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RESEARCH ARTICLE

A comparative study of cardiovascular autonomic function tests between second trimester pregnant women and non-pregnant women

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ABSTRACT

Background: Normal pregnancy has been documented to be accompanied by marked alteration in maternal circulation during the first and second trimesters. For adapting the cardiovascular hemodynamic changes during normal pregnancy, a well-controlled interaction between the sympathetic and parasympathetic system is very essential, failure of which may result in pregnancy-related complications. **Aims and Objectives:** To evaluate and compare the cardiovascular autonomic function tests (AFTs) between the second trimester pregnant women and controls. **Materials and Methods:** A cross-sectional study was conducted by random selection of 67 s trimester pregnant women and 67 controls in the age group of 19–29 years. The cardiovascular AFTs were carried out. The statistical analysis was done using unpaired *t*-test. **Results:** During isometric handgrip exercise, the maximum rise in diastolic blood pressure (DBP), and during cold pressor test, the maximum rise in systolic BP and maximum rise in DBP were significantly less in the second trimester of pregnancy than controls. There was significantly less increase in 30:15 ratio and E: I ratio of the second trimester pregnant women when compared to controls. **Conclusion:** The cardiovascular autonomic nervous activity was decreased in the second trimester of pregnancy when compared to controls.

KEY WORDS: Cardiovascular Autonomic Function Tests; Cold Pressor Test; Hypertension

INTRODUCTION

Normal pregnancy has been documented to be accompanied by marked alteration in maternal circulation during the first and second trimesters including, 30–60% increase in cardiac output and decrease in systemic vascular resistance in response to hemodynamic changes and, 10% fall in arterial pressure.[1] For adapting cardiovascular hemodynamic changes during normal pregnancy, a well-controlled interaction between the sympathetic and parasympathetic system is very essential, failure of which may result in pregnancy-related complications.[2,3] These physiological changes if unadapted over a period of time may lead to various complications such as cardiovascular diseases and hypertension.

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During pregnancy, alteration in autonomic cardiovascular control has an important etiological role in certain conditions such as insufficient uteroplacental blood flow pregnancy-induced hypertension (PIH).[4] Aortocaval compression by the gravid uterus becomes evident as the pregnancy advances. This may cause supine hypotension syndrome, leading to higher cardiovascular sympathetic activity, which is the main factor responsible for this change.[5] Higher sympathetic activity is noticed in the first trimester. This increased sympathetic activity leads to hypertension in some women during pregnancy called PIH.

Thus, cardiovascular monitoring during pregnancy helps in early detection of cardiovascular abnormalities, especially in developing countries like India.[3] In preventing complications, the antenatal visits are very much helpful. Hence, the present study was undertaken to evaluate the non-invasive cardiovascular autonomic function tests (AFTs) in the second trimester of pregnancy and compare them with non-pregnant controls.

Aims and Objectives

This study aims to evaluate and compare cardiovascular AFTs between the second trimester pregnant women and non-pregnant women.

MATERIALS AND METHODS

The present study was undertaken at the Department of Physiology with collaboration of the Department of Gynecology and Obstetrics, Belagavi Institute of Medical Sciences (BIMS) College and Hospital, Belagavi, Karnataka. The pregnant women were selected by random sampling, attending BIMS Civil Hospital for routine antenatal care. Control group comprised healthy non-pregnant women which included non-teaching staff, technicians, and relatives of patients who were randomly selected from BIMS College and Hospital, Belagavi.

The study was conducted after obtaining ethical clearance from Institutional Ethics Committee. The details, such as the purpose of the study, nature of the study, and methods used, were explained to the subjects and controls, in their own understandable language. Written informed consents were duly signed by the subjects and controls.

- Sample size
- Study design: Cross-sectional study.

By referring the article,[3] sample size was calculated using the formula,

Formula: $n = [(Z\alpha + Z\beta)^2 \times S^2 \times 2]/d^2$

Where,

$Z\alpha$ - Z value for alpha error = 1.96

$Z\beta$ - Z value for beta error = 0.84 with 80% power

S - Common standard deviation between two groups = 5.02

d - Clinically meaningful difference = 2.43

Z - Standard normal deviate (deviation from the mean)

By substituting above values in the formula, $Z\alpha = 1.96$, $Z\beta = 0.84$ with 80 % power, S = 5.02 and d = (mean 1 – mean 2) = (7.73 – 5.3) = 2.43, we get sample size as n = 67 in each group.

Second trimester – 67

Control – 67

Total – 134

Inclusion Criteria

1. Subjects: 19–29 years healthy pregnant women of the second trimester with singleton pregnancy were randomly selected.
2. Controls: 19–29 years healthy non-pregnant women were randomly selected from population of non-teaching staff, technicians, and relatives of patients.

Exclusion Criteria

All pregnant women in the age group of <19 or <29 years, with multiple pregnancies, gestational diabetes, preeclampsia and eclampsia, diabetes mellitus, asthma, thyroid diseases, history of cardiovascular or lung diseases, smokers, or on any drugs that might affect autonomic functions, for example, adrenergic receptor stimulants and blockers and those with hemoglobin <10 g% were excluded.

