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RESEARCH ARTICLE

Cardiac autonomic activity in preeclamptic pregnancy

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ABSTRACT

Background: Preeclampsia, a hypertensive disorder of pregnancy is a major cause of maternal and child mortality and morbidity. Although the exact aetiology is not known but many pathophysiological factors were unveiled by recent researches. The association of preeclampsia with autonomic nervous system is not much studied. **Objectives**: The objective of this study is assessment of the heart rate variability (HRV) in preeclamptic pregnancy to find if there is any difference between preeclamptic and normal pregnancies. **Methodology**: In this study already diagnosed preeclamptic pregnant and normal pregnant woman of same age group in their third trimester were assessed. Anthropometric parameters like height, weight, BMI, and pulse, blood pressure were recorded by using standard procedure. HRV was recorded by heart rate variability module for lab Chart Software and Power Lab. **Result**: Pulse, blood pressure were found significantly higher in preeclamptic group. The parameters of heart rate variability TP, HF, RMSSD, SDRR, which represent parasympathetic activities are decreased significantly in preeclamptic group in comparison to the normal pregnant women. Another parameter LF which signifies the sympathetic activity was significantly more in preeclampsia. **Conclusion**: This study concluded that in preeclampsia, there occurs imbalance of cardiac autonomic activity. There occurs withdrawal of parasympathetic activity with overactivity of sympathetic nervous system in preeclampsia.

Keywords: Autonomic nervous system, HRV, preeclampsia, cardiac autonomic activity.

Preeclampsia, a hypertensive disorder of pregnancy after 20th week of gestation with rise in blood pressure to the extent of 140/90 mm of Hg or more with proteinuria in previously normal woman [1]. It significantly contributes to neonatal and maternal morbidity and mortality, especially in developing countries of South-East Asia [2]. In developing countries, the prevalence of preeclampsia ranges from 1.8 and 16.7% which is seven times higher than the developed countries as estimated by WHO [3, 4].

Although the exact pathophysiology of preeclampsia is not very clear but the most accepted theory is defective remodelling of the uterine spiral arteries, not meeting the metabolic demands of the placenta and foetus by maternal perfusion, coupled with a maternal predisposition to inflammation and high BMI [5, 6]. When stressed, the placenta releases factors such as pro-inflammatory cytokines, exosomes, anti-angiogenic agents, and cell-free foetal DNA, into the maternal circulation, which causes dysfunction of endothelial cells affecting many maternal organs like nervous system, liver, kidney, coagulation cascade leading to maternal symptoms [7, 8].

Considering these chronological events of pathophysiology, various tests can be done to predict the onset of preeclampsia and prevent its major complications. Doppler velocimetrical study to assess placental perfusion [9], flow-mediated dilation (FMD) of the brachial artery to assess endothelial function [10], ophthalmic artery Doppler velocimetry for perfusion of the CNS [11], and assessment of biological markers like angiogenic or anti-angiogenic factors [12, 13]. But all these investigations are either complicated requiring high skills, costly or invasive.

Moreover, profound adaptive haemodynamic changes

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occur during pregnancy and autonomic nervous system helps in adaption of these cardiovascular changes. In recent years, the role of cardiac autonomic activity in the pathophysiology of pre-eclampsia has gained increasing attention. Physiologically, autonomic nervous system plays an important role in controlling blood pressure. Usually, hypertension is generated either due to vasoconstriction or due to increased blood volume [14]. Preeclampsia is characterized by low volume and high vascular resistance, so most likely cause of hypertension in preeclampsia may be the vasoconstriction induced by sympathetic overactivity [15]. The cardiac autonomic function or sympathovagal balance of cardiac activity can be assessed by heart rate variability [16]. HRV is a sophisticated tool and especially suitable for pregnant women because it is non-invasive and does not produce any stress on mother and infant.

HRV provides a sensitive predictor as well as diagnostic and prognostic indicator of many health impairments [17]. But its role in preeclampsia is not much investigated specially in this part of the globe. Recent studies have shown prominent sympathetic dominance in preeclampsia [18] but contrast reports are also available where researchers failed to demonstrate and change in HRV in preeclampsia [19]. There is still a paucity of comprehensive studies exploring the exact nature. It is now of paramount importance to understand the interplay between cardiac autonomic activity and the development of pre-eclampsia. Because of this inconsistency in reports, this study was designed to investigate the changes that occur in cardiac autonomic activity in preeclamptic pregnancy.

