STUDY ON PERSISTENT UTERINE ARTERY DIASTOLIC NOTCH: A PREDICTOR OF HYPERTENSIVE DISORDERS OF PREGNANCY AND FOETAL GROWTH RESTRICTION

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ABSTRACT

BACKGROUND

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with haemorrhage and infection that contribute greatly to maternal morbidity, mortality and responsible for 20% of perinatal mortality and morbidity. Incidence of foetal growth restriction is close to 10% of all births and contributes to increased perinatal morbidity and mortality. This prospective study is on persistent uterine artery diastolic notch as a predictor of hypertensive disorders of pregnancy and foetal growth restriction.

METHODS

The study population consisted of 200 antenatal women attending outpatient clinic, Institute of Social Obstetrics and Government Kasturba Gandhi Hospital with the 16-28 weeks of gestation.

RESULTS

Persistence of notch was seen in 27.17% of cases. Among them 47.16% of cases had hypertensive disorders of pregnancy, 39.62% of cases had foetal growth restriction, 22.64% of cases had FGR with HTD.

CONCLUSION

This study highlights that the persistence of uterine artery diastolic notch, especially bilateral notch should be specifically evaluated so that necessary timely intervention can be made. Persistent uterine artery notch in high risk women is a good predictor of hypertensive disorders of pregnancy and foetal growth restriction.

KEYWORDS

Hypertensive Disorders of Disorders of Pregnancy, Foetal Growth Restriction, Uterine Artery Diastolic Notch.

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INTRODUCTION

Uteroplacental bed perfusion increases in normal pregnancy and decreases in foetal growth restriction and hypertensive disorders of pregnancy.¹ The alterations in the uteroplacental circulations precedes the onset of foetal growth restriction and hypertensive disorders of pregnancy.

Doppler ultrasound is an innovation in foetal surveillance, which would indicate the state of uteroplacental and fetoplacental blood flow from which implications about the foetal condition can be made.²

Uterine artery flow velocity wave forms recorded throughout the menstrual cycle and early pregnancy are usually characterized by an early diastolic notch, which indicates high resistant uterine blood flow. In normal pregnancies, the early diastolic notch persists until approximately 24 weeks gestation and it is rarely recorded

on placental side after 24 weeks due to conversion of high resistance uterine blood flow to low resistance flow. FGR and hypertensive disorders of pregnancy is due to defective placentation, which leads to persistence of diastolic notch.

Ramsay and Donner (1980) presented a summary of their anatomical studies of the uteroplacental vasculature. The first wave occurs before 12 weeks post fertilization and consists of invasion and modification of the spiral arteries of the decidua, reaching its border with the myometrium. Between 12-16 weeks post fertilization, the second wave occurs. This involves invasion of the intramyometrial parts of the spiral arteries converting narrow lumen, muscular spiral arteries into dilated, low resistance uteroplacental vessels and decreased responsiveness to pressor substances. A lack of endovascular infiltration by trophoblasts into the myometrial portion of the placental bed spiral arteries results in persistence of high resistance flow and early diastolic notch. Defective trophoblastic invasion is the consistent finding in hypertensive disorder/FGR.

To evaluate uterine artery Doppler wave forms, colour flow mapping is used to locate the uterine arteries as they cross from medial to the iliac arteries.

The Doppler gate is placed within the straight portion of uterine artery before it enters the myometrium.

Hence, this study is done to predict the occurrence of these two disorders by using persistence of uterine artery diastolic notch.

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AIM AND OBJECTIVE

To find out the correlation between persistence of uterine artery diastolic notch by Doppler and development of foetal growth restriction and hypertensive disorders of pregnancy.

MATERIALS AND METHODS

Study Design: Prospective study.

Study Period: July 2012 to June 2014.

Sample Population

The antenatal mothers were clinically evaluated at the Antenatal OP Department and were allocated into two groups as follows.

Group I: 100 antenatal mothers at 16-28 weeks primi/multi.

Group II: 100 antenatal mothers at 16-28 weeks with previous history of FGR/hypertensive disorders of pregnancy.

Inclusion Criteria**Group I**

Antenatal mothers primi/multi without any previous H/O FGR/Hypertensive disorders of pregnancy/IUD.

