The Assessment of Association between Uterine Artery Pulsatility Index at 30–34 Week's Gestation and Adverse Perinatal Outcome

Abstract

Background: Given the high prevalence of adverse perinatal outcome in the developing countries and the association between uterine artery (UtA) blood flow and fetal status in the uterine, in the current study, we assess the association between UtA pulsatility index (UtA-PI) at 30–34 week's gestation and adverse perinatal outcome. **Materials and Methods:** This cohort study included 100 pregnant women at 30–34 weeks' gestation. At baseline, UtA-PI was evaluated with color Doppler through abdominal ultrasound. Then, adverse perinatal outcomes including preterm labor, intrauterine fetal death, preeclampsia, low 5-min Apgar score (<7), low umbilical arterial cord blood pH, admitted to Intensive Care Unit in the first 3 days of birth, low birth weight, infant with low weight, death of newborns, cesarean section for respiratory distress, and meconial amniotic fluid were recorded. Ultimately, the collected data were analyzed using SPSS, version 20. **Results:** The presence of small-for-gestational-age fetuses indicated the highest prevalent adverse prenatal outcome with the incidence of 13.3% and 58.5%, respectively, among pregnancies with normal UtA-PI as well as those with high UtA-PI ($P < 0.001$). Overall, given that sensitivity and specificity of high UtA-PI were 37.5% and 73.3%, respectively, it could not properly predict adverse perinatal outcome ($P = 0.360$). **Conclusion:** According to the results, although the incidence of some of adverse perinatal outcomes in pregnant women with high UtA-PI was higher compared to those with normal UtA-PI, this factor alone cannot predict adverse perinatal outcome well. Therefore, this factor may predict these outcomes well, in the subgroups with high-risk pregnancies or with some blood factors or with pregnancy complications.

Keywords: *Adverse prenatal outcome, gestational age, uterine artery pulsatility index*

Elahe Zarean,
Shahrzad
Shabaninia

From the Department of Obstetrics and Gynecology, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction

Placentation when it is impaired, on the one hand, may result in high residence to blood flow of uterine arteries (UtAs) during pregnancy, particularly within first, second, and third trimesters. On the other hand, this can lead to developing preeclampsia (PE) subsequently and birth of small-for-gestational-age (SGA) newborns.[1-5] The evidence suggests that there is an association between persistence of increased residence to blood flow in the UtAs within the third trimester of pregnancy and the increased risk of adverse outcomes in perinatal period such as stillbirths or force to use cesarean section when fetal distress and low cord blood pH occurred.[6-10]

Whereas adverse perinatal outcomes are prevalent in developing countries, the importance of perinatal mortality index which reflects the health of a country is undeniable. Annually, 4 million newborns die within the first 4 weeks of life, while 3 million of these cases occur in the perinatal period (early death). By taking into account the cases of stillbirth, nearly 6 million perinatal deaths come about each year; however, 98% of perinatal deaths occur in developing countries.[11,12] Due to the fact that one-third of perinatal deaths occur during labor, it can be effectively prevented.[13,14] In this regard, using Doppler ultrasound is one of the noninvasive methods to assess uterine blood flow. It works based on variations in frequencies of the sound waves that have been sent from the probe to the red blood cells in vessels and reflected to the probe.[15] In most studies, some of the Doppler indices including resistive index (RI) or pulsatility index (PI) have been measured. PI is measured at 11–14 weeks' gestation. Many studies have been conducted on the association between UtA blood flow

and fetal status,[16-18] which reflects the importance of reduced trend of PI in the final stages of pregnancy. An increased risk of hypertension, epilepsy during pregnancy, intrauterine growth restriction (IUGR), placental abruption, and stillbirth has been reported during the first and second trimesters of pregnancy in pregnant women with a high UtA-PI.[19-22]

The results of another study indicated that high UtA-PI can help us predict adverse perinatal outcome, since its diagnostic potential was higher in pregnancies with an SGA fetus compared to others in the prediction of adverse perinatal outcome. The diagnostic potential in the prediction of stillbirth in two groups of high UtA-PI and normal UtA-PI was 24% and 13%, in the prediction of cesarean section for respiratory distress was 15% and 5%, and in the prediction of decreased umbilical arterial/venous cord blood pH was 22% and 9%, and in the prediction of low 5-min Apgar score was reported 20% and 3%, respectively.[23]

