

Relationship between Umbilical Artery Pulsatility Index of Doppler Velocimetry and Umbilical Venous Blood Gases Measured by Cordocentesis

Woo Jin Kim, Syng Wook Kim

*Department of Obstetrics and Gynecology, Seoul National University
College of Medicine, Seoul 110-744, Korea*

= Abstract = Cordocentesis of umbilical vein to obtain fetal blood pH, PCO₂, and PO₂ and Doppler velocimetry as a preceding evaluation procedure were performed in 41 fetuses to assess fetal status in utero. The results of the two evaluation techniques, namely pH, PCO₂ and PO₂ of fetal venous blood and pulsatility index (PI) of Doppler velocimetry, were individually correlated to determine if the procedure of Doppler velocimetry could be performed in lieu of cordocentesis in assessing fetal acid-base status in utero. The indications for cordocentesis were small-for-gestational age fetus (n=9), suspected fetal thrombocytopenia (n=7), isoimmunization (n=5), need for rapid karyotyping (n=2), paternity determination (n=1), cancer chemotherapy (n=1), congenital malformation (n=15), and nonimmune hydrops fetalis (n=1). The prevalence of fetal acidemia was 34% (14/41). There was no significant difference in median gestational age at cordocentesis between patients with acidemic fetus and those with nonacidemic fetus (P<0.5). Significant differences were found in both gas values and PI between acidemic and nonacidemic fetus groups as PI and PCO₂ were significantly higher (P<0.00001, P<0.00001) while PO₂ was significantly lower (P<0.005) in acidemic fetus group. Linear regression lines drawn to see the relationships between PI and pH, PCO₂, PO₂, respectively, showed fair to good relationships with r values of -0.6334, 0.5747 and -0.4699, in the same order, all with significance. In conclusion, it is conceivable that for close and continuous in utero monitoring of hypoxia-complicated fetuses, non-invasive Doppler velocimetry could be performed in place of invasive cordocentesis and also for assisting in decision-making for early delivery to avoid fetal compromise in utero.

Key words : *Cordocentesis, Doppler velocimetry, fetal acid-base status*

INTRODUCTION

Doppler velocimetry and cordocentesis are two of the major modes currently employed to determine fetal well-being in utero. The former is a non-invasive evaluation technique whereas the latter

is an invasive one. Doppler velocimetry makes use of the fact that changes in fetal development are always accompanied by corresponding hemodynamic changes which can be detected by the technique. Determination of fetal blood pH and gas values by cordocentesis is a very objective means of assessing fetal well-being in utero (Silverman *et al.*, 1985). However, invasive nature of the cordocentesis technique limits its applicability to usually evaluation of abnormal fetuses and normal fetuses with various hematologic peculiarities such as Rh- blood typing. The intent of this study was to see if there are any significant relationships between PI of Doppler velocimetry and individual fetal blood gas and pH values obtained by cordocentesis of umbilical vein. If any significant relationships between the results of the two techniques could be found, there would be more freedom of choice in employing either technique without having doubts about the results or both techniques could be performed to strengthen the reliability of the results.

This study was undertaken to find out if there are any significant relationships between pulsatility index of Doppler velocimetry and individual fetal blood gas and pH values obtained by cordocentesis of umbilical vein. If there exists any significant relationship between the results of the two evaluation techniques of fetal well-being, Doppler velocimetry could be employed in place of invasive cordocentesis without having doubts regarding outcome. In addition, the predictive accuracy of Doppler pulsatility index in the diagnosis of unfavorable status of fetal cord blood was assessed by plotting receiver-operator characteristic curves.

MATERIALS AND METHOD

1. Study design

The candidates for the Doppler velocimetry were the patients who were referred to our unit (Seoul National University Hospital) for cordocentesis. The gestational age of the patients ranged from 25 to 40 weeks and those with multiple pregnancy, rupture of membranes, and in labor were excluded from the study group. The indica-

tions for cordocentesis were small-for-gestational age fetus (n=9), suspected fetal thrombocytopenia (n=7), isoimmunization (n=5), need for rapid karyotyping (n=2), paternity determination (n=1), cancer chemotherapy (n=1), congenital malformation (n=15), and nonimmune hydrops fetalis (n=1). A written informed consent was obtained from all the patients prior to performing cordocentesis.

