Original Research Article

First Trimester Screening for Prediction of Preeclampsia with Maternal Characteristics, Uterine Artery Doppler and Mean Arterial Pressure

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Abstract

Aim: First trimester screening for prediction of preeclampsia with maternal characteristics, uterine artery doppler and mean arterial pressure.

Materials and Methods: The present study was done in pregnant women attending outpatient Department of Obstetrics and Gynaecology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala, Haryana. This study was conducted from Jan 2020 – June 2021. Women, giving consent for participation in the study; between 11-13+6 weeks; Spontaneous conception were included in the study. Fetal Congenital abnormalities detected any time during pregnancy.

Results: 129 pregnant women were included. Majority of pregnant women included were in the age group of 25-29 years. Out of the total 129 women in our study group, 18(13.95%) developed preeclampsia. Incidence of preeclampsia was highest (33.0%) in the age group of 20-24 years and 30-35 years. 7.0% female developing preeclampsia were aged 25-29 years and above 35 years. 3 (16.6%) Women developed early onset pre-eclampsia whilst the rest 83.4 % i.e. 15 females had late onset pre-eclampsia amongst which 5 gestational hypertension followed by proteinuria and eventually late onset pre-eclampsia. In 45% (5/11) women who had past history of pre-eclampsia/ gestational hypertention developed pre-eclampsia in present pregnancy. 4 out of 6 women (66%) with past history of chronic hypertension developed pre-eclampsia. In our study 3 out of 3 women (100%) who were APS positive had pre-eclampsia in present pregnancy. 72% of the women with preeclampsia had a mean arterial pressure of more than 90mmHg. On bilateral uterine artery Doppler, 39% of women had a raised palatability value. Majority of women (89%) with the presence of a diastolic notch developed pre-eclampsia. Past history of pre-eclampsia, advanced maternal age, gestational, raised pulsatility index, presence of diastolic notch showed association with adverse pregnancy outcome.

Conclusion: A detailed history for first trimester (11-13+6 weeks) detection of maternal characteristics, MAP along with uterine artery Doppler (PI, RI and diastolic notch) are helpful in early prediction of preeclampsia. There is a statistically significant correlation of presence of

diastolic notch on uterine artery doppler with development of preeclampsia. In a low resource country like India prediction of preeclampsia with maternal characteristics, mean arterial pressure and uterine artery doppler is not only cost effective but a non-invasive modality for prediction of pre-eclampsia so that preventive measures can be implemented well in time to avoid catastrophic maternal and fetal outcomes.

Keywords: Preeclampsia, Uterine artery Doppler, Maternal characteristics, Mean arterial Pressure.

Introduction

Hypertensive disorders complicate 5 to 10 percent of all pregnancies, and together they form one of the deadliest triad along with hemorrhage and infection that contributes greatly to maternal morbidity and mortality rates. Of hypertensive disorders, the preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous. New- onset hypertension during pregnancy, termed gestational hypertension, is followed by signs and symptoms of preeclampsia almost half the time, and preeclampsia is identified in 4 to 5 percent of all pregnancies. The World Health Organization (WHO) systematically reviews maternal mortality worldwide, and in developed countries, 16 percent of maternal deaths were attributed to hypertensive disorders. In the United States from 2011 to 2013, more than half of these hypertension-related deaths were deemed preventable.[1] Therefore we conducted this study to evaluate the maternal characteristics in all antenatal women in first Trimester (11to 13±6 weeks) record, Mean Arterial pressure, bilateral uterine artery Doppler study from 11to 13±6 weeks POG in all antenatal women for prediction of Preeclampsia and to study incidence of preeclampsia and maternal fetal outcome in women with high risk factors.

Aims And Objectives

- Prevalence of preeclampsia on study group.
- Prediction of preeclampsia using maternal characteristics as per UPSTF Criteria 2014, MAP and Bilateral uterine artery Doppler (PI, RI, diastolic notch) study from 11 to 13 ± 6 weeks POG in all antenatal women.
- To study adverse maternal fetal outcome in women with high risk factors with preeclampsia.

Material and Method

The Prospective observational study was done on 129 pregnant women attending antenatal clinics of Department of Obstetrics and gynecology, tertiary care hospital in India. This study was conducted in the Department of Obstetrics and Gynecology in collaboration with the Department of Radiodiagnosis for a period of 18 months. Patients with Spontaneous conception and Between 11 to 13 ± 6 weeks were included in the study.

