Fetal and placental Doppler velocimetry in hypertensive pregnant women and perinatal outcomes according to gestational age*

Dopplervelocimetria fetoplacentária em gestantes hipertensas e resultados perinatais segundo a idade gestacional

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Abstract **OBJECTIVE: To evaluate the pulsatility index of umbilical artery (UAPI) and middle cerebral artery (MCAPI), as well as the umbilical-cerebral pulsatility (UAPI/MCAPI) ratio in fetuses of hypertensive pregnant women and associated adverse perinatal outcomes. MATERIALS AND METHODS: The authors have analyzed UAPI, MCAPI and UAPI/MCAPI ratio in 289 fetuses of hypertensive women, correlating the results with the presence of adverse perinatal outcomes. Results were compared with and without adjustment for gestational age. RESULTS: Apgar score < 7 at the 5th minute was associated with altered outcomes after adjustment for gestational age. The risk for small-for-gestational-age infant increased three times after such adjustment, with statistical significance for all the Doppler parameters. The increase in risk for neonatal hypoxia after adjustment for gestational age was statistically significant for UAPI and UAPI/MCAPI ratio. No increase was observed in the risk for respiratory distress syndrome in the adjusted analysis. A three-time higher risk for perinatal mortality and altered UAPI with statistical significance was observed after adjustment. CONCLUSION: In fetuses of hypertensive pregnant women, UAPI demonstrated better correlations with perinatal outcomes than MCAPI and UAPI/MCAPI ratio. The risk for adverse gestational outcome should be evaluated taking the gestational age into consideration.**

Keywords: Doppler velocimetry; Hypertension; Perinatal outcome.

Resumo **OBJETIVO: Avaliar índices de pulsatilidade das artérias umbilical (IPAU) e cerebral média (IPACM) e relação do índice de pulsatilidade umbilico-cerebral (IPAU/IPACM) em fetos de gestantes hipertensas e presença de resultados perinatais adversos. MATERIAIS E MÉTODOS: Analisamos IPAU, IPACM e IPAU/IPACM de 289 fetos de gestantes hipertensas quanto à previsão dos resultados perinatais adversos. Os resultados foram comparados sem e com ajuste pela idade gestacional. RESULTADOS: O índice de Apgar < 7 no 5º minuto foi associado com resultados alterados após o ajuste por idade gestacional. O risco para recém-nascidos pequenos para a idade gestacional aumentou em três vezes após o ajuste, com significância estatística em todos os parâmetros do Doppler. Na síndrome da hipóxia neonatal o aumento do risco ajustado pela idade gestacional foi estatisticamente significante no IPAU e IPAU/IPACM. Não houve aumento no risco de síndrome do desconforto respiratório na análise ajustada. A mortalidade perinatal e o IPAU alterado apresentaram um risco três vezes maior e foram estatisticamente significantes após o ajuste. CONCLUSÃO. Em gestantes hipertensas, o IPAU apresentou melhor correlação com os resultados perinatais do que o IPACM ou relação IPAU/IPACM. O risco de resultados adversos deve considerar a idade gestacional.**

Unitermos: Dopplervelocimetria; Hipertensão; Resultados perinatais.

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INTRODUCTION

Currently, one of the main preoccupations in obstetrics is to assure good vitality conditions for the fetus at risk. Such preoccupation is even greater in the presence of maternal diseases that are known to cause placental insufficiency and intrauterine growth restriction (IUGR) as is the case, mainly, of arterial hypertension(1). This is the clinical entity that is mostly associated with IUGR and placental insufficiency(2–7).

The Doppler technique allows the noninvasive study of the uterine and

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fetoplacental circulation, allowing the early diagnosis of hypoxia states and the prediction of adverse perinatal outcomes[6,8-10].

The Doppler scan allows the analysis of the main vessels resistance index, with the most utilized ones being the umbilical artery and the middle cerebral artery[11–14]. In the compensation phase of hypoxia, the placental resistance increases and the umbilical arteries resistance indices rise. Subsequently, a progressive reduction of the cerebral vascular resistance is observed, progressing to "centralization". Such phenomenon precedes severe fetal involvement by 10 to 12 days, with fetal acidosis and higher perinatal morbimortality[6].

