ORIGINAL RESEARCH

Role of level 2 doppler waveforms in prediction of abnormal trophoblastic invasion and adverse pregnancy outcomes

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Abstract
Introduction- Doppler ultrasonography is used to evaluate uteroplacental circulation by analysing the systolic and diastolic waveforms. Given the ethnic and geographical differences in PIH and IUGR, it is crucial to comprehend the methods used to predict it in different populations. The aim of present study was to assess the role of level 2 doppler waveforms (at the time of anomaly scan) in assessing abnormal trophoblastic invasion and predicting adverse pregnancy outcomes in the form of PIH and IUGR.
Material and methods- The present prospective study was conducted in department of obstetrics and gynaecology at SMGS Hospital among 100 pregnant females visiting the OPD during the study period of one year. As detailed level 2 anomaly scan is mandatory in our settings at 18-22 weeks, the required data on doppler study at 18-22 weeks could easily be extracted from the study patients, thus being economical on the part of patients in low resource settings.The doppler study was performed on all cases throughout the 18-22 weeks period of pregnancy and the two Indices like Pulsatility Index and Diastolic notch of uterine artery were recorded. The patients were followed up for the development of PIH and IUGR.
Results- Out of 100 cases, pregnancy induced hypertension was found in 20 cases while 80 cases did not show pregnancy induced hypertension.30 cases developed IUGR and 70 remained non IUGR cases. Diastolic notch was found in 16 of PIH and 22 of nonPIH patients. 8 of PIH cases had a pulsatility index (PI) of greater than 1.71, compared to 10 of non PIH cases, which had a PI of greater than 1.71 (p=0.01). The sensitivity of diastolic notch in diagnosis of PIH was 65.3% whereas, that of PI was 53.48%. Similarly, diastolic notch was present in 19 of IUGR cases and 10 of non IUGR cases.8 of IUGR patients had PI of >1.7 and 20 of non IUGR cases had PI of > 1.7 giving the statistically significant results. Thus, second trimester doppler changes in the uterine artery has a role in prediction of IUGR too.
Conclusion– Uterine artery doppler is a potentially effective method for predicting the occurrence of PIH and IUGR by examining both the pulsatility index (PI) and the presence of a diastolic notch in the uterine artery. The Doppler technique demonstrated a high level of diagnostic accuracy in detecting preeclampsia.
Keywords- Diastolic notch, Doppler, Induced Hypertension, Investigation, Pregnancy, Uterine Artery

Introduction

Pregnancy induced hypertension (PIH) is a complex disorder that affects various organ systems and occurs in the early stages of pregnancy. It can result in significant maternal mortality and morbidity. Fetal growth restriction can occur with or without PIH. Nevertheless, the exact mechanism by which PIH affects both the fetal/placental and maternal variables remains unclear [1]. The relationship between abnormal doppler waveforms and development of adverse pregnancy outcomes in the form of PIH and IUGR is well established [2].Pregnancies that are destined to have normal outcome show loss of diastolic notch at 22 weeks whereas pregnancies that result in adverse outcomes show early diastolic notch [3]. The main factor leading to PIH and IUGR is the insufficient supply of blood and oxygen to the placenta, which is likely caused by the aberrant formation of blood vessels in the placenta during early pregnancy. The estimated prevalence of pulmonary embolism (PE) is approximately 10%, and it is a significant contributor to iatrogenic pre-term births [4].

Several factors that have been hypothesized to impact the risk of PIH and IUGR in mothers include diabetes, obesity, multiple pregnancy, and primiparity, age above 30 years, prior occurrence of Hypertension or chronic hypertension in family [5]

The process of implantation and trophoblastic invasion is vital for the formation of the placenta as an organ responsible for the transportation of nutrients and oxygen to the fetus. The depletion of smooth muscle and elastin from the spiral arterioles results in the transformation of the uteroplacental circulation into a system with low resistance and high capacitance. PIH and IUGR occurs as a result of compromised trophoblastic invasion into the spiral arterioles of the mother. The process of trophoblastic invasion can be observed by Doppler ultrasonography examinations, which represent the physiological changes occurring in the body [6,7].

