A Comparative Study of Cardiovascular Sympathetic Activity in Three Trimesters of Pregnancy
Ghuge S H*, Patil V V*, Latti R G**, Thorat K D*

Abstract
The autonomic nervous system is known to play a major role not only in various pathophysiological circumstances, such as haemorrhage and shock, but also in physiological states such as pregnancy. Normal pregnancy is associated with changes in the hemodynamics especially in the cardiac output, stroke volume and blood pressure. Systemic vascular resistance is decreased in response to these hemodynamic changes. So the present study was planned, to investigate the sequential changes in cardiovascular sympathetic activity during the three trimesters of pregnancy. Total 100 healthy pregnant women having no major illness or any additions, were considered for the study. All subjects were evaluated by “CANWIN- Cardiac Autonomic Neuropathy Analyzer”, using the tests like Blood pressure response to standing and Blood pressure response to sustained handgrip. The results indicate that Sympathetic variation was present in all three groups but more in 2nd trimester as compared to 1st and 3rd trimesters. So study concludes that there is decreased Sympathetic activity up to mid-trimester and return of Sympathetic activity towards prepregnant level in last trimester of pregnancy.

Key Words: Pregnancy, Sympathetic activity, Blood Pressure, Cardiovascular.

Introduction
Normal pregnancy is associated with substantial changes in the cardiovascular system. It has been noted that blood volume, cardiac output and stroke volume begin to change after the first trimester to accommodate the growing foetus. Most of the 30-60% increase in cardiac output and at least half of the approximately 10% fall in arterial pressure in human pregnancy is accomplished in the first trimester. It might be anticipated that baroreflex function would be decreased in pregnancy because the physiologic hypervolemia of pregnancy would be expected to dampen large changes in blood pressure induced by a given stimulus. Systemic vascular resistance is also decreased in response to hemodynamic changes. Arterial blood pressure shows a progressive fall in the first and middle trimesters.

As pregnancy advances, aortocaval compression by the gravid uterus gradually becomes evident, which may cause supine hypotensive syndrome in late pregnancy. It has been noted that cardiovascular sympathetic nervous activity shifted to higher sympathetic modulation in late pregnancy. Aortocaval compression is the main suggested factor responsible for this change. This theory was supported by observations that moving to an upright position could lead to lessening of sympathetic activation and that delivery of the foetus led to return of normal cardiovascular autonomic nervous activity within 3 months. All these adaptations are associated with autonomic nervous system changes that produce alteration in cardiac autonomic modulation. Failure of these adaptations may result in pregnancy related complications such as pregnancy induced hypertension, pre-eclampsia and eclampsia.

As the cardiovascular sympathetic nervous system plays an important role in adaptation of the maternal body to nurturing foetus, it is important to understand the sequential changes in cardiovascular sympathetic nervous activity at various stages of pregnancy. The
present study was undertaken to investigate the sequential changes in cardiovascular sympathetic activity in three trimesters of pregnancy.

**Materials and Methods**

Total 100 healthy normotensive pregnant women ranging in age group between 18 to 28 years attending regular Antenatal Clinic of Pravara Rural Hospital were considered for the study as soon as pregnancy was established. Pregnancy was confirmed by urinary human chorionic gonadotropin determination test. The study design was approved by ethical committee of the institute.

Subjects were divided into three groups.

- **GROUP I** - 33 subjects of 1st TRIMESTER (Up to 12 weeks)
- **GROUP II** - 33 subjects of 2nd TRIMESTER (13 to 28 weeks)
- **GROUP III** - 34 subjects of 3rd TRIMESTER (29 weeks onwards).

Study protocol was explained to the subjects and written informed consent was obtained. Subjects with any major illness in the past or at present such as hypertension, diabetes, any cardiovascular abnormality; with any addiction, history of caesarean section, or previous abortions were not included in this study.

**CANWIN**

Canwin is the-state-of-the-art window based computer having cardiac autonomic neuropathy (CAN) analysis system with interpretation. It has an extensive data base to keep track of subject’s history and for archive test retrieval and comparisons. Being fully automatic, the need of manual recordings, readings and calculation is eliminated. Inbuilt time domain waveform analysis and Blood pressure measurements make the task of conducting all the Autonomic Nervous System tests very easy.