Methodology A written informed consent was taken from all the women included in the study after explaining to them the methodology of study. Maternal characteristics, past medical, family and past obstetric history of patients were recorded as per the proforma. Blood pressure was taken under standard operating procedure two times for each participant, to correctly diagnose preeclampsia. All pregnant women visiting antenatal clinic in first trimester willing to participate in the study were questioned regarding the high risk and moderate risk factors as per UPSTF. Maternal characteristics were noted. Systolic

and diastolic BP was noted and mean arterial blood pressure was calculated. Pregnant women were kept under follow-up and their outcomes were noted till delivery. Patient with high risk OR 1 or 2 moderate risk factors and increased MAP > 90mmHg or increased pulsatile index in uterine artery were followed up. MAP = Diastolic pressure + 1/3rd Pulse pressure, Baseline investigations CBC, PBF, RFT, LDH, LFT, Platelet count and urine for proteins were done in these cases with high risk. Patients were followed up for development of preeclampsia. Adverse maternal and fetal outcome preeclampsia (early and late onset preeclampsia), preterm labour, eclampsia, PPH, need for NICU admission, still birth was noted. Data was compiled and statistically analysed.

Statistical Analysis

The data was described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Student t-test. For comparing categorical data, Chi square ($\chi 2$) test was performed, and exact test was used when the expected frequency is less than 5.

Results

In the present study majority of women 35.7% were in the age group of 25-29 years and (3.9%) were in the age group of more than 35 years. The mean age of the study population was 26.88 years with standard deviation of 4.4 whereas the mean age of preeclampsia group was slightly higher 28.78 with a standard deviation of 5.77. 60% of women in the age group >35 years developed preeclampsia. Out of the total 18 women who developed preeclampsia majority of 14 women were of the age <35 years and the rest of 4/18 (22%) women were of the age >35 years. Advanced maternal age had statistically significant association with development of preeclampsia in our study (p-value 0.022). Majority of study subjects in present study had BMI in the range of 18.5-24.9 Kg/m^2 (normal) and 26.4% women were overweight (25-29.9). The mean BMI of the study group was 24.2 kg/m^2 and the mean BMI of women with preeclampsia in the study group was 24.28 kg/m^2 which were comparable. In present study, preeclampsia was more frequently found amongst primigravida (33%) and second gravidas (33%). However, the incidence of preeclampsia was found to be 1 in 6 in primigravida (16.2%) and 1 in 5(20%) in fourth gravida. Out of the total 18 women in our study group who developed preeclampsia, three women were gravida three and more with a significant p value of 0.002. In the present study, 5/18 (28%) women who developed preeclampsia had apast history of preeclampsia. 11% women had family History of preeclampsia. Four out of six (66%) women who had a past history of chronic hypertension developed preeclampsia. In the present study, 5/18 (28%) women who developed preeclampsia gave history of gestational hypertension in previous pregnancy.

Table 1: Demographic profile

Age (year)	Frequency n=129	Percentage
<18	0	0.00%
18-20	1	0.80%
20-24	44	34.10%
25-29	46	35.70%
30-35	33	25.60%
>35	5	3.90%

Religion		
Hindu	63	48.80%
Muslim	66	51.20%
GRAVIDA		
1	37	28.70%
2	45	34.90%
3	39	30.20%
4	5	3.90%
5	1	0.80%
6	2	1.60%
BMI (kg/m2)		
<18.5	7	5.40%
18.5- 24.9	75	58.10%
25-29.9	34	26.40%
>30	19	14.70%

In our study, 18/129 (13.95%) women developed preeclampsia, out of these 3/18(16.6%) women developed early onset preeclampsia and 10/18 (56%) developed late onset preeclampsia, five out of these 18 women (28%) developed gestational hypertension but over a span of further 3 to 4 weeks developed proteinuria and were thus included in the late onset preeclampsia. Thus, a total of 15/18(83.3%) women developed late onset preeclampsia. One patient in the early onset preeclampsia had eclampsia with IUD.

Table 2: Distribution of women according to past obstetric and medical Risk factors

1	Past Obstetrical History (N=129)	No risk factors		Risk factors	
		N	%	N	%
A	Pre-eclampsia	123	95.35%	6	4.65%
B	Gestational hypertension	124	96.12%	5	3.88%
C	Eclampsia	128	99.22%	1	0.78%
D	FGR	125	96.90%	4	3.10%
E	Preterm Labour	123	95.35%	6	4.65%
F	GDM	123	95.35%	6	4.65%
G	APS	126	97.67%	3	2.33%
H	IUD	123	95.35%	6	4.65%
	Past Medical History n=129	Absence of Risk factors		Presence of Risk factors	
2	Chronic hypertension	124	96.12%	6	4.65%
3	Overt Diabetes Mellitus	125	96.90%	4	3.10%
4	Chronic Kidney disease	128	99.22%	1	0.78%
5	Family History of Preeclampsia	No family history		Had a family history	
6	Family History of Eclampsia	127	98.45%	2	1.55%
7	Interconception period of >10 years	128	99.22%	1	3.10%

