Correlation of Adverse Neonatal Outcomes of Pregnant Women with Hypertensive Disorders Using the Middle Cerebral Artery and Umbilical Artery Pulsatility Index Ratio*

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ABSTRACT

Background: Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being providing an opportunity to improve fetal outcome. The present study was undertaken to evaluate the role of middle cerebral to umbilical artery pulsatility index ratio (MCA/UA PI Ratio) as a predictor of perinatal outcome in hypertensive pregnant patients admitted from January 2009- December 2011 at the De La Salle-University Medical Center

Objectives: To correlate the neonatal outcomes of hypertensive pregnant women at 28-34 weeks AOG with the middle cerebral artery and umbilical artery pulsalitility index ratio.

Study Design: A retrospective cohort was done on records of patients with hypertension who delivered from January 2009 - December 2011. Doppler ultrasound results of said patients that were available at the OB-GYN ultrasound section were recorded and the MCA/UA PI Ratio computed. Doppler results were then compared to neonatal outcomes

Results: Results of the study shows that 10 out of the 17 hypertensive patients with decreased MCA/UA PI Ratio developed Intrauterine growth restriction. 62.5% of those patients who had normal MCA/UA PI Ratio results delivered term, while 87.5% of those who had decreased MCA/UA PI Ratio delivered preterm (P <0.002). However results of the MCA/UA PI ratio has no association on APGAR scores at 1 and 3 minutes.

Conclusion: Decreased MCA/UA PI Ratio results have an association on the development of adverse neonatal outcomes in hypertensive pregnant women.

INTRODUCTION

The role of ultrasonography in obstetrics has evolved during the years and its usefulness in predicting adverse neonatal outcomes has been deemed life saving in complicated pregnancies. Hypertension in pregnancy has long been a problem that has alarmed practicing obstetricians over the years and termination of pregnancy has been the only treatment option.

Ultrasound has become the essential tool of modern obstetric practice. With advances in technology and computer processing, what was once a mere curiosity has become crucial for the assessment of the placenta, membranes, fluid and fetal anomaly. [1]

The use of ultrasound in pregnancy complicated with hypertension has aided obstetricians in its management. Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being providing an opportunity to improve fetal outcome.

Doppler ultrasound studies have been used in predicting adverse perinatal outcomes among hypertensive patients and valuable in decision-making in the management of these patients. Recently, the Middle Cerebral Artery /Umbilical Artery Pulsatility Index Ratio have been used by sonologists as a tool in predicting intrauterine growth restriction in pregnancies complicated by chronic medical conditions like hypertension.

OBJECTIVES

General Objective

To correlate the neonatal outcomes of hypertensive pregnant women at 28-34 weeks AOG with the middle cerebral artery and umbilical artery pulsalitility index ratio.

Specific Objectives

1. To determine the adverse outcomes of pregnancies based on the onset of development of hypertension and timing of delivery with the Middle Cerebral Artery / Umbilical Artery Pulsatility Index Ratio.

2. To correlate the Middle Cerebral Artery /Umbilical Artery Pulsatility Index Ratio values to the different age of gestation of each pregnancy complicated with hypertension.

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REVIEW OF RELATED LITERATURE

According to Williams, hypertensive disorders complicate 5 to 10 percent of all pregnancies, and together they form one member of the deadly triad, along with hemorrhage and infection, that contribute greatly to maternal morbidity and mortality rates. With hypertension, the preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous.

New-onset nonproteinuric hypertension during pregnancy—termed gestational hypertension—is followed by signs and symptoms of preeclampsia almost half the time, and preeclampsia is identified in 3.9 percent of all pregnancies (Martin and colleagues, 2009). The World Health Organization systematically reviews maternal mortality worldwide (Khan and colleagues, 2006). In developed countries, 16 percent of maternal deaths were due to hypertensive disorders. This percentage is greater than three other leading causes: hemorrhage—13 percent, abortion—8 percent, and sepsis—2 percent. In the United States from 1991 to 1997, Berg and colleagues (2003) reported that almost 16 percent of 3201 maternal deaths were from complications of pregnancy-related hypertension. Importantly, Berg and co-workers (2005) later reported that over half of these hypertension-related deaths were preventable. [2]

