ORIGINAL ARTICLE

EFFECTS OF VARIATION IN UMBILICAL ARTERY RESISTIVE INDEX ON PLACENTAL MORPHOLOGY AND BIRTH WEIGHT IN PREGNANCY INDUCED HYPERTENSION

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Background: Pregnancy induced hypertension results from defective trophoblast invasion and increased umbilical artery resistance which in turn results in decreased blood supply to the placenta and hence to the foetus. This arterial resistance varies in different cases of PIH thus causing variable effects on placenta and foetus. The objective of this study was to study the morpho-metric changes in placenta and alterations in birth weight with differences in umbilical artery resistive index in hypertensive pregnancies. **Methods:** Ninety pregnant women with pregnancy induced hypertension were selected with gestational age greater than 35weeks. Doppler ultrasound examinations were carried out to record umbilical artery resistive index (UARI). 2 groups were made on the basis of median values of UARI. Plain ultrasound examination was then carried out to record presentation, site of placentation, grade of maturity, insertion of the cord, cord thickness, placental thickness, vacuolation and amniotic fluid index (AFI). After delivery, foetal birth weight was noted and placentae examined for placental weight, infarcts, number of cotyledons, umbilical cord insertion, cord thickness and placental thickness were noted. Foeto-placental weight ratio was also calculated. **Results:** Significantly higher UARI was seen in the high-resistance group. Significantly lower values of placental thickness, AFI, birth weight, placental weight and placental thickness, whereas greater number of grade-III maturity, infarcts and marginal cord insertion were noted in the high-resistance group. **Conclusion:** Increased UARI leads to a spectrum of changes in the placenta and also decreased birth weight. Marginal cord insertion causes greater risk of increased UARI.

Keywords: PIH, Umbilical Artery, Resistive Index, Placenta.

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INTRODUCTION

Pregnancy induced hypertension (PIH) has been haunting pregnancies the world over due to its greater risk of stillbirths and neonatal and maternal mortality.[1,2] Although not much data is available on the global prevalence of this condition, it is suggested that its prevalence seems to vary in different parts of the demographic map.[3,4] Many hypotheses have been proposed on the mechanism of development of PIH. However, none have been completely elucidated. Different factors such as hypoxia, endothelial injury, imbalance between prostacyclins and thromboxanes, decreased intravascular volume, diet and genetic predisposition have been considered to be responsible.[5] Whatever the underlying cause, it seems to be the disease of a diseased trophoblast in which defective trophoblast invasion seems to lie at the centre of the spectrum of changes occurring in this condition.[6]

Studies have shown that impaired blood supply to the placenta causes it to release certain factors into the maternal circulation which lead to altered metabolic pathways, eventually resulting in an increased maternal blood pressure.[7] It has also been proven that hypoxia results in the increase of soluble fms-like tyrosine kinase (sFlt-1) which is an antagonist of vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), the latter being a vasodilator.[8] As these factors responsible for angiogenesis are antagonized, normal invasion of maternal uterine vessels by the trophoblast cannot take place resulting in a decreased foeto-placental circulation. Relationship between the rising levels of soluble endoglin and ratios of sFlt1: PlGF, and the onset of preeclampsia has also been demonstrated.[9] Raised maternal serum uric acid and decreased prostacyclin levels have also been found to be related to hypertensive pregnancies. In fact, studies have shown that uric acid is as important as proteinuria in identifying foetal risk in PIH.[10] Differences have been seen between placental morphology of normal and hypertensive pregnancies.[11,12]

Macroscopically, the invasion of maternal spiral arteries by the trophoblast occurs in two stages known as the first phase and second phase trophoblast invasions. The first phase trophoblast invasion occurs at about the 12th week of gestation and involves invasion of the tunica intima and media of maternal endometrial arteries. In the second phase invasion which occurs around the 18th week of gestation invasion of the endothelium and tunica media of the arteries in the myometrium takes place. As the trophoblast invades the media of these vessels, the smooth muscle layer

encircling them is disrupted, thus resulting in loss of vasoconstrictive ability of these vessels. These two processes collectively render a low resistant high flow system which maintains a constant blood supply to the developing foetus.[13,14]

We know that the arteries mentioned above are medium sized muscular arteries. Researchers have shown that as the tunica media of these arteries is invaded, apoptosis of the smooth muscles in the walls of these arteries occurs. These results in loss of vasoconstrictive ability of these arteries hence, maintaining a constant and continuous blood flow throughout the cardiac cycle.[15] Inability of the trophoblast to invade maternal vessels in either of the two phase's leads to persistence of vasoconstrictive ability of the vessels, thus leading to decreased foeto-placental blood flow and to compensate this, maternal blood pressure rises.