The overall mean value of mean arterial pressure of women in our study group was 87.5 mmHg with a standard deviation 3.7 while in women who developed preeclampsia

in our study group the mean value of mean arterial pressure was 90.67 mmHg with a standard deviation 5.49. 72% of women who developed preeclampsia had MAP 90 mmHg at 11-13+6 weeks compared to 28% who had normal MAP in present study. The difference between MAP was between preeclampsia and non-preeclampsia was statistically significant in our study (0.0001). In the present study the overall mean value of pulsatility index was 1.8 with a standard deviation of 0.8. while in those who developed preeclampsia in our study group the mean of pulsatility index was 2.15 with a standard deviation of 0.78. However, the difference was statistically significant. In the present study the overall mean value of resistance index was 0.7 with a standard deviation of 0.3 while in the women who developed preeclampsia in our study group the mean of resistance index was 0.76 with a standard deviation of 0.09. However, the results were statistically non-significant. In the present study diastolic notch was present in 16/18 (89%) women with preeclampsia and this association was found to be higly

statistically significant. (p- value of 0.0001). Out of 129 women in the study group adverse pregnancy outcome were seen in 70 cases while 59 cases were uneventful. In this study maternal, past history of hypertensive disease of pregnancy (preeclampsia and gestational hypertension), past history of chronic hypertension, advanced maternal age, family history of preeclampsia/eclampsia were all found to have significant association with development of preeclampsia in the present pregnancy. However, no statistically significant association could be established between adverse pregnancy outcome and maternal past obstetric, medical and family history. In Present study adverse maternal and fetal outcome show association with uterine artery pulsatility index (p-value 0.041) and with diastolic notch (p-value0.001). There was only one (0.8%) stillbirth in our study group. The woman with eclampsia had a stillbirth. A total of ten out of the 129 babies required NICU admission. All the NICU admissions were in the preeclampsia group.

Table 3: Prevalence of Preeclampsia in our study group

	Frequency (n=129)	Percentage
Total no. of females	129	
Patuents who developed Pre-eclampsia:		
Early onset < 34wk	*3****	17%
Late onset> 34wk	*10*** *	56%
Gestational hypertension progressed to late onset pre- Eclampsia	5	28%
Total female developed late onset pre- Eclampsia	(10+ 5) =15	
Total	18	100%

**oneoutofthe3womenhadeclampsia.
*** five women who had gestational hypertension. In a span of further 3-4 weeks they developed proteinuria thus included in late onset preeclampsia

Table 4: Indication for induction

Indication for induction	Number(n=129)	Percentage
Pre-eclampsia	18	13.95%
Early onset < 34wk	*3*	
Late onset > 34wk	*15*	
Preeclampsia with FGR	7	5.43%

GDM with PE/gestational hypertension	2	1.55%
Post-dated pregnancy	2	1.55%
Premature Rupture of Membranes	3	2.33%
Severe Oligohydramnios with preeclampsia	5	3.88%

Table 5: Association of maternal characteristics with Pre-eclampsia

Maternal characteristics	Total	Unaffected (n=111)	Pre- eclampsia (n=18)	%	P Value
Past History Pre-eclampsia/Gestational hypertension	11	6	5	28%	0.002
Multifetal Gestation	1	0	1	6%	0.14
Known case of Chronic Hypertension	6	2	4	22%	0.002
Diabetes Mellitus	4	0	4	22%	1
Chronic Kidney Disease	1	0	1	6%	0.14
Nulliparous	47	40	7	39%	0.6
Parity, P-/3	5	2	3	17%	0.002
Body Mass index < 25	76	65	11	61%	0.838
> 25	53	46	7	39%	
Family H/O Preeclampsia/Eclampsia	2	0	2	11%	0.019
Maternal Age < 35	120	106	14	78%	0.022
> 35	5	1	4	22%	
> 10 year Interconeption Period	1	0	1	6%	0.14

Table 6: NICU Admission and Fetal outcome amongst study population

	Frequency	Percentage
NICU Admission	10	7.80%
Still birth	1	0.80%

Table 7: Association of mean arterial pressure with Pre-Eclampsia

MAP(mmHg)	Distribution of women according to Mean Arterial Pressure (Total 129)	No of women developed Preeclampsia (Total 18)	Percentage
<90 mmHg	88	5	28%
>=90 mmHg	41	13	72%

Table 8: Association of uterine arterial indices(PI) and Resistance Index withpre-eclampsia

