A Study Of Risk Factors Of Fall In Elderly

[1]Dr. R. Subashree, [2*]Dr. S. Oorvasi, [3]Dr. C.P Abinaya
[1,2,3]Assistant Professor, Department Of Obstetrics & Gynecology,
Government Medical College& Hospital, Thiruvarur, Tamil Nadu, India

*Corresponding Author:
Dr. S. Oorvasi
3Assistant Professor, Department Of Obstetrics & Gynecology, Government Medical College& Hospital,
Thiruvarur, Tamil Nadu, India

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Abstract

Background: Hypertension complicates nearly 10% of pregnancies. Hypertensive disorders vary from mild gestational hypertension to severe preeclampsia. Pre-eclampsia, which complicates 2-8% of all pregnancies, as a rule, develops after 20 weeks of gestation and it is characterized by elevated blood pressure along with proteinuria. The method of choice to indirectly monitor the status of the spiral artery bed is provided by uterine artery waveform and serves as a predictor of preeclampsia. Performing a uterine artery Doppler study at 22-24weeks gestation increases the predictive value of adverse pregnancy outcomes.

Aim: To study the role of elevated mid-trimester Serum Beta HCG levels and Uterine Artery Doppler in predicting the occurrence of Hypertensive disorders of pregnancy.

Material and Methods: A prospective randomized double-blinded study was conducted after obtaining institutional ethical committee approval. Normotensive pregnant women between 13-24 weeks of gestation as per last menstrual period or ultrasound scan. Singleton pregnancies between 13-24 weeks of gestation as per the last menstrual period or ultrasound scan are included in this study. Gestational age < 13 weeks and > 24 weeks, Chronic Hypertension, Multiple Pregnancies, Molar Pregnancy, and History of Down syndrome patients are excluded from this study. The study was conducted from December 2021 to November 2022. Serum beta HCG and uterine artery doppler were performed.

Results: In our study, 142 cases were finally evaluated, and 123 cases (82%), had Beta-HCG levels, < 2MOM. Whereas 27 cases (18%), had values >2 MOM. The multiple of the median was calculated and Beta-HCG values for that particular gestational age group were analyzed. Out of 123 cases with Beta- HCG levels < 2 MOM, only 1 case (4.8%) developed preeclampsia. And out of 27cases (18%) with Beta- HCG values >2MOM, 20 cases (95.2%) developed pregnancy-induced hypertension, and 7 cases (18%) were normotensive. In our study, the increasing Beta-HCG levels (in mIU/ml) showed a direct association with the severity of pregnancy-induced hypertension. Out of 142 patients, 26 had abnormal Uterine Artery Doppler changes. Out of which 18 had increased RI, 18 had Increased PI, and 26 had Diastolic Notching.

Conclusion: There is a strong association between high maternal serum ß-hCG levels and abnormal uterine Doppler studies in the prediction of preeclampsia. Diastolic notch in the uterine artery as a single parameter is better than the individual Doppler indices in the uterine artery. In our study BhCG,>2 MOM in the early second trimester is an excellent screening tool for the prediction of pre-eclampsia with a sensitivity of 95.2% and specificity of 94.2%.