Alterations in the Doppler pattern of the umbilical artery, particularly absent or reversed diastolic flow, are indicative of placental dysfunction[15], with high risk of fetal distress and, particularly, vulnerability to prematurity complications[16], which determines a balance between fetal risk *versus* neonatal risk in the identification of the appropriate moment for intervention[17–19].

For some authors, obstetric management is still predominantly based on the umbilical artery Doppler analysis[4,18,20–22], although some studies point towards the inclusion of more than one vessel in the assessment of vitality of fetuses at risk[7,23].

It is important to highlight that severe dopplervelocimetric alterations indicative of intensive fetal monitoring or interruption occur in premature fetuses, particularly in cases of extreme prematurity[24].

With the purpose of clarifying the capability of different Doppler indicators to predict the risk of perinatal complications, the authors have simultaneously evaluated the risk of bad perinatal outcomes in the presence of dopplervelocimetric changes in the umbilical artery, middle cerebral artery and in the umbilical-cerebral indices. At the same time, the authors have evaluated the occurrence of substantial changes in results after control according to gestational age at birth.

MATERIALS AND METHODS

The initial series comprised 497 hypertensive pregnant women in the period from January 2002 to August 2006. For the studies of the fetoplacental circulation, a Shimadzu ultrasonography unit model SDU-2200 (Shimadzu; Kyoto, Japan) with a Doppler device with color blood flow mapping and a 3.5 MHz convex transducer, was utilized. The window filter was set between 50 and 100 Hz. With the patient lying in semi-Fowler position and in the absence of body motion and fetal breathing movements, utilizing real-time images, the blood flow color mapping was initiated, thus obtaining the color mapping of the vessels to be studied, which were evaluated by means of the Doppler device, with adjustments of the sample volume for each vessel, in the absence of fetal movements.

The Doppler scan of the umbilical artery was performed in open loop, close to the placental insertion and insonation angle always below 60°. The spectral analysis was considered appropriate in cases where at least three similar velocity waves were observed in the same spectrum (Figure 1). The analysis was considered as abnormal in cases where the diastole was absent or reversed in the umbilical artery, or the pulsatility index was above the 95th percentile[25].

The middle cerebral artery was visualized from the circle of Willis and was insonated immediately after its origin in the internal carotid artery. The angle between the sound beam and the flow was captured the closest possible to 0°, with the pulsatility index being measured (Figure 2). A middle cerebral artery pulsatility index (MCAPI) < 5th percentile and umbilical artery/cerebral artery (UAPI/MCAPI) ratio > 95th percentile for the gestational age were considered as abnormal[25].

Exclusion criteria were the following: cases with intervals between the last dopplervelocimetric study and the labor > 7 days, absence of data on perinatal outcomes at birth, presence of congenital defects or fetal or neonatal chromosomal abnormalities, maternal disease leading to congenital infection, and gestational age at birth < 24 weeks. With these criteria, 208 patients were excluded, so the final sample included the remaining 289 pregnant women.

The software EPI-Info, version 1.0 was utilized for data organization. The cases were divided into three gestational age groups (< 33 weeks, 33 to 36 weeks and ≥ 37 weeks) and classified according to the presence or absence of each adverse perinatal outcome as follows: Apgar score at the 5th minute < 7; newborn small for gestational age (SGA); occurrence of neonatal hypoxic-ischemic syndrome (HIS); occurrence of respiratory distress syndrome (RDS) and perinatal death.