Methods

In the present study, five simple, non-invasive cardiovascular reflex tests had been used to assess autonomic functions. All the tests were conducted between 10.00 am and 4.00 pm. The subjects had been instructed to abstain from coffee, tea, cola, etc., for a minimum period of 12 h before the tests. After thorough examination of subjects as per pro forma, subjects were asked to relax in supine position for 30 min. The resting heart rate (HR) was recorded on a standard electrocardiogram (ECG) from lead II and blood pressure (BP) was measured from Omron digital BP monitor. The standard cardiovascular AFTs were performed, as per Ewing *et al*. and Hines Jr criteria.[6,7]

The tests included

BP response to standing.

BP response to sustained handgrip.

HR response to standing.

HR response to deep breathing.

Cold pressor test (CPT).

Procedure

BP response to standing

BP was recorded when the subject is lying down quietly for 5–10 min. Three basal readings were taken. The subject stood up suddenly, taking <5 s; then, BP was recorded at 30 s, 60 s, and 90 s after standing. The postural fall in BP is taken as the difference between systolic BP (SBP) in lying and lowest SBP on standing.[6]

BP response to sustained handgrip

The subject was asked to exert maximal hand grip strength on hand grip dynamometer with dominant hand. The maximum voluntary contractions were first determined. Handgrip was then maintained at 30% of that of maximum for as long as possible (3 to 5 minutes). Blood pressure was measured three times before and at one-minute intervals during handgrip for 3 minutes in the non-dominant hand. The result is expressed as difference between highest diastolic blood pressure during handgrip exercise and the mean of the three diastolic blood-pressure readings before handgrip began.[6]

Immediate HR response to standing

The test was done with the subject lying quietly while the HR was recorded continuously for 30 s, on an ECG. The subject then stood suddenly and the point at starting to stand was marked on the ECG. ECG was recorded for 30 s after standing. The shortest relative risk (RR) interval at the 15th beat and the longest RR interval at around the 30th beat were measured. The HR response was expressed by 30:15 ratio.[6]

The ratio was expressed as follows:

Ratio = [Longest R-R interval at around 30th beat]/[Shortest R-R interval at around 15th beat]

HR variation during deep breathing

The subject sits quietly and was instructed to start deep breathing on verbal command as trained earlier (5 s deep inspiration and 5 s deep expiration) for 30 s and the ECG was recorded throughout the period of deep breathing. The mean of difference between maximum and minimum RR interval during each breathing cycle was measured.[6] The ratio was expressed as:

Ratio = [Maximum R-R interval]/[Minimum R-R interval]

CPT

After the subject had rested supine for 5–10 min, resting BP was recorded with the subject sitting comfortably in the right upper arm. The left hand was then immersed to just above the wrist in cold water (3–5° C) for 1 min. BPs were measured from the right arm at 30 and 60 s after immersion. Maximum increase in SBP and DBP was noted.[7]

Statistical Analysis

The basic data were presented as mean ± standard deviation. The statistical analysis was done using unpaired *t*-test (SPSS 22 version) to compare the data and $P < 0.05$ was considered as significant.

RESULTS

The comparison of cardiovascular AFTs was done between the 67 s trimester pregnant women and 67 healthy non-pregnant women who were the controls.[Table 1].

DISCUSSION

We found that in our study, the fall in SBP in response to standing was not significant in the second trimester of pregnancy when compared to controls. In our study, the maximum rise in DBP during isometric handgrip exercise, the maximum rise in SBP and maximum rise in DBP in response to CPT were significantly less in the second trimester than compared to controls. We also found that in HR response to standing, the 30:15 ratio and also, in HR response to deep breathing, the ratio of maximum-to-minimum RR-interval during respiratory cycles, that is, the E/I ratio of RR intervals, was found to be significantly less in the second trimester of pregnancy than compared to controls.

In our study, the fall in SBP in response to standing was not significant in the second trimester of pregnancy when compared to controls. Previous study had shown that, on orthostatic hypotension test, no significant change was found in BP among the second trimester pregnant women, which correlates with our study.[8] A decrease in baroreceptor sensitivity, especially observed in early pregnancy may be attributed to this observed result signifying an incomplete adaptation of the cardiovascular system to the pregnant state. It has been noted that during second half of pregnancy, the increase in blood volume seemed to improve hemodynamic stability.[9] In our study, the maximum rise in DBP during isometric handgrip exercise was significantly less in the second trimester when compared to controls. This is in accordance with many studies[4,8,10-12] which have shown that there is decreased sympathetic activity more in the second trimester, which explains the decreased peripheral vascular resistance in the second trimester is by decreased sympathetic activity.[8] The reduced BP response reported could be due to an antagonistic effect of products of uteroplacental unit such as progesterone or a diminished contractile response of the blood vessels to adrenaline.[13,14] According to other study, BP decreases in early pregnancy, reaching a minimum in mid-pregnancy, which again correlates with our study.[15] A lower viscosity potentiates fall in vascular resistance. Both factors independently contribute to fall in afterload. These changes combined are responsible for decrease in BP in the second trimesters of pregnancy.[8] In contrast, a study showed increase in BP in response to isometric handgrip test in the second trimester of pregnancy, who subsequently developed PIH as compared to women with normal outcome,

