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Original Article

Diminished Vagal Tone and Enhanced Sympathetic Drive During Third Trimester of Gestation Among Healthy Women – A Cross Sectional Study

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Abstract

Background: The haemodynamic adaptations during pregnancy are associated with the changes in autonomic nervous system. Heart rate variability (HRV) is an accurate, noninvasive tool to assess autonomic modulation of cardiovascular system. A vast array of studies have assessed HRV throughout pregnancy and assessed the risk of cardiovascular disease during pregnancy. The present study involves a simple non invasive assessment of the cardiac autonomic modulation during third trimester of pregnancy when compared with non pregnant women.

Methodology: Anthropometric parameters (Height, Weight, body mass index), resting heart rate, blood pressure of pregnant women (n=30) and age matched healthy women (n=30) were recorded using standard techniques. Resting HRV of healthy pregnant women was recorded during third trimester and compared with the age matched healthy non-pregnant female volunteers. HRV variables were compared between two groups using Independent T-test.

Results: Cardio vagal modulation as assessed by high frequency power of HRV in normalized units was significantly lower in pregnant women when compared to control group. Low frequency power in normalized units was significantly higher in pregnant women when compared with non pregnant controls. The LF:HF ratio which denotes cardiac sympathovagal balance, was also found to be significantly higher in pregnant subjects.

Conclusion: The study concludes that third trimester of gestation in healthy females is associated with diminished vagal tone and an enhanced sympathetic drive compared to that of their non-pregnant counterparts. These autonomic adaptations during healthy pregnancy might be an additional risk for cardiovascular disease among pregnant women.

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Introduction

The prevalence of cardiovascular disease (CVD) has increased among women during childbearing age (1).

The global burden of CVD during pregnancy and postpartum has not yet been contemplated (2), with increasing attention mainly on pre-eclampsia, eclampsia and its complications (3). Apart from developed countries, presently, 80% of CVD related deaths is known to occur in developing countries (4). Also, morbidity and mortality due to CVD in developing countries occur at younger age and affect women mainly, during pregnancy (3).

Pregnancy is characterized by maternal cardiovascular adaptations, like increase in heart rate, blood volume resulting in increased cardiac output and decreased systemic vascular resistance. Cardiovascular changes during pregnancy are important not only for maternal adaptations to pregnancy, but also for maintaining fetal nutrition (5). These hemodynamic changes begin in first trimester, peaks during second trimester and plateau during third trimester (6). These hemodynamic adaptations are associated with changes in autonomic nervous system (ANS) that produces cardiac autonomic modulation (5). Although, ANS plays a major role in these adaptations; its role during pregnancy is poorly studied. However, failures of these adaptations are associated with risk of pregnancy related complications (5).

Heart rate variability (HRV) is an accurate, non-invasive tool to assess autonomic modulation of cardiovascular system. Those patients with decreased HRV, characterized by increased sympathetic and decreased parasympathetic modulation of heart rate are known to have an increased cardiovascular risk (5). A multi-centric follow up study (7), of atheroscrelotic risk factors in healthy young adults, showed that women with cardiovascular risk had decreased vagal cardiac control. Also, epidemiological studies like Framingham Heart Study that studied association between HRV and hypertension among either gender indicated that several measures of both time and frequency domain indices of HRV were significantly lower in hypertensive men and women than in normotensives (8). ANS activity during early pregnancy may vary little from that of non-pregnant state. The autonomic modulation that occurs due to hemodynamic changes as well as aortocaval compression by gravid uterus is marked especially in third trimester (9). Therefore, the objective of the study is to assess the cardiac autonomic modulation among healthy women during third trimester of pregnancy when compared with non pregnant controls.

Methods

Thirty healthy pregnant women in the age group of 20-35 years, visiting K S Hegde charitable hospital were recruited. Thirty age and gender matched non-pregnant volunteers were recruited as control group. Subjects with acute illness in preceding two weeks, Diabetes mellitus/gestational diabetes mellitus, hypertension or other medical illness requiring treatment, history of breathlessness, chest pain, orthopnoea, habitual use of tobacco and alcohol were excluded. All subjects were requested to refrain from strenuous physical activity for 24 hours, and any caffeinated/ non-caffeinated beverages for 2 hours prior to recording. In control subjects, HRV recordings were performed between the 5th to 10th day of menstrual cycle (follicular phase) to minimize hormonal variations influenced by progesterone (10). The experimental protocol used in the study was reviewed and approved by the Institutional Ethical Committee. Written informed consent was obtained from all subjects.