Gomez-Roig *et al.* on the assessment of the association between IUGR and PE and UtA-PI suggested that UtA-PI with the measurement of serum level of placental growth factor (PIGF) can be useful in early diagnosis of adverse perinatal outcome caused by IUGR and PE in the third trimester of pregnancy, but this study demonstrated that UtA-PI measurement alone can be identified as a poor predictor in this regard.[24] Considering the high incidence of adverse perinatal outcome as well as the lack of precise criteria for assessing and screening the newborns at risk off, and given that the results from previous studies on the performance of UtA-PI are contradictory, the current study investigates the association between UtA-PI at 30–34 weeks' gestation and adverse perinatal outcome.

Materials and Methods

This cohort study included 100 pregnant women at 30–34 weeks' gestation referred to Beheshti Hospital during March 2015–March 2016. Since this study only follows diagnostic purposes with no invasive and therapeutic intervention, there is no danger to patients. Therefore, to participate in the study, written informed consent was obtained from these women. History of chronic hypertension, diabetes mellitus, systematic lupus erythematosus and autoimmune diseases, fetal anomalies diagnosed by ultrasound, thrombophilia, abnormal karyotype, fetal growth restriction, pregnancy-induced hypertension and preterm labor (PTL) in recent pregnancy, multiple pregnancies, and lack of consent to continue cooperation were considered as the exclusion criteria in this study.

Following being included in the study, the maternal basic information including age and medical history of hypertension, hyperglycemia, birth, and PE was recorded at baseline.

Afterward, at 30–34 weeks of pregnancy, an ultrasound was performed by Mindray DC7 device (made in China) with abdominal probe. First, through transabdominal probe, uterus and ovarian size, endometrial thickness, and amniotic fluid were measured and examined. Then, UtA-PI was evaluated with color Doppler through abdominal ultrasound after voiding. Evaluation of UtA-PI at the level of the internal cervical os from its ascending branch on the right and left sides of cervix was performed and measured in all three areas, and then, their mean was recorded. It should be noted that all measures related to ultrasound and color Doppler were performed by an experienced person in the morning.

Then, after delivery of newborns, the information on adverse perinatal outcome, including PTL, intrauterine fetal death, PE, low 5-min Apgar score (<7), low umbilical arterial cord blood pH, admitted to Intensive Care Unit in the first 3 days of birth, low birth weight, infant with low weight, death of newborns, cesarean section for respiratory distress, and meconial amniotic fluid, was recorded.

Finally, collected data were entered into Statistical Package for the Social Sciences (SPSS) software version 20 (SPSS, Inc., Chicago, IL, USA), and as descriptive statistics, we used mean and standard deviation for quantitative data and frequency and frequency percentage for qualitative data. As inferential statistics, we applied Chi-square test, Fisher's exact test, and independent *t*-test to compare maternal and pregnancy characteristics to UtA-PI, and we used receiver operating characteristic curve (ROC curve) analysis to assess the diagnostic value of UtA-PI in the prediction of adverse perinatal outcome. For all analyses, we considered a significance level of <0.05.

Results

In the current study, according to the results from Doppler ultrasound, of the 100 pregnant women, there were 40 women (40%) with high UtA-PI (mean age = 28.50 ± 6.03 years) and 60 women (60%) with normal UtA-PI (mean age = 30.53 ± 5.51 years) ($P = 0.085$). Gestational age was 36.49 ± 2.51 and 37.93 ± 1.96 weeks in high UtA-PI and normal UtA-PI groups, respectively ($P = 0.002$). Adverse perinatal outcome was observed in 12 cases (30%) of high UtA-PI group versus in nine cases (15%) of normal UtA-PI ($P = 0.047$). However, the number of male births in high UtA-PI group with the frequency of 30 (75%) was significantly higher compared to the frequency of 31 (51.7%) in normal UtA-PI group ($P = 0.012$). Moreover, the birth weight in normal UtA-PI group (mean weight = 3236.50 ± 592.64 g) was significantly higher compared to high UtA-PI group (mean weight = 2422.75 ± 473.95 g) [Table 1].