Keywords: Pre-eclampsia, B hCG, uterine doppler

Introduction

Gestational Hypertension is defined as Blood pressure >= 140 mm Hg systolic and/or >=90 mmHg diastolic in a previously normotensive woman after 20 weeks of gestation. Pre-eclampsia, which complicates 2-8% of all pregnancies, as a rule, develops after 20 weeks of gestation and it is characterized by elevated blood pressure along with proteinuria (≥300mg/24hr or ≥+1 dipstick). It can be categorized into mild and severe forms based on the level of hypertension and proteinuria [1]The proposed etiology for preeclampsia is abnormal placentation. In normal placental development, the placental cells invade the uterine spiral arteries and transform them from small-caliber resistance vessels to high-caliber capacitance vessels to enable adequate perfusion.[2]In Preeclampsia, this transformation does not occur in the spiral artery bed leading to increased resistance to flow into intervillous space. Several methods are under trial to predict pre-eclampsia at an earlier gestational age.[3]The method of choice to indirectly monitor the status of the spiral artery bed is provided by uterine artery waveform and serves as a predictor of preeclampsia. Performing a uterine artery Doppler study at 22-24weeks gestation increases the predictive value of adverse pregnancy outcomes.[4]Abnormal uterine artery doppler in the second trimester has been shown to identify pregnancies that could develop pre-eclampsia. Persistence of an early diastolic notch, unilateral or bilateral in the main uterine artery, or elevated resistance index or RI of 0.6, or an elevated pulsatility index of 1.4 or both is considered as abnormal flow velocity waveforms.[5]Other screening tests include measurement of urinary and plasma angiogenic factors like VEGF, placental growth factor, soluble endoglin and soluble FMS-like tyrosine kinase-1, plasma uric acid levels, and maternal serum markers such as alpha-fetoprotein, human chorionic gonadotropin, inhibin A, and activin A. Among these, Serum beta HCG is a reliable marker.[6]The human chorionic gonadotropin (hCG) is a glycoprotein made of two subunits, α, and β, released from syncytiotrophoblasts. Maternal serum hCG peaks at 8 – 10 weeks of gestation and declines at 18-20 weeks. Immunological changes occurring in the trophoblasts during the mid-trimester result in secretary response which is seen as a rise in serum beta hCG levels.[7] In pre-eclampsia, there is focal cellular necrosis of syncytiotrophoblast and increased mitotic activity with the proliferation of cytotrophoblasts. Also, there is the rapid transformation of the proliferating trophoblast into syncytiotrophoblast resulting in elevated hCG production by hyperplasic cytotrophoblasts. This leads to a rise in mid-trimester serum beta HCG levels which can be used as a non-invasive biomarker in predicting the development of hypertension later in that pregnancy.[8]

Materials and Methods: This study was performed by the principles of the Declaration of Helsinki. After obtaining institutional ethical committee approval written informed consent was taken from all the patients. A study was conducted at Government Thiruvarur Medical College from December 2021 to November 2022. Normotensive pregnant women between 13-24 weeks of gestation as per the last menstrual period or ultrasound scan are taken as the study population. Singleton pregnancies between 13-24 weeks of gestation as per the last menstrual period or ultrasound scan were included in this study. Exclusion criteria include patients with Gestational age < 13 weeks and > 24 weeks, Chronic Hypertension, Multiple Pregnancies, Molar Pregnancy, History of Down syndrome, and Congenital Malformations. A total of 150 normotensive pregnant women attending antenatal OPD or admitted as patients over the study period, fulfilling the inclusion and exclusion criteria will be recruited in the study after obtaining informed consent. On admission, a detailed history will be taken and individuals would be subjected to general, systemic, obstetric examination and ultrasonological assessment. History regarding Age, Parity, Gestational age, Height, Weight, Weight gain during pregnancy, Weeks of collecting beta HCG samples, past medical and obstetric history, and family history will be collected. Systemic examination with special reference to edema and blood pressure will be done.

Estimation of serum Beta HCG: Around 3 ml of venous blood was collected between 13 -20 weeks of gestation and serum beta hCG was determined using Chemiluminescent Microparticle Immunoassay. Results were analyzed based on the beta-hCG reference range at a particular gestational age.

**Measurement of Uterine artery waveforms:** Uterine artery Doppler was performed by a

Radiologist between 22-24 weeks of gestation. The pulsatility index, Resistance index, and presence of any notch (bilateral or unilateral) will be taken as a positive predictor for developing hypertension later in the pregnancy. Subsequent development of preeclampsia can be predicted when the resistance index is more than 0.7 and /or pulsatility index is more than 1.4 and/or the presence of a notch. All patients were followed up and examined for 4 weeks to 28 weeks, fortnightly up to 34 weeks, and thereafter weekly till delivery. At every visit, a General examination including blood pressure recording, urine examination for albumin and sugar were recorded, Abdominal examination to assess fetal growth and well-being, and liquor status was assessed. Several women developing PIH subsequently will be noted. Statistical analysis will be performed using Microsoft Excel and SPSS software.