In the light of this knowledge gap, the present study aims to investigate cardiac autonomic activity in preeclamptic pregnancies, shedding light on its potential role in the pathogenesis of this condition. The objectives were to assess heart rate variability for the sympathetic and parasympathetic regulation in preeclamptic women compared to the normotensive pregnant individuals. The findings from this research hold promise in unravelling the possible role of autonomic nervous system in underlying mechanisms of pre-eclampsia and may have implications for early detection in non-invasive simple way, risk stratification and targeted intervention to improve maternal and foetal outcome.

The implication of this study may pave the path towards prevention and better management of pre-eclamptic complications. As we delve into the realm of cardiac autonomic activity in pre-eclampsia, we strive to make valuable contributions to both obstetrics and cardiovascular research, ultimately striving for improvement of maternal and neonatal health during pregnancy and beyond.

Methodology

This original research employed a cross-sectional study design to investigate the effect of preeclampsia on cardiac autonomic function, as assessed by heart rate variability.

This study was done in the Department of Physiology, Gauhati Medical College & Hospital, Guwahati in collaboration with Department of Obstetrics and Gynaecology, Gauhati Medical College & Hospital Guwahati, Assam from July 2019 to March 2021. After getting Institutional Ethical Committee clearance, data was collected from those subjects only who have given informed consents. We had selected the cases by simple random selection method.

Sample size calculation - For unlimited population (i.e., when the population size is not known), Sample size, $N = z^2 \times p(1-p)/\varepsilon^2$, Where, N is the required sample size, z is the z score associated with the desired level of confidence, P is the estimated proportion of the population, ε is the desired margin of error. For this study, we consider a z-score of 1.96 aiming for a 95% confidence level, and a margin of error of 10%. Assume a population proportion of 0.5.

$N = (1.96)^2 \times 0.5(1 - 0.5)/(0.1)^2 = 96.04 \cong 96 = 100$. So, in this study we had taken 100 preeclamptic cases and for comparison another 100 pregnant woman of same trimester but not having preeclampsia was taken.

Mode of selection of subjects – In this study we had selected 100 diagnosed cases of preeclamptic pregnant females in the third trimester of pregnancy, visiting Obstetrics and Gynaecology Department of Guwahati Medical College and Hospital. For comparison separate group of 100 normal normotensive pregnant females of same trimester (third trimester), as that of preeclamptic pregnant group were selected.

Exclusion criteria - Females with previous history of hypertension, hypotension, cardiovascular disease, diabetes mellitus, chronic renal failure, liver diseases, thyrotoxicosis, vascular diseases and multigravida were excluded.

Data collection - Anthropometric parameters: Height, weight, and body mass index (BMI) of all participants were recorded using standard procedures.

Hemodynamic parameters: Pulse rate and blood pressure (systolic and diastolic) were measured for each participant using validated and calibrated instruments.

Heart rate variability (HRV) assessment: HRV was recorded using the Heart Rate Variability Module for Lab

Chart Software and Power Lab. A 15-minute basal ECG recording was obtained, and a 5-minute artefact free segment was analysed to derive time-domain and frequency-domain parameters of HRV.

Statistical method - Data were analysed using SPSS 21 software. Descriptive statistical analysis was done for calculation of mean of various parameters and independent t test was done for comparison of those parameters among the preeclamptic and normal pregnant women. The significance level (p-value) was set at 0.05.

Results

This cross-sectional study was conducted on 100 preeclamptic women and 100 normal third trimester pregnant women. The participants were of 20 to 30 years of age. In this study we did not get any statistically significant differences in body weight and BMI among normal pregnancy and preeclamptic pregnancy. But there was significant difference in pulse rate with 94.71beats per minute and 84.76 beats per minute in preeclamptic and normal pregnant woman respectively. Significant differences were also seen in systolic and diastolic blood pressures with (SBP=145.61 mm Hg, DBP=94.66 mm Hg) in preeclamptic and (SBP=114.32 mm Hg, DBP=75.24 mm Hg) in normal third trimester pregnant woman. P≤0.05 was considered to be significant. These were shown in the table 1.