How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Indeed, hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics.[2]

Hypertensive Complications of Pregnancy are more likely to develop in a woman who is exposed to abnormal chronic villi for the first time, is exposed to super abundance of chorionic villi, or with twins or hydatidiform mole, has preexisting vascular disease, or is genetically predisposed to hypertension developing during pregnancy. [2]

According to the Philippine Clinical Practice Guidelines on Hypertension in Pregnancy of 2010 that regardless of the lack of existing prophylactic and therapeutic means to address preeclampsia, the search for non-invasive markers that could predict the development or assist in the detection of this life-threatening pregnancy disorder is still of utmost importance. The availability of such markers could have decisive impact not only on the medical management of pregnant women and their child, such as referral to a tertiary center, but also on the health costs associated with this prevalent medical condition. There are many proposed strategies on the detection or prediction of hypertensive complication of pregnancy. [3]

Doppler velocimetry is one of the most recent predictor for outcomes complicated with hypertension. It is based simply on the principle of the Doppler Effect. Doppler interrogation of the the fetal arterial system provides an indirect assessment of placental resistance.

In a study done by Yalti and colleagues in 2004, they evaluated the role of middle cerebral to umbilical artery blood velocity waveform's systolic/diastolic ratio (MCA/UA) and biophysical profile as a predictor of perinatal outcome in hypertensive and preeclamptic pregnant women during the late third trimester. The MCA/UA was valuable for predicting the outcome of preeclamptic and hypertensive pregnancies. [4]

In a study done by Shahiraj and colleagues on the value the middle cerebral to umbilical artery Doppler ratio in the prediction of neonatal outcomes in patient with preeclampsia and gestational hypertension; they investigated on the diagnostic value of MCA/UA PI ratio. Neonates of mothers with abnormal MCA/UA PI Ratio results had significantly lower gestational age at delivery (34.8 vs 38.4, P<0.0001), lower birth weight (2174.6 g vs 3215.0 g, P<0.001), significantly greater risk for perinatal death (30.8% vs 0.23%, P0.0001), significantly greater risk of admission to intensive care unit (77.8% vs 47.4%, P<0.0001), longer duration of treatment in NICU (10.6 days vs 6.5 days, P<.0001) greater rate of cesarean delivery for fetal distress (71.9% vs 62.5%, P<0.0001), a great number of fetus IUGR (7.18% vs 1.76%, P<0.0001). [5]

Also in a study done by Ozerenet. Al., there were significant differences found between normal pregnancies and preeclamptic patients without IUGR using the mean MCA PI and the MCA PI/UA PI ratio. In the preeclamptic patients with IUGR, all the mean Doppler indices were different from those of the normal pregnancies. In the preeclamptic patients with IUGR the values were different from the preeclamptic patients without IUGR, except for the MCA PI at 31-35 weeks. The UA S/D had the highest sensitivity (88%) and diagnostic accuracy (94%) in predicting the adverse perinatal outcome. The MCA PI/UA PI ratio showed the highest predictive value in determining IUGR by a sensitivity of 84% and a diagnostic accuracy of 87%. Also in a study done by Ozerenet. Al., there were significant differences found between normal pregnancies and preeclamptic patients without IUGR using the mean MCA PI and the MCA PI/UA PI ratio. In the preeclamptic patients with IUGR, all the mean Doppler indices were different from those of the normal pregnancies. In the preeclamptic patients with IUGR the values were different from the preeclamptic patients without IUGR, except for the MCA PI at 31-35 weeks. The UA S/D had the highest sensitivity (88%) and diagnostic accuracy (94%) in predicting the adverse perinatal outcome. The MCA PI/UA PI ratio showed the highest predictive value in determining IUGR by a sensitivity of 84% and a diagnostic accuracy of 87%. [6]

Doppler ultrasound has been used as a reliable tool in assessing fetal well-being.

