Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical Anatomy and Physiology

Journal homepage: https://www.ijcap.org/

Original Research Article

Study of sympathetic and parasympathetic control of haemodynamics in mid pregnancy by cardiac autonomic neuropathy analyzer

Jeewandeep Kaur[1,*], **Arvinder Pal Singh Batra**[2]

[1] *Dept. of Physiology, BPS GMC For Women, Sonepat, Haryana, India*
[2] *Dept. of Anatomy, BPS GMC For Women, Sonepat, Haryana, India*

ARTICLE INFO

Article history:
Received 21-06-2021
Accepted 27-08-2021
Available online 01-10-2021

Keywords:
Pregnancy
Autonomic nervous system
Hypertension
Isometric hand grip test

ABSTRACT

Background: Pregnancy is associated with substantial changes in cardiovascular system. The action of autonomic nervous system is essential for circulatory adaptations in pregnancy and nourishing growing fetus.
Aims and Objective: The study was conducted to assess the significance of autonomic function tests amongst women of mid pregnancy and non pregnant women.
Materials and Methods: A comparative study was carried out amongst pregnant and non pregnant women in Department of Physiology. A total of 60 women (30 pregnant as study group and 30 non pregnant healthy women as control group) aged between 18- 30 years were included in study.
Results: The results indicated that there was statistically significant change in resting heart and highly statistically significant change to deep breathing in mid pregnancy reflecting higher parasympathetic activity in study group (pregnant female) as compared to control group (non pregnant female) while sympathetic activity assessed by isometric hand grip test didn't show any statistically significant change among pregnant as compared to non pregnant.
Conclusions: Our study showed role of parasympathetic activity in controlling haemodynamics in mid pregnancy and it may help to return the arterial pressure to non pregnant level by causing haemodilution, although when the increase in activity is excessive, hypertension may ensue.

1. Introduction

Pregnancy is associated with substantial changes in cardiovascular system.[1] The action of autonomic nervous system is essential for circulatory adaptations in pregnancy and nourishing growing fetus. The autonomic nervous system is divided anatomically and functionally into two distinct system i.e. the sympathetic and parasympathetic in first half of pregnancy systemic vascular resistance and blood pressure decreases, during last trimester systemic vascular resistance increases.[2] A well controlled interaction between sympathetic and parasympathetic system is necessary for adapting the cardiovascular system to various haemodynamic needs not only under pathophysiological conditions like hemorrhage and shock, but also in physiological states such as pregnancy.[3]

During pregnancy there is an increase in blood volume, heart rate and cardiac output while peripheral resistance and resting blood pressure decreases.[4] It might be anticipated that baroreflex function would be decreased in pregnancy because the physiological hypervolemia of pregnancy would be expected to dampen large changes in blood pressure induced by a given stimulus.[5] Systemic vascular resistance is also decreased in response to haemodynamic changes. Arterial blood pressure shows a progressive fall

* *Corresponding author*.
E-mail address: jeewandeepk@gmail.com (J. Kaur).

https://doi.org/10.18231/j.ijcap.2021.053

in first and middle trimester.[6] As gestational age increases further aortocaval compression caused by enlarging gravid uterus further compromises venous return and cardiac output leading to shift in sympathetic nervous system activity towards an even higher sympathetic and lower vagal modulation in third trimester of pregnancy.[1]

Aortocaval compression is the main suggested factor responsible for this change. Failure of these adaptations may result in pregnancy related complications such as pregnancy induced hypertension, preeclampsia and eclampsia.[2] Autonomic nervous control can be non-invasively studied with the cardiovascular reflex tests, such as the orthostatic test, the isometric handgrip test and by measuring heart rate variability. Common to the tests is that they all disturb the circulatory system. By examining the recovery of the cardiovascular system, information may be obtained on the autonomic nervous control of the haemodynamics.[7] A combination of tests is needed to elucidate overall autonomic nervous control.[8] This study was undertaken to investigate the changes in autonomic nervous system activity and its control over haemodynamics in mid pregnancy in pregnant females as compared with non pregnant females.