Uterine Arterial Doppler Indices	Pre-eclampsia (n=18)		Unaffected (n=111)		P value
	Raised	WNL	Raised	WNL	
Pulsatility index	7 (39%)	11 (61%)	16 (14%)	95 (86%)	0.012
Resistance Index	7 (39%)	11 (61%)	23 (21%)	88 (79%)	0.091

Table 9: Association of age with adverse pregnancy outcome

Age (year)	Distribution of women according to age (n= 129)	No of women with APO (n= 70)	Percentage
<20	1	1	1%
20-24	44	20	29%
25-29	46	29	41%
30-34	33	14	20%
35-39	5	5	7%

Table 10: Association of adverse pregnancy outcomes with uterine artery Doppler indices (PI)

Uterine Arterial Doppler Indices	APO (N=70)		Unaffected (n=59)		P value
	Raised	WNL	Raised	WNL	
Pulsatility Index	17	53	6	53	0.041
Resistance Index	22	48	8	51	0.021

Table 11: Association of diastolic notch with adverse pregnancy outcome

Diastolic notch	Distribution of women according to diastolic Notch (n= 129)	No of women with APO (n=70)	Percentage
Absent	66	25	36%
Diastolic notch	63	45	64%

Table 12: Association of Diastolic notch with Pre-eclampsia

Diastolic notch	No of women (Total=129)	No. of Women developed Pre- eclampsia (Total=18)	Percentage
Absent	66	2	11%
Present	63	16	89%

Discussion

The mean age of the study population was 26.88 years with standard deviation of 4.4 whereas the mean age of preeclampsia group was slightly higher 28.78 with a standard deviation of 5.77. 80% of women in the age group >35 years developed preeclampsia. No detection could be made from age group of < 20 years because of lesser number of patients in that particular age group. Leite *et al* [2] in 2019, found mean age of control group as 29.8 6.5. in their study age of women developing early onset preeclampsia was significantly higher (33.1) than control group and late onset preeclampsia group. In study conducted by Poon LC *et al* [3] 2009, no significant difference in median age of women was seen between cohort and case group. Median age of women was 32.3 in overall population and median age of women

with early onset preeclampsia was 31.7 and median age of women with late onset preeclampsia was 31.5. Bramham *et al* (2011) and Zhu J *et al* (2021) also did not find any significant difference in the maternal age in the preeclampsia and non- preeclampsia group.[4,5]

BMI

Majority of study subjects in present study had BMI in the range of 18.5- 24.9 Kg/m^2(normal) and 26.4% women were overweight (25-29.9). The mean BMI of the study group was 24.2 kg/m^2 and the mean BMI of women with preeclampsia in the study group was 24.28 kg/m^2 which were comparable. Similar findings of BMI were observed in a study conducted by Leite *et al* 2019 where study population had mean BMI

of 26.0 ±5.0 and BMI of women with preeclampsia was 25.6± 3.9.[2] In a study conducted by Kapuk SA *et al* 2019 the mean BMI was 28.3±3.3 and mean 29.3 with standard deviation 6.7 in women who developed preeclampsia.[6]

Gravidity

In present study, preeclampsia was more frequently found amongst primigravida (33%) and second gravidas (33%). However, the incidence of preeclampsia was found to be 1 in 6 in primigravida (16.2%) and1 in 5(20%)in fourth gravida Out of the total 18 women in our study group who developed preeclampsia, three women were gravida three and more with a significant p value of 0.002. Similar results were seen in study by Rindawati H *et al* 2021, 35.71% primigravida developed preeclampsia, 16% of Second gravida and 12.5%multigravida developed preeclampsia.[7]

Primigravida was found to be risk factor for preeclampsia on the multivariable analysis. The odds of developing pre-eclampsia were 2.68 times higher in primigravida women compared to multigravida (AOR: 2.68 95% CI: 1.38, 5.22). In the present study,5/18(28%) women who developed preeclampsia had a past history of preeclampsia. Similar results in which 23% of women developed preeclampsia who had a past history of preeclampsia were observed by Braham *et al* 2011[4]. In contrast with study conducted by Aabidha *et al* 2015 [8] 7.52% women developed preeclampsia who had past history of preeclampsia. In a study conducted by Baschat*et al* 2014 2.2% developed early onset preeclampsia and 18.7% of women developed late onset preeclampsia who had a past history of pre-eclampsia.[9] In our study 5 patients with preeclampsia had past history of preeclampsia, out of 5, 1 had early onset preeclampsia and 4 had late onset preeclampsia. Similarly 4 patients who were

a known case of chronic hypertension developed preeclampsia in our study, 2 of them had early onset preeclampsia and 2 had late onset preeclampsia .