2. Doppler velocimetry

Umbilical artery Doppler studies were performed on a free loop of cord with the use of pulsed Doppler equipment with a 3.5 MHz transducer (Diasonics SPA 1000). A high-pass filter and the sample volume were set at 100 Hz and at 6 to 9 mm respectively. After making at least four separate measurements for each examination, the pulsatility index (PI) of the flow waveform (Maximum velocity-Minimum velocity/Mean velocity) was obtained and the average was used for calculations. The test was performed with the mother in a semirecumbent position and the fetus in a quiet state.

3. Cordocentesis

Umbilical venous blood was obtained directly under the real-time ultrasonography (Aloka model SSD-650) without maternal sedation to be collected into heparinized plastic syringes. The syringes were capped with rubber lids, placed in ice, and blood gas level determinations were completed within 5 minutes. The cord blood gas analysis was performed with an automatic pH and blood gas analyzer (AVL model 995). The fetal origin of the blood sample was confirmed by the Kleihauer-Betke test. Confirmation of venous site sampling was made by ultrasonographic visualization and/or test injection of normal saline solution to see turbulence.

4. Statistical analysis

As values of all the variables concerned, namely PI of Doppler velocimetry, pH, PCO₂, PO₂ of umbilical venous blood, are known to change with gestation, they were expressed in terms of multiples of standard deviation from the mean for the

corresponding or nearest gestational week. The reference range of the Doppler umbilical PI employed was the standard obtained using a Korean population and those of pH and blood gas values were calculated using the equations cited from Ribbert *et al.* (1990). and Salvesen *et al.*, (1991). Fetal acidemia and hypoxia were defined to be venous pH and PO₂ values with a difference below 2SD respectively, while for hypercapnia, it was defined when the difference was greater than above 2SD from the mean for the corresponding gestation.

Statistical analysis was performed by Fisher's exact test for categorical variables or by Student's t test, or Mann-Whitney U test for continuous variables. The relationships between umbilical artery Doppler velocimetry and fetal acidemia, hypercapnia, and hypoxia, respectively were evaluated with linear regression analysis. In addition, receiver-operator characteristic curves were drawn to illustrate the accuracy of PI in predicting the umbilical venous blood acidemia, hypercapnia, and hypoxia.

RESULTS

1. Clinical characteristics of study population

According to the comparison in Table 1, there was no significant difference in gestational age at cordocentesis between the abnormal and normal Doppler pulsatility index groups. However, as shown by the p values, significant differences were found in all three biochemical parameters, namely, pH, PCO₂, and PO₂, of cord blood between the two compared groups.

In the comparison for the delivery outcome, significant differences were found between the two groups both in the birth weight and perinatal death rate, i. e., still birth and neonatal deaths combined.

There were a total of four stillbirths (SB) and eleven neonatal deaths (NND). Three of the four SB cases had both acidemia and abnormal PI while the remaining one had only abnormal PI, but with accompanying hydrops fetalis. Among the four SB cases, the outcome was bad despite

Table 1. Clinical characteristics and delivery outcomes of normal and abnormal Doppler pulsatility index group

	Doppler	Pulsatility Index	P-value
	normal(n = 25)	abnormal(n = 16)	
Cordocentesis			
Gestational age (WK, mean ± SD)	33.9 ± 3.9	32.1 ± 3.0	NS
pH (mean ± SD)	7.37 ± 0.03	7.27 ± 0.11	P < 0.01
PCO ₂ (mmHg, mean ± SD)	39.04 ± 4.83	49.63 ± 16.05	P < 0.05
PO ₂ (mmHg, mean ± SD)	44.08 ± 10.20	33.38 ± 13.96	P < 0.01
Delivery outcome			
Birth weight (gm, mean ± SD)	2707 ± 484*	1751 ± 885	P < 0.0005
Perinatal death (still birth plus neonatal death)	16.7% (4/24)*	68.8% (11/16)	P < 0.005

* : One patient lost in follow-up was excluded.

good body weight in one case, probably explainable by the fact that the mother had severe acute thrombocytopenic purpura and abnormal values for all measured parameters concerned. Of the eleven NND cases, seven had both abnormal PI and acidemia while one had only abnormal PI and the remaining three were affected by less significant hypercapnia only. Further examination of NND cases showed that the majority, i. e. , eight cases, had birth weight over 1500 gm, and of them six had one type of major recognizable anomalies with the presence of ventriculomegaly in three cases being the most frequent. A noteworthy finding is that two of the NND cases without abnormality in either pH or PI were affected with ventriculomegaly in comparison to one case with ventriculomegaly, abnormalities in both pH and PI, and outcome of NND and another ventriculomegaly-associated case without abnormalities in any values and good fetal outcome. There were three cases, all free of anomalies, with good delivery outcome despite abnormalities in both pH and PI.