A brief medical history and clinical/antenatal examination was done. All the examinations including assessment of HRV were done after voiding of the urine. Resting HRV measurements were performed in single session in a quiet, temperature-controlled room (23±1°C). Basal blood pressure was measured using non-invasive intermittent automated blood pressure monitoring device (Omron IA2 model) in supine position. Anthropometric measurements like height, weight were measured using standard techniques and body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.

Resting HRV assessment: Heart rate was obtained from R-R interval for which lead II ECG was recorded using a bio-amplifier data acquisition module,

Powerlab 26T, AD Instruments, Australia. Following 15 minutes of rest, Lead II ECG was recorded in supine position for 5 minutes. Subjects were instructed to breathe normally during the recording. ECG was recorded at a sampling rate of 1000 Hz. Ectopics and artifacts were identified and excluded from the raw recordings manually. Power spectral analysis was performed using non-parametric Fast Fourier transformation (FFT) based approach with HRV module of Lab Chart V7, AD Instruments. Power spectrum was expressed as LF (0.04-0.15 Hz), HF (0.15-0.4 Hz), total power in absolute units, LF normalized unit (LFnu), HF normalized unit (HFnu) and LF/HF ratio.

Statistical analysis: Data was managed in SPSS version 17. Variables were expressed as Mean±SD. Due to fluctuations in HRV measurements, HRV parameters are expressed as Mean±Standard error. Variables were tested for normality by Kolmogorov-Smirnov test and analyzed by Independent t-test. P value less than 0.05 was considered to be significant.

Results

Data from thirty pregnant volunteers in third trimester of pregnancy and thirty age, gender matched non-pregnant volunteers was available for the final analysis. Baseline characteristics of the study population are provided in Table I. This shows that the resting systolic and diastolic blood pressures were significantly higher in pregnant subjects during third trimester when compared with non-pregnant subjects.

Table II shows frequency domain HRV parameters among the study groups. High frequency power in normalized units, which indicates cardiac vagal tone was significantly lower in pregnant women when compared to control group. Also, low frequency power in normalized units which signifies cardiac sympathetic tone was significantly higher in pregnant women. The LF:HF ratio which denotes cardiac sympathovagal balance, was found to be significantly higher in pregnant subjects when compared with non-pregnant controls.

TABLE I: Anthropometric measurements and Baseline parameters (n=60).

Variables	*Pregnant (n=30) (Mean±SD)*	*Non-pregnant (n=30) (Mean±SD)*	*p-value*
Age (years)	24.03±1.47	23.70±0.65	0.262
Height (cm)	154.07±6.62	161.03±4.74*	0.000
Weight (kg)	53.07±8.29	55.26±8.79	0.324
BMI (kg/m^2)	22.41±3.57	21.41±3.02	0.249
Resting Heart rate (beats per minute)	78.20±8.10	75.11±12.25	0.255
SBP (mmHg)	117.47±8.79	102.06±7.59*	0.000
DBP (mmHg)	77.51±6.94	65.27±5.00*	0.000

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; S.D: Standard Deviation; *p-value <0.01

TABLE II: Basal heart rate variability parameters (n=60) (Independent T test)

Variables	*Pregnant (n=30) (Mean±SD)*	*Non-pregnant (n=30) (Mean±SD)*	*p-value*
HF (ms^2)	1058.75±221.57	2226.31±446.23	0.061
LF (ms^2)	1770.39±585.88	1064.32±253.60	0.715
HF(nu)	35.39±2.11	52.78±3.24*	0.000
LF(nu)	53.30±2.18	32.85±3.28*	0.000
Total power (ms^2)	5579.35±1349.73	4820.15±798.11	0.620
LF/HF ratio	1.80±0.20	0.77±0.16*	0.000

HF: High frequency power, LF: Low frequency power, ms^2: millisecond squared, HF(nu): high frequency power normalized unit, LF(nu): Low frequency power normalized unit, TP: Total power, S.E: standard error; *p-value <0.01

Discussion

Present study involves assessment of HRV among normal pregnant women during third trimester of pregnancy when compared with age matched non pregnant females (mean age of 24 years). The two groups did not differ significantly in anthropometric parameters like height, weight and BMI. Present study found that, high frequency power (normalised units) which indicates cardiac vagal tone was significantly lower in pregnant women. Low frequency power (normalised units) was significantly higher in pregnant subjects. LF/HF ratio which reflects sympathovagal balance was significantly higher in the pregnant women. No significant difference was found in total power between the two groups.