## Results:

The majority of patients in our study were in the age group of 26 -30 years (43.3%). Only 4 cases (2.7%) were in the age group of <20 years and 3 cases were in the age group of >35 years (2%). The majority of patients who developed preeclampsia were in the age group of 21-25 years (47.6%). Out of 4 cases in the age group <20 years 3 (14.3%) developed preeclampsia and out of 3 cases in the age group >35 years 2 (9.5%) developed preeclampsia. The majority were Primigravida 79 patients. (52.7%). Out of 21 cases who developed preeclampsia, 15 (71.4%) were primigravida indicating that the incidence of preeclampsia is more among primigravida. In our study, most of the patients were within normal BMI of 18.6 -24.9, and only 7.3% had a BMI of >30. Around 71.4% of cases who developed preeclampsia were within normal BMI (18.6 to 24.9) and only

14.3% of cases were obese (>30). Out of 150 cases,9 patients (6%) had a history of preeclampsia in a previous pregnancy. Out of 21 patients who developed preeclampsia,4 cases (19%) had a history of hypertension in a previous pregnancy. Out of 21 cases who developed preeclampsia, 33.3% cases were diagnosed with gestational hypertension within 4 weeks duration and 14.4% had a duration of >4 weeks, and 52.3 % cases presented with preeclampsia for the first time. In our study, the majority of beta hCG samples were taken at 16 weeks of gestation (34.7%). Out of 150 cases,121 cases (80.7%) were normotensive,21 cases (14%) developed preeclampsia,4% cases were lost to follow up and 1.33% had a spontaneous abortion. Out of 21 patients who developed preeclampsia, the majority of them 52.4% presented between 32 -36 weeks of gestation and 33.3% presented at term (>37 weeks). Around 7.3% of patients had systolic blood pressure falling in the mild preeclampsia cut-off range (i.e.) between 141-159 mmHg and 6.7% had severe preeclampsia cut-off (i.e.) >160mmHg. Around 6.7% of patients had diastolic blood pressure falling in the mild preeclampsia cut-off range (i.e.) between 91-109 mmHg and 6% had severe preeclampsia cut-off (i.e.) >110mmHg. In our study, 42.9% of patients with preeclampsia had imminent symptoms and 57.1% didn't have imminent symptoms. Around 85.7% who developed preeclampsia had proteinuria and only 1.7% of normotensive had proteinuria. In my study,12% of Cases were delivered as preterm and 88% delivered at term, out of which, 42.9% preeclamptic patients delivered as preterm and 57.1 % delivered at term. which is statistically significant. In my study,69% of patients delivered by labor natural, and 30.3% had LSCS. Out of which, 71.4 % of preeclamptic patients delivered by labour natural.

Graph: 1 Distribution Of Patients With Preeclampsia According To Gestational Age At Which Betahcg Taken
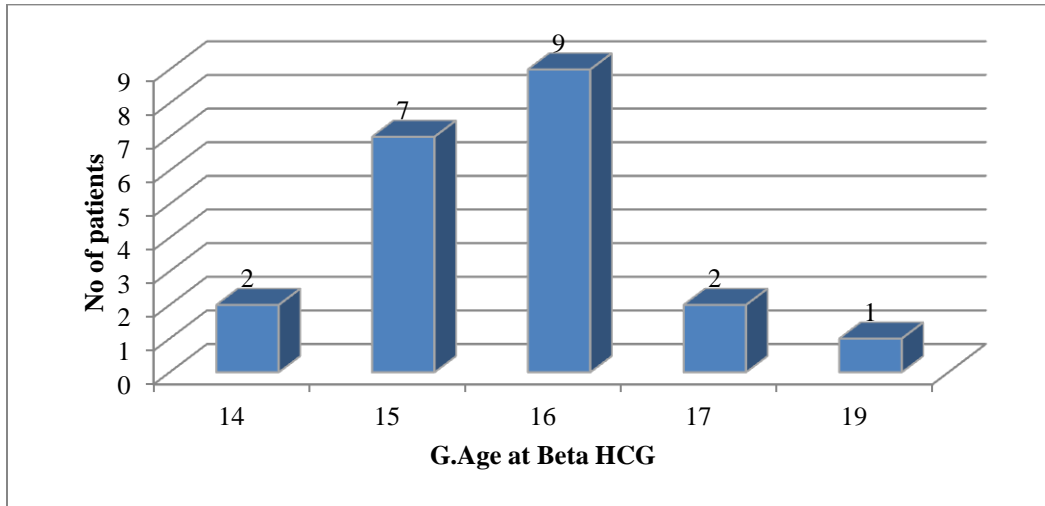