Nowadays, Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring, allowing the non-

invasive assessment of fetal circulation. [5]

METHODS

I. Setting:

The subjects came from De La Salle University Medical Center

II. Subjects:

Inclusion Criteria:

All deliveries from 2009-2011 complicated with hypertension at De La Salle-University Medical Center.

Exclusion Criteria:

Pregnant patients with other maternal risk factors such as diabetes mellitus, premature rupture of membranes, multifetal pregnancies and Immunoreproductive Disorders.

III. Data Collection:

Records of hypertensive pregnancies and neonatal outcomes from 2009-2011 using the OB-GYN weekly census and Perinatology records were reviewed and recorded. Doppler ultrasound results from OB Ultrasound Section from 2009-2011 of each patient were reviewed and available MCA/UA PI ratio was computed.

Methods of the Study:

The independent variable used in this study is the Middle Cerebral Artery/ Umbilical Artery Pulsatility Index Ratio. Values were taken from Doppler ultrasound results from 2009-2011. A value of less than 1 was assigned as decreased and a value of > or =1 was assigned as normal. Results of MCA/UA PI ratio were then compared with neonatal outcomes from the 2009-2011 admissions.

The dependent variable analyzed included are birth weight, appropriate weight for age of gestation, and presence of maternal and fetal complications like prematurity, intrauterine growth restriction and intrauterine fetal demise.

Study Design:

The study used is a retrospective, cohort analytical study.

Statistical Analysis:

The data gathered (independent and dependent variables) were analyzed using the Analysis of Variance, Chi square Test, Pooled T-Test, test for independence, which ever was appropriate to determine the statistical significance and determine the association of these variables.

Significance of the Study:

This study aims to determine the significance of Middle Cerebral Artery/ Umbilical Artery Pulsatility Index Ratio of Doppler Ultrasound Studies in predicting poor perinatal outcomes on pregnant women complicated with hypertension. If results were proven to be statistically significant, Middle Cerebral Artery/Umbilical Artery Pulsatility Index Ratio would be useful in predicting adverse perinatal outcomes in pregnancies complicated with hypertension and would not only reduce mortality but also morbidity.

Definition of Terms:

1. *Gestational Hypertension* - elevated blood pressure of 140/90mm Hg without proteinuria develops in a woman after 20 weeks of gestation and blood pressure levels return to normal 12 weeks postpartum
2. *Chronic Hypertension* - Blood pressure of 140/90 mm Hg before pregnancy or diagnosed before 20 weeks' gestation not attributable to gestational trophoblastic disease
3. *Chronic Hypertension with Superimposed Preeclampsia* - New-onset proteinuria 300 mg/24 hours in hypertensive women but no proteinuria before 20 weeks' gestation. A sudden increase in proteinuria or blood pressure or platelet count < 100,000/L in women with hypertension and proteinuria before 20 weeks' gestation
4. *Preeclampsia* - BP of 140/90 mm Hg after 20 weeks' gestation and proteinuria 300 mg/24 hours or 1+ dipstick
5. *Eclampsia* - Seizures that cannot be attributed to other causes in a woman with preeclampsia
6. *Intrauterine Growth Restriction* - Low-birthweight infants below the 10th percentile who are small-for-gestational age
7. *Intrauterine Fetal Demise* - stillbirth deliveries
8. *Doppler velocimetry ultrasound* - waveform measures from the fetal arterial and venous circulation to assess fetal well-being