Doppler ultrasound (USG) is a non-invasive and highly effective tool for managing high-risk situations. Although the direct evaluation of trophoblastic invasion is not possible, doppler ultrasonography can be used to measure uteroplacental circulation by comparing systolic and diastolic waveforms [8,9]. The uterine artery is the vessel that is most frequently examined in doppler examination. The metrics utilized for evaluating uteroplacental insufficiency encompass the presence of an early diastolic notch, as well as the pulsatility or resistance index of the uterine artery [10,11]. Research indicates that doing doppler ultrasonography on the uterine arteries between 12 and 16 weeks of gestation is highly beneficial for identifying preeclampsia [12,13]. Nevertheless, certain studies have emphasized the usefulness of this technique during the third trimester for anticipating changes in blood flow and inadequate blood supply to the uterus and placenta [14].

Identifying individuals at risk, particularly in the early stages of pregnancy, can be beneficial in implementing appropriate management techniques. This can ultimately decrease the likelihood of negative outcomes for both the mother and baby [15,16]. Hence the present study was conducted to assess the role of level2 doppler waveforms in prediction of adverse pregnancy outcomes in the form of PIH and IUGR.

Material and methods

The present prospective study was conducted at department of obstetrics and gynaecology of SMGS Hospital among pregnant females visiting the OPD during the study period of one year. Ethical clearance was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure.

All patients with single pregnancy having gestational age between 18 to 22weeks were included in the study. Patients with gross foetal malformation on Ultrasonography (USG)

(like anencephaly, meningo myelocele), known case of essential hypertension, who were on treatment with aspirin, heparin or antihypertensives, history of Pregnancy Induced Hypertension (PIH) in previous pregnancy, with multiple pregnancy, who had abortion on follow-up, critically ill patients were excluded from the study. Sample size was calculated by using the formula

" N=Zα2 [pxq]/d2"

 Where, Zα is from probability table and 2 Standard Errors (SE) corresponds to 1.96

p was prevalence if PIH i.e. 6%.

 q was 1-p, when p is in decimal terms (1-0.06=0.94).

 d was precision of estimate i.e. 5%

Substituting these values,

N=(1.96)2[0.06*0.94]/(0.05)2=90.24

Actual sample size= 90.24+10%of 90.24=100

All study participants were surveyed to collect comprehensive data on socio-demographic factors, including age, education, and socio-economic position. A comprehensive obstetric history was collected, and any previous pregnancy difficulties were carefully documented. In addition, all the cases underwent thorough general, systemic, and obstetric evaluation. The blood pressure was measured following a 10-minute period of rest, with the individual positioned at a 45-degree angle and the cuff placed at the level of the heart. Standard investigations were performed, including liver function assessment, kidney function assessment, Bleeding Time (BT), Clotting Time (CT), activated partial thromboplastin time/international normalized ratio, prothrombin time, and urine for albumin

The doppler study was performed on all cases throughout the 18-22 week period of pregnancy. As Level 2 scan is mandatory in our setting, the required data about uterine artery doppler could easily be extracted from the study patients. The purpose was to observe and record the two Indices like Pulsatility Index and Diastolic notch of uterine artery.

Subsequently, all the participants underwent regular screening during their antenatal visits to detect the occurrence of symptoms associated with hypertension, such as headache, blurred vision, epigastric pain, vomiting, high blood pressure, presence of albumin in urine, presence of pedal edema or abdominal wall edema, and weight gain. Also, growth scans were done and regular antenatal check ups were done to know for the development of IUGR.

The results were reported as the mean value plus or minus the standard error of the mean (SEM), or as a number or median, depending on the situation. Comparisons between the two groups were conducted using Fischer's test or Chi-square test, depending on the suitable circumstances. A significance level of P < 0.05 was used to determine statistical significance.

Results

Out of 100 cases, pregnancy induced hypertension was found in 20 cases while 80 cases did not show pregnancy induced hypertension.Also,30 cases developed IUGR and 70 were non IUGR cases. Less educated and nulliparous females had a higher frequency of induced hypertension. Between the two groups of PIH, there was a statistically significant difference in gestational age at delivery (p-value=0.01) as shown in figure 1, table 1.