Group II

Antenatal mothers with previous H/O FGR/Hypertensive disorders of pregnancy.

Exclusion Criteria

1. Women with medical disorders complicating pregnancy like diabetes, cardiac diseases, chronic hypertension, SLE complicating pregnancy, chronic renal disease.
2. Multiple gestation.
3. Women with congenitally malformed fetus.

Method of Study

All mothers were registered at 16 wks. for basic evaluation. For all mothers a thorough general, obstetric history was elicited and a complete general, obstetric examination was done. All the basic investigations were done. Uterine artery Doppler was done between 24 & 28 weeks of gestation. Doppler characteristics evaluated for predicting foetal growth restriction/hypertensive disorders of pregnancy was persistence of uterine artery diastolic notch.

Method of Doppler Study

The selected cases are subjected to a colour Doppler which included biometry, Doppler evaluation for persistence of diastolic notches in the uterine arteries of both sides. The Doppler equipment consisted of a colour Doppler system with a carrier frequency of 3.5 MHZ. The Doppler evaluation was carried out as follows. Antenatal mother is placed in a supine, slightly left lateral position and wedge is placed under the left flank. It is important to avoid supine hypotension syndrome due to vena caval compression. For uterine artery Doppler, the probe is placed 2-3 cm medial to the anterior superior iliac spine.

The transducer is pointed laterally and downward toward the parametrial area where the iliac vessels pierce the myometrium.

The presence of diastolic notch was noted. Main outcome variables for analysis were the development of hypertension

with or without proteinuria, FGR, mode of delivery, gestational age at delivery and perinatal outcome.

RESULTS AND ANALYSIS

In group I 100 cases and in group II 100 cases were selected and prospectively followed up; 3 cases in group I and 2 cases in group II were lost for followup. These cases not reported back after Doppler study. The selected cases had uterine artery evaluation between 24-28 weeks gestation and followed up for development of hypertensive disorders, foetal growth restriction, gestational age at delivery, mode of delivery and perinatal outcome. Cases included were mainly belonging to class IV/class V socioeconomic status.

The following Observations were made

Age	No. of Cases	
	Group I	Group II
18-20 yrs.	27(27.8%)	13(13.2%)
21-30 yrs.	66(68%)	76(77.5%)
31-35 yrs.	4(4.1%)	9(9.1%)

Table I: Age Distribution of Cases

In this study, 66 cases (68%) in group I and 76 cases (77.5%) in group II belonged to the age group of 21-30 yrs.; 27 cases (27.8%) in group I and 13 cases (13.2%) in group II belonged to the age group of 18-20 yrs. and the remaining belonged to the age group of 31- 35 years.

Fig. 1: Age Distribution of Cases

Table II: Group I

Parity	Count	%
Multi	31	31.96
Primi	66	68.04
Total	97	100

Table II: Parity Distribution of Cases

In Group I, 66 cases (68.04%) were primi gravida and 31 cases (31.96%) were multigravida.

Table III: Group II

Parity	Count	%
Multi	98	100
Primi	0	0
Total	98	100

In Group II, all were multigravida 98 cases (100%).

Fig. 2: Parity Distribution of Cases

Notch Distribution

Table IV: Group - I

Notch	Count	%
Absent	75	77.32
Bilateral	11	11.34
Unilateral	11	11.34
Total	97	100

In Group I, bilateral notch was present in 11 cases (11.34%) and unilateral notch was present in 11 cases (11.34%).

Table V: Group - II

Notch	Count	%
Absent	67	68.37
Bilateral	24	24.49
Unilateral	7	7.14
Total	98	100

In Group II, bilateral notch was present in 24 cases (24.49%) and unilateral notch was present in 7 cases (7.14%).

Fig. 3: Notch Distribution

NOTCH AND HTD/FGR

Table VI: Group - I

Notch	Number	Normal Outcome	HTD	FGR
Bilateral	11 (11.34%)	6 (54.5%)	4 (36.36%)	3 (27.27%)
Unilateral	11 (11.34%)	7 (63.63%)	2 (18.18%)	2 (18.18%)
Total	22 (22.68%)	13 (59.09%)	6 (27.27%)	5 (22.72%)
Absent	75 (77.31%)	72 (96%)	2 (2.6%)	1 (1.3%)

In group I, 4 cases (36.36%) had HTD, 3 cases (27.27%) had FGR in the cases with persistence of bilateral uterine artery notch.