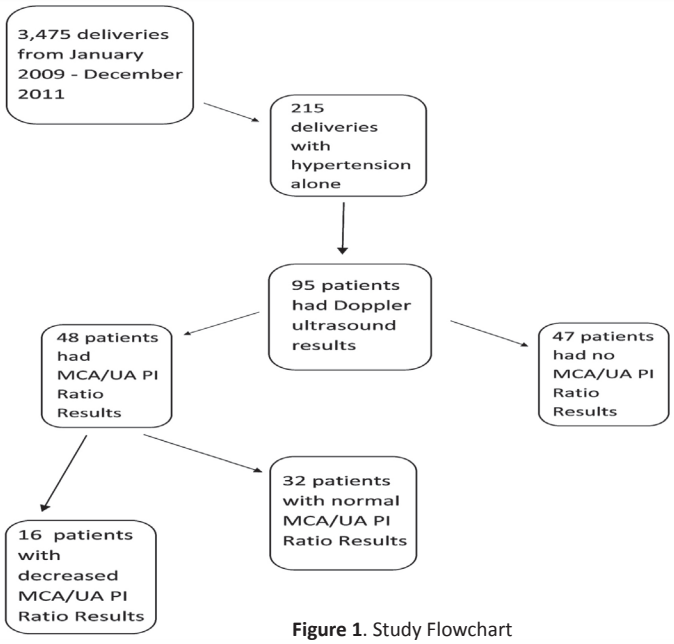

Figure 1. Study Flowchart

RESULTS

There were a total of 3, 476 deliveries at the De La Salle University Medical Center from January 2009 to December 2011. A total of 215 deliveries were complicated with hypertension alone. 23% of the total 215 deliveries had Doppler ultrasound results with MCA/UA PI Ratio computation.

Table 1 shows the 3 leading types of hypertension admitted were Preeclampsia Severe, Gestational Hypertension and Chronic Hypertension. Intrauterine Growth Restriction among infants developed among Chronic Hypertension with Superimposed Preeclampsia at 21%, Preeclampsia Severe patients at 14 %, and Chronic Hypertension at 10%. Intrauterine Fetal Demise developed among patients with Antepartum Eclampsia and Preeclampsia Severe at 7%, Chronic Hypertension with Superimposed Preeclampsia at 5%, and Chronic Hypertension at 3%.

Table 1. Types of Hypertension in pregnancy and corresponding adverse neonatal outcomes

Type of Hypertension	Count	Complications		Count (Patients who are 28-34 weeks old)	Complications	
		IUGR	IUFD		IUGR (patients who are 28-34 weeks old)	IUFD (patients who are 28-34 weeks old)
Antepartum Eclampsia	13	0	1	6	0	2
CHVD	51	5	3	7	2	10
CHVD with SPE	33	7	1	5	1	2
CHVS	1	0	0	0	0	2
Gestational Hypertension	53	0	0	0	0	8
Impending Eclampsia	2	0	0	0	0	8
Intrapartum Eclampsia	1	0	0	1	0	3
Preeclampsia	1	0	0	0	0	1
Preeclampsia Mild	3	0	0	0	0	0
Preeclampsia non severe	2	0	0	0	0	0
Preeclampsia severe	55	8	4	12	4	10
TOTAL	**215**	**20**	**9**	**31**	**7**	**2**

Table 2 shows that 63% delivered abdominally for varying indications such as uncontrolled hypertension, malpresentation, dystocia and repeat cesarean section. 28 % delivered vaginally and the remaining 8% delivered via outlet forceps extraction.

Table 2. Manner of delivery and adverse neonatal outcomes

Manner of Delivery	Count	Complications		Count (Patients who are 28-34 weeks old)	Complications	
		IUGR	IUFD		IUGR (patients who are 28-34 weeks old)	IUFD (patients who are 28-34 weeks old)
Classical CS	1	0	0	0	0	0
LTCS	132	18	3	19	7	1
LTCS I	1	0	0	0	0	0
LTCS II	3	0	0	2	0	0
OFE	17	0	0	0	0	0
VSD	61	2	6	10	0	4
TOTAL	**215**	**20**	**9**	**31**	**7**	**5**

Table 3. MCA/UA PI Ratio and adverse neonatal outcome

MCA/UMA Ratio	Count	Complications		Count (Patients who are 28-34 weeks old)	Complications	
		IUGR	IUFD		IUGR (patients who are 28-34 weeks old)	IUFD (patients who are 28-34 weeks old)
None	164	6	8	19	1	4
Decreased	17	10	1	8	5	1
Normal	33	4	0	4	1	0
TOTAL	**214**	**20**	**9**	**31**	**7**	**5**

Table 3 shows association between the MCA/UMA ratios values with the different age of gestation of each pregnancy complicated with hypertension, a contingency table between the four classification variables via the r x c Test for Independence was used.