2. A comparison of acidemic and nonacidemic fetus groups

The prevalence of fetal acidemia was 34% (14/41). There was no significant difference in median gestational age at cordocentesis between patients with acidemic fetus and those with nonacidemic fetus. Significant differences were found, as shown in Table 2, in both gas values and PI between acidemic and nonacidemic fetus groups. While

PCO₂ and PI were significantly higher, PO₂ was significantly lower in acidemic fetus group.

3. The relationships between Doppler PI with the three respective biochemical cord blood values

The relationships between Doppler PI with the three respective biochemical cord blood values are illustrated by linear regression lines in Figs. 1, 2, and 3. The r values between PI and pH, PCO₂, PO₂ respectively were, in the same order, -0.6334,

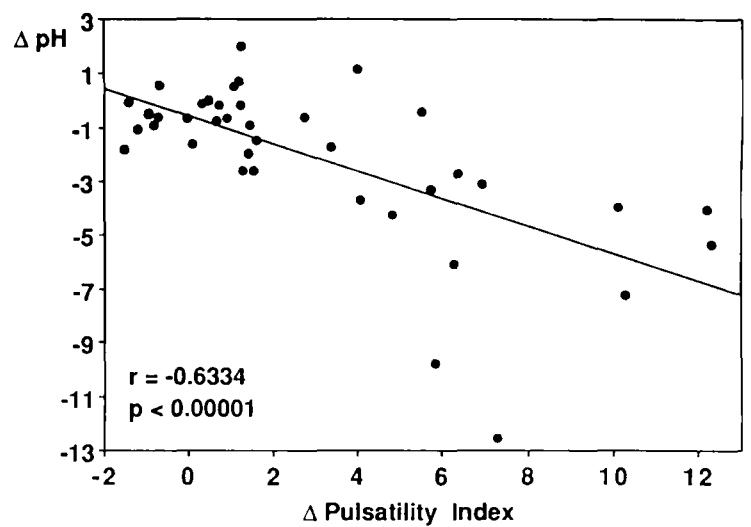


Fig. 1. Relationship between umbilical artery pulsatility index of Doppler velocimetry and degree of fetal acidemia. The values of pH and PI were expressed in terms of multiples of standard deviation from the mean for the corresponding or nearest gestational week.

Table 2. Comparison of acidemic and nonacidemic fetuses in terms of median and range of PI, PCO₂, and PO₂ and corresponding P-values

		Acidemic fetuses(n = 14)	Nonacidemic fetuses(n = 27)	P-value
PI	median	1.92	0.94	P<0.00001
	range	1.0-2.86	0.68-1.87	
PCO ₂	median	48.0	37.0	P<0.00001
	range	40.0-86.0	26.0-47.0	
PO ₂	median	32.5	41.0	P<0.005
	range	2.0-57.0	29.0-69.0	