GRAPH:2 DISTRIBUTION OF CASES ACCORDING TO DIAGNOSIS AND BetaHCG in mIU/L
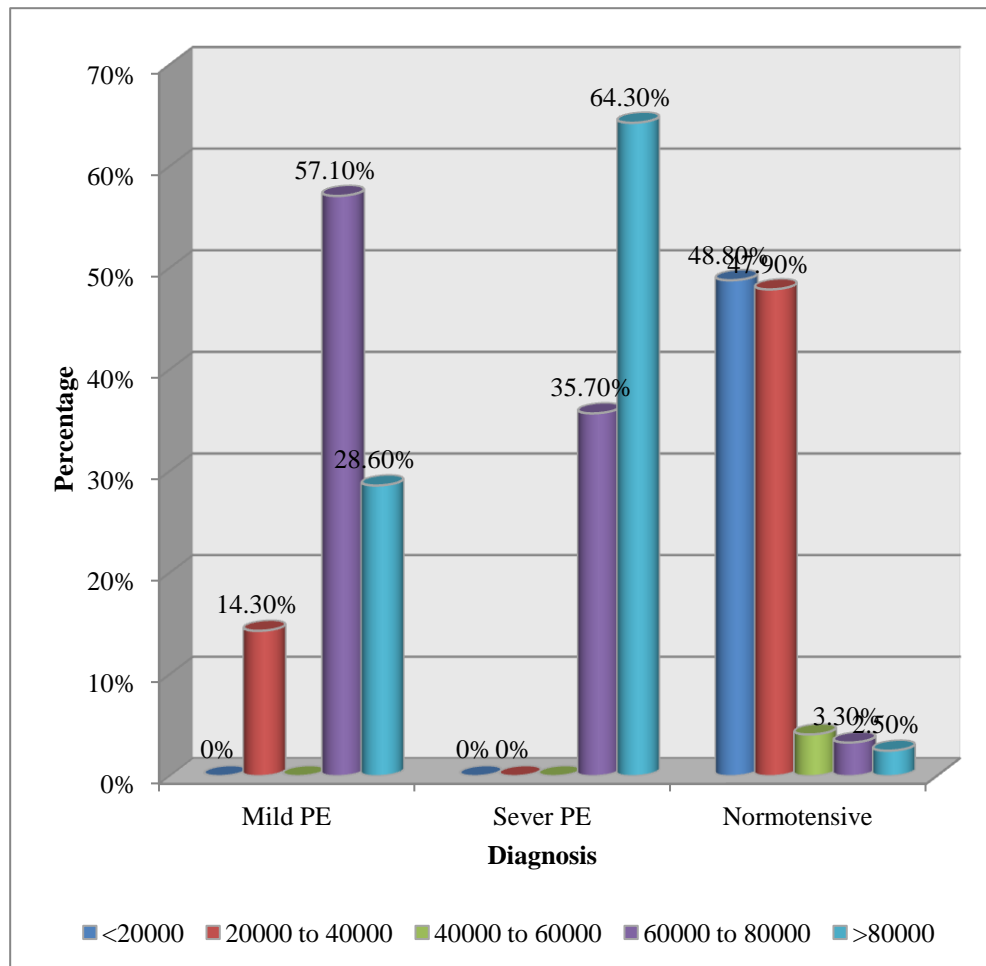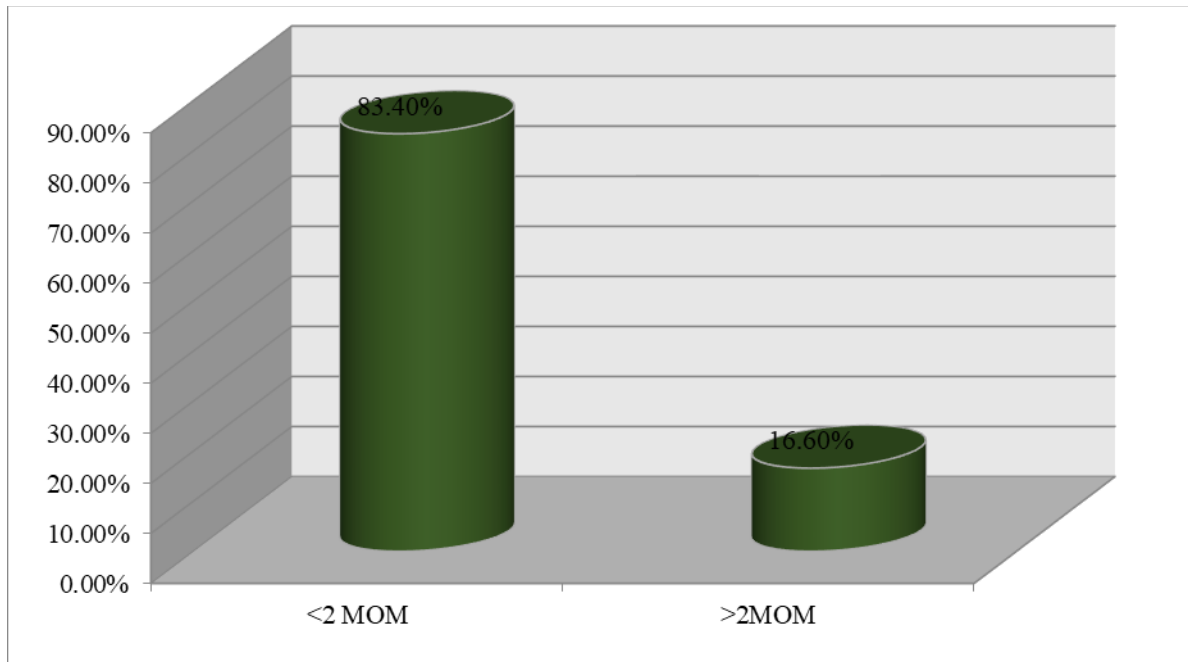
In our study, the incidence of preeclampsia increased with rising maternal serum BetaHCG levels. Out of 21 preeclamptic patients, 11 cases (92.9%) developed preeclampsia when Betahcg was >80000 mIU/L, 9 cases (92.8%) developed when values were between 60000-80000 mIU/L compared to 3 cases (2.5%) who were found to normotensive when values were >800000.which is statistically significant (p-value <0.001).