Doppler Ultrasound is a good tool to pick up alterations in foeto-placental circulation.[16] Research has proven umbilical artery Doppler waveforms as an important predictor of pregnancy outcome.[17,18] Foetal middle cerebral artery and foetal aortic Doppler indices have also been used as predictors of foetal well-being.[19] Whatever the mechanism, the altered blood flow leads to a large spectrum of changes in the utero-placental circulation which eventually leads to structural changes in the placenta and foetus.

Objective of study is to study the morphological changes in placenta and differences in birth weight with variation in umbilical artery resistive index in hypertensive pregnancies.

MATERIAL AND METHODS

This was a cross-sectional study. After taking written consent from the patients for participation in the study, 99 patients were selected out of which 9 patients were lost to follow-up.

Pregnancy induced hypertension was defined as a reading of 140/90 mmHg or above or an increase of 30/15 mmHg or more above the baseline reading on two separate occasions, at least 2 weeks apart. Diagnosed cases of gestational hypertension who were normotensive up to the 20th week of gestation with para 1 to 3 were included in the study. Women with accurate gestational age (with known LNMP and also confirmed by 1st trimester ultrasound) were only included. These women were registered at Ziauddin Hospital (North Nazimabad and Nazimabad Campus) and Habib Medical Centre before 18thweek of gestation. Patients with essential Hypertension previous Caesarean Section or any uterine surgery, placenta previa, fibroids, abnormal uterine anatomy, abnormal vaginal discharge or bleeding, autoimmune disorders, vascular disorders, gestational diabetes, diabetes mellitus, congenital anomalies in foetus, history of preterm delivery and history of Nicotine use, alcoholism or any other street drug use were excluded from the study.

Doppler ultrasound examinations were carried out by the same operator in which the Umbilical Artery Resistive Index (UARI) was noted down from the foetal end of the artery. Three readings were taken and mean values were recorded. On basis of median values of UARI (0.70), the subjects were divided into two groups:

1. Low Resistance Flow Group (LRG) which had 47 subjects and UARI $\leq$0.70
2. High Resistance Flow Group (HRG) which had 43$\leq$ subjects and UARI >0.70

After this the placenta and foetus were examined by ultrasound for site of placentation, grade of maturity, cord insertion, cord thickness, placental thickness, amniotic fluid index, foetal movements and foetal heart rate. After delivery, foetal birth weight was noted and placenta was collected and examined for placental weight, number of infarcts, number of cotyledons, cord thickness and central placental thickness were noted. Foeto-placental weight ratio was also calculated.

The study was approved by the Ethical Review Committee and Board of Advanced Studies and Research of Ziauddin University, Karachi.

Data analysis was done on SPSS-17. Test of proportion was used for comparison of categorical variables and student's t-test was used for comparison of quantitative data. A *p*-value $\leq$0.05 was considered statistically significant.

RESULTS

Umbilical artery Doppler ultrasound showed significantly higher resistive index in the high resistance group (Table-1). The two groups were equally matched in age, gestational age at scan, parity, weight, systolic blood pressure, diastolic blood pressure and pulse (Table-2).

On ultrasound, significantly lower values were noted in placental thickness and amniotic fluid index in the HRG. No statistically significant difference was found in cord thickness and foetal heart rate between the two groups. (Table-3)Also on ultrasound, greater number of grade III maturity and marginal cord insertions were the HRG. No significant differences were found in foetal movements and site of placentation between the two groups (Table-4). On gross examination, it was seen that birth weight, placental weight and placental thickness were significantly lower in the HRG with significantly greater number of infarcts in this group. No significant difference could be found in the foeto-placental weight ratio, number of cotyledons of

placenta and cord thickness between the two groups (Table-5).

Table-1: Umbilical Artery Resistive Index (on Doppler Ultrasound)

	LRG Mean±SD	HRG Mean±SD	*p*
Resistive Index	0.6326±0.04551	0.7444±0.02281	0.001*

Table-2: General Characteristics

	LRG (Mean±SD)	HRG (Mean±SD)	*p*
Age (Years)	24±3.57	23.23±3.31	0.295
Gestational age at scan (Weeks)	36.6383±1.03	36.46±1.10	0.442
Parity	0.7234±0.99	0.60±0.88	0.551
Weight (kg)	65.234±5.47	65.44±5.10	0.852
Systolic Blood Pressure	141.28±3.37	142.33±4.27	0.198
Diastolic Blood Pressure	75.32±12.31	77.21±7.01	0.379
Pulse	85.70±8.49	88.65±11.31	0.163