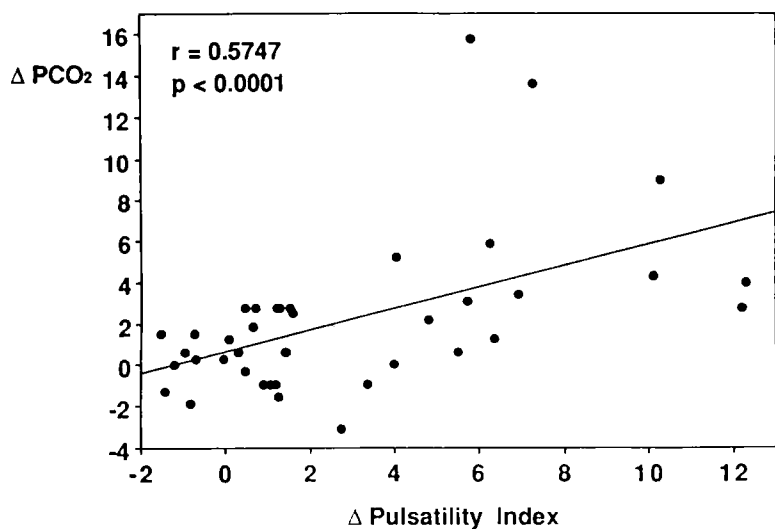


Fig. 2. Relationship between umbilical artery pulsatility index of Doppler velocimetry and degree of fetal hypercapnia. The values of PCO_2 and PI were expressed in terms of multiples of standard deviation from the mean for the corresponding or nearest gestational week.

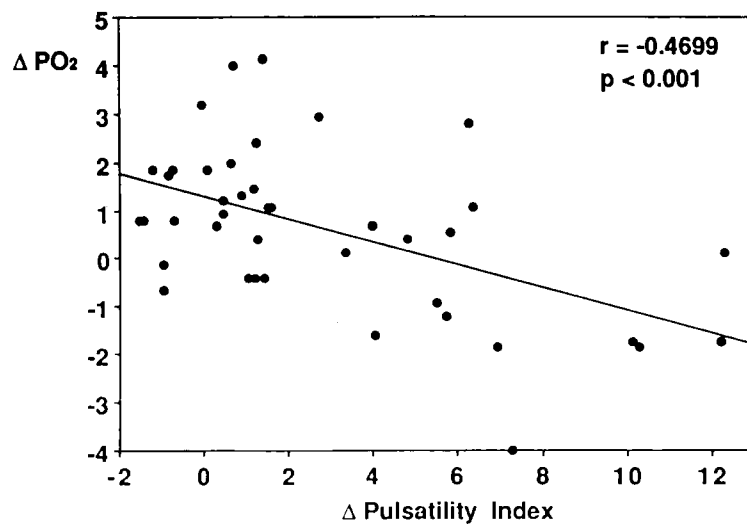
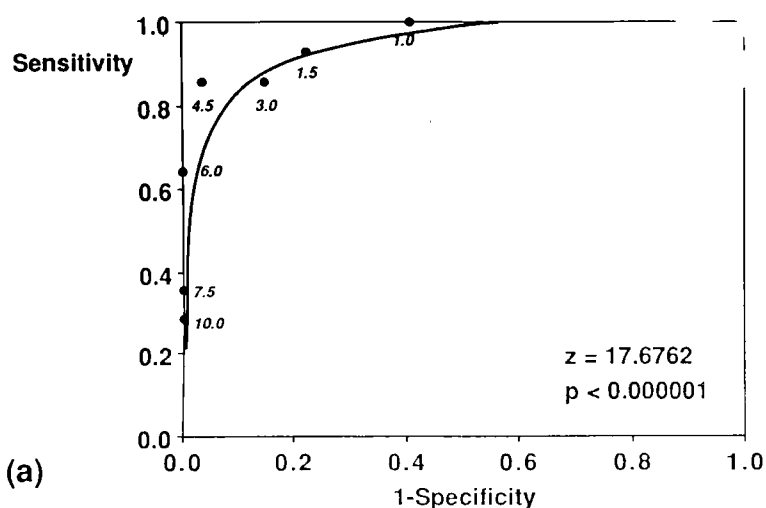
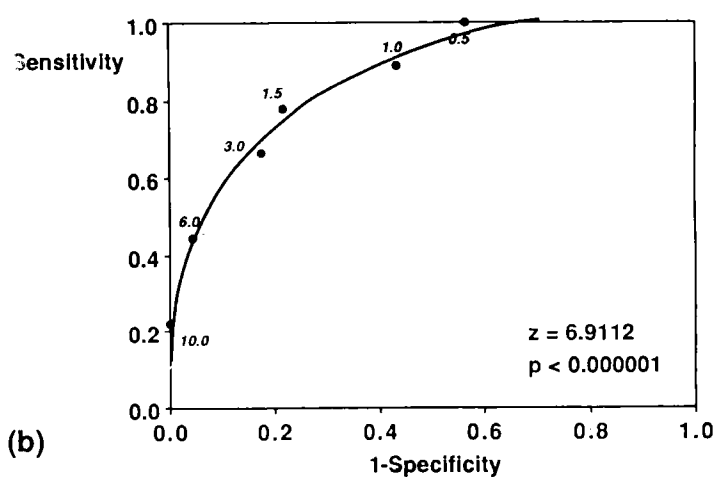