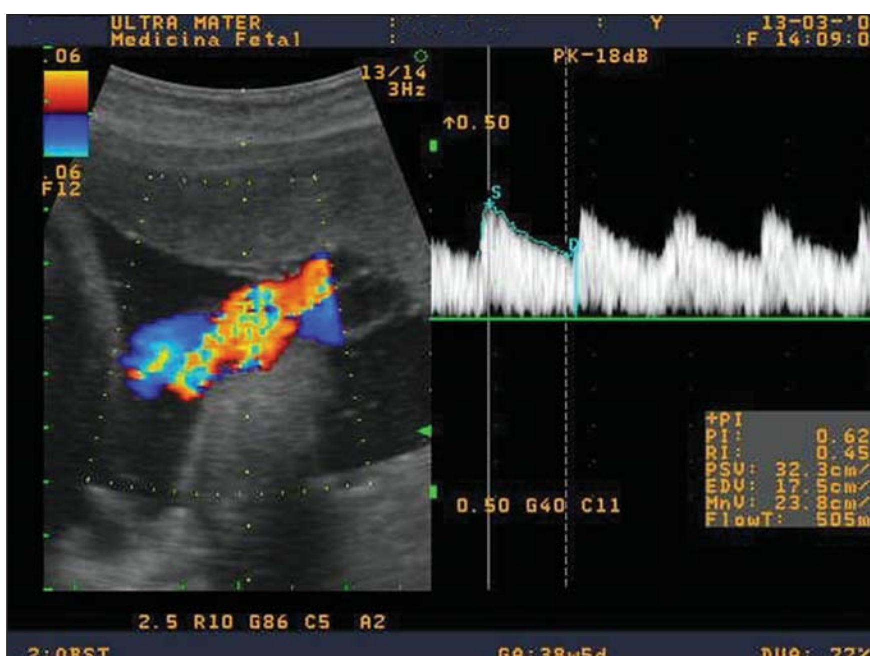

Figure 1. Doppler velocimetry of the umbilical artery close to the placental insertion.

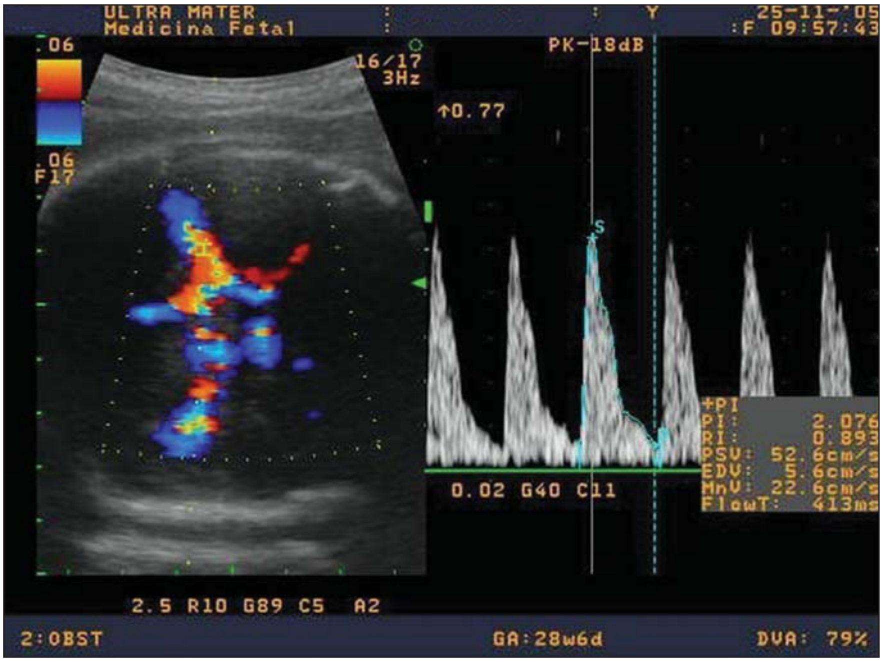

Figure 2. Doppler velocimetry of the cerebral artery visualized from the circle of Willis and insonated immediately after its origin in the internal carotid artery. The angle between the sound beam and the flow was captured as close as possible to 0°.

A prospective analysis of risk of bad perinatal outcomes calculated by the relative estimated risk (*odds ratio*) of the studied outcomes was performed, in accordance with results of Doppler velocimetry performed up to seven days before the labor. Later, the same calculation was carried out, this time adjusted according to gestational age.

The present study was developed in compliance with Resolution 196/1996 of Conselho Nacional de Saúde (Brazilian Council of Health), and the recommendations of the Helsinki Declaration VI for research with humans, and was duly submitted and approved by the Committee for Ethics in Research of Centro Integrado de Saúde Amaury de Medeiros of Universidade de Pernambuco.