Table 1: Comparison of cardiovascular AFT between the second trimester pregnant women and controls

Parameters	2nd trimester (Mean±SD)	Controls (Mean±SD)	Significance	
			t value	*P* value
I. Sympathetic tests:				
1. BP response to standing (mmHg):				
Supine SBP	110.96±8.58	106.57±10.68	2.622	0.010*
On standing SBP	104.54±10.98	103.04±9.16	0.854	0.394
Fall in SBP	6.48±7.40	4.18±6.56	1.902	0.59
2. BP response to sustained handgrip (mmHg):				
Baseline DBP	62.78±0.82	63.46±8.79	−0.508	0.612
Maximum DBP during handgrip	80.57±9.58	88.99±15.77	−3.734	0.000*
Maximum rise in DBP	17.79±10.01	25.49±15.21	−3.461	0.001*
3. CPT:				
i. Comparison of SBP response during CPT (mmHg):				
Supine SBP	110.96±8.58	107.43±9.31	2.277	0.024*
Maximum SBP reached	123.73±9.87	131.34±16.22	−3.281	0.001*
Maximum rise in SBP	12.84±8.70	23.94±13.91	−5.538	0.000*
ii. Comparison of DBP response during CPT (mmHg):				
Supine DBP	62.78±6.71	62.69±6.45	0.079	0.937
Maximum DBP reached	79.58±10.16	85.88±13.10	−3.110	0.002*
Maximum rise in DBP	16.98±8.66	23.16±12.63	−3.303	0.001*
II. Parasympathetic tests:				
HR response to standing - 30: 15 ratio	1.02±0.10	1.08±0.18	−2.588	0.011*
HR response to deep breathing - ratio of maximum to minimum RR interval	1.37±0.16	1.50±0.19	−4.272	0.000*

All the values in mmHg except ratios. *Indicates significant value. AFTs: Autonomic function tests, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, BP: Blood pressure, HR: Heart rate, RR: Relative risk, CPT: Cold pressor test, SD: Standard deviation

which was attributed to increased vascular reactivity during early pregnancy before clinical manifestation of the disease.[16] In our study, the maximum rise in SBP and maximum rise in DBP in response to CPT were significantly less in the second trimester than compared to controls, indicating decreased sympathetic activity in the second trimester than controls. Increase in BP in response to CPT was more in the second trimester of pregnancy, who subsequently developed PIH as compared to women with normal outcome, which was attributed to increased vasoconstrictive response to physiological stimulus (cold in this case).[16] In our study of HR response to standing, the 30:15 ratio was found to be significantly less in the second trimester of pregnancy compared to controls. Previous study showed the 30:15 ratio was significantly low in the second trimester of pregnancy than controls, correlating with our study. Furthermore, significant response was found in the study by Ekholm *et al*. in the second trimester, again correlating with our study. Duration of pregnancy seems to influence the HR difference between supine and standing posture. This HR response is reduced during pregnancy, indicating a diminished baroreflex induced slowing of HR which suggests a rearrangement of autonomic tone takes place in normal pregnancy.[17] In our study of HR response to deep breathing, the ratio of maximum-to-minimum RR-interval during respiratory cycles, that is, the E/I ratio of RR intervals, was found to be significantly less in the second trimester compared to controls. In accordance with our results, many studies[4-21] showed HR response to deep breathing expressed as deep breathing difference (DBD), a measure of cardiac parasympathetic function was observed to be significantly lower in pregnant women when compared to control group and generally followed a decreasing trend with increase in gestation.[4] This finding was in conformity with observation of Ekholm *et al*. who suggested a multifactorial basis for it.[19] A diminished parasympathetic input to the heart during pregnancy has been attributed to, reduced baroreceptor sensitivity, impaired vagal afferents to brain and altered efferent signals to the heart.[20] A reduction in oscillation of the right atrial distension arising from diminished pulsatility of venous return from the growing uterus has been described in pregnant subjects, which may account for the lowering of DBD in pregnancy.[4]

Strength and Limitations of this Study

Strength: The cardiovascular AFTs can be used as screening tests in all the three trimesters of pregnancy to detect any altered cardiovascular autonomic responses.

Limitations: Less sample size of both pregnant and non-pregnant women, not included the pregnant women of all the three trimesters, not correlated the urinary catecholamine levels with that of the cardiovascular autonomic functions.

CONCLUSION

From the above results, we can conclude that, on comparison of cardiovascular AFTs between pregnant women and controls, the cardiovascular autonomic nervous activity was decreased during pregnancy than controls. There was decreased sympathetic and parasympathetic nervous activity in the second trimester of pregnancy when compared to controls. Thus, cardiovascular AFTs can be used as screening tests among pregnant women to detect any cardiovascular autonomic alterations which may lead to complications like PIH, and thus may give valuable information in this regard.

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