In group I, 2 cases (18.18%) had HTD, 2 cases (18.18%) had FGR in the case with persistence of unilateral uterine artery notch.

In group I, 2 cases (2.6%) had HTD and 1 case (1.3%) had FGR in the absence of notch.

Group I

Fig. 4: Notch and HTD/FGR

Table VII: Group - II

Notch	Number	Normal Outcome	HTD	FGR
Bilateral	24 (24.49%)	5 (20.8%)	14 (58.33%)	14 (58.33%)
Unilateral	7 (7.14%)	1 (14.28%)	5 (71.4%)	2 (28.57%)
Total	31 (31.6%)	6 (19.35%)	19 (61.22%)	16 (51.61%)
Absent	67 (68.36%)	62 (92.53%)	3 (4.4%)	2 (2.98%)

In group II, 14 cases (58.33%) had HTD, 14 cases had FGR in the cases of persistence of bilateral uterine artery notch.

In group II, 5 cases (71.4%) had HTD, 2 cases (28.57%) had FGR in the cases of persistence of unilateral uterine artery notch.

In the absence of notch 3 cases (4.4%) had HTD and 2 cases (2.9%) had FGR.

Group - II

Notch and HTD/FGR

Fig. 5: Notch and Perinatal Outcome

Table VII: Group I

Notch	Number of Cases	Perinatal Outcome	
		Abnormal	Normal
Bilateral	11	5(45.45%)	6(54.54%)
Unilateral	11	2(18.18%)	9(81.81%)
Total	22	7(31.81)	15(68.18%)
Absent Notch	75	6(8%)	69(92%)

CONCLUSION

In Group I, in the presence of bilateral notch, 5 cases (45.45%) had abnormal perinatal outcome and in the presence of unilateral notch 2 cases (18.18%) had abnormal perinatal outcome.

Abnormal perinatal outcome was noted as Apgar <7/10, Meconium aspiration syndrome, respiratory distress, small for gestational age, preterm delivery and its complications, NICU admission.

Group - II: Persistence of Notch and Perinatal Outcome

Group - I Group II

Notch	Number of Cases	Perinatal Outcome	
		Abnormal	Normal
Bilateral	24	13 (54.16%)	11 (45.83%)
Unilateral	7	5 (71.42%)	2 (28.57%)
Total	31	18 (58.06%)	13 (41.93%)
Absent Notch	67	12 (17.9%)	55 (82.03%)

CONCLUSION

In Group II, in the presence of bilateral notch, 13 cases (54.16%) had abnormal perinatal outcome and in the presence of unilateral notch 5 cases (71.42%) had abnormal perinatal outcome.

Persistence of Notch and Perinatal Outcome Group - II

DISCUSSION

Doppler velocimetry is a non-invasive technic, which uses high frequency sound for the investigation of blood flow. The feasibility of its foetal application was first reported by Fitzgerald and Drumm.³ It made non-invasive investigation of uteroplacental circulation possible. Diastolic notch is defined as the slower velocity just after systolic flow, but before maximum diastolic flow.

In this study, there was statistically significant association between the persistence of both unilateral, bilateral notching and development of hypertensive disorders of pregnancy, foetal growth restriction when compared to notch absent groups.

In Group I, 36.36% had HTD of pregnancy and 27.27% had FGR in the presence of bilateral notch, 18.18% had HTD and 18.18% had FGR in the presence of unilateral notch. In Group II, 58.33% had HTD and 58.33% had FGR in the presence of bilateral notch and 71.4% had HTD and 28.57% had FGR in the presence of unilateral notch.

Persistence of bilateral notching was associated significantly with severe forms of hypertensive disorders of pregnancy (31.42%) when compared to unilateral notching (5.5%).

A prospective trial of Zimmermann et al⁴ evaluated the utility of uterine artery Doppler between 21-24 wks. in the prediction of preeclampsia and FGR. He selected 172 low risk pregnancies and 175 women at risk for hypertensive disorders of pregnancy/FGR. Presence of persistent notch accounted for 3-4 fold increased risk in developing preeclampsia/FGR. In this group, preeclampsia/FGR was found in 58.3% compared to 8.3% if Doppler results were normal. Doppler was less informative in low risk population. Here preeclampsia/FGR were 6.1-6.4% in this low risk group and 5.2% in notch absent group.