The results from ROC curve analysis, meanwhile, on the assessment of diagnostic value of UtA-PI in the prediction of adverse perinatal outcome indicated that sensitivity and

2

Advanced Biomedical Research | 2018

Variables	Totally (n=100)	Normal UtA-PI (n=60)	UtA-PI >95th centile (n=40)	P
Table 1: Maternal and pregnancy characteristics in two groups				
GA at assessment (weeks)	37.35±2.29	37.93±1.96	36.49±2.51	0.002
Maternal characteristics				
Age (year)	29.72±5.78	30.53±5.51	28.50±6.03	0.085
Weight (kg)	76.92±11.03	75.51±12.03	79.04±10.65	0.233
Height (m)	1.64±0.71	1.65±0.68	1.63±0.74	0.913
Cigarette smoker, n (%)	0	0	0	-
Obstetric history, n (%)				
Parous	55 (55)	36 (60)	19 (47.5)	0.397
Nulliparous	45 (45)	24 (40)	21 (52.5)	
Adverse pregnancy outcome, n (%)				
Preeclampsia	3 (3)	0	3 (7.5)	0.047
Gestational diabetes	9 (9)	8 (13.3)	1 (2.5)	
Hypertension	3 (3)	0	3 (7.5)	
Hypertension with preeclampsia	2 (2)	0	2 (5)	
IUGR	4 (4)	1 (1.7)	3 (7.5)	
Mode of delivery, n (%)				
Natural vaginal delivery	75 (75)	47 (78.3)	28 (70)	0.357
Cesarean section	25 (25)	13 (21.7)	12 (30)	
Newborn characteristics				
Sex, n (%)				
Boy	61 (61)	31 (51.7)	30 (75)	0.012
Girl	39 (39)	29 (48.3)	10 (25)	
Weight (g)	2911.00±677.004	3236.50±592.64	2422.75±473.95	<0.001
Admission to the NICU, n (%)	13 (13)	4 (6.7)	9 (22.5)	0.021

GA: Gestational age, IUGR: Intrauterine growth restriction, UtA-PI: Uterine artery pulsatility index, NICU: Neonatal Intensive Care Unit

specificity of this index for identification of adverse perinatal outcome were equal to 37.5% and 73.3% respectively; thereby, the possibility of high UtA-PI would be as a diagnostic criterion to identify adverse perinatal outcome, which is ruled out statistically significant (area under the curve = 0.554, P = 0.360) [Figure 1].

Furthermore, the results from the assessment of adverse perinatal outcome with high UtA-PI suggested that, in general terms, in the current study, there were no 5-min Apgar score <7, abnormal umbilical arterial and venous cord blood pH, and stillbirth while all pregnancies resulted in live birth. The newborns with a birth weight <2500 g in high UtA-PI group and normal UtA-PI group were 57.5% and 13.3%, respectively; however, SGA in high UtA-PI group showed the highest incidence for both cesarean and normal deliveries (SGA: odds ratio [confidence interval 95%] = 8.794 [3.323–23.272], P < 0.001). Furthermore, overall, the incidence of PE observed in five cases. Of these five cases in high UtA-PI group, there were 2 (5%) and 3 (7.5%) cases with gestational age <37 weeks and with gestational age ≥37 weeks, respectively (P > 0.05) [Table 2].

Discussion

In developing countries, there is a high prevalence of adverse perinatal outcomes, of which perinatal mortality is indicative of health development in the country. In the
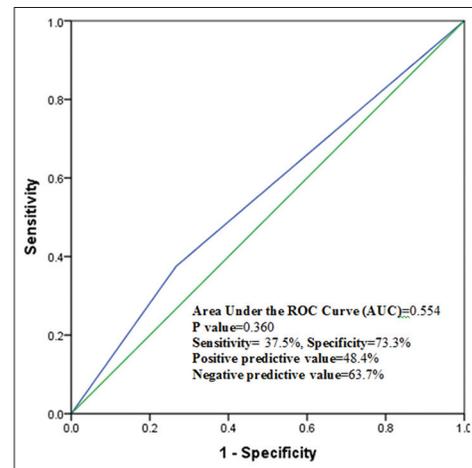

