA	26w	Vaginal IUD	530 g	Unexpected IUD
Case 9	25 w	Group 6 Doppler: UA AEDF DV PI>95th centile MCA PI<5th centile	26 w 5 d	Vaginal IUD	550 g	IUD*
Case 10	25 w	Group 7 Doppler: normal UA DV normal MCA<5th centile	26 w	Vaginal Severe preeclamsia and worsening maternal symptoms	530 g	IUD during antepartum period
Case 11	24 w 4 d	Group 6 Doppler: UA REDF DV reverse a wave	26 w 4 d	Vaginal IUD	550 g	IUD*
Case 12	26 w	Group 2 Doppler: UA AEDF DV normal MCA normal	27 w 4 d	CS HELLP syndrome	700 g	Neonatal death at 5. day due to grade 4 intracranial hemorrhage
Case 13	26 w	Group 8 Doppler: UA PI 95th çentile DV normal MCA PI<5th centile	29 w	Vaginal IUD	740 g	IUD Parents refused ing perform CS due to late decelerations
Case 14	26 w 3 d	Group 8 Doppler: UA REDF DV PI>95th centile MCA PI<5th centile	26 w 6 d	Vaginal IUD	580	IUD*

GA, Gestational age; UA, Umbilical artery; DV, Ductus venousus; MCA, Middle cerebral artery; PI, Pulsatility index; w, Week; d, Day; IUD, Inutero death; CS, Cesarean; AEDF, Absent end diastolic flow; REDF, Reverse end diastolic flow. *Patient decision for non-intervention because of considered poor prognosis.

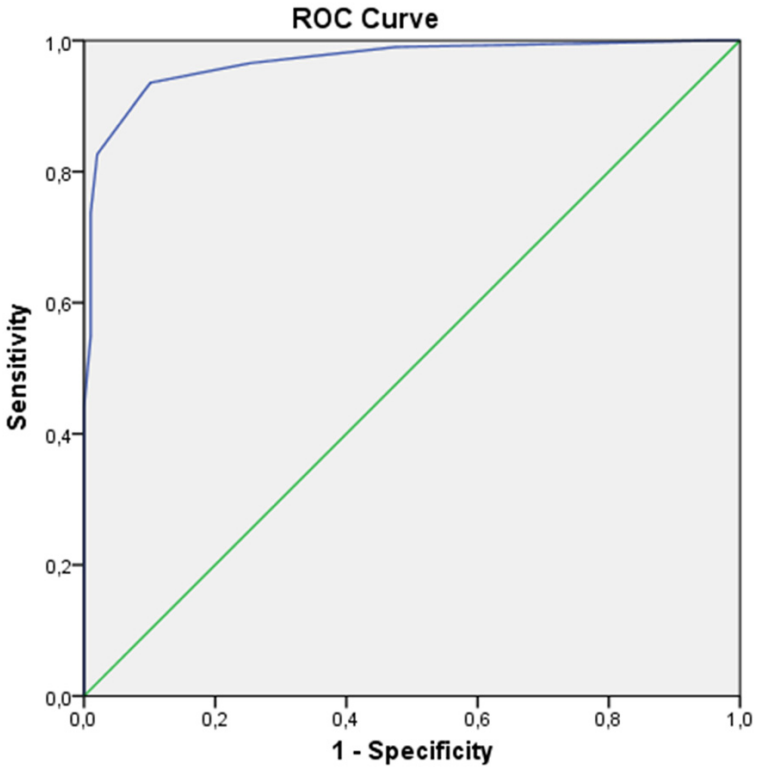

Figure 1. Receiver-operating curves for the prediction of NICU admission for gestational age at delivery.

and 33 weeks of gestation. In the third case with inutero fetal death at 29 weeks of gestation, parents refused delivery who was offered cesarean section due to late decelerations. Characteristics of cases with perinatal mortality was shown in **Table 4**.

