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Prediction of Preeclampsia by uterine artery doppler

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Abstract
Aims and Objectives: To evaluate the predictive value of uterine artery Doppler in gestational hypertensive disorders and to evaluate the best single marker (Doppler index) with highest sensitivity & specificity in the screening of pre-eclampsia.
Materials and Methods: This prospective study was conducted in the department of Obstetrics & Gynaecology at SKIMS Medical College Bemima) Srinagar. 226 enrolled subjects were subjected to uterine artery Doppler velocimetry at 22 to 24 weeks gestation and were followed throughout their antenatal course & outcome measured as pre eclampsia & gestational hypertension.
Results: This was tabulated and calculated with statistical analysis. Among 226 nullipara, uterine artery Doppler abnormalities were detected in 34 (15%) of cases. 8 patients developed proteinuric hypertension (pre-eclampsia/eclampsia) with sensitivity & specificity of 80% and 88% respectively with positive predictive value & negative predictive value of 23.5% &98% respectively. 4 patients among 34 patients with abnormal second trimester uterine artery Doppler developed non-proteinuric hypertension (gestational hypertension) with sensitivity & specificity of 33.3% and 89% respectively with a negative predictive value of 96%.
Conclusion: Uterine artery Doppler velocimetry is one of the vital tools for prediction of pre-eclampsia (proteinuric hypertension). Women with normal second trimester uterine artery Doppler velocimetry have low risk of developing obstetric complication-hypertensive disorders.

Keywords: Doppler velocimetry, pre eclampsia, gestational hypertension, uterine artery Doppler

Introduction

Hypertensive disorders of Pregnancy are important causes of maternal & peri-natal morbidity & mortality [1, 2]. In developed countries hypertensive disorders rank 2nd only to anemia with approximately 7-10% of all pregnancies complicated by some form of hypertension [3]. Berg & colleagues (1996) reported almost 18% of 1450 maternal deaths in U.S.A were complications of pregnancy related hypertension [4]. Hypertension in pregnancy is also responsible for 18% of fetal & infant mortality as well as 46% of infant born SGA [5].

Hypertensive disorders of pregnancy is generally regarded as a multi-system disorder specific to pregnant women characterised by wide spread endothelial damage which originates from utero-placental circulation but ultimately involves the variety of other organs such as kidney, liver & brain. It is characterised by imbalance between prostacycline & thromboxane production [6] as well as failure of second wave trophoblastic invasion of endometrio-myometrial vasculature. Result is abnormal utero-placental blood flow. Therefore it should be possible to predict the risk by using Doppler-Ultrasonography (uterine artery flow velocity wave forms) as method of screening for the ante-natal complications [7].

Aims and Objectives

To evaluate the predictive valve of uterine artery Doppler in pre-eclampsia /PIH
To evaluate the best single marker (Doppler index) with highest sensitivity &specificity in the screening test of pre-eclampsia.

Materials and Methods

This study was conducted in the department of Obstetrics & Gynaecology at Sher-I-Kashmir Institute of Medical Sciences (SKIMS) Srinagar. In all the cases, informed consent was taken from the patient. Total of 234 subjects were enrolled during the study after proper consent & fulfilling the inclusion & exclusion criteria which are as follows:

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Inclusion Criteria
- Singleton nulliparous pregnant women
- Following their antenatal care at SKIMS in their pregnancy period
- Professor OBGYN, SKIMS, Soura Srinagar
- Expected delivery at SKIMS

Exclusion Criteria
- Multiparous pregnant women
- Multiple gestations like twins, triplets, etc.
- Subjects with chronic hypertension, renal disease, cardiac disease.
- Congenital anomalies of fetus
- Unreliable LMP & not confirmed by 1st trimester scan
- Loss at follow up

Methods
This was the prospective cohort study. All subjects enrolled in the study were subjected to the following investigations, after measurement of arterial blood pressure to rule out chronic hypertension:
- Baseline investigations
- PIH profile
- Baseline fundoscopy
- Two routine ultrasound examinations. The first at 11-14 weeks for pregnancy dating. The second, at 2O-22 weeks for assessment of fetal growth & examination for fetal defects.