Deutinger et al believed that early diastolic notch persistence was thought to represent the persistence of inherent total impedance of the uteroplacental circulation.

Rofinas et al⁵ found that the persistence of uterine artery diastolic notch indicates severe hypertensive disorder and associated with increased rate of FGR, caesarean delivery, foetal distress and preterm delivery.

In 1983, Campbell et al⁶ was the first to demonstrate a correlation between pregnancies complicated by hypertensive disorder/FGR, increased caesarean rate, foetal distress, low APGAR scores and persistence of uterine artery notch. Furthermore, proteinuria and severe hypertension correlated significantly with persistent notch.

Flesicher et al⁷ in 1986 demonstrated the presence of an early diastolic notch in the uterine artery after 26 weeks gestation correlated significantly with the clinical diagnosis of preeclampsia, abnormal perinatal outcome, increased caesarean rate.

Trudinger⁸ in 1990 did Doppler uterine artery in a highly selected population for prediction of severe PIH.

Thaler et al, demonstrated the persistence of an early diastolic notch after 26 weeks of gestation in 25-40% of

preeclampsia. Presence of notch is significantly a better predictor of poor pregnancy than the S/D ratio (or) resistive index.

Pai.⁹ found persistent diastolic notch to be a better parameter than abnormal RI in predicting the hypertensive disorders of pregnancy/foetal growth restriction.

Bower.¹⁰ et al also predicted the hypertensive disorders of pregnancy/foetal growth restriction by persistence of uterine artery notch.

Aristidou et al noted that the uterine artery notch was a good predictor of poor perinatal outcome, increased rate of FGR, caesarean delivery for foetal distress, preterm delivery.

In 2001, Christopher Lees carried out a colour Doppler assessment of uterine artery in 5121 women attending routine antenatal clinic and concluded that persistent uterine artery notch associated with adverse perinatal outcome.

Validity of tests in Group I and II for any notch and bilateral notch for hypertensive disorder/foetal growth restriction when compared to other studies were,

For Prediction of Hypertensive Disorders

Author	Sensitivity%	Specificity%	Positive Predictive Value	Negative Predictive Value
Pai. ⁹	45.45	92	38	93.87
Bower et al ¹⁰	78	96	28	99.5
Agarwal. ¹¹	84	71.4	72	-
May Backos et al ¹²	38	85	27	90
Papageorghiou et al ¹³	41	-	-	-

In this study, Group I

Notch	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	LR for + Test	LR for - Test	FP	FN
Any notch	75%	82.0%	27.27%	97.33%	4.16	0.3	6.7%	25%
Bilateral	66%	92%	36%	97.67%	8.25	0.36	7.61%	33.3%

Group II

Notch	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	LR for + Test	LR for - Test	FP	FN
Any notch	86.36%	84.21%	61.29%	95.52%	5.46	0.16	15.78%	13.63%
Bilateral	82.34%	87.65%	58.33%	95.94%	6.66	0.2	12.34%	21.42%

For Prediction of Foetal Growth Restriction

Author	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Papageorghiou et al ¹³	24%	-	-	-
May Backos et al ¹⁴	41%	85%	30%	90%

Group I

Notch	Sensi	Speci	Positive Predictive Value	Negative Predictive Value	LR for + test	LR for - test	FP	FN
Any notch	83.33%	81.31%	22.7%	98.66%	4.36	0.2	18.68%	16.66%
Bilateral	75%	91.39%	27.27%	98.83%	8.3	0.27	8.6%	25%

Group II

Notch	Sensi	Speci	Positive Predictive Value	Negative Predictive Value	LR for + Test	LR for - Test	FP	FN
Any notch	88.8%	81.25%	51.61%	97.01%	4.74	0.13	18.75%	11.11%
Bilateral	87.5%	87.80%	58.3%	97.29%	7.17	0.14	12.1%	12.5%

The most useful part of the test is the negative predictive value. A negative test at 24 wks. in a high risk population indicates a 97-99% probability that HTD/FGR will not be present.¹⁰ So in the absence of notch, reassurance can be given to the high risk cases.