GRAPH :3 DISTRIBUTION OF CASES ACCORDING TO BetaHCG in MULTIPLE OF MEDIAN (MOM)
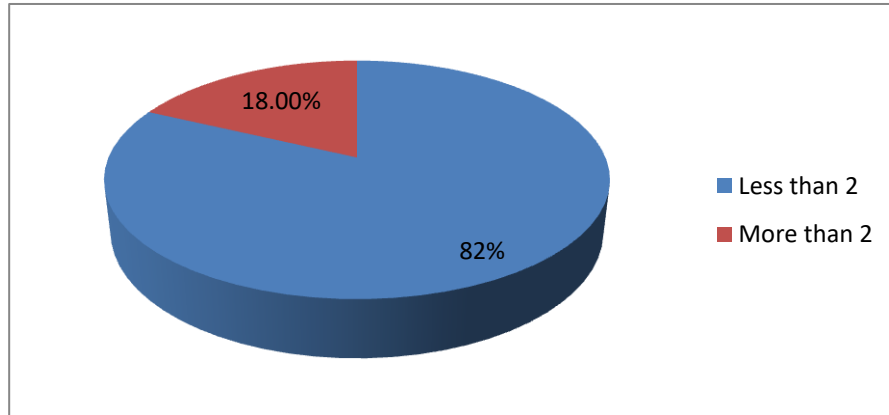

In our study,82% of patients had BetaHCG >2 MOM and 18% had values <2 MOM.. The incidence of Preeclampsia is more (i.e.) 95.2% when maternal serum BetaHCG was >2 MOM

GRAPH 4:CORRELATION BETWEEN EARLY ONSET PREECLAMPSIA (<34 Weeks) AND SERUM βhCG >2 MOM

The incidence of Early-onset preeclampsia occurring before 34 weeks of gestation is more (i.e.) 83.4% when BetaHCG was >2 MOM

