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Analysis Of Physiological Variables Of Pregnancy Pathology

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Abstract

Introduction: Pre-eclampsia is a multifactorial hypertension condition that is peculiar to pregnancy and has a 2-5% global prevalence. Symptoms start to show up after 20 weeks of pregnancy. Changes in physiological parameters like systolic blood pressure, diastolic blood pressure, Mean arterial pressure and BMI were investigated. The difference in physiological parameters in early onset and late onset of preeclampsia were compared with normal pregnant women.

Methods: In several hospitals in South India, 99 pregnant women participated in the cohort study. Data was gathered from the patients upon their admission for delivery. ANOVA was used to determine the differences in physiological characteristics among three study groups such as height, weight, BMI, systolic blood pressure, diastolic blood pressure, mean arterial pressure.

Results: The three study groups varied in several physiological indicators, according to the study. Pregnancy difficulties can result from altered physiological parameters, and there was a difference in parameters like BMI and Blood pressure among the groups with early and late-onset preeclampsia.

Conclusions: Altered physiological parameters during pregnancy challenge the health of the mother and fetus. So study of physiological parameters is necessary for the early identification of various kinds of pregnancy disorders. Analysis of the health status in early- and late-onset preeclampsia in comparison to controls has been reported in very little Indian literature.

Keywords: Biomarker, Early onset preeclampsia, Late-onset preeclampsia.

INTRODUCTION

Preeclampsia is a pregnancy-specific disorder typically identified by new-onset hypertension in the second half of pregnancy. Worldwide, PE complicates 2%-8% of pregnancies and is one of the main causes of maternal death in both developed and developing nations each year. In India, the prevalence rate is 8-10%.PE can cause a wide range of symptoms, such as headaches, vision abnormalities, epigastric pain, and the beginning of edema, in addition to the frequently observed new-onset proteinuria.

Preeclampsia is characterized by new-onset hypertension with a rise in systolic blood pressure of 140 mmHg and diastolic blood pressure of 90 mmHg.In severe conditions, it rises to 160 mmHg systolic and 110 mmHg diastolic(**1**). The International Society for the Study of Hypertension in

Pregnancy (ISSHP) has endorsed the diagnosis of new-onset hypertension in pregnancy (systolic > 140 mmHg and diastolic > 90 mmHg) in conjunction with one or more additional features, such as proteinuria, other maternal organ dysfunction (including liver, kidney, neurological), or hematological involvement, and uteroplacental dysfunction, such as fetal growth restriction and abnormal Doppler ultrasound (2)Manson et al,1995).

Risk factors of preeclampsia.

The main risk factors for the development of preeclampsia are obesity, antiphospholipid syndrome, pregestational diabetes mellitus, history of preeclampsia, hypertension before pregnancy, and advanced maternal age(3). Other risk factors include nulliparity, history of chronic kidney disease, and use of assisted reproductive technologies. (4) According to a cross-sectional study, poor maternal outcome in preeclampsia correlates with maternal age (5). According to a study by Goldman et al., women aged 40 years and older are more likely to suffer from low birth weight, premature birth, stillbirth, and neonatal death (6). Many studies have been done on the genetic basis of preeclampsia. Similarly, maternal age was positively correlated with higher diastolic blood pressure (0.5 mmHg for each subsequent 10 years) in a prospective cohort study of 8,623 women. Gestational preeclampsia is associated with a distinct risk of obesity. Obese individuals have metabolic syndrome (MS), defined by insulin resistance, excessive fatty acid flux, and a proinflammatory state (7).

Pathogenesis of preeclampsia

In the course of typical placental implantation, cytotrophoblasts enter into the uterine spiral arteries to create vascular canals that nourish the developing fetus at the interface between the mother and fetus. Due to this invasion's deep penetration into the spiral artery at the myometrial level, which causes high capacitance and vascularity, maternal spiral arteries undergo extensive remodeling throughout a typical pregnancy. (8)