RESULTS

Sample characteristics

The patients' ages ranged from 14 to 43 years (mean age, 26 years); with respect to parity, 57.1% of the women were primigravidas. Nearly two thirds of cases corresponded to preeclampsia. Vaginal deliveries comprised only 25.6% of the cases. The last Doppler scan was performed up to one day before delivery in 51.2% of the cases (Table 1).

In almost two thirds of the cases the newborns were preterm, and among them 27.7% had less than 33 weeks of gestational age at birth. The newborns weight ranged from 550 g to 4,580 g. In 21.5%, the Apgar scores were < 7 at the 5th minute, and 31.5% of the cases were SGA. Almost 20% of the neonates presented HIS and 16%, RDS. Fetal death occurred in 2%, and neonatal death in 6.5% of cases (Table 2).

Association between the dopplervelocimetric results and perinatal outcomes

No association was observed between UAPI, MCAPI and of the UAPI/MCAPI ratio and Apgar score < 7 at the 5th minute before the adjustment for gestational age. After the adjustment, the risk of Apgar < 7 at the 5th minute was more than two times and almost twice higher in fetuses in whom the UAPI and MCAPI, respectively, were altered. However, only the association with UAPI alteration reached statistical significance (Table 3).

The authors observed that alterations in UAPI, MCAPI and UAPI/MCAPI ratio increased from five to seven times the risk of the occurrence of SGA newborns in the analysis without adjustment and around three times in the adjusted analysis according to gestational age (Table 4). The increase in risk was statistically significant for all studied dopplervelocimetric parameters.

Alterations in UAPI, MCAPI and in the UAPI/MCAPI ratio increased two to five times the risk of HIS before adjustment, and between one and one half and more than three and a half times after the adjustment according to gestational age. The increase in the adjusted risk was significant only for UAPI and the UAPI/MCAPI ratio (Table 5).

Table 1 Characteristics of the 289 pregnant women.

	n	Rate
Parity		
Gravida I	165	57.1%
Gravida II and III	96	33.2%
Gravida > III	28	9.7%
Type of hypertension		
Systemic arterial hypertension	69	23.9%
Preeclampsia	182	63.0%
Superimposed preeclampsia	38	13.1%
Mode of delivery		
Vaginal delivery	74	25.6%
Elective Cesarean section	172	59.5%
Intrapartum Cesarean delivery	43	14.9%
Interval: last Doppler study and delivery		
1 day	148	51.2%
Between 2 and 3 days	71	24.6%
Between 4 and 7 days	70	24.2%

Table 2 Perinatal outcomes.

	n	Rate
Gestational age		
< 33 weeks	80	27.7%
33–36 weeks	95	32.9%
≥ 37 weeks	114	39.4%
Weight of newborns in grams (g)		
< 1500 g	53	18.4%
1500–2.499 g	85	29.4%
≥ 2500 g	151	52.2%
Apgar at 5 minutes < 7	61	21.5%
Newborn small for gestational age	91	31.5%
Hypoxic-ischemic syndrome	56	19.8%
Respiratory distress syndrome	46	16.3%
Perinatal death		
Fetal death	5	2.0%
Neonatal death	16	6.5%

Table 3 Relative estimated risk (odds ratio) for Apgar score < 7 at 5 minutes, without adjustment and after adjustment for gestational age according to altered indicator at Doppler velocimetry.

Altered indicator	Gross odds ratio	CI 95%	Adjusted odds ratio	CI 95%
UAPI	1.31	(0.55–2.89)	2.65	(1.03–6.85)
MCAPI	1.36	(0.71–2.57)	1.85	(0.96–3.58)
UAPI/MCAPI	0.89	(0.44–1.37)	1.45	(0.66–5.99)

UAPI, umbilical artery pulsatility index; MCAPI, middle cerebral artery pulsatility index; IUAPI/MCAPI, umbilical/cerebral pulsatility index.

Table 4 Relative estimated risk (odds ratio) for small gestational age, without adjustment and after adjustment for gestational age according to altered indicator at Doppler velocimetry.