The observed value of the statistic is 30.50. The probability of observing a value of 30.50 or greater is between 0.99 and 1. That is the P value of the test is between 0.99 and 1. We will therefore conclude that the age of gestational delivery is independent to the MCA/UA PI Ratio. In other words, there is clearly no association between MCA/UMA Ratio and AOG at the time of delivery. Therefore, AOG has no effect with the outcome of MCA/UA PI ratio.

Table 4. Weight for gestational age and adverse neonatal outcomes

Weight for Gestational Age	Count	Complications		For patients who are 28 - 34 weeks old		
		IUGR	IUGR	Count	IUFD	IUGR
AGA	169	1	0	17	0	0
LGA	7	0	0	1	0	0
SGA	31	0	20	8	0	7
TOTAL	**207**	**1**	**20**	**26**	**0**	**7**

Small for gestational age babies with intrauterine growth restriction complicated 10% of hypertensive pregnancies.

Table 5. Age of gestation at delivery and MCA/UMA Ratio Result

Age of Gestational Delivery	MCA/UA PI Ratio			Marginal Row Total
	None	Decreased	Normal	
26-28 weeks	4	1	1	6
29-31 weeks	8	1	1	10
32-34 weeks	9	6	2	17
35-37 weeks	25	6	6	37
38-40 weeks	96	2	20	118
41-43 weeks	15	0	2	17
Marginal Column Total	**157**	**16**	**32**	**205**

Table 5 shows the association between the MCA/UA PI ratios; values to the different age of gestation of each pregnancy complicated with hypertension, a contingency table between the four classification variables via the r x c Test for Independence was used. With this method, a multivariate distribution was done and the Chi-Squared Goodness of Fit formula extended.

62.5% of those patients who had normal MCA/UA PI Ratio results delivered term, while 87.5% of those who had decreased MCA/UA PI Ratio delivered preterm.

Table 6. Cell expectation for types of hypertension complicating pregnancy and MCA/UA PI Ratio for each observation

Type of Hypertension	Adverse Outcomes of Pregnancy	Normal	Decreased	Normal
Antepartum Eclampsia	1.00	0.48	0.38	0.14
CHVD	8.00	3.86	3.03	1.10
CHVD with SPE	8.00	3.86	3.03	1.10
CHVD	-	-	-	-
Gestational Hypertension	-	-	-	-
Impending Eclampsia	-	-	-	-
Intrapartum Eclampsia	-	-	-	-
Preeclampsia	-	-	-	-
Preeclampsia Mild	-	-	-	-
Preeclampsia non severe	-	-	-	-
Preeclampsia severe	12.00	5.79	4.55	1.66

Table 8 shows the observed value of the X^2_{30} statistic is 5.27. The probability of observing a value of 5.27 or greater is between 0.002 and 0.001. That is the, the P value of the test is between 0.002 and 0.001. Since this probability is fairly small we shall reject the null hypothesis and conclude that the adverse outcome of pregnancy is not independent to the MCA/UMA Ratio.

Since it is established that there is an association between the adverse outcomes of pregnancy with the MCA/UA PI Ratio, then we can proceed in determining which is more likely the adverse neonatal outcome with an abnormal MCA/UA PI Ratio result.

The table below shows the frequency of all patients with the onset of development of hypertension versus the adverse outcome of pregnancy having a decreased MCA/UMA ratio.

Table 7. Adverse neonatal outcome and type of hypertension

Type of Hypertension	IUGR	IUFD
Antepartum Eclampsia	0	0
CHVD	3	1
CHVD with SPE	4	0
CHVD	0	0
Gestational Hypertension	0	0
Impending Eclampsia	0	0
Intrapartum Eclampsia	0	0
Preeclampsia	0	0
Preeclampsia Mild	0	0
Preeclampsia non severe	0	0
Preeclampsia severe	3	0

mean :	0.91	0.09
variance :	2.49	0.09
n :	11	11

In comparing the variance we get 27.67 as the observed value of the F test statistic. The numbers of degrees of freedom associated with the statistic are both 10, which will give us