Sympathetic activation is usually accompanied by the reduction in the total power (11). In the present study no such association was found, which may be attributed to very low frequency power (VLF) which is known to influence total power.

Research studies have reported that both systolic blood pressure (BP) and diastolic BP decreases during early pregnancy, reaches minimum in mid pregnancy (20 weeks), remains low till 32 weeks, returns to baseline at term. Also, diastolic BP is known to decrease more when compared to systolic BP, which may be attributed to decrease in vascular tone during pregnancy. During early pregnancy, peripheral resistance is markedly reduced leading to a state of systemic vasodilatation (12). This pregnancy associated fall in systemic vascular resistance may also be due to hormonal influence mainly circulating estrogen, prostaglandins (13). However, in contrast to above findings, present study showed a significant increase in both systolic and diastolic BP. Similar findings were obtained by Moertl et al. which showed a significant increase in BP during late gestation especially in diastolic measurements (14). MacDonald-Wallis et al, in an attempt to establish BP reference values during pregnancy, have found higher mean systolic BP and diastolic BP values at 12 and 37 weeks of normal pregnancies which is in par with our study (15). All these authors concluded that, BP changes during pregnancy is related mainly to BMI during pre-pregnancy and early pregnancy (16). However, due to study design, present study do not have pre-pregnancy, early pregnancy measurements and was restricted to third trimester, hence changes that occur during pregnancy cannot be compared with non pregnant values.

Resting heart rate abruptly increases in the first trimester of pregnancy, followed by a moderate increase later till term. However, in present study heart rate was measured only in 3rd trimester and it was higher in pregnant women when compared to control group. Resting heart rate is known to be an independent predictor of cardiovascular and all-cause mortality in either gender with and without diagnosed CVD. However, the changes in resting heart rate may be attributed to hemodymnamic adaptations during pregnancy (17, 18).

Assessment of short term HRV could determine early risk of underlying abnormal physiologic states like preeclampsia (19, 20), preterm deliveries and gestational diabetes (21). A 24 hour Holter monitoring based study of HRV throughout pregnancy showed that all indices of HRV decreased during early pregnancy as well as late pregnancy when compared with non-pregnant state (5).

Studies have reported that hypertensive disorders during pregnancy, mainly in preeclamptic women is characterized by sympathetic overactivity, however, these studies used invasive measurement techniques (22). Apart from this, research that studied maternal cardiac autonomic changes during pregnancy using non-invasive tools have reported that cardiac autonomic parasympathetic activity was decreased and sympathetic activity was increased during late gestation (23, 24). These findings are similar to that obtained in present study. This indicates that, there is sympathetic predominance during late pregnancy. This may be due to aortocaval compression caused by enlarging gravid uterus with increasing gestational age, which compromises venous return and hence, cardiac output. This leads to a shift towards higher sympathetic activity and lower vagal modulation during late gestation (25).

In contrast to these findings, the research that focused on study of various parameters like HRV, blood pressure variability and baroreflex sensitivity though out pregnancy found no difference in these autonomic indices during different gestational ages (14). Another study showed that there is no difference in cardiac autonomic activity among pregnant and non pregnant women; however, here the autonomic function tests were performed during first trimester (26). Ekholm et al demonstrated a decrease in parasympathetic responsiveness during pregnancy that returned to normal following delivery (27).

Presently most of the studies have focused on echocardiographic recording of fetal heart beat as it is a part of routine clinical practice, due to its prognostic tool in normal and pathological pregnancies (28). However, the maternal HRV

analysis has advantage over fetal HRV, in that ECG records can be obtained from early pregnancy till delivery by non invasive procedures. Recent studies have investigated prognostic value of assessment of HRV in various clinical conditions (29). The presence of a high vagal tone seems to be a marker of physiological as well as psychological flexibility (30). Decreased HRV during normal pregnancy may reflect impaired adaptations of maternal cardiovascular system to pregnant state. However, research studies that specifically focused on; the risk of CVD during normal pregnancy, in otherwise healthy females without underlying structural cardiac abnormalities is meagre. The main focus of the present study was to assess cardiac autonomic responses among healthy pregnant females and upcoming risk of CVD in them due to the pregnant state. A timely life style modification like yogic meditation, regular exercise can improve cardiac autonomic modulation.

Conclusion:

The present study involving healthy females during third trimester of pregnancy concludes that, decreased vagal tone in 3rd trimester of gestation; as depicted by decreased HRV. This may be linked with the fact that, even normal pregnancy can have impact on dynamic autonomic control of heart.

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None

Conflict of Interest:

None declared

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