Altered indicator	Gross odds ratio	CI 95%	Adjusted odds ratio	CI 95%
UAPI	7.48	(3.57–16.09)	2.98	(1.36–6.56)
MCAPI	5.43	(3.05–9.70)	3.24	(1.78–5.89)
UAPI/MCAPI	7.37	(4.06–13.41)	3.15	(1.66–5.99)

UAPI, umbilical artery pulsatility index; MCAPI, middle cerebral artery pulsatility index; IUAPI/MCAPI, umbilical/cerebral pulsatility index.

Table 5 Relative estimated risk (odds ratio) for newborn hypoxic-ischemic syndrome, without adjustment and after adjustment for gestational age according to altered indicator at Doppler velocimetry.

Altered indicator	Gross odds ratio	CI 95%	Adjusted odds ratio	CI 95%
UAPI	4.93	(2.30–10.43)	3.66	(1.77–7.57)
MCAPI	2.36	(1.23–4.49)	1.54	(0.80–2.99)
UAPI/MCAPI	4.49	(2.32–8.68)	2.79	(1.34–5.82)

UAPI, umbilical artery pulsatility index; MCAPI, middle cerebral artery pulsatility index; IUAPI/MCAPI, umbilical/cerebral pulsatility index.

Table 6 Relative estimated risk (odds ratio) for respiratory distress syndrome, without adjustment and after adjustment for gestational age according to altered indicator at Doppler velocimetry.

Altered indicator	Gross odds ratio	CI 95%	Adjusted odds ratio	CI 95%
UAPI	6.06	(2.69–13.39)	1.56	(0.68–3.60)
MCAPI	2.35	(1.15–4.74)	1.04	(0.48–2.25)
UAPI/MCAPI	3.93	(1.92–8.03)	0.90	(0.38–2.09)

UAPI, umbilical artery pulsatility index; MCAPI, middle cerebral artery pulsatility index; IUAPI/MCAPI, umbilical/cerebral pulsatility index.

The observed increase in the risk of RDS in cases with altered UAPI, MCAPI and UAPI/MCAPI ratio was between two and six times in the analysis without adjustment. However, after adjustment by gestational age, no increase was observed in the risk of this neonatal complication in the cases with these alterations at Doppler (Table 6).

In spite of the fact that the gross risk of perinatal mortality having been between three to ten times greater in cases with alterations in UAPI, MCAPI and UAPI/MCAPI ratio in the analysis adjusted according to gestational age, only the altered UAPI presented a statistically significant risk almost three times higher for perinatal death (Table 7).

Table 8 shows the summarized results for a better visualization and comparison of the different indicators of Doppler alterations. It can be observed that the UAPI is the best indicator o risk of bad perinatal outcomes, particularly when the risk evaluation is adjusted by gestational age of the neonate.

DISCUSSION

The results of the present study suggest that the evaluation of blood flow in the umbilical artery was the best indicator of risk of adverse perinatal outcome, as compared with the evaluation of the middle cerebral artery and with the IAPI/MCAPI ratio. Before the adjustment for gestational age, the three indicators seem to have a similar capability of predicting adverse perinatal outcomes. It is important to note that the increase in risk was always greater when one considers the Doppler results for the umbilical artery compared with the ones for the middle cerebral artery. It should be highlighted that the difference between these two indicators is more noticeable when one observes the risks of adverse perinatal outcomes after adjustment for gestational age. Various authors have not considered the factor of gestational age in their studies[7,9,11,13,18,26].

In the present study, alterations in UAPI allowed the prediction of a higher risk (about three times higher) in four out of five indicators of the adverse perinatal outcomes studied. For RDS, the risk was 50%

Table 7 Relative estimated risk (odds ratio) for perinatal death, without adjustment and after adjustment for gestational age according to altered indicator at Doppler velocimetry.

Altered indicator	Gross odds ratio	IC 95%	Adjusted odds ratio	CI 95%
UAPI	9.84	(3.80–25.67)	2.87	(1.10–7.45)
MCAPI	2.81	(1.15–6.98)	1.18	(0.48–2.94)
UAPI/MCAPI	6.08	(2.37–16.08)	1.57	(0.56–4.35)

UAPI, umbilical artery pulsatility index; MCAPI, middle cerebral artery pulsatility index; IUAPI/MCAPI, umbilical/cerebral pulsatility index.

Table 8 Relative estimated risk of adverse perinatal outcomes according to altered indicator at Doppler velocimetry.