Figure 1: Incidence of pregnancy induced hypertension and IUGR
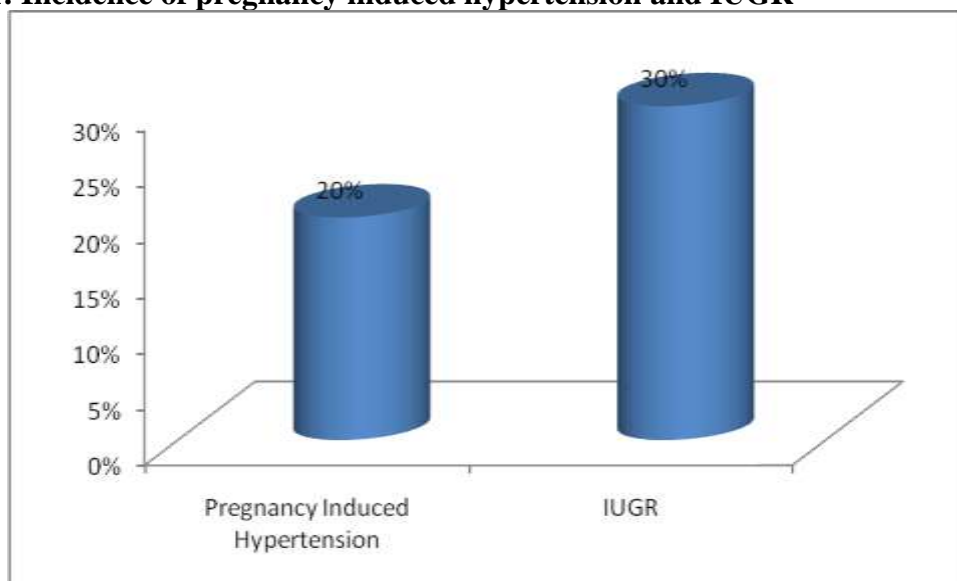
Table 1 Association between different variables and PIH

Variable		With PIH	Non PIH	P value
Age (years)	>18	2	5	0.034
	18-30	16	65	
	>30	2	10	
Education	Primary	1	10	0.01
	Secondary	2	30	
	Intermediate	17	38	
	Graduation	0	2	
Parity	0	14	25	0.03
	1	5	50	
	>1	1	5	
Mean gestational age		35.32±2.34	39.89±2.89	0.01

Diastolic notch was found in 16 of PIH and 22 of non PIH patients. 10 of non PIH cases had a pulsatility index (PI) of greater than 1.71, compared to 12 of PIH cases, which had a PI of less than 1.71. There was a statistically significant (p-value=0.01) difference in the diastolic notch and PI between with PIH and non PIH subjects as shown in table 2.

Table 2 Association of diastolic notch and pulsatility index in PIH and non PIH cases

Level 2 Doppler		Non PIH	With PIH	P value
Diastolic notch	Present	22	16	0.01
	Absent	58	4	
Pulsatility index	<1.71	70	12	0.01
	≥1.71	10	8	

The sensitivity of diastolic notch in diagnosis of PIH was 65.3% whereas, that of PI was 53.48% as shown in table 3.

Table 3 Sensitivity and specificity of diagnostic notch and pulsatility index in diagnosis of PIH

Doppler	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Diastolic notch	65.30%	74.20%	43.90%	89.21%	73.21%
Pulsatility index	53.48%	97.21%	88.23%	88.21%	81.20%

Diastolic notch was found in 10 of non IUGR and 19 of IUGR patients. 20 of non IUGR cases had a pulsatility index (PI) of greater than 1.71, compared to 22 of IUGR cases, which had a PI of less than 1.71. There was a statistically significant (p-value=0.01) difference in the diastolic notch and PI between with non IUGR and IUGR subjects as shown in table 4.