The predictive accuracy of GA at delivery as a marker for NICU admission and perinatal mortality were determined by receiver-operating curves (ROC) analysis. Area under curve (AUC) were 0.97 (95% CI: 0.95-0.99) and 0.93 (95% CI: 0.87-0.99) for NICU admission and perinatal mortality, respectively in **Figures 1** and **2**. When <32.5 weeks of gestation was used as a cut-off for GA at delivery to predict NICU admission and perinatal mortality; sensitivity and specificity were determined to be 55%, 99% and 93%, 64%, respectively (**Table 5**).

Discussion

Our data suggest that GA at delivery is the significant independent predictor for NICU admission and perinatal mortality. None of the remaining variables including presence of preeclampsia, abnormal UA Doppler, oligohydramnios, preeclampsia, birthweight and EFW percentile were detected to be independent predictors of NICU admission and perinatal mortality. Our data also showed that there was a 72% reduction in the incidence of NICU admission for every additional week of gestation at delivery. In contrast to present study; Prospective Observational Trial to Optimize Pediatric Health in Intrauterine Growth Restriction (PORTO Study), including 1116 fetuses EFW <10th centile, demonstrated the strong association between NICU admission and abnormal UA artery. In addition EFW <3rd centile was reported to be associated with NICU admissions in the absence of abnormal UA Doppler. Moreover, PORTO study reported lower NICU admission rate compared with present study (28% vs 64%). Population of PORTO study including pregnants up to 37 weeks is the possible reason of lower NICU admission rate [8]. Ozyuncu et al also revealed higher NICU admission rates in cases with UA Doppler abnormality compared to cases with normal UA Doppler findings (63% vs 82%). NICU admission rate was increasing proportional to severity of UA Doppler abnormality [9].

In the present study; there were 11 stillbirths and 3 neonatal deaths corresponding to a perinatal mortality rate of 4.5%. The most important independent determinant of perinatal mortality was the GA at delivery. Thirteen (92%) of perinatal deaths occured in cases with abnormal UA Doppler. However; none of the predictors beside gestational age at delivery; were associated with perinatal mortality. Despite the lack of statistical significance association was reported for abnormal UA Doppler, the small number of deaths may have limited the ability of UA Doppler abnormalities to predict perinatal morbidity. PORTO study reported 6 perinatal deaths between 24 and 35 weeks. In contrast to our results; authors emphasized association between perinatal death and abnormal

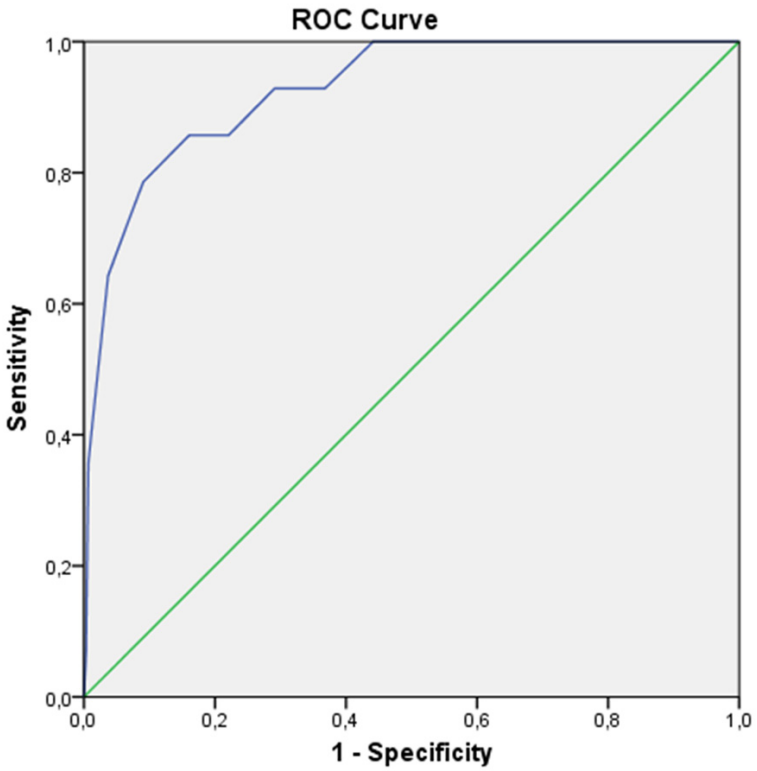

Figure 2. Receiver-operating curves for the prediction of perinatal mortality for gestational age at delivery.

