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# Autonomic functions in pre-eclampsia and normal pregnancy

Anita Herur[1,2], Manjunath Aithala[2], Kusal Das[2], Ashalata Mallapur[1]

S. Nijalingappa Medical College, Bagalkot, Karnataka[1]
Shri B. M. Patil Medical College, BLDE (Deemed to be University), Vijayapura, Karnataka[2]

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**ABSTRACT**

Pre-eclampsia (PE) is a major complication of pregnancy that could lead to maternal and fetal morbidity and mortality. The analysis of heart rate variability (HRV) is a noninvasive diagnostic tool that provides important information about autonomic functioning and individual's risk of developing cardiovascular disease. The aim of the present study was to compare the frequency and time domain heart rate variability parameters in pre-eclampsia (PE) with that of normal healthy (NP), as a measure of the autonomic functions. This was a case-control study. Pregnant women diagnosed to have pre-eclampsia according to ACOG guidelines and aged 18-35 years were included as cases. Healthy pregnant women, matched for age, gravida and gestational weeks were included as controls. Gestational age was calculated from first trimester USG. Blood pressure was recorded using a mercury sphygmomanometer (Diamond). Heart rate and heart rate variability (HRV) was recorded by Powerlab (AD instruments). HRV analysis was done in the frequency and time domains. Statistical analysis was done using Student's t test. There was a significant increase in the systolic and diastolic blood pressures, low frequency (LF) domain, LF/HF ratio and a decrease in high frequency (HF) components of the HRV analysis in pre-eclampsia. The time domain parameters of HRV, SDNN, SDANN, RMSSD and pNN50%, showed a fall in preeclampsia. Sympathetic over activity combined with parasympathetic withdrawal is seen in pre- eclampsia, which may suggest cardiovascular risk in these patients. Autonomic function testing of heart rate variability may be used as a tool for early diagnosis, management and prevention of future cardiovascular diseases in pre-eclampsia women.

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## 1. INTRODUCTION

One among the many major disorders that complicate pregnancy is pre-eclampsia (PE), which may significantly affect maternal and fetal morbidity and mortality [1]. Pre-eclampsia manifests after 20th week of pregnancy and is characterized by an increase in blood pressure (BP≥140/90 mmHg) and protein in maternal urine (urinary albumin protein ≥300 mg/24 h) [2]. Pre-eclampsia occurs in 2–8% of pregnancies

worldwide, and is the second leading cause of direct maternal and fetal deaths [2], [3] Blood pressure is mainly influenced by the autonomic nervous system. The interaction of the two branches of the autonomic nervous system (ANS): sympathetic and parasympathetic and their activity may be assessed by heart rate variability (HRV) [4]. The analysis of heart rate variability (HRV) is a non-invasive diagnostic tool that provides important information about the risk for cardiovascular disease [5]. Hence, HRV analysis tells us about the involvement of the sympathetic and parasympathetic system in pre-eclampsia. HRV studies in pre-eclampsia have shown varied results. Some have observed a reduced variability [6] and others an increase in variability [7]. The aim of the present study was to compare the heart rate variability parameters in pre-eclampsia (PE) with that in normal pregnancy (NP), as a measure of the autonomic functions.

## 2. Materials and Methods

This was a case-control study for which Institutional Ethics committee clearance was obtained and subjects were recruited from the department of Obstetrics and Gynaecology. Pregnant women diagnosed to have pre-eclampsia according to ACOG guidelines [8] and aged 18-35 years were included as cases (PE). Healthy pregnant women, matched for age, gravida and gestational weeks were included as controls (NP). Pregnant women with past history of hypertension, diabetes mellitus, or heart disease were excluded from both the groups. Informed consent was taken from all the participants. The sample size was 30 in each group. Gestational age was calculated from first trimester USG and according to ACOG guidelines [9]. After 15 minutes of rest, blood pressure was recorded using a mercury sphygmomanometer (Diamond) in lying down position twice with a gap of 15 minutes between each recording. Heart rate and heart rate variability (HRV) was recorded and analyzed by Powerlab (AD instruments). ECG electrodes were connected in lying down position for Lead II and recording was obtained for 15 minutes. Ectopics and artifacts were removed from the recording. HRV analysis was done in the frequency and time domains [4]. Frequency domain indices such as relative power of the low-frequency band (0.04–0.15 Hz) in normalized units (LFnu), relative power of the high-frequency band (0.15–0.4 Hz) in normalized units (HFnu) and ratio of LF-to-HF power (LF/HF) were noted. Time domain indices such as standard deviation of normal to normal intervals (SDNN), standard deviation of the average NN intervals for each 5 min segment (SDANN), root mean square of successive RR interval differences (RMSSD) and percentage of successive RR intervals that differ by more than 50 ms (pNN50) were also noted. Statistical analysis was done using SPSS 19.0 version software by Student's t test and a p value $<0.05$ was considered statistically significant.

## 3. Results

Thirty subjects were recruited in each group and as one sample HRV could not be analyzed due to many errors, analysis was done for the rest twenty-nine samples. The mean age and the gestational age of the mothers in both NP and PE groups were comparable and did not show any statistical difference (Table 1).

**Table 1.** Mean maternal and gestational age in NP and PE groups

| | **Normal pregnancy (NP) (n=29)** | **Preeclampsia (PE) (n=29)** | **t value** | **P value** |
|---|---|---|---|---|
| **Maternal age (years)** | 22.93 ± 3.17 | 22.62 ± 3.89 | 0.355 | 0.740 |
| **Gestational Age (weeks)** | 37.59 ± 3.20 | 35.97± 4.30 | 1.668 | 0.109 |

Both the systolic and diastolic blood pressures were significantly higher in preeclampsia as compared to normal pregnancy (Figure 1).