GRAPH:5 COMPARISON OF GESTATIONAL AGE AT DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS
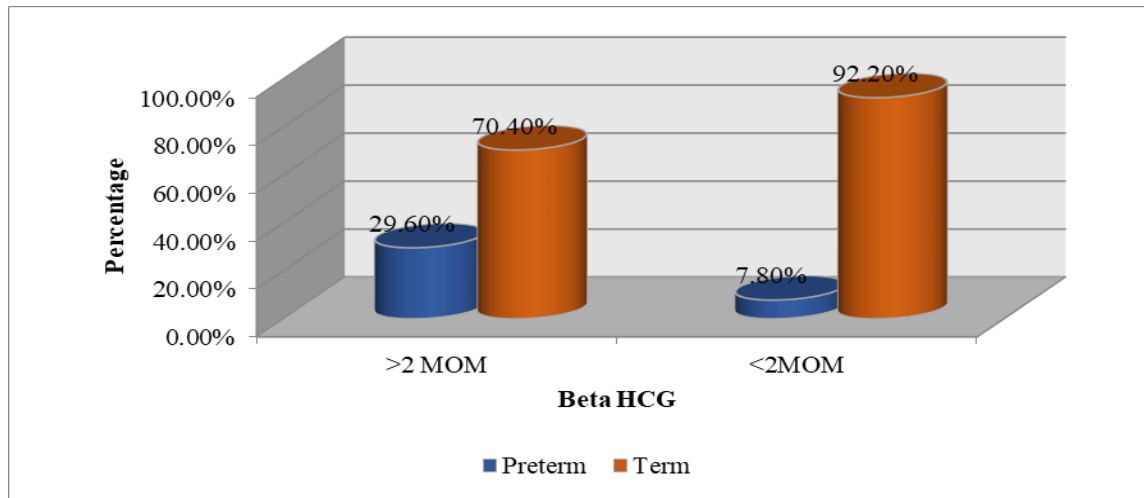
In our study, Preeclamptic patients with elevated serum βhCG had more preterm delivery (<37 weeks), i.e. 29.6% of preterm delivery among preeclamptic patients when   BetaHCG was   > 2 mom, which is statistically significant (0.002).

TABLE:1 COMPARISON OF DOPPLER WITH DIAGNOSIS

Doppler	Diagnosis			Total	Chi-square	P value
	Mild PE	**Sever PE**	**Normotensive**			
Rt- PI						
Abnormal	5 (71.4%)	10 (71.4%)	3 (2.5%)	18 (12.7%)		
Normal	2 (28.6%)	3 (28.6%)	119 (97.5%)	124 (87.3%)	76.85	<0.001
Lt-PI						
Abnormal	2 (28.6%)	11 (78.6%)	5 (4.1%)	18 (12.7%)	64.496	<0.001
Normal	1 (71.4%)	3 (21.4%)	120 (95.9%)	124 (87.3%)		
Rt-RI						
Abnormal	4 (57.1%)	11 (78.6%)	4 (3.3%)	19 (13.4%)	73.50	<0.001
Normal	3 (42.9%)	1 (21.4%)	119 (96.7%)	123 (86.6%)		
Lt-RI						
Abnormal	2 (28.6%)	11 (78.6%)	0 (0%)	13 (9.2%)	96.481	<0.001
Normal	3 (71.4%)	2 (21.4%)	124 (100%)	129 (90.8%)		
B/L Notch						
Abnormal	4 (57.1%)	12 (85.7%)	10 (8.3%)	26 (18.3%)	57.746	<0.001
Normal	3 (42.9)	2 (14.3%)	111 (91.7%)	116 (81.7%)		