Table 5. Predictive accuracy of gestational age at delivery in detecting NICU admission and perinatal mortality for different cut-offs

Cut-off value (GA at delivery)	For NICU admission		For perinatal mortality	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
<28.5 weeks	14	100	79	91
<30.5 weeks	33	100	86	78
<32.5 weeks	55	99	93	63
<34.5 weeks	74	99	100	51
<36.5 weeks	94	90	100	34

UA Doppler and EFW <3rd percentile [8]. In the present study, perinatal mortality rate was 8% (13 of 175) in cases with abnormal UA Doppler. TRUFFLE trial (Trial of Umbilical and Fetal Flow in Europe), including 542 pregnants at 26-32 weeks of gestation, with abdominal circumference <10th percentile and UA Doppler pulsatility index >95th percentile, reported perinatal mortality rate of 8%. In contrast; our study included cases at 24 and 25 weeks gestations in which poor perinatal outcomes were expected. So present study describe somewhat better than expected perinatal outcomes in this high risk group of fetuses with abnormal UA Doppler. In addition, in TRUFFLE trial; presence of gestational hypertensive morbidity at study entry (OR=1.7; 95% CI, 1.11-2.62), GA at admission (OR=0.8 per week of gestation; 95% CI, 0.65-0.99) and EFW at study inclusion (OR=0.84 per 100 g of EFW; 95% CI, 0.72-0,99) were the most important independent determinants of the composite poor outcome (death or severe morbidity) [10]. Present study also revealed that there was a 50% reduction in the incidence of perinatal mortality for every additional week of gestation at delivery. Mari et al reported that GA at delivery predicted perinatal mortality in 41 patients who delivered at 32 weeks gestation or earlier with fetuses EFW below 3rd percentile and UA PI above the 95th percentile. Also no other Doppler parameters predicted perinatal mortality. Similar to our results, perinatal mortality decreased by 48% for each additional week the fetuses remained in utero [11]. Twelve of 14 perinatal deaths occured in cases diagnosed below 27 gestational weeks. In 7 of them antepartum deaths were caused by a decision for non-intervention because of considered poor prognosis below 26 gestation weeks. Data of IUGR infants born before 26 weeks revealed a very poor outcome at neonatal period and 2 years of age. From 2 observational studies neonatal survival increased from 13% at 24 weeks to 43% at 25 weeks and to 58-76% at 26 weeks of gestation. Intact neonatal survival rates was reportes as 0%, 13%, 31% at 24, 25 and 26 gestational weeks, respectively [10, 12]. Similar to our recommendation Visser et al suggested that active intervention by delivery of early

IUGR fetuses, with or without concomitant maternal preeclampsia, should not be recommended before 26 weeks of gestational age, unless the parents decide otherwise [13].

Present study reported no association between oligohydramniosis and NICU admission or perinatal deaths. Limited evidence is available on the role of oligohydramniosis to predict perinatal complications in IUGR fetuses managed with Doppler. Chauhan et at demonstrated that oligohydramniosis is associated with an abnormal 5-min Apgar score, but no association was reported with acidosis or perinatal death in SGA (RR 1.6 95% CI 0.9-2.6) [14]. PORTO trial reported an association with adverse perinatal outcomes when combined with an EFW <3rd centile. But no association was reported neither with NICU admission nor with prenatal mortality. So it is still questionable to include oligohydramniosis in management protocols.

Major strength of the study is the large number of cases in this very high-risk group. All cases were subjected to a high degree of fetal surveillance using the most advanced Doppler techniques available, which were performed by experienced perinatologists. But there are some limitations deserving critiques. As there were no published data demonstrating Turkish intrauterine growth curves, curves from France were used to determine SGA fetuses [5]. From a socioeconomic perspective, severe morbidities such as neurological impairment including cerebral palsy or broncopulmonary dysplasia enough to require home oxygen therapy are more critical problems. Unfortunately perinatal outcomes associated with neonatal morbidity such as intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, necrotizing enterocolitis, bronchopulmonary dysplasia, sepsis could not be evaluated due to lack of neonatal data in most cases. Although NICU admission rates may reflect these morbidity, such association can not be evidence based.