Table-3: Ultrasound Findings

	LRG (Mean±SD)	HRG (Mean±SD)	*p*
Cord Thickness (cm)	1.1489±0.12136	1.1419±0.13135	0.791
Placental Thickness (cm)	3.3872±0.27475	3.2±0.25820	0.001*
AFI	14.436±1.98192	13.244±2.38091	0.011*
Foetal Heart Rate	141.15±5.66829	141.26±6.01622	0.931

Table-4: Ultrasound Findings (Qualitative Variables)

		LRF	HRF	*p*
Site of placentation	**Anterior (n)**	37	32	0.877
	Fundo-posterior (n)	4	4	
	Posterior (n)	6	7	
Placental Maturity	**Grade II (n)**	32	16	0.006*
	Grade III (n)	15	27	
Insertion of cord	**Central (n)**	42	29	0.019*
	Marginal (n)	5	14	
Foetal movements	**Normal (n)**	47	41	0.135
	Sluggish (n)	0	2	
	Absent (n)	0	0	

Table-5: Gross Findings (After Delivery)

	LRF (Mean±SD)	HRF (Mean±SD)	*p*
Birth Weight (gm)	2825.53±192.77	2723.26±193.76	0.014*
Placental Weight (gm)	413.34±29.97	390.42±39.35	0.002*
Foeto-placental Weight Ratio	6.87±0.65	7.05±0.97	0.295
Number of Infarcts	8.72±1.77	9.65±1.59	0.011*
Number of Cotyledons	16.06±0.70	16.26±0.62	0.175
Cord thickness (cm)	1.1936±0.14	1.14±0.13	0.085
Placental Thickness (cm)	3.45±0.43	3.21±0.22	0.001*

DISCUSSION

It can be seen that with increasing resistance, the placentae tend to get significantly thinner and amniotic fluid gets scanty. These are directly attributed to the diminishing blood flow to the placenta with increasing resistance. Studies done in the past have shown an association of these parameters with increasing severity of hypertension[20] but none to our knowledge have associated it with UARI.

It is also noted that placental maturity is achieved at an earlier stage with increasing resistance. As in other tissues, cell death and degeneration also occurs normally in placenta. These minute degenerated areas tend to calcify and when this occurs the placenta is said to have attained Grade-III maturity.[21] The early placental maturity seen in the HRG indicates that due to decreased blood supply, the placental cells tend to die quicker which in turn leads to increased rate of calcification.

Greater number of marginal insertion of umbilical cord indicates that asymmetrical insertion of the cord also increases risk of increased resistance in umbilical artery flow. Marginal cord insertion has been attributed in the past to an abnormal umbilical artery systolic-diastolic ratio, but in the same study, no relation could be found with UARI.[22]

On gross examination, the birth weight was found to be significantly lower in the group with higher resistive index. The weight of placentae in this group was also significantly lower. These two findings when seen collectively indicate that as the resistance increases, the blood flow to the placentae and hence to the foetus decreases. This leads to decreased tissue blood supply, thus leading to decreased tissue nutrition and decreased weight of these structures. These findings are similar to findings in studies carried out before.[23,24] No significant difference however, was seen in the foeto-placental ratio between the two groups indicating a proportional effect of blood flow on both, the foetus and placenta.

Another observation on gross examination was the significantly increased number of infarcts in the HRG. This indicates unequal blood flow to different parts of the placenta. Gross examination also confirmed the ultrasound findings of decreased placental thickness in the HRG.

CONCLUSION

The study shows umbilical artery resistive index does affect the morphology as well as morphometry of both, the placenta and foetus. The current study suggests that increasing resistance in umbilical arteries leads to:

- Decreased placental thickness and placental weight
- Earlier placental maturity
- Greater number of placental infarcts
- Decreased amniotic fluid production
- Lower birth weight

The study also suggests that marginal cord insertion leads to a greater incidence of increased umbilical artery resistance.

REFERENCES

1. Ananth CV, Basso O. Impact of Pregnancy-Induced Hypertension on Stillbirth and Neonatal Mortality in First and Higher Order Births: A Population-Based Study. Epidemiology. 2010;21(1):118–23.