Table 4 Association of diastolic notch and pulsatility index with Non IUGR and IUGR cases

Level 2 Doppler		Non IUGR	IUGR	P value
Diastolic notch	Present	10	19	0.01
	Absent	60	11	
Pulsatility index	<1.71	50	22	0.01
	≥1.71	20	8	

Discussion

Pregnancy induced hypertension is a prevalent factor that is strongly linked to higher rates of illness and death among mothers worldwide. In order to decrease the risk of negative outcomes during pregnancy, it is crucial to promptly identify and treat PIH, thereby reducing the related problems including maternal morbidity and death. The use of USG doppler has been suggested as a beneficial method for evaluating uteroplacental circulation and detecting preeclampsia at an early stage [17]. Two variables are found and associated with uteroplacental insufficiency and indicators of preeclampsia. The parameters mentioned are the pulsatility index, and diastolic notch of uterine artery [11].

In our study the number of women with PIH case was 20% of overall cases selected. They were mostly in the age group of 18 to 30 years with mean gestational age of 25 years. A recent study found that the frequency of pregnancy-induced hypertension (PIH) was 11.5% in cases where the resistance index (RI) was greater than 0.58 and the mothers were between 18-24 weeks pregnant [18]. In a separate research, it was discovered that 6% of mothers had Pregnancy-Induced Hypertension (PIH) during the gestational period of 20-24 weeks, with a Resistive Index (RI) of 0.58 [19]. A study found that mothers who had a bilateral uterine artery notch at 24 weeks of pregnancy had an incidence of pregnancy-induced hypertension (PIH) of 55%. This rate climbed to 81% at the time of delivery, and all of these mothers gave birth before 35 weeks of pregnancy [20].

The current study found that the pulsatility index was elevated (>1.71) in patients with PIH, compared to patients without PIH. Bindal J and Chugh N found that a greater percentage of PIH cases had a PI (pulsatility index) more than 1.71, with a statistically significant p-value of less than 0.05. Köpük S¸ Y et al. found concordant results, documenting a significantly higher proportion of patients with high PI values in the preeclampsia group (p-value=0.023) [21,22].

In this study, both the pulsatility index and diastolic notch were found in more of PIH cases and as compared to PIH cases. Unlike Bindal J and Chugh N, who found both the pulsatility index and diastolic notch in just 12% of cases [21], Gomez O et al. reported a statistically significant increase in placental insufficiency (PI) and a higher occurrence of bilateral notching in patients diagnosed with preeclampsia [12].

The current investigation found that the sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the diastolic notch for diagnosing PIH were 65.30, 74.20%, 43.90% and 89.21% correspondingly. The diagnostic accuracy was determined to be 73.21%. At a cut-off of 1.71, the sensitivity of PI was 53.48%, but the specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of PI were higher than those of the diastolic notch. Köpük S¸ Y et al. reported a sensitivity of 42.31% and specificity of 82.10% when using a cut-off value of >2.23 to detect preeclampsia [22]. Carbillonl found that uterine artery doppler had a high sensitivity for predicting preeclampsia at 11-14 weeks of pregnancy, but with a low positive predictive value [23].

As far as IUGR is concerned, Torres C and Raynor B et al., also studied uterine artery waveforms and adverse pregnancy outcomes in low risk population..They showed that for IUGR, the score had sensitivity of 16.7% and specificity of 86.3% [24].It is comparable with our study which shows the similar results. According to a systemic review in 2004, doppler study blood flow in uterine artery is valuable in predicting pre eclampsia and IUGR [2]. In study conducted by Barati M et al; doppler screening was done at 16 to 22 weeks and it had predicted pre eclampsia and IUGR with acceptable sensitivity and specificity [25].

Conclusion

Our research indicates that utilising Doppler ultrasound at 18-24 weeks to assess the notching of the uterine artery and its pulsatility index (PI) was effective in predicting pregnancy-induced hypertension (PIH) and intra uterine growth restriction (IUGR) in most patients, particularly those with aberrant uterine artery notching. It is economical for the patients in developing countries like India where they can get screened for the anomalous fetus and possibility of developing PIH and IUGR in future at the same time of sonologic examination. However, we suggest conducting more large-scale prospective investigations to confirm these observations within our population.

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