TABLE :1 Shows In our study,47.6% of patients had abnormal Doppler changes between   22-23 weeks of gestation. In our study, out of 142 patients, 26 had abnormal Uterine Artery Doppler changes. Out of 26

patients,18 had increased RI, 18 had Increased PI, and 26 had Diastolic Notching. It was found that, among 26 patients (18.3%) with abnormal uterine artery Doppler parameters, 16 patients (61.5%) developed preeclampsia and 10 patients (38.5%) were normotensive. Abnormal uterine artery Doppler parameterUterine artery PI - Abnormal (Right PI- 12.7%, Left PI-12.7%) Uterine artery RI -Abnormal (Right PI-13.4%, Left RI -9.2%) Uterine artery Notching –Bilateral -18.3%About 83.4% patients with abnormal Doppler velocimetry developed early onset preeclampsia before 34 weeks of gestation. In our study, a total of 142 cases were finally evaluated, 27 cases had abnormal BetaHCG value (>2MOM) out of which 20 patients developed preeclampsia and 1 patient with normal value(<2MOM) developed preeclampsia. The p-value for this parameter when calculated for the development of preeclampsia came out to be <.001, which is highly significant. Similarly, it was found that 26 patients had abnormal Doppler changes, out of which 16 patients developed preeclampsia and 5 patients with normal Doppler developed preeclampsia. Diastolic notch is the best predictor compared to the other two Doppler parameters.

TABLE:2 SHOWS THE CORRELATION BETWEEN BOTH BETAHCG AND UTERINE ARTERY DOPPLER WITH THE DEVELOPMENT OF PREECLAMPSIA

Doppler			Preeclampsia		Total	P value
			Yes	No		
BHCG (AN and N)		Abnormal	20	7	27	<0.001
		Normal	1	114	115	
		Total	21	121	142	
RI	Right	Abnormal	15	3	18	<0.001
		Normal	6	118	124	
		Total	21	121	142	
	Left	Abnormal	13	5	18	<0.001
		Normal	8	116	124	
		Total	21	121	142	
PI	Right	Abnormal	15	4	19	<0.001
		Normal	6	117	123	
		Total	21	121	142	
	Left	Abnormal	13	0	13	<0.001
		Normal	8	121	129	
		Total	21	121	142	
B/L Notch		Abnormal	16	10	26	<0.001
		Normal	5	111	116	
		Total	21	121	142	

TABLE :3 DISTRIBUTION OF VALIDITY PARAMETERS OF UTERINE ARTERY DOPPLER TESTING AND BETA-HCG FOR PREECLAMPSIA (POSITIVE PREDICTIVE VALUE)

G. Age at Doppler	TP	TN	FP	FN	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	P value
PI	15	118	3	6	71.43%	97.52%	83.33%	95.16%	93.66%	<0.001
RI	15	117	4	6	71.43%	96.69%	78.95%	95.12%	92.96%	<0.001
B/L Notch	16	111	10	5	76.19%	91.74%	61.54%	95.69%	89.44%	<0.001
Combined (PI+RI+Notch)	19	104	17	2	90.48%	85.95%	52.78%	98.11%	86.62%	<0.001
Beta HCG	20	114	7	1	95.24%	94.21%	74.07%	99.13%	94.37%	<0.001

TABLE :3 Uterine Artery Doppler Parameters: Sensitivity and Positive predictive value of PI - 71.43%,83.33%Sensitivity and Positive predictive value of RI-71.43%,78.95%Sensitivity and positive predictive value of Notch-90.48%,52.78%Notch as a single parameter is the best predictor of Preeclampsia but the combination of the parameter is the best indicator. Beta HCG: BetaHCG alone has a sensitivity of 95.24% and a positive predictive value of 74%.