2. Aims and Objective

The current study is planned to learn how to assess the significance of autonomic function tests amongst women of mid pregnancy and non pregnant women.

3. Materials and Methods

A comparative study was carried out amongst pregnant and non pregnant women in Department of Physiology. A total of 60 women (30 pregnant as study group and 30 non pregnant healthy women as control group) aged between 18-30 years were included in study after approval of protocol by institutional ethical committee.

3.1. Study group

Healthy pregnant female.

3.2. Control group

Healthy non pregnant female.

3.3. Inclusion criteria

1. 18-30 years age limit
2. Healthy pregnant and non pregnant females
3. No history of complicated pregnancy

3.4. Exclusion criteria

1. Twin gestation
2. History of preeclampsia
3. Gestational diabetes
4. Placenta previa
5. Bad obstetric history
6. Chronic hypertension
7. Chronic renal disease
8. Diabetes
9. Cardiopulmonary disease
10. Chronic respiratory illness
11. On any medication like anti hypertensive's

All subjects were explained of the procedure to be undertaken and a written consent was obtained. All 30 pregnant women attending antenatal clinic along with healthy controls were assessed for variation in sympathetic and parasympathetic system during mid pregnancy. Cardiac autonomic function test for assessing sympathetic and parasympathetic control was done by CANWIN- 504 (Cardiac Autonomic Neuropathy Analyser- 504).

3.5. CANWIN- 504 (Cardiac Autonomic Neuropathy Analyser)

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. Cardiac Autonomic Neuropathy Analyser model CANS 504 is an important tool to measure and diagnose autonomic dysfunctions using ECG of R- R intervals and automatic BP measurement.

Fig. 1: CANWIN- 504

3.5.1. Test for assessing parasympathetic activity include

1. **Resting Heart Rate** was calculated from ECG by using standard limb leads.
2. **Heart rate response to standing (30:15)** was calculated as ratio between R- R interval at beats

30 and 15 of the ECG recorded immediately upon standing. This test evaluates the cardiovascular response elicited by change from horizontal to vertical position. The typical heart rate response to standing is largely attenuated by parasympathetic blockade.

3. **Heart rate response to deep breathing:** Heart rate was recorded first during normal breathing at rest and then during deep breathing (6/ min). ECG 3^{rd} and 6^{th} respiration, minimum R- R interval and corresponding heart rate were calculated.

3.5.2. Test for assessing sympathetic activity

Isometric hand grip exercise test: Before the exercise, subjects were allowed to rest for 10 minutes in a quiet room. Resting blood pressure of all subjects was measured by auscultatory method with help of mercury sphygmomanometer (DIAMOND). First kortk of sound indicated systolic blood pressure (SBP) and fifth kortk of sound indicate diastolic blood pressure (DBP). Isometric handgrip test was done in both study and control group. After recording basal blood pressure, subjects were asked to perform isometric handgrip exercise. Subjects were told to hold the handgrip spring dynamometer in dominant hand to have full grip. Handles of dynamometer were compressed by subject with maximum effort for few seconds. Then subject were told to perform 30% of maximum handgrip for 3 min. During the test blood pressure was recorded from non exercising arm and again recorded after 5 min after exercise.

4. Observation and Results

Mean and standard deviation of sympathetic and parasympathetic tests were carried out for study as well as control group. Statistical analysis was done by calculation of “p” value and “t” test.

The results indicated that there was statistically significant change in resting heart and highly statistically significant change to deep breathing in mid pregnancy reflecting higher parasympathetic activity in study group (pregnant female) as compared to control group (non pregnant female) while sympathetic activity assessed by isometric hand grip test didn’t show any statistically significant change among pregnant as compared to non pregnant.

Table 1 Mean and Standard deviation values for parasympathetic test for study and control group.

Table 2 showed Mean and Standard deviation values for sympathetic test for study and control group.

Table 3 showed comparison of Mean values of study and control group for parasympathetic test. Parasympathetic parameters for study and control group showed that study group had higher value of 81±15.67 for resting heart rate as compared to value of 75.4±5.35 for control group which showed statistically significant change ($p<0.05$). Study group had lower value of 46.15±26.32 for deep breathing as compared to value of 63±21.0 for control group which showed statistically highly significant change($p<0.01$). Study group had lower value of 1±0.5 for standing 30:15 ratio as compared to value of 1.03±0.32, which showed no statistically significant change ($p>0.05$).