	Indicator of Doppler alteration		
	Umbilical artery	Middle cerebral artery	U/C index
Without adjustment			
Apgar at 5 minutes < 7	(1.31)*	(1.36)	(0.89)
Newborn small for gestational age	7.48	5.43	7.37
Hypoxic-ischemic syndrome	4.93	2.36	4.49
Respiratory distress syndrome	6.06	2.35	3.93
Perinatal death	9.84	2.81	6.08
Adjusted for gestational age			
Apgar at 5 minutes < 7	2.65	(1.85)	(1.45)
Newborn small for gestational age	2.98	3.24	3.15
Hypoxic-ischemic syndrome	3.66	(1.54)	2.79
Respiratory distress syndrome	(1.56)	(1.04)	(0.90)
Perinatal death	2.87	(1.18)	(1.57)

* Values in parentheses were not statistically significant.

higher, but it was not statistically significant. In contrast, MCAPI alterations allowed the prediction of a higher risk only for SGA, and alterations in the UAPI/MCAPI ratio allowed predictions only for SGA and HIS.

For some authors, the study of more than one vessel contributes to improve the diagnosis of the fetal situation, evaluating the Doppler velocimetry capability to predict perinatal outcomes, including only fetuses with confirmed IURG diagnosis[3,6,7,12,27,28]. In the present study, hypertensive pregnant women were included, as it may lead to placental insufficiency potentially presenting a risk of fetal damage, without being necessarily present.

Another important information is related to the evaluation of perinatal outcomes in cases with zero diastole or reversed flow, which are severe alterations in the dopplervelocimetric pattern[9,10,13,26]. The present study considered not only absent or reversed diastole as altered results of the umbilical artery, but also cases in which the pulsatility indices were above the 95th percentile.

Another factor considered as relevant in the present study was that approximately 75% of the cases had an interval of up to three days between the Doppler study and the labor, and in 50% the interval was one day. In the study developed by Baschat et al.[7] the mean interval between the last Doppler study and delivery has not been informed, while in other studies the mean interval was > 7 days[9,29]. Variations in the Doppler study-delivery interval may explain differences in results, considering that severe alterations in the Doppler pattern of the umbilical and cerebral arteries precede the worsening in the fetal status[6] by 10–14 days.

Prematurity remains as the single most important determinant of neonatal complications and mortality[9,27,28,30]. In the literature, some authors have analyzed only premature fetuses, particularly at gestational ages < 32 weeks, differently from the cases in the present study, in which different gestational ages were included, allowing a separate analysis of outcomes in extremely premature neonates, premature neonates and term neonates, and evaluate the impact of prematurity on the perinatal outcomes[3,7,11,13].

The change in results after adjustment for gestational age was significant. It is known that in cases where placental insufficiency and fetal hemodynamic alterations are diagnosed, the tendency is to interrupt the pregnancy to avoid intrauterine fetal death. Therefore, the association between alterations at Doppler and lower gestational ages is evident. Additionally, considering that the lower the gestational age is, the worst the perinatal outcomes are, it is understood that gestational age is a confusing variable in the study of the association between alterations at Doppler and perinatal outcomes.

The most typical example is RDS. Before adjusting by gestational age, the Doppler alterations of the umbilical artery seemed to be associated with a six-time higher risk of RDS, but after the adjustment, this association was not significant. Among the studied adverse perinatal outcomes indicators, RDS is exactly the one more closely related to gestational age, more so than the situation of chronic intrauterine hypoxemia. It is therefore clear that the increase in risk of RDS in cases with alterations at Doppler is mostly due to the premature interruption of pregnancy induced by the Doppler result than the hypoxia condition of the fetus.

It would be very attractive if the assessment of the fetal *status* were more important than the gestational age effects on perinatal outcomes, so that the moment of delivery could be based on the tests of fetal assessment.

Therefore, the authors' opinion is that the gestational age should not be ignored in the analysis of the data evaluated in the present study. This is the most important contribution of the present study, and hopefully the publication of such results will contribute with future studies to confirm the relevance of the gestational age factor in their analyses to the performance of Doppler velocimetry for assessing fetal vitality.

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