Preeclampsia (PE) is primarily thought to be caused by abnormal spiral artery remodeling, which in turn causes placental cell ischemia and an imbalance between pro- and anti-angiogenic factors. All maternal organ systems are adversely affected by this imbalance favoring antiangiogenic chemicals, which results in extensive endothelial dysfunction.(9) Additionally, it raises the risk that the mother and kid will experience diabetes and cardiovascular issues in the future. It is believed that reduced blood flow or prolonged hypoxia plays a greater role in the development of placental injury in preterm infants than do the main causes. As a result, it has been proposed that the damage might instead be the outcome of free radical damage, such as damage from reactive oxygen species (ROS) or damage from hypoxia-reoxygenation (HR). Antiangiogenic chemicals, including soluble endoglin and soluble fms-like tyrosine kinase-1 (sFlt-1), are released into the circulation by the ischemic placenta (10)

Early detection of the disease

Collaboratively, scientists searched for novel biomarkers that would enhance preeclampsia prognosis. They typically come from organs like the placenta, heart, and urinary system that are implicated in the pathophysiology of preeclampsia. Evaluation is done on physiological data, including respiration rate, heart rate, body mass index, systolic and diastolic blood pressure, and certain biochemical indicators. Early disease prediction is also aided by markers such as serum and urine creatinine, PLGF, SFLT, and urine protein levels(11).

Physiological parameters for the detection of preeclampsia

One way to diagnose preeclampsia and gestational hypertension is by looking at elevated blood pressure. Numerous retrospective and prospective studies have looked into the possibility of predicting this problem using blood pressure taken during routine prenatal appointments. Blood pressure fluctuations most likely represent undiagnosed hypertension or act as a proxy for heightened maternal vascular vulnerability to PE (12,13) . An additional risk linked to PE is an elevated body mass index. Research has demonstrated a positive correlation between BMI and PE. PE is also caused by obesity and excessive lipid levels, particularly TG, which impair endothelial function (14). A gradually higher incidence of early and late pregnancy-related hypertension is linked to obesity (15). Another study found that women with late-onset disease were more likely than those with early-onset disease to have metabolic syndrome and pre-existing hypertension (16). Exemplary obesity is a powerful indicator of subsequent obesity, which is frequently linked to the development of type 2 diabetes, dyslipidemia, and chronic hypertension. It was discovered in two randomized clinical trials including middle-aged, obese individuals who were intolerant to glucose that losing weight, upping physical activity, and changing nutrition might reduce type 2 diabetes by 50%. According to linear models, a 0.54% drop in gestational weight can result in a comparable reduction of preeclampsia for every 1 kg/m2 weight loss (17). An additional link between aging and preeclampsia is the assumption. Older moms are more likely to get preeclampsia. An increased risk of negative consequences is associated with advanced maternal age in primiparous women with preeclampsia. For preterm PE, a mother's age of 35 years or older was linked to an increased chance of premature delivery before 28 weeks. (18).

Aim of the study

To investigate physiological factors such as age, blood pressure, and body mass index in early preeclampsia, late-onset preeclampsia, and normal pregnancy groups.

Hypothesis

The research hypothesis states that (i) there are changes in physiological parameters such as age, blood pressure, and body mass index in early-onset preeclampsia, late-onset preeclampsia, and normal pregnant women.

Materials and Methods

Ethical considerations

The present study was approved by the institutional ethical committee and also by the ethical committees of the hospitals where the samples were collected. EC approval numbers: Saveetha Medical College and the Hospital Institutional Human Ethics Committee (.008/09/2019/IEC/SMCH); ESIC Hyderabad(ESIC-ESICMC/SNR/IEC-S101/12-2020)

The participants in the study voluntarily signed the informed consent.

We made certain that the study conforms with all relevant international ethical standards by the Helsinki Declaration - Ethical Principles for Medical Research Involving Human Subjects. The study was conducted from January 2020 to March 2022).

Inclusion and exclusion Criteria:

The control group included 33 normal pregnant women. The preeclamptic group included 33 early-onset preeclamptic and 33 late-onset preeclamptic women between the age group of 18-45. Women with diabetes or any other pregnancy complication and early history of hypertension were excluded from the study.