Figure 1: The receiver operating characteristic curve used to assess diagnostic value of high uterine artery pulsatility index in prediction of adverse perinatal outcome

recent decade, Doppler ultrasound has been identified as a part of examination in midwifery. Due to the incidence of hemodynamic changes in uteroplacental vessels and fetus before clinical incidence of midwifery complications, the placental and fetal immaturity could be diagnosable through blood flow measurement. Doppler ultrasound can be applied for IUGR and oligohydramnios, but it is not a routine approach to screen high-risk pregnancies. Doppler ultrasound is used as a simple nonintensive

Table 2: Comparison of adverse perinatal outcome between normal and high uterine artery pulsatility index groups

Perinatal outcome	Totally (n=100), n (%)	Normal (n=60), n (%)	UtA-PI >95th centile (n=40), n (%)	P
Preeclampsia	5/100 (5)	0/60 (0)	5/40 (12.5)	0.686
Preeclampsia with delivery <37 weeks	2/100 (2)	0/60 (0)	2/40 (5)	0.158
Preeclampsia with delivery ≥37 weeks	3/100 (3)	0/60 (0)	3/40 (7.5)	0.273
SGA	31/100 (31)	8/60 (13.3)	23/40 (57.5)	<0.001
SGA and cesarean section for fetal distress	12/100 (12)	1/60 (1.7)	11/40 (27.5)	<0.001
SGA and vaginal delivery	19/100 (19)	7/60 (11.7)	12/40 (30)	0.036
PTL	2/100 (2)	0/60 (0)	2/40 (5)	0.158
Abruption	2/100 (2)	0/60 (0)	2/40 (5)	0.158
ROM	2/100 (2)	2/60 (3.3)	0/40 (0)	0.515
Abnormal amniotic fluid	3/100 (3)	1/60 (1.7)	2/40 (5)	0.562
Stillbirth	0/100 (0)	0/60 (0)	0/40 (0)	-
Arterial pH ≤7.0 or venous pH ≤7.1	0/100 (0)	0/60 (0)	0/40 (0)	-
5-min Apgar <7	0/100 (0)	0/60 (0)	0/40 (0)	-

SGA: Small-for-gestational age with birth weight <10th percentile, PTL: Preterm labor, ROM: Rupture of membranes, UtA-PI: Uterine artery pulsatility index

approach to distinguish high-risk pregnancies from low-risk pregnancies. It can reduce perinatal mortality by 50% in high-risk pregnancies. Today, adverse fetal condition can be recognizable through assessing Doppler indices of middle cerebral artery (MCA) and umbilical artery (UMA). The novelty of this study is the assessment of UtA due to existing limited studies with contradictory results.

The results of the current study showed that high UtA-PI at 30–34 weeks' gestation has been associated with adverse pregnancy outcome, number of male newborns, and low birth weight. The birth weight in high UtA-PI group was <2500 g whereas in normal UtA-PI group was >3000 g, and the percentage of male newborns was higher than normal UtA-PI group as well. However, overall, 31% of pregnant women participating in the study have experienced adverse prenatal outcome, of which 21% result in male newborns and 10% lead to female newborns.

In this respect, considering the vulnerability of male newborns, the "male fetuses" will need more prenatal care because some studies expressed that perinatal mortality and low birth weight are more common in male newborns compared to female newborns.[25,26]

In the current study, high UtA-PI has no acceptable diagnostic value in the prediction of adverse perinatal outcome since its sensitivity and specificity were 37.5% and 73.3%, respectively. Contrary to many studies in which PI and RI, as the critical and useful factors in Doppler ultrasound, are identified as appropriate criteria in the prediction of adverse perinatal outcome, high-risk pregnancies and etc., in this study the mean of each of these criteria has been measured and showed that PI can be used as an appropriate predictor at the second trimester of pregnancy; since this criterion has a high specificity as well as an acceptable sensitivity compared to RI, in prediction of high-risk pregnancies and PE complications.[18,27,28]