Table 4 showed the sympathetic parameter for study and control groups that study group had lower value of 3.63±7.45 for sustained hand grip exercise as compared to value of 5.63±6.65 for control group which showed no statistically significant change ($p>0.05$).

5. Discussion

To study the effects of pregnancy on autonomic functions (sympathetic and parasympathetic) the analysis was done separately in two groups (pregnant and non pregnant). The results indicated that there was statistically significant change to resting heart and highly statistically significant change to deep breathing in mid pregnancy reflecting higher parasympathetic activity in study group (pregnant female) as compared to control group (non pregnant female) while sympathetic activity assessed by isometric hand grip test didn’t show any statistically significant change among pregnant as compared to non pregnant. We observed a significant association between cardiovagal and sympathetic baroreflex gains in the pregnant women, suggesting a common underlying mechanism, such as the baroreceptors themselves, in the etiology of this reduction in sympathetic baroreflex gain.

Our data showed increased parasympathetic activity in study group(pregnant females) as compared to control group(non pregnant female) whereas test for sympathetic activity didn’t show any difference between both groups, indicating a reduced role of the sympathetic nervous system in the long- term regulation of blood pressure during normotensive pregnancy. In a study here is shown that peripheral resistance continued to decrease up to 25^{th} week. There was evidence that increased nitric oxide activity that plays major role for pregnancy associated decrease in systemic resistance and this decrease in systemic resistance continued up to 25^{th} weeks of pregnancy.[9] The statistically significant increase in resting heart rate of pregnant group in our study may be explained by the Bainbridge reflex occurring due to increase in end diastolic volume caused by haemodilution.

A significant response in heart rate was found in the study done in the second trimester but the difference became insignificant only when the resting heart rate was used as a covariate.[2] Use of non invasive methods for assessment of autonomic functions has been an area of special interest since they have the advantage of having minimal risk for the mother and fetus.[10] The beginning of pregnancy is associated with sympathetic reactivity, whereas the latter half of pregnancy is characterized by increased hemodynamic stability during orthostatic test.[11]

Table 1: Distribution of Mean and Standard deviation amongst study and control group for parasympathetic tests

Parasympathetic tests		N	Mean	Std. Deviation
RHR(BPM)	Study group	30	81.63	15.677
	Control	30	75.40	5.354
DB(E-I Diff)	Study group	30	46.93	26.322
	Control	30	63.00	21.006
Standing (30:15)	Study group	30	1.00	.525
	Control	30	1.03	.320

Table 2: Distribution of Mean and Standard deviation amongst study and control group for sympathetic tests

Sympathetic test		N	Mean	Std. Deviation
SHG(Change in Diastolic BP)	Study group	30	3.63	7.453
	control	30	5.03	6.054

Table 3: Comparison of Mean values of parasympathetic test between study and control group

Para Sympathetic test	Study group Mean±SD	Control Mean±SD	t-value	p-value
RHR (BPM)	81±15.67	75.4±5.35	2.061	0.043*
DB (E-I Diff)	46.15±26.32	63±21.0	2.613	0.01**
Standing (30:15)	1±0.5	1.03±0.32	.297	0.77

* considered as statistically significant; **considered as statistically highly significant

Table 4: Comparison of Mean values of Sympathetic test between study and control group

Sympathetic test	Study group Mean±SD	Control Mean±SD	t-value	p-value
SHG(Change in Diastolic BP)	3.63±7.45	5.03±6.05	-.799	0.43

* considered as statistically significant; **considered as statistically highly significant
P-value <0.05 considered as statistically significant

Deep breathing is sensitive non invasive manoeuvre to quantify cardiac parasympathetic reactivity.[12]