Physiological measurements

The Pre-eclampsia group was then subdivided into early onset and late onset based on gestational age.(Early -Onset Preeclampsia-<34weeksGA, Late-Onset Preeclampsia>34 weeks of gestation).(19)

During the study, the participants remained in a sitting position, supporting the right arm at the level of the heart. An adult blood pressure cuff was used to select the correct size for each participant. The pressure reading in phase V of the Korotkoff sounds corresponded to the diastolic pressure.(20) Mean arterial blood pressure was obtained using the equation (2DBP + SBP)/3. Data is gathered, including demographics, height, and BMI. A stadiometer was used to measure the height. A digital scale was used to determine weight. The World Health Organization's standards of BMI (weight (kg) / height (m)2) were used to classify the results as underweight (≤ 18.4), normal (18.5-24.9), overweight (25.0-29.9), obesity class I (30.0-34.9), and obesity class II-III (≥35.0). (21)

Statistical methods

The means, standard deviation, and standard error were used to express the data. Analysis of variance (ANOVA) was used to examine the means, and Tukey's post hoc test was used for multiple comparisons. A probability was deemed statistically significant if it was 0.05 or less. - Software called SPSS was used to create graphs and perform statistical analysis.

RESULTS

FIG-1:Mean Maternal age in Three study groups

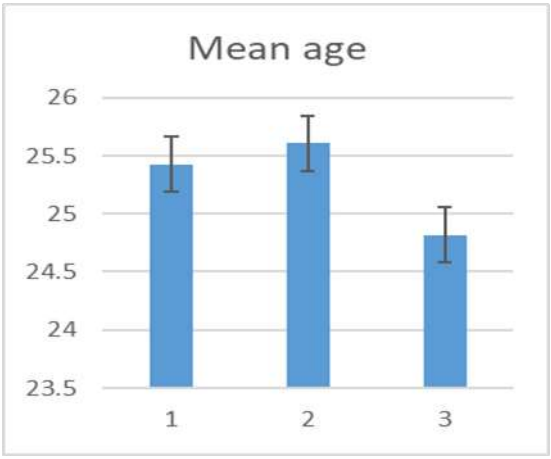

Fig-1:Mean maternal age in Control(1),EOPE(2)&LOPE(3).The figure shows that there is no correlation between maternal age and preeclampsia.

An ANOVA test across the three groups showed a less value of 0.25047when the mean maternal age was compared to that of normal pregnant women and preeclampsia patients, but there was no significant difference in mean maternal age between the other two groups. The test was further validated using F-statistics analysis, and the level of significance between the groups was explained using Post HOC Tukey HSD. Less significant differences were seen between EOPE and LOPE and between control and LOPE when the p-value was greater than 0.05.

Fig-2:Mean Arterial Pressure in three groups

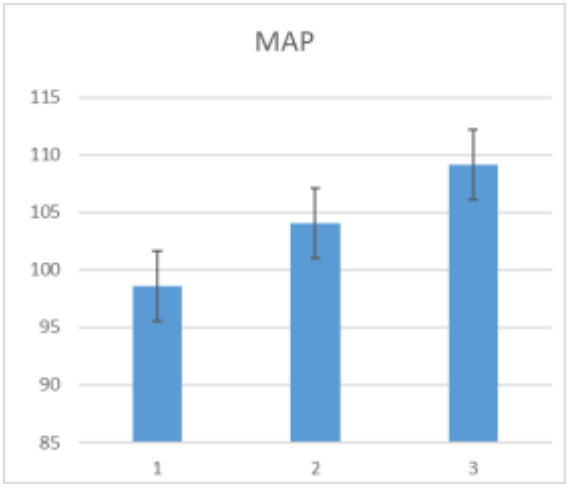

Fig-2:Mean arterial pressure in Control(1),EOPE(2)&LOPE(3). The figure shows that Mean Arterial Pressure is higher in preeclampsia as compared to control.

Mean Arterial Pressure

Between the three groups, there was a significant difference in mean arterial pressure. When comparing the mean arterial pressure of preeclampsia patients to that of normal pregnant women, an ANOVA test between the groups revealed a higher value. F-statistics analysis was used to further validate the test, and Post HOC Tukey HSD explained the level of significance between the groups. A p-value of less than 0.05 showed a significant difference between control and LOPE and EOPE and LOPE. The difference between Control and EOPE was less significant.