In agreement with this study, Gomez-Roig et al. on 156 complicated pregnancies and 344 uncomplicated pregnancies found that UtA-PI measurement alone can be identified as a poor predictor for early diagnosis of adverse perinatal outcome caused by IUGR in the third trimester of pregnancy although more precise assessment revealed that its diagnostic value can be acceptable in this respect if it was accompanied by the measurement of serum level of PIGF.[24]

Contrary to the current study, Valiño et al., in their study of 30,780 singleton pregnancies at 30–34 weeks to evaluate high UtA-PI in prediction of each perinatal outcome, found out that high UtA-PI at 30–34 weeks' gestation may well predict adverse perinatal outcome while pregnancies result in SGA newborns; however, in the absence of SGA, it could not predict adverse outcome well.[23]

Furthermore, Rani et al. in their study on 223 pregnant women composed of preeclampsia group (n = 115) and control group (n = 108) demonstrated that maximum specificity (97%–98%) among all MCA and UMA Doppler indices was observed in MCA/UMA PI and RI ratios and UMA RI, despite their poor sensitivity (9.3%–17.6%) in the prediction of adverse perinatal outcome.[29]

Hofstaetter et al. in their study of 110 uncomplicated pregnancies suggested that increased UtA score had been associated with increased risk of adverse outcome. They concluded that the unilateral notch can be considered as a better predictor of the perinatal outcome than the unilateral high PI.[30]

In other studies, it has been expressed that high PI value representing high resistance on the one side of the uterine circulation has been in association with increased risk of adverse outcome.[31-34]

Therefore, overall, through transabdominal ultrasound and analysis of calculated indices, the status of blood flow in

UtAs can be examined to a great extent and it seems that high-risk pregnancies can be assessed by using Doppler ultrasound. Although, in this study, high UtA-PI was not identified as an acceptable predictor, this could be achieved due to some limitations including small sample size or low incidence of adverse perinatal outcome.

In this study, the incidence of complications such as decollement, rupture of membranes, abnormal amniotic fluid, and PTL was very low, and there was no difference between two groups in this respect. However, newborns with SGA were observed in high UtA-PI group and normal UtA-PI group in 57.5% and 13.3% of cases, respectively ($P < 0.001$). However, among pregnancies with high UtA-PI, the PE occurred in gestational age <37 weeks although, among pregnancies with normal UtA-PI, the PE was observed in gestational age ≥37 weeks.

In line with this study, Mitao *et al*. (2016) in their study of 37,799 singleton births suggested that low birth weight is associated with adverse perinatal outcome. Therefore, early identification of risk factors of low birth weight through prenatal surveillance of high-risk pregnant women can be useful in the prevention of these adverse perinatal outcomes.[35]

Furthermore, in many other studies, the incidence of complications including PE, IUGR, SGA, and prenatal mortality in the group with abnormal RI or PI has been reported higher compared to normal group. In fact, PE occurs with reduced organ perfusion following a severe vasospasm and, therefore, appears to be associated with high UtA-PI. This conflict and lack of significant difference between the incidence of PE and the UtA-PI status in the current study may be achieved due to small sample size and its low incidence since in some studies has been stated that indices of RI, PI, and notch at the first and second trimester can be useful in the prediction of PE.[23,34,36,37]

Conclusion

Finally, it can be concluded that although high UtA-PI in the current study could not be identified as an acceptable criterion in the prediction of adverse perinatal outcome, substantial proportion of incidence of some adverse including SGA or PE, birth of male newborn, and adverse pregnancy outcome were observed in pregnancies with high UtA-PI. Therefore, according to the results of this study and conflicting results of previous studies representing PI as a preferred criterion in the examination of pregnant women particularly at second trimester that is more valuable if it is performed with prediastolic notch assessment and the use of other indices including end-diastolic velocity, peak systolic velocity, and RI to identify adverse perinatal outcome and high-risk pregnancies, it seems that more studies with larger sample size in this regard are required.

Conflicts of interest

There are no conflicts of interest.