Measurement of Blood Pressure
- Mercury manometer
- Comfortable sitting position, arm at the level of heart
- Record systolic & diastolic pressures the latter as Korotkoff Vth (disappearance).
- Confirmed by two readings at least 4 hours apart

Doppler
All uterine artery Doppler studies were performed by transabdominal Sonography by Radiologist accompanied by experienced obstetrician and Student. The ultrasonography and Doppler examination was performed using Aloka Prosound SSD-3500SX Ultrasound-Doppler machine using a 3.5 MHz transducer. Both the Uterine Arteries were studied for wave form morphology and various indices like SD ratio, RI and PI (calculated using automated Software). In addition, baseline fetal study including the examination of placenta was carried out in the same sitting. Screening was performed at 22-26 weeks of gestation with uterine artery Doppler velocimetry.

Results and Observations
234 singleton women were included in our study over a period of 2 years. Out of 234 cases, 8 were lost to follow up.Therefore, 226 nulliparous women were available for analysis. All the subjects after proper history, examination, baseline investigations, fundoscopy & PIH profile were subjected to Uterine Artery Doppler Velocimetry at 24-26 period of gestation.

These cases were followed regularly throughout there antenatal course & outcome measured as gestational hypertension, pre-eclampsia & eclampsia.
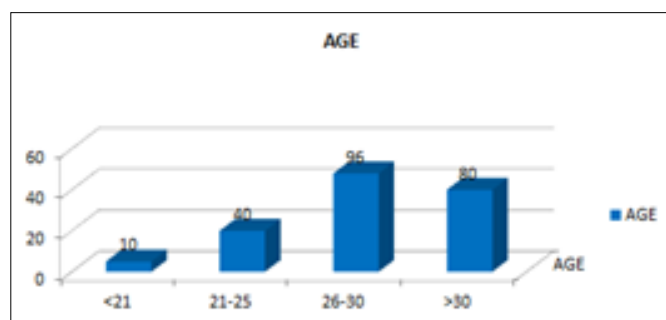

Fig 1: Age Distribution

40% were in age group 26-30 years & only 9% were<21 years. In the<21year age –group, 5(23%) developed PIH, in 21-25year age group 4(18%), in 26-30year age group 3 (14%) & 10 (45%) patients >30year age developed PIH.
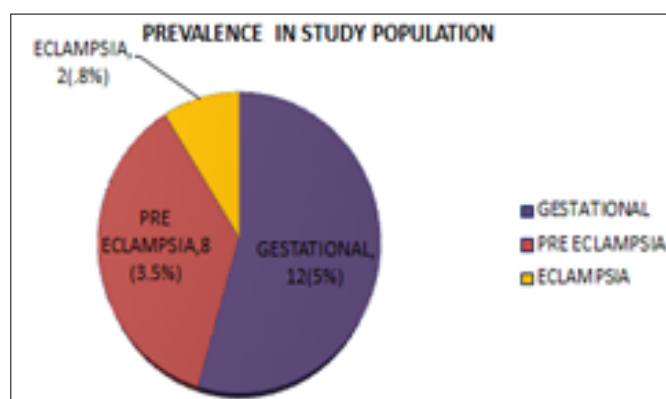

Fig 2: Prevalence of hypertension

Among 22 women who developed hypertension, 12 (5%) had gestational or non-proteinuric hypertension. Preeclampsia (proteinuric hypertension) was seen in 8 women with prevalence of 3.5%. Eclampsia developed in only 2 patients (8%).