Discussion

Our study was Comprised of 150 asymptomatic pregnant women subjected to both mid-trimester maternal serum BHCG estimation and uterine artery Doppler velocimetry. BetaHCG estimation was done using chemiluminescent immunoassay between 13-20 weeks of gestation and uterine artery Doppler parameters were measured between 22-24 weeks of gestation. Their Baseline blood pressure recording, laboratory investigations and general physical examination, and obstetric examination were assessed during each visit. They were followed till delivery .out of 150 antenatal women included in the study,142 cases were followed till delivery, 6 cases (4%) were lost to follow up and 2 cases (1.3%) had a spontaneous abortion. Out of 142 cases studied, the Incidence of preeclampsia was found to be 14 % (i.e.) 21 cases developed preeclampsia. Out of which 9.3% developed severe preeclampsia and 4.7% developed mild preeclampsia. Age has an important influence on the incidence of hypertensive disorders during pregnancy. Development of preeclampsia and eclampsia before 20 years of age have been attributed to initial trophoblastic invasion and maternal immune response to it. The failure of the normal invasion of trophoblastic cells leads to mal-adaptation of the spiral arterioles, which are related to the causation of preeclampsia/eclampsia.[9] While in women greater than 30 years of age, the risk is due to the increased villous reaction. It is proposed that preeclampsia/eclampsia syndrome is because by a maternal immune reaction against paternal antigens expressed in the placenta and this reaction leads to defective trophoblast invasion and subsequent placental dysfunction. [10]The lower risk of pre-eclampsia among multiparous women has been attributed to desensitization after exposure to paternal antigens in the placenta during previous pregnancies and due to smoother trophoblastic invasion after modification of maternal spiral arteries during the first pregnancy. [11]Serum beta hCG was measured between 13-20 weeks, out of which 35 % of samples were collected around 16 weeks of gestation in this study. In our study, a total of 142 cases were finally evaluated, 123 cases (82%), had Beta-HCG levels, < 2MOM. Whereas 27 cases (18%), had values >2 MOM. The multiple of the median was calculated and Beta-HCG values for that particular gestational age group were analyzed. [12]Out of 123 cases with Beta- HCG levels < 2 MOM, only 1 case (4.8%) developed preeclampsia. And out of 27cases (18%) with Beta- HCG values >2MOM, 20 cases (95.2%) developed pregnancy-induced hypertension, and 7 cases (18%) were normotensive. The p-value for this

parameter when calculated for the development of pregnancy-induced hypertension, came out to be <.001, which is highly significant. Pankaj Desai et al, found that 62 cases out of 90 (68.9%) with values of Beta-HCG >2MOM developed pregnancy-induced hypertension against 21 cases out of 130 (16.15%), having a Beta-HCG value <2 MOM.[13] While 3 cases out of 21, (14.28%) with a Beta-HCG value <80,000mIU/ml developed severe disease. In our study, the increasing Beta-HCG levels (in mIU/ml) showed a direct association with the severity of pregnancy-induced hypertension. While 3 cases out of 21, i.e., 2.5% with a Beta-HCG value <80,000mIU/ml, group had severe preeclampsia compared to, >80,000 mIU/ml group where 11 out of 21 i.e., 92.9% developed preeclampsia,28.6% had mild preeclampsia and 64.3% had severe preeclampsia, giving a p-value of <0.001, which is statistically significant. So, it was concluded that as the Beta-HCG levels rise, the probability of developing severe preeclampsia also increases with a positive association between these parameters. [13]It was evident that Preeclamptic patients with elevated serum βhCG had more preterm delivery (<37 weeks), i.e 29.6% of preterm delivery among preeclamptic patients when BetaHCG was > 2 mom, which is statistically significant (0.002). [14]Out of which 18 had increased RI, 18 had Increased PI, and 26 had Diastolic Notching. Out of 21 preeclamptic patients, 61.5% (16 cases) with abnormal uterine artery Doppler parameters (Either increased RI or PI or notching or combination of three) developed preeclampsia and 4.31% (5 cases) with normal doppler parameters developed preeclampsia. [15]

Conclusion: Our study concluded that there is a strong association between high maternal serum ß-hCG level and abnormal uterine Doppler studies in the prediction of preeclampsia. Doppler assessment is a non -a invasive method and thus easily accessible and acceptable to patients Among all uterine artery Doppler parameters studied, pulsatility index and bilateral notching are the promising Doppler indices to predict the risk of preeclampsia. Diastolic notch in the uterine artery as a single parameter is better than the individual Doppler indices in the uterine artery. It has a good predictive value, especially for early onset pre-eclampsia and severe pre-eclampsia. Also, a good association was found between high maternal serum ß-hCG levels and the rising severity of the

disease. Combined mid-trimester uterine artery Doppler and maternal serum BetaHCG estimation is the best predictor for Preeclampsia, These predictors help in risk stratification of women destined to develop pregnancy-induced hypertension in the same pregnancy, and these women can be followed up in a tertiary care center for further management.

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