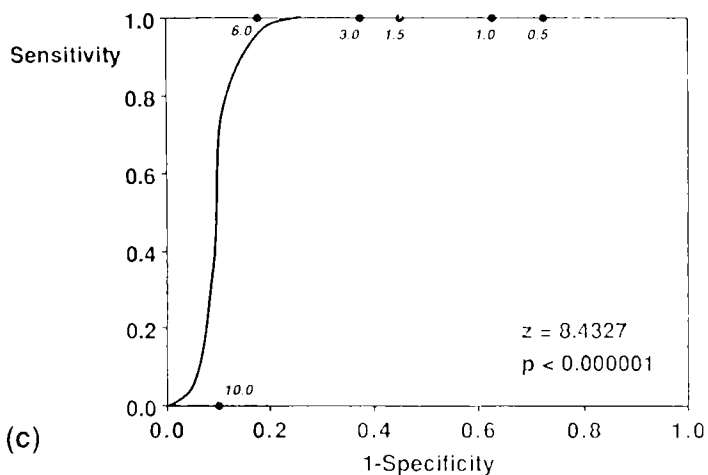
Fig. 3. Relationship between umbilical artery pulsatility index of Doppler velocimetry and degree of fetal hypoxia. The values of PO_2 and PI were expressed in terms of multiples of standard deviation from the mean for the corresponding or nearest gestational week.



(a)



(b)



(c)

4. Receiver-operator characteristic curve analysis of results of umbilical artery Doppler velocimetry (ΔPI) in prediction of fetal acidemia (a), hypercapnia (b), and hypoxia (c). Curves all lie above 45-degree line indicating a higher ΔPI increase the probabilities of fetal acidemia (ΔPI : $z=17.17$, $p<0.000001$), hypercapnia (ΔPI : $z=6.9$, $p<0.000001$) and hypoxia (ΔPI : $z=8.4$, $p<0.000001$).

0.5747, and -0.4699, all with significance. interpretable as having good to fair relationships. In Fig. 4, receiver-operator characteristic curves have been drawn to see the predictive accuracy of Doppler PI in the diagnosis of the three biochemically unfavorable status of fetal cord blood. All three curves are drawn well above the dividing 45-degree line and reflect that the higher the PI, the higher the likelihood of fetal acidemia, hypercapnia, and hypoxia, respectively.

DISCUSSION

In this study, it has been possible to obtain good to fair relationships between PI of Doppler velocimetry and fetal cord blood pH and gas values obtained via cordocentesis, respectively, with a sample of 41 fetuses subjected to both evaluation techniques for diagnostic purpose. There have been many other studies relating the results of these two evaluation techniques, with the majority of them finding some kind of high to significant relationships between indices of Doppler velocimetry and biochemical values of cord blood (Weiner *et al.*, 1990, Ferrazzi *et al.*, 1988, Bilardo *et al.*, 1990, Yoon *et al.*, 1992, Guyot *et al.*, 1992). However, there have also been few studies opposing such a relationship. Vintzileos *et al.*, (1991) had found no significant relationship between S/D and pH, although their study design was different from this one in that their cutoff for the umbilical arterial acidosis was 7.20 whereas a venous pH value 2 SD below the mean for gestational age was the cutoff in this study, and also the constituents of the two study populations were quite different since in this study, congenital anomaly and isoimmunization cases had also been included. Moreover there is another major difference in the methodology of the two studies in that while cordocentesis of this study was performed in utero, i. e. in intact circulation, Vintzileos's cordocenteses were performed at the time of cesarean section, results of which thus obtained could have been affected by various intrapartum changes such as fall in maternal blood pressure which could have had bearing on fetal acidosis but not PI measured prior to Cesarean

section.