In conclusion fetuses with EFW <10th centile for gestation should alert clinicians to potential small fetal size due to association with poor perinatal outcomes. Present study provided evidence that GA at delivery is the significant independent predictor for NICU admission and perinatal mortality. Moreover, this study may provide contemporary information for counseling women at the time of antenatal diagnosis in respect of short-term outcomes.

Disclosure of conflict of interest

None.

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References

[1] American College of Obstetricians and Gynecologists. Intrauterine growth restriction. Washington, DC: American College of Obstetricians and Gynecologists; 2000.

[2] Royal College of Obstetricians and Gynecologists. The investigation and management of the small-for-gestational-age fetus (guideline no. 31). London: Royal College of Obstetricians and Gynecologists; 2002.

[3] Lausman A, McCarthy FP, Walker M, Kingdom J. Screening, diagnosis, and management of intrauterine growth restriction. J Obstet Gynaecol Can 2012; 34: 17-28.

[4] 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: 333-7.

[5] Zeitlin J, Ancel PY, Saurel-Cubizolles MJ, Papiernik E. The relationship between intrauterine growth restriction and preterm delivery: an empirical approach using data from a European case-control study. BJOG 2000; 107: 750-8.

[6] Arduini D, Rizzo G. Normal values of Pulsatility Index from fetal vessels: a cross-sectional study on 1556 healthy fetuses. J Perinat Med 1990; 18: 165-72.

[7] Barfield WD; Committee on Fetus and Newborn. Standard terminology for fetal, infant, and perinatal deaths. Pediatrics 2011; 128: 177.

[8] Unterscheider J, Daly S, Geary MP, Kennelly MM, McAuliffe FM, O'Donoghue K, Hunter A, Morrison JJ, Burke G, Dicker P, Tully EC, Malone FD. Optimizing the definition of intrauterine growth restriction-results of the multicenter prospective PORTO Study. Am J Obstet Gynecol 2013; 208: 290, e1-6.

[9] Ozyuncu O, Saygan-Karamursel B, Armangil D, Onderoglu LS, Yigit S, Velipasaoglu M, Deren O. Fetal arterial and venous Doppler in growth restricted fetuses for the prediction of perinatal complications. Turk J Pediatr 2010; 52: 384-92.

[10] Lees C, Marlow N, Arabin B, Bilardo CM, Brezinka C, Derks JB, Duvekot J, Frusca T, Diemert A, Ferrazzi E, Ganzevoort W, Hecher K, Martinelli P, Ostermayer E, Papageorghiou AT, Schlembach D, Schneider KT, Thilaganathan B, Todros T, van Wassenaer-Leemhuis A, Valcamonico A, Visser GH, Wolf H; TRUFFLE Group. 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.

[11] Mari G, Hanif F, Treadwell MC, Kruger M. Gestational age at delivery and Doppler waveforms in very preterm intrauterine growth-restricted fetuses as predictors of perinatal mortality. J Ultrasound Med 2007; 26: 555-9.

[12] Baschat AA, Cosmi E, Bilardo CM, Wolf H, Berg C, Rigano S, Germer U, Moyano D, Turan S, Hartung J, Bhide A, Müller T, Bower S, Nicolaides KH, Thilaganathan B, Gembruch U, Ferrazzi E, Hecher K, Galan HL, Harman CR. Predictors of neonatal outcome in early-onset placental dysfunction. Obstet Gynecol 2007; 109: 253-261.

[13] Visser GH, Bilardo CM, Lees C. Fetal growth restriction at the limits of viability. Fetal Diagn Ther 2014; 36: 162-5.

[14] Chauhan SP, Sanderson M, Hendrix NW, Magann EF, Devoe LD. Perinatal outcome and amniotic fluid index in the antepartum and intrapartum periods: A meta-analysis. Am J Obstet Gynecol 1999; 181: 1473-8.