Fig 3:BMI in three study groups

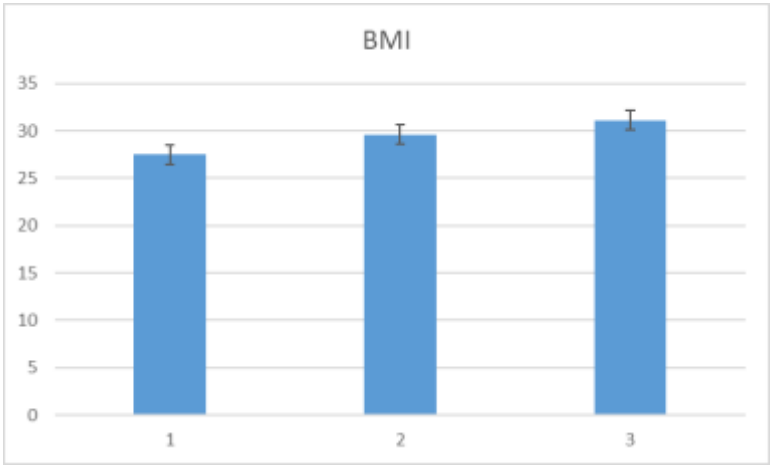

Fig-3:shows the difference in BMI in 1(control),2(EOPE) and 3(LOPE).BMI shows a higher value in preeclampsia as compared with normal pregnancy.

BMI was found to be higher in Preeclampsia groups as compared to Normal pregnant women. The study in 3 groups was statistically performed using one-way ANOVA and pairwise comparison was done using f-statistics. The statistical analysis was later confirmed using F-statistics. The values were significantly different among Control samples and LOPE and between EOPE and LOPE. The difference in BMI between Control and EOPE showed less significance.

TABLE-1:Statistical analysis of physiological parameters in three study groups

Parameters	Groups	Mean value	SD	F-value	p-value
Maternal Age(18 -45)	Control	25.4	3.91	0.25047	C: E=0.99955
	EOPE	25.6	4.69		C: L =0.80581
	LOPE	24.8	3.94		E: L =0.82139
Gestational age(25-40weeks)	Control	37.7	1.93	161.43	C: E=4.831E-10
	EOPE	30.2	1.98		C: L=2.557e-9
	LOPE	34.8	0.88		E: L=4.831e-10
SBP(mmHg)	control	124.8	5.09	150.73	C: E=4.831e-10
	EOPE	144.6	3.39		C: L=4.831e-10
	LOPE	147.1	5.43		E: L=0.1792e-10
DBP(mmHg)	CONTROL	79.09	4.45	31.24	C: E=1.025e-7
	EOPE	89.9	7.87		C: L=6.019e-10
	LOPE	92.5	8.83		E: L=0.3194
MAP	CONTROL	91.9	4.56	11.631	C: E= 0.168
	EOPE	109.7	13.06		C: L=0.00002
	LOPE	111.3	5.43		E: L=0.00934
Ht	CONTROL	157.1	5.45	0.9167	C: E= 0.544
	EOPE	155.8	4.5		C: L=0.4201
	LOPE	156.2	4.3		E: L=0.977
wt.	CONTROL	68	8.8	5.99	C: E= 0.142
	EOPE	72	7.6		C: L=0.0023
	LOPE	75	9.5		E: L=0.2723
BMI	CONTROL	27.3	2.38	11.63	C: E= .16862
	EOPE	29.9	2.14		C: L=00002
	LOPE	30	3.86		E: L=.00934

Table-1:shows the different demographic and physiological variables investigated in control(c),early onset preeclampsia(E)and late onset preeclampsia group(L).A p-value of <0.05 shows significant difference among the groups.

1.1.1. DISCUSSION

Preeclampsia is a multifactorial illness with distinct clinical and pathophysiological manifestations. In hypertensive pregnant women, physiological measures such age, SBP, DBP, MAP, and BMI are different from normal.