$$P[F_{10,10} > 2.323] = 0.10$$

The probability of observing a value greater than 0.177742 is larger than this. Since this P value is large, we are unable to reject the null hypothesis and therefore we shall pool both sample variances to estimate the common population variance. In this case, the pooled variance is 1.29. We will be using the Pooled T Test Statistic to know if it is significant to say that our alternative hypothesis (that is, IUGR is more likely to happen given a particular stage of hypertension). Using the Pooled Test Statistic, we will obtain 1.6932 which is less than the T20 distribution at 95% confidence level. With this value, we can say that IUGR is significantly more likely to happen given the onset of the development of hypertension, particularly in the case of chronic hypertension, chronic Hypertension with superimposed preeclampsia and severe Preeclampsia.

DISCUSSION

Ultrasonography has been available to aid obstetricians for 4 decades. Recently, doppler studies have been used to assess the fetoplacental circulation in

Table 8. Doppler MCA/UMA PI Ratio for each Apgar score at 1 min.

Apgar Score (at 1 min)	Doppler MCA/UMA PI Ratio			Marginal Row Total
	None	Decreased	Normal	
0	1	9	1	11
1	0	1	0	1
2	1	0	0	1
3	5	0	0	5
4	1	0	0	1
5	3	1	1	5
6	7	1	3	11
7	13	1	3	17
8	13	3	1	17
9	112	9	24	145
Marginal Column Total	**156**	**25**	**33**	**214**

Table 9. Shows the Doppler MCA/UMA PI Ratio for each Apgar score at 5 min.

Apgar Score (at 5 min)	Doppler MCA/UMA PI Ratio			Marginal Row Total
	None	Decreased	Normal	
0	9	1	1	11
5	1	1	0	2
6	6	0	0	6
7	3	1	1	5
8	4	3	2	9
9	141	11	29	181
Marginal Column Total	**164**	**17**	**33**	**214**

complicated pregnancies to assess fetal status.

Results of the study shows the significance of the MCA/UA PI Ratio as a good predictor on the development of poor perinatal outcomes on pregnant women complicated with hypertension. A decreased value of less than 1 was shown to have an increased risk for intrauterine growth restriction and intrauterine fetal demise.

The study also shows decreased results for the MCA/UA PI Ratio were more prevalent on patients diagnosed to have Preeclampsia Severe, Chronic Hypertension and Chronic Hypertension with Superimposed Preeclampsia.

Although, there was no association seen between the ages of gestation at the time of delivery with the results of the MCA/UA PI Ratio done at 28-34 weeks age of gestation. 62.5% of those patients who had normal MCA/UA PI Ratio results delivered term, while 87.5% of those who had decreased MCA/UA PI Ratio delivered preterm.

SUMMARY AND CONCLUSION

There was a strong association between decreased results of MCA/UA PI Ratio and the development of adverse neonatal outcomes like intrauterine growth restriction and intrauterine fetal demise among hypertensive women who delivered from January 2009 to December 2011. We can therefore conclude that the MCA/UA PI Ratio on Doppler ultrasound result is a valuable tool and a strong predictor of adverse neonatal outcomes in pregnant patients with hypertension.

Among the types of hypertension, the MCA/UA PI Ratio proved to be significantly decreased among patients with preeclampsia, chronic hypertension and chronic hypertension with superimposed preeclampsia. No association were found among patients with gestational hypertension alone.

There was no strong correlation among the timing of delivery and results of the MCA/UA PI Ratio. However, a large percentage of those with decreased MCA/

UA PI Ratio results were delivered preterm and a significant percentage of those with normal MCA/UA PI Ratio were carried to term. We can therefore safely say that the MCA/UA PI Ratio can help prevent fetal morbidity and mortality.

RECOMMENDATIONS

Based on the results of the study, a study encompassing a longer time period should be done to increase the sample size in order to better test the association of MCA/UA PI Ratio and adverse neonatal outcomes among hypertensive patients.

Also, the MCA/UA PI Ratio should be included in all Doppler studies done in all hypertensive patients to assess fetal well-being and prevent the development of adverse neonatal outcomes as the pregnancy progresses.

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