In order to more accurately interpret the metabolic status of the fetal tissues, cord arterial blood, biochemical values of which reflect fetal tissue acid-base status, should have been used to obtain fetal blood pH, PCO₂, and PO₂ instead of venous blood, biochemical values of which reflect placental tissue acid-base status (Johnson *et al.*, 1990). However, this was not the case of this study as arterial puncture was not feasible due to technical difficulty and also there were established normal ranges for cord venous blood biochemical values only.

As biochemical values of each blood sample give us only an instantaneous information of fetal status and not the course the fetus will subsequently take, it obviously would seem helpful to obtain serial samples if not for the invasiveness of the procedure; however, with the likelihood of the many strong relationships between indices of Doppler velocimetry and cord blood pH and gas values thus far elucidated (Weiner *et al.*, 1990, Ferrazzi *et al.*, 1988, Bilardo *et al.*, 1990, Yoon *et al.*, 1992, Guyot *et al.*, 1992), Doppler velocimetry measurements could be made in lieu of the invasive cordocentesis for close follow-up of acidotic fetuses.

According to the study of Yoon *et al.*, (1993), there was a stronger relationship with fetal acid-base status in the case of umbilical artery Doppler velocimetry than that between biophysical profile and also it is reported (James *et al.*, 1992) the sequence test results become abnormal are in the order of umbilical artery Doppler velocimetry and then BPP score.

In view of the above-mentioned findings, it would be wise to make follow-up of hypoxic fetus first with Doppler velocimetry, and additionally with BPP.

As stated earlier, anomaly-associated cases have been included in the analysis of this study as this study was concerned with only the relationships between the results of the two procedures and not the outcome at delivery. Although values obtained from the two procedures per individual case has not been displayed by a table, there have been three academic cases among the fif-

teen anomaly-associated cases, with two of them also having abnormal PI values and there were three anomaly-associated cases with only abnormal PI and no acidemia accounting for three of four such cases; but with two cases having good fetal outcome. The latter finding could somewhat have resulted in lowering the correlation between pH and PI. However it would be very difficult to interpret whether anomalies involved somehow had bearing on producing the abnormal PI values.

Although criteria of acidemia is not well defined, clinically significant umbilical arterial pH favored by many is a pH cutoff of 7.20 and 7.26, respectively for arterial and venous blood (Vintzileos *et al.*, 1992) on the basis of fetal outcome and by common practice. Some studies contend that pH cutoff should be even lower, to as low as less than 7.00 (Goldaber *et al.*, 1991). However, this study has shown that even at mild acidotic states, i. e., above the usual cutoff but satisfying the 2SD cutoff ranging from 7.26 to 7.31, the outcomes excluding three anomaly-associated cases were not good as only three of six small for gestational age fetuses were well at delivery. Therefore we cannot easily confine our surveillance to only clearly acidotic fetuses and to further support this, study by Soothill *et al.*, (1992). has shown that, with cord blood acidemia defined to be pH less than 2 SD for gestational age, there was a significant correlation between the degree of fetal acidemia and developmental quotient and suggested that acidemia may be too late in the disease process to be used as an indication for delivery to prevent handicap. The results of this study has provided a good ground to further infer that non-invasive Doppler velocimetry can replace the invasive procedure of cordocentesis, a measure which can best provide us the presence and severity of fetal acidosis, in follow-up of acidemic fetuses, regardless of association with anomaly, who are most likely distressed with hypoxia.

However, there are a few drawbacks associated with the technique of Doppler velocimetry measurements such as lack of extensive study, availability of special equipment, and concerns about accuracy and reproducibility problems in com-

parison to the BPP scoring.

In summary, it is conceivable that for close in utero monitoring of hypoxia-complicated fetuses once confirmed by cordocentesis, Doppler velocimetry could be performed in lieu of repeat cordocentesis and for assisting in decision-making for early delivery to avoid fetal compromise in utero.

CONCLUSION

The results pertaining to the relationship between umbilical artery pulsatility index of Doppler velocimetry and umbilical venous blood gases measured by cordocentesis for the 41 subjects are as follows:

1. Significant differences were found in both gas values and PI between acidemic and nonacidemic fetus groups. In acidemic fetus group, PI and PCO_2 were significantly higher ($P < 0.00001$, $P < 0.00001$) while PO_2 was significantly lower ($P < 0.005$).