Valensise et al 1993.¹⁵ has better sensitivity of 88% for the prediction of preeclampsia. Conde-Agudelo et al 1993.¹⁶ found that the sensitivity of the test was 72-92% in prediction of hypertensive disorders of pregnancy. On evaluating the likelihood ratio for positive and negative tests, presence of any notch is mild predictor of these disorders in group I and was moderate predictor of hypertensive disorders/foetal growth restriction in group II.

It can be evaluated along with routine scan in all women if possible. But in high risk women, it should be specifically evaluated for better antenatal care so that necessary timely intervention can be done.

Several factors are likely to influence the performance of screening tests and these include anatomical site of measurement of uterine artery Doppler. Test to be done at standard reference point for better prediction.

SUMMARY

In Group - I

- 68% of cases belonged to 21-30 yrs. of age.
- 68.04% of cases were primigravida and 31.96% were multigravida.
- Bilateral notch was present in 11.34% of cases (primi- 81.81%, multi- 18.18%).
- Unilateral notch was present in 11.34% of cases (primi- 72.72%, multi- 27.27%).
- 36.36% of cases had hypertensive disorders of pregnancy, 27.27% of cases had foetal growth restriction, 18.18% of cases had hypertensive disorder with foetal growth restriction, 36.36% had caesarean delivery, 27.27% of cases had preterm delivery, 45.45% had abnormal perinatal outcome in the presence of bilateral notch.
- In cases with unilateral notch, 18.18% of cases had hypertensive disorders of pregnancy, 18.18% of cases had foetal growth restriction, 18.18% had caesarean delivery, 9.09% had preterm delivery, 18.18% had abnormal perinatal outcome.
- In the absence of notch, 2.6% of cases had hypertensive disorders, 1.3% cases had foetal growth restriction, 16% had caesarean section, 10.66% had preterm delivery, 8% had abnormal perinatal outcome. There is significant association between notch and HTD, FGR, abnormal perinatal outcome, mode of delivery and no significant association between notch and HTD with FGR, gestational age at delivery. In the presence of notch, there is increased incidence of HTD, FGR, caesarean delivery.

In Group II

- 77.5% of cases belonged to the age group of 21 to 30 years of age.
- 100% were multigravida.
- Bilateral notch was present in 24.49% of cases.
- Unilateral notch was present in 7.14% of cases.
- In the presence of bilateral notch, 58.33% had hypertensive disorders, 58.33% had foetal growth

restriction, 37.5% had hypertensive term delivery, abnormal perinatal outcome disorders with foetal growth restriction, 41.66% had caesarean delivery, 16% had preterm delivery, 54.16% had abnormal perinatal outcome.

- In the presence of unilateral notch 71.4% had hypertensive disorders, 28.57% had foetal growth restriction, 14.28% had hypertensive disorders with foetal growth restriction, 57.14% had caesarean delivery, 14.28% had preterm delivery, 71.42% had abnormal perinatal outcome.
- There is significant association between notch and HTD, FGR, abnormal perinatal outcome, mode of delivery, HTD with FGR, gestational age at delivery. In the presence of notch, there is increased incidence of HTD, FGR, caesarean delivery, preterm delivery, abnormal perinatal outcome.

CONCLUSION

1. Persistent uterine artery notch is a predictor of development of hypertensive disorders of pregnancy and foetal growth restriction. Presence of bilateral notch is significantly associated with severe form of hypertensive disorders.
2. In high risk pregnancies, an abnormal uterine artery Doppler is an indication for a closer antenatal followup and normal uterine artery Doppler is reassuring and allows less frequent foetal surveillance when compared to positive test.
3. To improve the predictive value of tests, it can be combined with clinical high risk factors, also with estimation of serum inhibin A, serum β HCG concentration.
4. In developing countries like India, cost effectiveness of the tests should also be taken into consideration.
5. Hence in high risk women, persistence of uterine artery notch especially bilateral notch should be specifically evaluated so that necessary timely intervention can be made. Persistent uterine artery notch in high risk women is a good predictor of hypertensive disorders of pregnancy and FGR.

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