References

1. Khong TY, De Wolf F, Robertson WB, Brosens I. Inadequate maternal vascular response to placentation in pregnancies complicated by pre-eclampsia and by small-for-gestational age infants. Br J Obstet Gynaecol 1986;93:1049-59.
2. Pijnenborg R, Anthony J, Davey DA, Rees A, Tiltman A, Vercruysse L, *et al*. Placental bed spiral arteries in the hypertensive disorders of pregnancy. Br J Obstet Gynaecol 1991;98:648-55.
3. Poon LC, Syngelaki A, Akolekar R, Lai J, Nicolaides KH. Combined screening for preeclampsia and small for gestational age at 11-13 weeks. Fetal Diagn Ther 2013;33:16-27.
4. Tayyar A, Garcia-Tizon Larroca S, Poon LC, Wright D, Nicolaides KH. Competing risk model in screening for preeclampsia by mean arterial pressure and uterine artery pulsatility index at 30-33 weeks' gestation. Fetal Diagn Ther 2014;36:18-27.
5. Bakalis S, Stoilov B, Akolekar R, Poon LC, Nicolaides KH. Prediction of small-for-gestational-age neonates: Screening by uterine artery Doppler and mean arterial pressure at 30-34 weeks. Ultrasound Obstet Gynecol 2015;45:707-14.
6. Severi FM, Bocchi C, Visentin A, Falco P, Cobellis L, Florio P, *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;19:225-8.
7. Li H, Gudnason H, Olofsson P, Dubiel M, Gudmundsson S. Increased uterine artery vascular impedance is related to adverse outcome of pregnancy but is present in only one-third of late third-trimester pre-eclamptic women. Ultrasound Obstet Gynecol 2005;25:459-63.
8. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. BJOG 2009;116:424-30.
9. Shwarzman P, Waintraub AY, Frieger M, Bashiri A, Mazor M, Hershkovitz R, *et al*. Third-trimester abnormal uterine artery Doppler findings are associated with adverse pregnancy outcomes. J Ultrasound Med 2013;32:2107-13.
10. Figueras F, Savchev S, Triunfo S, Crovetto F, Gratacos E. An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome. Ultrasound Obstet Gynecol 2015;45:279-85.
11. Department of Measurement and Health Information Systems (MHI), Evidence and Information for Policy (EIP). WHO Under-Five Mortality. Unpublished Country Estimates Computed for the World Health Report 2005. Geneva: World Health Organization; 2004.
12. Bayou G, Berhan Y. Perinatal mortality and associated risk factors: A case control study. Ethiopian J Health Sciences 2012;22:153-62.
13. National Statistical Service (Armenia)/Ministry of Health (Armenia)/ORC Macro. Armenia Demographic and Health Survey (ADHS) 2000. Yerevan/Calverton, MD: National Statistical Service/ORC Marco; 2001.
14. World Health Organization. WHO Mortality Database. Geneva: World Health Organization; 2003. Available from: http://www.who.int/whosis. [Last accessed on 2007 Apr 04].

15. Campbell S, Diaz-Recasens J, Griffin DR, Cohen-Overbeek TE, Pearce JM, Willson K, *et al.* New Doppler technique for assessing uteroplacental blood flow. Lancet 1983;1:675-7.

16. Deurloo KL, Spreeuwenberg MD, Bolte AC, Van Vugt JM. Color Doppler ultrasound of spiral artery blood flow for prediction of hypertensive disorders and intra uterine growth restriction: A longitudinal study. Prenat Diagn 2007;27:1011-6.

17. Fratelli N, Rampello S, Guala M, Platto C, Frusca T. Transabdominal uterine artery Doppler between 11 and 14 weeks of gestation for the prediction of outcome in high-risk pregnancies. J Matern Fetal Neonatal Med 2008;21:403-6.

18. Meler E, Figueras F, Mula R, Crispi F, Benassar M, Gómez O, *et al.* Prognostic role of uterine artery Doppler in patients with preeclampsia. Fetal Diagn Ther 2010;27:8-13.

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;193:429-36.

20. Papageorghiou AT, Roberts N. Uterine artery Doppler screening for adverse pregnancy outcome. Curr Opin Obstet Gynecol 2005;17:584-90.