2. The relationships between Doppler PI and the three respective biochemical cord blood values reflected by r values of linear regression lines, which were -0.6334 ($P < 0.00001$), 0.5747 ($P < 0.0001$), and -0.4699 ($P < 0.001$) in the order of pH, PCO_2 and PO_2 , were interpretable as good to fair.

3. The receiver-operator characteristic curves drawn to see the predictive accuracy of PI for umbilical venous blood acidemia, hypercapnia, and hypoxia, respectively, were drawn above the dividing 45-degree line to infer that the higher the PI, the higher the likelihood of fetal acidemia, hypercapnia, and hypoxia, respectively. In this study, it has been possible to obtain good to fair relationship between PI of Doppler velocimetry and fetal cord blood pH and gas values, respectively and that increase in Doppler PI increases the likelihood of fetal acidemia, hypercapnia and hypoxia. From the results, it is further conceivable that for close and continuous in utero monitoring and for decision-making for possible early delivery of hypoxia-complicated fetuses, non-invasive Doppler velocimetry could provide very useful information to or be performed in place of invasive cordocentesis.

REFERENCES

- Bilardo CM, KH Nicolaidis, Campbell S. Doppler measurements of fetal and uteroplacental circulations: Relationship with umbilical venous blood gases measured at cordocentesis. *Am J Obstet Gynecol* 1990,162:115-20.
- Ferrazzi E, Pard G, Bauscaglia M, Marconi AM, Gementi B, Bellotti M, Makowski EL, Battaglia FC. The correlation of biochemical monitoring versus umbilical flow velocity measurements of the human fetus. *Am J Obstet Gynecol* 1988, 159:1081-7
- Goldaber KG, Gilstrap LC, Leveno KJ, Dax JS, McIntire DD. Pathologic fetal acidemia. *Obstet Gynecol* 1991, 78:1103-7
- James DK, Parker MJ, Smoleniec JS. Comprehensive fetal assessment with three ultrasonographic characteristics. *Am J Obstet Gynecol* 1992, 166:1486-95
- Johnson JWC, Richards DS, Wagaman RA. The case for routine umbilical blood acid-base studies at delivery. *Am J Obstet Gynecol* 1990. 162: 621-5
- Ribbert LSM, Snijder RJM, Nicolaidis KH, Visser GHA. Relationship of fetal biophysical profile and blood gas values at cordocentesis in severely growth-retarded fetuses. *Am J Obstet Gynecol* 1990, 163:569-71
- Salvesen DR, Brudenell MJ, Nicolaidis KH. Fetal polycythemia and thrombocytopenia in pregnancies complicated by maternal diabetes mellitus. *Am J Obstet Gynecol* 1992, 166:1289-93
- Silverman F, Suidan J, Wasserman J, Antoine C, Young BK. The Apgar score: is it enough? *Obstet Gynecol* 1985, 66:331-6
- Soothill PW, Ajayi RA, Campbell S, *et al.*, Relationship between fetal acidemia at cordocentesis and subsequent neurodevelopment. *Ultrasound Obstet Gynecol* 1992, 2:80-3
- Vintzileos AM, Campbell WA, Rodis JF, McLean DA, Fleming AD, Scorza WE. The relationship between fetal biophysical profile assessment, umbilical artery velocimetry, and fetal acidosis. *Obstet Gynecol* 1991, 77:622-6
- Vintzileos AM, Egan JFX, Campbell WA, *et al.*, Asphyxia at birth as determined by cord blood pH measurements in preterm and term gestations: correlation with neonatal outcome. *Journal of Maternal Fetal Medicine* 1992, 1:7
- Weiner CP. The relationship between the umbilical artery systolic/diastolic ratio and umbilical blood gas measurement in specimens obtained by cordocentesis. *Am J Obstet Gynecol* 1990, 162:1198-202
- Yoon BH, Syn HC, Kim SW. The efficacy of Doppler umbilical artery velocimetry in identifying fetal acidosis: a comparison with fetal biophysical profile. *J Ultrasound Med* 1992, 11:1-6
- Yoon BH, Romero R, Roh CR, Kim SH, Ager JW, Syn HC, Cotton D, Kim SW. Relationship between the fetal biophysical profile score, umbilical artery Doppler velocimetry, and fetal blood acid-base status determined by cordocentesis. *Am J Obstet Gynecol* 1993, 169:1586-94