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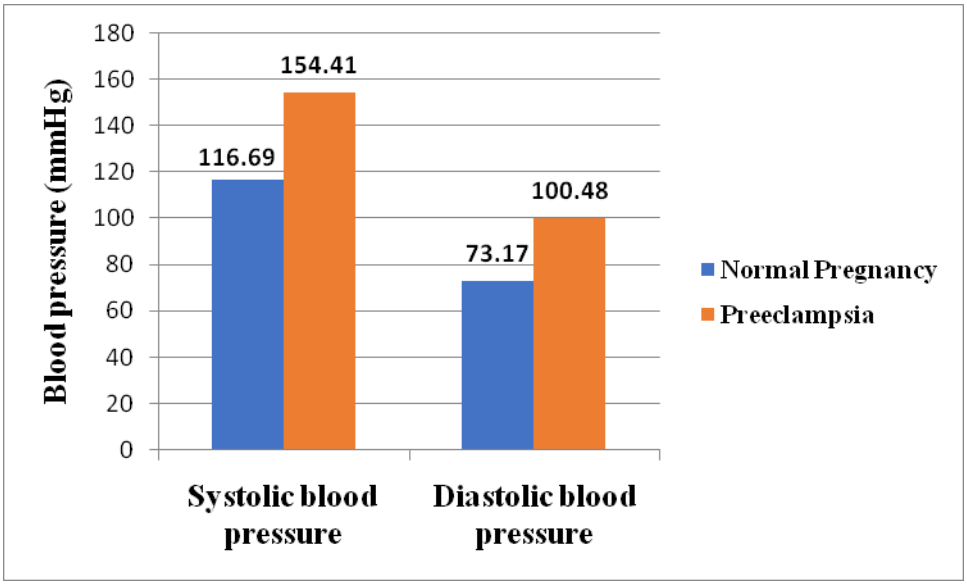


**Figure 1.** Blood pressures in normal pregnancy and preeclampsia

The mean heart rate (beats/min) was slightly lower (92.69 ± 12.10) in preeclampsia as compared to normal pregnancy (93.41 ± 9.51), but was not statistically significant (p=0.801).

Heart rate variability analysis revealed that there was a significant increase in the low frequency (LF) component, LF/HF ratio and a decrease in high frequency (HF) component in pre-eclampsia. The time domain parameters, SDNN, SDANN, RMSSD and pNN50, showed a fall in preeclampsia (Table 2).

**Table 2.** Heart rate variability analysis in NP and PE groups

| | **Normal Pregnancy (NP) (n=29)** | **Preeclampsia(PE) (n=29)** | **t value** | **p value** |
|---|---|---|---|---|
| **Frequency domain** | | | | |
| **LF(nu)** | 54.84 ± 15.93 | 67.01 ± 23.95 | 2.318 | **0.024** |
| **HF(nu)** | 41.07 ± 13.86 | 33.41 ± 12.50 | 2.245 | **0.029** |
| **LF/HF ratio** | 1.54 ± 0.77 | 2.44 ± 1.54 | 2.910 | **0.005** |
| **Time domain** | | | | |
| **SDNN (ms)** | 50.24 ± 23.62 | 35.17 ± 20.20 | 2.655 | **0.010** |
| **SDANN (ms)** | 18.46 ± 12.79 | 10.94 ± 8.49 | 2.684 | **0.009** |
| **RMSSD (ms)** | 37.39 ± 30.58 | 18.71 ± 12.80 | 3.087 | **0.003** |
| **pNN50 (%)** | 4.49 ± 3.97 | 2.37 ± 2.10 | 2.576 | **0.013** |

**4. Discussion**

Elevated levels of systolic and diastolic blood pressure in pre-eclampsia may depict an increase in

sympathetic activity in pre-eclampsia, with a resulting increase in the peripheral resistance [10]. Peripheral resistance influences the diastolic blood pressure, whereas cardiac output influences the systolic blood pressure, and cardiac output, in turn, is given by heart rate and stroke volume11 (Guyton). As there was no significant change in heart rate in the present study, the stroke volume would be responsible for a significant change in systolic blood pressure. Stroke volume would again depend on venous return and myocardial contractility [11] (Guyton). Reduction in the plasma volume is seen in pre-eclampsia [12] and hence, contractility of the myocardium would determine the systolic blood pressure. An increase in the sympathetic activity would thus explain the increase in myocardial contractility and peripheral resistance and hence, increase in both systolic and diastolic blood pressures. There was a significant increase in the low frequency (LF) component, LF/HF ratio and a decrease in high frequency (HF) component in pre-eclampsia, on frequency domain analysis of the heart rate variability in the present study and the same was also reported by other authors [13- 15]. LF component reflects sympathetic tone and HF component reflects parasympathetic tone; whereas the LF/HF ratio depicts the sympatho-vagal balance, an increase indicates sympathetic predominance and a decrease signifies parasympathetic predominance [4], [14]. The time domain parameters, SDNN, SDANN, RMSSD and pNN50, showed a fall in preeclampsia in the present study as observed by others too13. These time domain parameters of HRV indicate parasympathetic activity [4], [14]. In the present study, there was sympathetic over activity combined with parasympathetic withdrawal, which would influence the outcome of pre-eclampsia. This and even the magnitude of variability may also determine the risk of developing cardiovascular diseases even after the termination of pregnancy. Hence, autonomic function testing in the form of heart rate variability may be used as a tool for early diagnosis, management and prevention of future cardiovascular diseases in pre-eclampsia women.

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