**Precautions during measurements**

- All measurements were performed 60 minute under standardized resting condition between 09:00 to 12:00 hours as described by Voss et al\(^6\) to avoid the effects of circadian rhythms on heart rate and in a quiet room.

- Subjects were asked to have a light breakfast and to empty their bladder before commencing the study.

- Test was carried out only when the subject was fully relaxed.

- Subjects were advised to restrict the movements during the test.

**Following Cardiovascular Sympathetic Tests were Carried Out**

1. **Blood pressure response to standing (Orthostatic/Postural Hypotension)**

   **Procedure:** The subject was asked to relax and lie down comfortably. Blood pressure was measured for the first time in supine position when the green light glows on the screen, then when red light glows, the subject was asked to stand up quickly and the blood pressure was recorded immediately after standing for the second time. Then the blood pressure was recorded again after 1 minute of standing. At the end of test, the result is displayed.

2. **Blood pressure response to sustained handgrip:**

   **Procedure:** The blood pressure was recorded in sitting position. Then the subject was asked to hold a spring dynamometer in the dominant hand and instructed to compress the dynamometer with full effort for a period of 5 minutes. The blood pressure was recorded thrice during these 5 minutes automatically. The alterations in blood pressure just before the release of spring dynamometer was taken as index of response to hand grip test.

   All the data for the above tests was recorded and statistical analysis was carried out.

**Result**

The statistical analysis for sympathetic tests was carried out separately in all the three groups. After analysing
all the three groups, the cardiovascular sympathetic functions were compared within the three groups. 

Table 1 shows Mean and Standard Deviation values for sympathetic parameters (Orthostatic Hypotension Test and Sustained Hand Grip Test) for all the three groups.

**Table No.1: Group wise distribution of Mean and SD values for Sympathetic tests**

<table>
<thead>
<tr>
<th>Sympathetic tests</th>
<th>Group I (n=33)</th>
<th>Group II (n=33)</th>
<th>Group III (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Orthostatic Hypotension Test</td>
<td>2.91 ± 2.92</td>
<td>4.09 ± 3.38</td>
<td>5.38 ± 3.47</td>
</tr>
<tr>
<td>Hand Grip Test</td>
<td>7.91± 7.14</td>
<td>4.54 ± 5.3</td>
<td>10.97 ± 4.2</td>
</tr>
</tbody>
</table>

Table 2 shows the sympathetic parameters in group I and group II subjects. Group I had lower value of 2.91 ± 2.92 for orthostatic hypotension as compared to the value for group II of 4.09 ± 3.38, but showed no statistically significant change (P>0.05). Group I had higher value of 7.91± 7.14 for sustained handgrip as compared to the value for group II of 4.54 ± 5.3 which showed statistically significant change (p < 0.05).

**Table No.2: Group wise comparison of mean values of Sympathetic tests in Group I & II**

<table>
<thead>
<tr>
<th>Sympathetic tests</th>
<th>Group I (n=33)</th>
<th>Group II (n=33)</th>
<th>'t' value</th>
<th>'p' value</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthostatic Hypotension Test</td>
<td>2.91 ± 2.92</td>
<td>4.09 ± 3.38</td>
<td>1.51</td>
<td>P&gt;0.05</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hand Grip Test</td>
<td>7.91± 7.14</td>
<td>4.54 ± 5.3</td>
<td>2.19</td>
<td>P&lt;0.05</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Table 3 shows the sympathetic parameters in group I and group III subjects. Group I had lower value of 2.91 ± 2.92 and 7.91± 7.14 for orthostatic hypotension and sustained handgrip respectively compared to the values group III of 5.38 ± 3.47 and 10.97 ± 4.2, respectively with P value of less than 0.01 which is highly significant for orthostatic hypotension and P value of less than 0.05 which is significant for sustained handgrip.