21. Papageorghiou AT, Yu CK, Cicero S, Bower S, Nicolaides KH. Second-trimester uterine artery Doppler screening in unselected populations: A review. J Matern Fetal Neonatal Med 2002;12:78-88.

22. Ghi T, Contro E, Youssef A, Giorgetta F, Farina A, Pilu G, *et al.* Persistence of increased uterine artery resistance in the third trimester and pregnancy outcome. Ultrasound Obstet Gynecol 2010;36:577-81.

23. Valiño N, Giunta G, Gallo DM, Akolekar R, Nicolaides KH. Uterine artery pulsatility index at 30-34 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol 2016;47:308-15.

24. Gomez-Roig MD, Mazarico E, Sabria J, Parra J, Oton L, Vela A, *et al.* Use of placental growth factor and uterine artery Doppler pulsatility index in pregnancies involving intrauterine fetal growth restriction or preeclampsia to predict perinatal outcomes. Gynecol Obstet Invest 2015;80:99-105.

25. Peacock JL, Marston L, Marlow N, Calvert SA, Greenough A. Neonatal and infant outcome in boys and girls born very prematurely. Pediatr Res 2012;71:305-10.

26. Pongou R. Why is infant mortality higher in boys than in girls? A new hypothesis based on preconception environment and evidence from a large sample of twins. Demography 2013;50:421-44.

27. Arias F. Accuracy of the middle-cerebral-to-umbilical-artery resistance index ratio in the prediction of neonatal outcome in patients at high risk for fetal and neonatal complications. Am J Obstet Gynecol 1994;171:1541-5.

28. Rai L, Lekshmi S. Value of third trimester uterine artery Doppler in high-risk pregnancies for prediction of adverse perinatal outcome. J South Asian Fed Obstet Gynecol 2010;2:31-5.

29. Rani S, Huria A, Kaur R. Prediction of perinatal outcome in preeclampsia using middle cerebral artery and umbilical artery pulsatility and resistance indices. Hypertens Pregnancy 2016;35:210-6.

30. Hofstaetter C, Dubiel M, Gudmundsson S, Marsal K. Uterine artery color Doppler assisted velocimetry and perinatal outcome. Acta Obstet Gynecol Scand 1996;75:612-9.

31. Zimmermann P, Eiriö V, Koskinen J, Kujansuu E, Ranta T. Doppler assessment of the uterine and uteroplacental circulation in the second trimester in pregnancies at high risk for pre-eclampsia and/or intrauterine growth retardation: Comparison and correlation between different Doppler parameters. Ultrasound Obstet Gynecol 1997;9:330-8.

32. McCowan LM, Ritchie K, Mo LY, Bascom PA, Sherret H. Uterine artery flow velocity waveforms in normal and growth-retarded pregnancies. Am J Obstet Gynecol 1988;158:499-504.

33. Grunewald C, Kublickas M, Nisell H, Nylund L, Westgren M. The interpretation of uterine artery pulsatility index in normal and hypertensive pregnancy. Ultrasound Obstet Gynecol 1994;4:476-9.

34. Frusca T, Soregaroli M, Zanelli S, Danti L, Guandalini F, Valcamonico A, *et al.* Role of uterine artery Doppler investigation in pregnant women with chronic hypertension. Eur J Obstet Gynecol Reprod Biol 1998;79:47-50.

35. Mitao M, Philemon R, Obure J, Mmbaga BT, Msuya S, Mahande MJ. Risk factors and adverse perinatal outcome associated with low birth weight in Northern Tanzania: A registry-based retrospective cohort study. Asian Pac J Reprod 2016;5:75-9.

36. Ebrashy A, Azmy O, Ibrahim M, Waly M, Edris A. Middle cerebral/umbilical artery resistance index ratio as sensitive parameter for fetal well-being and neonatal outcome in patients with preeclampsia: Case-control study. Croat Med J 2005;46:821-5.

37. Zeisler H, Eppel W, Husslein P, Bernaschek G, Deutinger J. Influence of acupuncture on Doppler ultrasound in pregnant women. Ultrasound Obstet Gynecol 2001;17:229-32.