Differences in HRV parameters were also significant. We have seen statistically significant decrease in total power (TP) (1524.46), HF (31.6199) and increase in LF (67.2592) values of the frequency domain parameters of HRV in preeclamptic group than the TP (2593.40), HF (42.4472) and LF (56.6586) of normal third trimester pregnant group. In our study, preeclamptic group also showed statistically significant decrease in RMSSD (14.097), SDRR (25.58) value of time domain parameters of HRV than the RMSSD (20.840), SDRR (35.325) values of normal pregnant group. We have also found high LF/HF ratio among preeclamptic women but the value is not statistically significant as p value is 0.056. All these results are shown in table 1.

Table 1: Distribution and comparison of various anthropometric and HRV parameters

Parameters		Preeclamptic study group (n=100)	Normal control group (n=100)	P value
Age (in years)		25.50	24.20	0.043*
Anthropometric parameters	Height (cm)	155.49	152.92	0.001*
	Weight (kg)	59.4286	57.08	0.082NS
	BMI	24.63	24.34	0.586NS
Pulse (beats/min)		94.71	84.76	0*
Blood pressure	SBP (mmHg)	145.61	114.32	0*
	DBP (mmHg)	94.66	75.24	0*
Frequency domain parameters of HRV	TP (ms^2)	1524.46	2593.40	0.000*
	LF (nu)	67.2592	56.6586	0*
	HF (nu)	31.6199	42.4472	0*
	LF-HF ratio	3.78	2.3985	0.056NS
Time domain indices of HRV	RMSSD	14.097	20.840	0.001*
	SDRR	25.58	35.325	.000*
	Prr50	3.3902	5.7872	0.104NS

BMI – Body mass index, SBP – Systolic blood pressure, DBP – Diastolic blood pressure, HRV – Heart rate variability, TP – Total power, HF – High frequency, LF – Low frequency, RMSSD - Root mean square of successive differences, SDRR - Standard deviation of RR intervals, Prr - Percentage of successive RR intervals. *p ≤0.05 statistically significant, NS – Statistically non-significant.

Discussion

Preeclampsia is a significant hypertensive disorder of pregnancy that poses considerable risks to maternal and foetal health. The current study investigated the cardiac autonomic function on preeclamptic persons, as assessed by HRV. HRV is a valuable non-invasive tool that provides insights into the sympathovagal balance of cardiac activity and autonomic nervous system regulation. Understanding the changes in cardiac autonomic activity during preeclamptic pregnancy can have important clinical implications for the management of this condition.

In contrast to another study [20], we did not get any significant difference in BMI between the preeclamptic and normal group. Probable reason for not getting statistically significant difference in BMI in our study may be due to selection of the sample from relatively homogeneous population with similar sociodemographic characteristics, lifestyle habits, and nutritional status. Studies are available suggesting contribution of high BMI in autonomic imbalance [21]. BMI has influence in autonomic activity, and it was not significantly different in the groups of our study so, we can say, BMI is not the cause of autonomic changes that we have seen in both the groups of our study.

Pulse rate, systolic blood pressure, diastolic blood pressure all are significantly higher in preeclamptic group of this study indicating elevated sympathetic activity and increased cardiovascular load in preeclampsia. These findings align with previous study where researchers

observed higher systolic and mean arterial blood pressure in preeclamptic pregnant women than normotensive pregnant women [20]. The significant increase in blood pressure in preeclamptic group which is characteristic of this disorder and also increased pulse rate in study group of this study may be at least in part be due to increase in sympathetic overactivity [15].