Longitudinal studies begun before pregnancy have shown that the maximal heart rate response to deep breathing diminishes progressively throughout pregnancy.[2,13] Several factors may be involved in these changes: the decrease in functional residual capacity of the lungs in pregnancy may reduce the difference in the breathing volume during spontaneous and deep breathing in pregnant subjects.[14] Furthermore, during deep breathing, the oscillation of venous return to the heart and thorax may be enhanced in pregnant subjects due to changes in thoraco abdominal pressures. These factors would change the afferent neural inflow differently in pregnant and non-pregnant subjects, and diminish the difference in heart rate variability in pregnant and non- pregnant subjects during deep breathing as compared with the difference in heart rate variability during spontaneous breathing.[15]

With the onset of isometric contraction, there is a prompt increase in the heart rate which causes a 30- 35% increase in cardiac output and blood pressure. A somatic pressor reflex and central nervous system regulation contribute to the hemodynamic changes.[16] The initial heart rate increase during isometric contraction is due to vagal withdrawal. The subsequent slower increase in heart rate is partly mediated by cardiac sympathetic stimulation.[17] The responses to the isometric handgrip test seem to be conflicting in pregnancy. Longitudinal studies starting before pregnancy have shown that the heart rate response to the isometric handgrip test is unaltered.[18] In contrast to this, maximal isometric exercise near to fatigue with leg extension has been reported to raise the total peripheral resistance without a change in cardiac output during the second half of pregnancy.[19] The heart rate and pressor response to maximal isometric exercise of short duration is unaffected by pregnancy. Since the initial blood pressure increase is due to a rise in cardiac output, the result suggests that the vagal withdrawal induced by the somatic pressor reflex is unchanged in pregnancy.[15]

The results implicate that sympathoadrenal responsiveness to somatic provocation is essentially unchanged in pregnancy. The reduced blood pressure response reported could be due to an antagonist effect of the products of the uteroplacental unit, such as progesterone or a diminished contractile response of the blood vessels to adrenaline. The reproducibility of the blood pressure response in the isometric handgrip test is poor.[19] In our study multiple variables for control of haemodynamics in mid pregnancy were assessed reflecting that there was an increased parasympathetic activity as compared to sympathetic activity in mid pregnancy possibly explained by role of Bainbridge reflex and baroreceptors gain in mid pregnancy.

6. Summary

Cardiovascular regulation has to maintain stable BP conditions in spite of higher blood volume, less viscosity and a huge arteriovenous shunt coming from the uteroplacental circulation, while respiratory regulation has to assure chemical homeostasis allowing for increased metabolic needs of the fetus, placenta and several maternal organs. In normal physiologic conditions the cardiovascular system is closely linked to the respiratory system. In our study it was found that there were significant change to resting heart rate and deep breathing among the study group (pregnant females) as compared to control group(non pregnant females) reflecting higher parasympathetic activity in mid pregnancy while test for sympathetic system has not shown significant difference amongst both group. Our study showed role of parasympathetic activity in controlling haemodynamics in mid pregnancy and it may help to return the arterial pressure to non pregnant level by causing haemodilution, although when the increase in activity is excessive, hypertension may ensue. So adaptive control of haemodynamics in mid pregnancy is important to study whose dysfunction may lead to pregnancy related complications- pregnancy induced hypertension, pre eclampsia and eclampsia, therefore help in preventing them at early stage.

7. Conclusion

To conclude our study showed role of parasympathetic activity in controlling haemodynamics in mid pregnancy and it may help to return the arterial pressure to non pregnant level by causing haemodilution, although when the increase in activity is excessive, hypertension may ensue. So adaptive control of haemodynamics in mid pregnancy is important to study whose dysfunction may lead to pregnancy related complications- pregnancy induced hypertension, pre eclampsia and eclampsia, therefore help in preventing them at early stage. However further studies in this matter are required to correlate autonomic nervous system function with fluctuation in gestational hormones.

8. Source of Funding

None.

9. Conflict of Interest

The authors declare no conflict of interest.