Mean arterial pressure

The overall mean value of mean arterial pressure of women in our study group was 87.5 with a standard deviation 3.7 while in women who developed preeclampsia in our study group the mean value of mean arterial pressure was 90.67 with a standard deviation 5.49. 72% of women who developed preeclampsia had MAP 90 mmHg at 11-13+6 weeks compared to 28% who had normal MAP in present study. The difference between MAP was between preeclampsia and non-preeclampsia was statistically significant in our study (0.0001). A study conducted by Zhu Jung *et al* 2021[5] the MAP at 11-14 weeks [mean (95% CI)] in women who developed preeclampsia was 90 as compared to MAP of 79.9 in non-preeclampsia group.

Uterine arterial indices:

Pulsatility index

In the present study the overall mean value of pulsatility index was 1.8 with a standard deviation of 0.8. while in those who developed preeclampsia in our study group the mean of pulsatility index was 2.15 with a standard deviation of 0.78. However, the difference was statistically significant. In a study conducted by Prajapati RS *et al* 2013, the uterine artery PI in early onset preeclampsia group was 0.95 and the values were statistically significant depicting association of uterine artery PI with early onset PE.[10] However, no correlation was found between late onset preeclampsia and uterine artery PI. Zhu J *et al* 2021, observed the mean PI with 95% CIinnon- preeclampsia was 1.81 (1.77 to 1.84) in women who developed pre-eclampsia was 1.93 (1.68 to

2.19) Thus, the difference was not statistically significant. [5]

Resistance index:

In the present study the overall mean value of resistance index was 0.7 with a standard deviation of 0.3 while in the women who developed preeclampsia in our study group the mean of resistance index was 0.76 with a standard deviation of 0.09. However, the results were statistically non-significant Compared to study conducted by Sultana S *et al* [11] 2020, among the normal group, mean of RI was 0.571 with standard deviation ±0.058. and Mean RI was 0.825 and SD was 0.087 in preeclampsia group. Melchiorre *et al* [12] 2008, observed that in first trimester uterine artery resistance index (RI) was significantly higher in women who subsequently developed early onset preeclampsia (mean RI, 0.79) than in those with a normal outcome (mean RI, 0.70; P = 0.0001) or those who developed pre-eclampsia at term (mean RI, 0.72; P = 0.002).

Diastolic notch:

The presence of early diastolic notch in the uterine artery flow velocity waveforms is reported to be a good predictor of poor pregnancy outcome. In the present study diastolic notch was present in 16/18 (89%) women with preeclampsia and this association was found to be statistically significant. (p- value of 0.0001).

Compared to a study conducted by Sultana *et al* 2020, early diastolic notch was found in 36 (90%) subjects with preeclampsia while in only 2 (5%) subjects with normal pregnancy. Chi-square test showed that there was statistically significant difference regarding presence of early diastolic notch between two groups. [11]

Adverse maternal and fetal outcome:

Adverse pregnancy outcome included preeclampsia (early and late onset), preterm labour, eclampsia, need for NICU admission, still birth. Out of 129 women in the study group adverse pregnancy outcome were seen in 70 cases while 59 cases were uneventful.

In this study maternal, past history of hypertensive disease of pregnancy (preeclampsia and gestational hypertension), past history of chronic hypertension, advanced maternal age, family history of preeclampsia/eclampsia were all found to have significant association with development of preeclampsia in the present pregnancy. In Present study adverse maternal and fetal outcome show association with uterine artery pulsatility index (p-value 0.041) and with diastolic notch (p-value-0.001).

Similar results were estimated in study by Prajapati SR [10] *et al* 2013, mean and standard deviation of PI value for subjects who had an adverse pregnancy outcome was significantly higher (0.84 ± 0.28) than mean and standard deviation of PI value for subjects who had normal pregnancy outcome (0.71 ± 0.16) with *p*-value <0.005). In a study conducted by Becter R *et al*56 2010, incidence of adverse pregnancy outcome was 5.3%; it increased from 4.6% for women without notch to 41.8% for those with a mean notch index≥ 0.2 and higher.[13]

Conclusion

A detailed history in first trimester (11 to13+6 weeks) for detection of maternal characteristics, MAP along with bilateral uterine artery Doppler (PI,RI and diastolic notch) are helpful in early prediction of preeclampsia. There is a strong co-relation of presence of diastolic notch on uterine artery doppler with development of preeclampsia. In a low resource countries early prediction of preeclampsia will help in implementation of preventive measures to decrease prevalence of preeclampsia and catastrophic adverse maternal and fetal effects.

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