HRV consists of frequency domain and time domain components. Frequency domain components measures TP, LF, HF, LF/HF values. Low frequency (LF) component primarily reflects sympathetic modulation of heart functions. Here we got significantly high LF in preeclamptic pregnancy which signified sympathetic overactivity in preeclamptic pregnancy. The high frequency (HF) represents vagal modulation of sinoatrial nodal discharge. It was decreased in preeclamptic pregnant women in this study, depicting that there was some degree of vagal withdrawal in addition to sympathetic overactivity in preeclamptic pregnancy. LH/HF ratio is the index of sympathovagal balance which represents the balance between sympathetic and parasympathetic activities of the individual at any given time in supine resting condition. Lesser value of this ratio indicates parasympathetic dominance and its greater values indicate sympathetic dominance [22]. In our study LF/HF ratio was high in preeclamptic pregnant women in comparison to normotensive pregnant women, signifying presence of sympathetic overactivity in preeclamptic pregnant women. But this high value was not statistically significant. The lack of statistical significance in this parameter may be attributed to the sample size or the variability in the study population. Nevertheless, the trend toward sympathovagal imbalance in preeclampsia is consistent with previous research [20, 23]. But an old study failed to demonstrate differences in HRV between preeclamptic and normal pregnant women [24].

The overall decrease in total power (TP) in the preeclamptic group is of particular interest, as TP reflects the overall magnitude of HRV and vagal potency of cardiac drive. The significant reduction in TP among preeclamptic women of this study indicates a dampened autonomic modulation, which has been associated with an increased risk of cardiac morbidity and sudden cardiac death [17]. This finding raises concerns about the cardiovascular health of women with preeclampsia beyond the perinatal period.

The time-domain indices (RMSSD, SDRR, pRR50) represent vagal modulation of cardiac functions. There was decrease in all these values in preeclamptic group in our study out of which decrease in RMSSD, SDRR values are statistically significant. This demonstrated decreased cardiac parasympathetic drive in preeclamptic pregnant women. These findings are consistent with a previous study, where researchers found decrease RMSSD, SDRR in late onset preeclampsia [25].

The exact cause of this sympathovagal disturbance in preeclampsia is not clearly known. But it may be due to release of some placental factors in the maternal circulation which cause endothelial dysfunction promoting vascular smooth muscle contraction or inhibiting vascular relaxation pathway [26]. The placental factors released peripherally in the maternal circulation can cross the blood brain barrier and affect various brain centres modulating parasympathetic outflow [27 - 29]. Overall, the findings of our study shed light on the potential role of autonomic nervous system dysfunction in the pathogenesis of preeclampsia and its implications for maternal health.

Implications of the study - The present study's findings have several implications for clinical practice and future research. Understanding the autonomic nervous system's dysregulation in preeclampsia can aid in risk stratification and early detection of complications. The observed sympathovagal imbalance may serve as a potential marker for identifying women at higher risk of adverse maternal and foetal outcomes. Utilizing HRV as a non-invasive tool in routine antenatal care may provide clinicians with valuable insights into the cardiovascular health of pregnant women and aid in personalized care for those with preeclampsia.

Limitations - Despite its valuable insights, this study has some limitations. The cross-sectional design restricts the establishment of causal relationships between HRV and preeclampsia. Longitudinal studies are needed to explore the dynamic changes in autonomic function throughout pregnancy and the postpartum period. Additionally, the relatively small sample size may have affected the statistical power to detect some significant differences. Further studies with larger cohorts are warranted to validate the findings.

Future scope - Future research should focus on investigating the heterogeneity of preeclampsia and its association with autonomic nervous system. Understanding how different subtypes of preeclampsia affect the autonomic nervous system could provide valuable insights into the disease's underlying pathophysiology and guide targeted interventions. Moreover, exploring the longitudinal changes in HRV during pregnancy and its relationship with maternal and foetal outcomes could help establish HRV as a predictive tool for preeclampsia and its complications.

Conclusion

This study highlights the presence of sympathovagal imbalance with reduced parasympathetic activity and increased sympathetic dominance in preeclampsia. The observed alterations in HRV parameters suggest an autonomic dysregulation that may contribute to the pathogenesis of hypertensive complications during pregnancy. By shedding light on the cardiac autonomic activity in preeclampsia, this research opens avenues for further investigations and potential applications of HRV assessment in antenatal care to improve maternal and foetal health outcomes.

Conflict of interest: None. **Disclaimer:** Nil.

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