References

1. Kuo CD, Chen GY, Yang MJ, Lo HM, Tsai YS. Biphasic changes in autonomic nervous activity during pregnancy. *Br J Anaesth*. 2000;84:323–9.
2. Ekholm EKM, Piha SJ, Antila KJ, Erkkola RJ. Cardiovascular autonomic reflexes in mid pregnancy. *Br J Obstet Gynecol*. 1993;100:177–82.
3. Schobel H. Autonomic function in normal pregnancy, the role of studying heart rate variability. *Clin Sci*. 2000;98:241–2.
4. Hytten FE, Leitch I. The Physiology of human pregnancy. 2nd ed. Oxford: Blackwell Scientific Publications; 1971. p. 69–131.
5. Thompson CA, Tatro DL, Convertino VA. Baroreflex responses to acute changes in blood volume in humans. *Am J Physiol*. 1990;259:792–8.
6. Phippard AF, Howarth JS, Glynn EM. Circulatory adaptation to pregnancy: serial studies on haemodynamics, blood volume, rennin and aldosterone in the baboon (Papio hamadryas). *J Hypertens*. 1986;4:773–9.
7. Sayers BM. Analysis of heart rate variability. *Ergonomics*. 1972;16:17–32.
8. Akselrod S, Gordon D, Madwed JB, Snidman NC, Shannon DC, Cohen RJ. Hemodynamic regulation: investigation by spec- tral analysis. *Am J Physiol*. 1985;249:867–75.
9. Morris NH, Eaton BM, Dekker G. Nitric oxide, the endothelium, pregnancy and pre-eclampsia. *Br J Obstet Gynecol*. 1996;103(1):4–15. doi:10.1111/j.1471-0528.1996.tb09508.x.
10. Cnossen JS, Post JAM, Mol BWJ, Khan KS, Meads CA, Riet G. Prediction of pre-eclampsia: a protocol for systematic reviews of test accuracy. *BMC Pregnancy Childbirth*. 2006;29(6). doi:10.1186/1471-2393-6-29.
11. Schobel HP, Fischer T, Heuszer K, Geiger H, Schmieder RE. Pre- eclampsia- astateofsympatheticoveractivity. *N Engl J Med*. 1996;335:1480–5.
12. Airaksinen KE, Salmela PI, Ikäheimo MJ, Kirkinen P, Linnaluoto MK, Takkunen JT, et al. Effect of pregnancy on autonomic nervous function and heart rate in diabetic and nondiabetic women. *Diabetes Care*. 1987;10:748–51.
13. Contreras G, Ez MG, Beroiza T. Ventilatory drive and respiratory muscle function in pregnancy. *Am Rev Respir Dis*. 1991;144:837–878.
14. Saul JP, Berger RD, Chen MH, Cohen RJ. Transfer function analysis of autonomic regulation 11. Respiratory sinus ar hyth- mia. *Am J Physiol*. 1989;256:153–61.
15. Shepherd JT, Blomqvist CG, Lind AR, Mitchell JH, Saltin B;.
16. Martin CE, Shaver JA, Leon DF, Thompson ME, Reddy PS, Leonard J. Autonomic mechanisms in hemodynamic responses to isometric exercise. *J Clin Invest*. 1974;54:104–15.
17. Matthews KA, Rodin J. Pregnancy alters blood pressure re- sponses to physiological and physical challenge. *Psychophysiology*. 1992;29(2):232–40. doi:10.1111/j.1469-8986.1992.tb01691.x.
18. Hook JV, Gill P, Easterling TR, Schmucker B, Carlson K, Benedetti TJ. The hemodynamic effects of isometric exercise during late normal pregnancy. *Ant J Obstet Gynecol*. 1993;169:870–3. doi:10.1016/0002-9378(93)90018-e.
19. Piha SJ, Puukka P, Seppänen A. Short- and long-term reproducibility of cardiovascular tests of autonomic function in normal subjects. *Clin Auton Res*. 1991;1(2):115–8. doi:10.1007/BF01826206.

Author biography

Jeewandeep Kaur, Associate Professor https://orcid.org/0000-0002-8435-314X

Arvinder Pal Singh Batra, Professor and Head

Cite this article: Kaur J, Batra APS. Study of sympathetic and parasympathetic control of haemodynamics in mid pregnancy by cardiac autonomic neuropathy analyzer. *Indian J Clin Anat Physiol* 2021;8(3):241-245.