Effect of maternal age on pregnancy outcome

Numerous studies have linked advanced maternal age to higher risk of specific pregnancy problems as well as unfavorable perinatal outcomes. Maternal conditions such as gestational diabetes, placenta previa, preeclampsia, miscarriage, pregnancy-induced hypertension, and cesarean delivery are particularly common in older mothers. Additionally, it is well recognized that women with advanced maternal age are more likely to need assistance, induce labor, and increase it with oxytocin.(22) Prenatal, neonatal, and fetal mortality are also impacted by an aging mother. Women with advanced maternal age are more likely to have chronic illnesses like diabetes and hypertension, which makes pregnancy more difficult for them.(23)

Prenatal, neonatal, and fetal mortality are impacted by maternal aging. Women with advanced maternal age are more likely to have chronic illnesses like diabetes and hypertension, which makes pregnancy more difficult in the current study, however, there was less of a correlation between preeclampsia and maternal age (Table1,Fig1). This is probably because the patients were close in age and a smaller sample number was required to get an overall statistically significant difference.

Estimation of Blood pressure for the prediction of PE.

An uninterrupted decrease in blood pressure during the first half of pregnancy is typically followed by an increase in blood pressure till delivery in a typical pregnancy. On the other hand, blood pressure often stays steady for the first half of pregnancy in women who have hypertension (also known as prenatal hypertension or preeclampsia) before rising till birth.

A 2001 study by that looked at over 2,000 blood pressure series obtained methodically by ambulatory monitoring revealed that while diastolic blood pressure rose by 7% in the normotensive group between mid-pregnancy and delivery, it increased by roughly 12–15% in the hypertensive group.(24)

Mean arterial blood pressure (MAP) has been studied over time as a potential indicator of the start of preeclampsia. It is a useful instrument for labor observation. Not much research has been done on blood pressure patterns in low-risk nulliparous pregnancies.

In the current investigation, there were notable differences in mean arterial pressure across the three groups (Table 2,Fig2). Preeclamptic patients' mean arterial pressure was found to be higher than that of typical pregnant women by a between-group ANOVA test. The test was further confirmed using F-statistic analysis, and Post HOC Tukey HSD was used to explain the degree of significance across groups. With a p-value less than 0.05, significant differences were seen between EOPE and LOPE as well as between control and LOPE. The differences between EOPE and control were less pronounced.

Correlation between BMI and Preeclampsia

Obesity and overweight are known to be connected with preeclampsia, and the risk rises with body mass index (BMI).

The preeclampsia group had marginally greater risks related to high BMI. Numerous studies indicate that mothers who are obese have a three to four times higher risk of developing preeclampsia compared to mothers who are normal weight (25).

It is well known that oxidative stress, insulin resistance and systemic inflammatory responses are associated with obesity. Increased oxidative stress, increased sympathetic tone and increased angiotensinogen expression are pathways by which obesity can lead to hypertension (26). In contrast, reduced cytotrophoblast migration and subsequent placental ischemia are associated with insulin resistance (27).

Since adipose tissue is a storage of triglycerides and an endocrine organ that synthesizes and secretes a variety of hormones and inflammatory factors, an aberrant metabolic environment may be linked to increased factor production (28). Because higher body fat is linked to increased circulating cytokines, obese women are more likely to conceive with a subclinical inflammatory state than normal-weight women. Research has indicated a positive relationship between women's BMI and blood pressure, neutrophil infiltration, and vascular inflammation (29). Furthermore, clinical research has demonstrated a positive link.

Many inflammatory diseases are caused by increased circulating inflammatory adipokines, particularly interleukin-1 and interleukin-6. Among these diseases, preeclampsia, depression, infertility, and polycystic ovary syndrome are the main clinical disorders related to pregnancy.(30) In this study (Table 3, Fig3), the body mass indices of the two PE groups were compared with the control group. be significantly higher. This shows that lifestyle management at an early age can reduce the likelihood of developing metabolic syndrome later in life, and obesity can be one of the risk factors for developing preeclampsia.

Conclusion

The investigation of physiological parameters, including maternal age, SBP, DBP, and MAP, is explained in this paper

In comparison to patients with normal pregnancies, the group of patients with preeclampsia had higher BMI and MAP values. Despite a wealth of research demonstrating a favorable correlation between maternal age and an elevated chance of pregnancy, this study's groups did not differ significantly in terms of parameters such as maternal age.

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