Table 1: Prevalence of uterine artery Doppler abnormalities

PREVALENCE OF UTERINE ARTERY DOPPLER ABNORMALITY IN THE STUDY POPULATION		
DOPPLER test	FREQUENCY(n)	PERCENTAGE (%)
NORMAL	192	85.0
ABNORMAL DOPPLER	34	15.0
DIASTOLIC NOTCH	10	5.0
S/D RATIO	12	6.0
PULSATILITY INDEX	12	6.0
COMBINED	14	7.0

In the study population, uterine artery Doppler abnormalities were detected in 34 (15%) of cases. Doppler findings were normal in 192 cases.

Table 2: Uterine artery Doppler in predicting pre eclampsia

DOPPLER TEST	TRUE POSITIVE	FALSE NEGATIVE	FALSE POSITIVE	TRUE NEGATIVE	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
S/D	4	6	8	208	40.0	96.2	33.3	97.0
D.N	6	4	8	208	60.0	96.2	43.0	98.0
PI	4	6	10	206	40.0	95.0	28.6	97.0
COM	8	2	8	208	80.0	96.3	50.0	98.8

In prediction of pre-eclampsia (proteinuric hypertension), persistent diastolic notch has sensitivity of 60% and positive predictive value of 43% and is therefore the single best predictive marker. However combination of parameters has the highest sensitivity and positive predictive value.

Table 3: Uterine artery Doppler in predicting Gestational hypertension

DOPPLER TEST	TRUE POSITIVE	FALSE NEGATIVE	FALSE POSITIVE	TRUE NEGATIVE	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
S/D	2	10	6	208	16.7	97.0	25.0	95.4
D.N	2	10	8	206	16.7	96.0	20.0	95.3
PI	4	8	8	206	33.3	96.2	33.3	96.0
COMB.	2	10	6	208	16.6	97.2	25.0	95.4

In prediction of gestational hypertension (non-proteinuric), pulsatility index has got highest sensitivity (33.3%) as single predictive marker. However, sensitivity of every single index as well as combined indices is low as compared to pre-eclampsia.

Discussion

This prospective cohort study was conducted in Department of Obstetrics & Gynaecology, Sher-I-Kashmir Institute of Medical Sciences (SKIMS), the tertiary care center in Srinagar over a period of 2 years, whose inflow includes women from both rural & urban sector. The study was done to evaluate the role of uterine artery Doppler in prediction of gestational hypertensive disorders i.e Pre –eclampsia & Gestational hypertension.

Among 226 nullipara, 8 developed Pre-eclampsia (3.5%), 12 developed gestational hypertension (5%), & 2 developed eclampsia (0.8%). The prevalence of pre-eclampsia in our study was 3.5%,which was comparable to studies conducted by Iron *et al.* & Bewely *et al.* While interpreting the results, eclampsia cases have been included as severe pre-eclampsia & evaluated as single group –pre-eclampsia.

Second trimester uterine artery Doppler was normal in 192 nullipara & 34 among 226 had abnormal uterine artery Doppler velocimetry when 95th percentile was taken as cut-off. Out of these 34 patients with abnormal Doppler results, 8 patients

developed proteinuric hypertension (pre-eclampsia/eclampsia) with sensitivity & specificity of 80% and 88% respectively. The results are comparable to the studies conducted by following authors….

Table 4: Patients with abnormal Doppler results, 8 patients developed

STUDY	YEAR	SENSITIVITY	SPECIFICITY
Valensise et al	1993	86%	93%
Bower et al	1993	75%	89%
Bhattacherya, Sanjay kumar	2010	73.3%	86.48%
SKIMS/PRESENT STUDY	2013	80%	88%

4 patients among 34 patients with abnormal second trimester uterine artery Doppler developed non-proteinuric hypertension (gestational hypertension) with sensitivity & specificity of 33.3% and 89% respectively. The results are comparable with the following authors.