2. Villar J, Carroli G, Wojdvla D, Ablos E, Giordano D, Ba'aqeel H *et al*. Gestational hypertension and intrauterine growth restriction, related or independent conditions? Am J Obstet Gynecol 2006;194:921–31.
3. Kaaja R, Kinnunen T, Luoto R. Regional differences in the prevalence of preeclampsia in relation to the risk factors for coronary artery disease in women in Finland. Eur Heart J 2005;26:44–50.
4. Muhammed Obaid-ur-Rehman M, Salah-ud-din, Siddiqui MA, Rehman S. Incidence of women having pregnancy induced hypertension in Karachi. J Pak Pharmacol 2003;20(1):5–8.
5. Kumar V, Abbas AK, Fausto N, eds. Robbins and Cotran. Pathologic Basis of Disease. 7th ed. Philadelphia: Saunders Elesware; 2005.
6. Naicker T, Khedun SM, Moodley J, Pijnenborg R. Quantitative analysis of trophoblast invasion in preeclampsia. Acta Obstet Gynecol Scand 2003;82:722–9.
7. Goldman-Wohl D, Yagel S. Regulation of trophoblast invasion: from normal implantation to pre-eclampsia. Mol Cell Endocrinol 2002;187(1-2):233–8.
8. Maynard S, Min J, Merchan J, Lim K, Li J, Mondal S, *et al*. Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. J Clin Invest 2003;111:649–58.
9. Levine RJ, Lam C, Qian C, Yu KF, Maynard SE, Sachs BP, *et al*. Soluble Endoglin and other circulating antiangiogenic factors in preeclampsia. N Engl J Med 2006;355:992–1005.
10. Roberts JM, Bodnar LM, Lain KY, Hubel CA, Markovic N, Ness RB, *et al*. Uric Acid Is as Important as Proteinuria in Identifying Foetal Risk in Women With Gestational Hypertension. Hypertension 2005;46;1263–9.
11. Majumdar S, Dasgupta H, Bhattacharya K, Bhattacharya A. A study of placenta in normal and hypertensive pregnancies. J Anat Soc India 2005;54(2):1–9.
12. Baloch AH, Memon SF, Ansari AK. Comparison of placentae from hypertension associated pregnancies and normal pregnancies. J Liquat Uni Med Health Sci 2012;11(1):3–6.
13. Kaufmann P, Black S, Huppertz B. Endovascular trophoblast invasion: Implications for the pathogenesis of intrauterine growth retardation and preeclampsia. Bio Reprod 2003;69:1–7.
14. Helwig JJ, Bouteiller PL. Physiological Smooth Muscle Cell apoptosis contributes to the uterine vascular remodeling in human early pregnancy. Circ Res 2007;100:754–6.
15. Pijnenborg R, Bland JM, Robertson WB, Brosens I. Uteroplacental arterial changes related to interstitial trophoblast migration in early human pregnancy. Placenta 1983;4:397–413.
16. Bhatt CJ, Arora J, Shah MS. Role of color Doppler in pregnancy induced hypertension (A study of 100 cases). Indian J Radiol Imaging 2003;3:417–20.
17. Yalti S, Oral O, Gürbüz B, Ozden S, Atar F. Ratio of middle cerebral to umbilical artery blood velocity in preeclamptic& hypertensive women in the prediction of poor perinatal outcome. Indian J Med Res 2004;120:44–50.
18. Dicke JM, Huettner P, Yan S, Odibo A, Kraus FT. Umbilical Artery Doppler Indices in Small for Gestational Age Foetuses: Correlation with adverse outcomes and placental abnormalities. J Ultrasound Med 2009;28:1603–10.
19. Khalid M, Wahab S, Kumar V, Khalid S, Haroon S, Noor AS. Doppler Indices in Prediction of Foetal Outcome in Hypertensive Pregnant Women. Nipal J Obstet Gynaecol 2011;6(1):28–34.
20. Rasmussen S, Irgens LM. Fetal Growth and Body Proportion in Preeclampsia. Obstet Gynecol 2003;101:575–83.
21. Stewart VL, Herling P, Dalinka MK. Calcification in soft tissues. JAMA 1983;250:78–81.
22. Nordenvall M, Ullberg U, Laurin J, Lingman G, Sandstedt B, Ulmsten U. Placental morphology in relation to umbilical artery blood velocity waveforms. Eur J Obstet Gynecol Reprod Biol 1991;40(3):179–90.
23. Bolz N, Kalache KD, Fotopoulou C, Proquitte H, Slowinski T, Hartung JP, *et al*. Value of Doppler sonography near term: can umbilical and uterine artery indices in low-risk pregnancies predict perinatal outcome? J Perinat Med 2013;41(2):165–70.
24. Torres PJ, Gratacós E, Alonso PL. Umbilical artery Doppler ultrasound predicts low birth weight and fetal death in hypertensive pregnancies. Acta Obstet Gynecol Scand 1995;74:352–5.

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