**Table No.3: Group wise comparison of mean values of Sympathetic tests in Group I & III**

<table>
<thead>
<tr>
<th>Sympathetic tests</th>
<th>Group I (n=33)</th>
<th>Group III (n=34)</th>
<th>'t' value</th>
<th>'p' value</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthostatic Hypotension Test</td>
<td>2.91 ± 2.92</td>
<td>5.38 ± 3.47</td>
<td>3.15</td>
<td>P&lt;0.01</td>
<td>Highly significant</td>
</tr>
<tr>
<td>Hand Grip Test</td>
<td>7.91± 7.14</td>
<td>10.97 ± 4.2</td>
<td>2.13</td>
<td>P&lt;0.05</td>
<td>Significant</td>
</tr>
</tbody>
</table>
Table No.4: Group wise comparison of mean values of Sympathetic tests in Group II & III

<table>
<thead>
<tr>
<th>Sympathetic tests</th>
<th>Group II (n=33) Mean ± SD</th>
<th>Group III (n=34) Mean ± SD</th>
<th>t' value</th>
<th>p' value</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthostatic Hypotension Test</td>
<td>4.09 ± 3.38</td>
<td>5.38 ± 3.47</td>
<td>1.54</td>
<td>P&gt;0.05</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hand Grip Test</td>
<td>4.54 ± 5.3</td>
<td>10.97 ± 4.2</td>
<td>5.5</td>
<td>P&lt;0.01</td>
<td>Highly significant</td>
</tr>
</tbody>
</table>

Table 4 shows the sympathetic parameters in group II and group III subjects. Group II had lower value of 4.09 ± 3.38 for orthostatic hypotension as compared to the value for group III of 5.38 ± 3.47, but showed no statistically significant change (P>0.05). Group II also had lower value of 4.54 ± 5.3 for sustained handgrip as compared to the value for group III of 10.97 ± 4.2 which showed highly statistically significant change (p < 0.01).

**Discussion**

To measure and compare the effects of pregnancy on cardiovascular sympathetic functions, the analysis was done separately in different trimesters of pregnancy. The results indicates that sympathetic activity was decreased more in 2nd trimester, less in 1st trimester and least in last trimester of pregnancy i.e. towards prepregnant level. In the early pregnancy an overall decrease in vascular tone leads to systemic vasodilatation and rise in arterial compliance. The vasodilatation may be directly responsible for down-regulation of baroreceptors. There is evidence that nonosmotically release of vasopressin causes hemodilution and with a reduction in viscosity. A lower viscosity potentiates fall in vascular resistance. Both factors independently contribute to fall in afterload. These changes combined are responsible for decrease in blood pressure in 1st and 2nd trimesters of pregnancy.

In a study by Morris et al showed that total peripheral resistance continued to decrease up to 25th week. Circulating estrogens increase early and progressively during pregnancy and may stimulate vascular function directly or indirectly by various means including increased NO availability. In vitro, oestrogen exerts an acute vasodilator effect by relaxing vascular smooth muscle directly, possibly by blocking cell membrane voltage-dependent Ca2+ channels.

The decline in systemic vascular resistance is probably caused by gestational hormones, increased concentrations of circulating prostaglandins, increased heat production by the developing foetus and development of a low-resistance circulation in the pregnant uterus. The decline in systemic vascular resistance may reduce the workload of the heart, leading to lower sympathetic modulation in the first trimester of pregnancy.

As gestational age increases further, aortocaval compression caused by the enlarging gravid uterus further compromises venous return and cardiac output leading to a shift in sympathetic nervous activity towards an even higher sympathetic and lower vagal modulation in the third trimester of pregnancy.

These findings emphasize that the most important maternal adaptation to pregnancy take place by change in cardiovascular sympathetic activity for the better perinatal outcome.

**Conclusion**

To conclude, cardiovascular nervous variation starts from the first trimesters of pregnancy. There is decreased sympathetic activity more in 2nd trimester, less in 1st trimester and least in last trimester of pregnancy i.e. towards prepregnant level. These results explain that
the decreased peripheral vascular resistance in 1st and 2nd trimester is mainly by decreased sympathetic activity and aortocaval compression responsible for higher sympathetic modulation in late pregnancy. A controlled and blind fold study is recommended to arrive at definite conclusions.

Acknowledgement
The authors wish to acknowledge thanks to all the technical and nonteaching staff members of Dept. of Physiology, and thanks to Dept of Obstetrics and Gynaecology, Rural Medical College, Loni for their time to time co-operation during the study.

References