Table 5: The results are comparable with the following authors

STUDY	YEAR	SENSITIVITY	SPECIFICITY
Valensise et al	1993	50%	96%
Bhattacherya, Sanjay kumar	2010	57%	95%
North et al	1994	51%	88%
SKIMS	2013	33.3%	89%

The results in the study showed that uterine artery Doppler findings in patients who developed proteinuric (pre-eclampsia/eclampsia) hypertension were significantly different from those who were destined to develop non-proteinuric hypertension (gestational hypertension). Those women who developed pre-eclampsia, Doppler abnormalities were present in 80% of cases compared to those who developed gestational hypertension. Doppler abnormalities were present in only 33.4% of cases with gestational hypertension. The results are comparable with the studies done by Llurba *et al.* in 2009, revealing that Uterine artery Doppler can identify 71% of pregnancies that will subsequently develop proteinuric hypertension [9].

The predictive role of various Doppler indices was evaluated in the present study. Out of 34 patients with abnormal Doppler,10 developed pre-eclampsia with sensitivity of 60%, 40% and 40% for diastolic notch, S/Dratio, Pulsatility index respectively. The specificities of these indices ranged from 95% to 96%. The values are comparable to the study conducted by Kurdi *et al.* [10]

In predicting proteinuric hypertension (pre-eclampsia-eclampsia), persistence of diastolic notch was the single best Doppler index among other indices with positive predictive value of 43%. However, combined parameters has highest

sensitivity and positive predictive value of 96.3% and 50% respectively. This is similar to the results obtained by Bower *et al.* [11] Antsaklis *et al.* 2000 [12] and Chan *et al.* 1995 [13]

Out of 12 patients with gestational hypertension, abnormal uterine artery Doppler was seen in 4 patients with sensitivity of 16.6% for all indices except 33.3% for pulsatility index when 95th percentile was taken as cut-off. The specificity was from 96%-97.2%. Among various Doppler indices, pulsatility index was better predictive index with positive predictive value of 33.3%. PI was seen in 3.3% of cases, which is comparable to study done by Suchila *et al.* (2007) [14].

In our study the important finding is that,the Doppler abnormalities were higher in women with proteinuric hypertension or pre-eclampsia. This indicates defective placentation as one of the causative factors in this form of disease. Our findings support the theory presented by Ness and Roberts. The theory states that Pre-eclampsia is the clinical result of maternal as well as placental disorders [15].

Defective placentation due to impaired trophoblastic invasion in first half of pregnancy leads to the pre-ecalampsia. In contrast maternal factors may be the cause of less severe form of hypertension in pregnancy i.e. Gestational hypertension or non-preteinuric hypertension. It seems that uterine artery Doppler is one of the best available test for the early detection of pre-eclampsia of placental origin.

Our study is in accordance with other studies done by H Valensise, V Bezzeccheri *et al.* (1993) which suggest that second trimester abnormal uterine artery Doppler velocimetry has better sensitivity for the prediction of pre-eclampsia than for the prediction of gestational hypertension [8].

The sensitivity of uterine artery Doppler velocimetry in prediction of pre-eclampsia in our study is 80%. However, the positive predictive value is only 23.5%, comparable to study by Albaiges *et al.* 2000 (PPV 10% and sensitivity of 70%) [16]. This limits its use as sreening test in general population. However, In high risk pregnancies an abnormal uterine Doppler is an indication for a closer pre-natal follow up. In the same high risk population, a normal second trimester uterine Doppler is reassuring and allows a less frequent fetal surveillance than when the test is positive.

Conclusion
- Uterine artery doppler velocimetry is one of the tools for prediction of pre-eclampsia (proteinuric hypertension)
- Diastolic notch in the uterine artery as a single parameter is better than other individual indices.
- Women with normal second trimester uterine artery Doppler velocimetry have low risk of developing obstetric complication -----hypertensive disorders.
- Second trimester uterine artery Doppler velocimetry may be included in hospitals with facilities and infrastructure to identify the group of patients at risk of developing pre-eclampsia.
- However, as the power of study is low, further studies have to be done to know Doppler predictive value in general population.

Recommendations
The patients with abnormal Doppler can be advised
- Regular antenatal follow up.
- Anti-oxidants
- Calcium supplements
- Early detection of hypertension, followed by vigilant feto-maternal surveillance.

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