National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Maternal heart rate variability during different trimesters of pregnancy

Tanwir Alam[1], Arbind Kumar Choudhary[2], Sendil Kumaran D[3]

[1]Department of Physiology, Integral Institute of Medical Science and Research, Lucknow, Uttar Pradesh, India, [2]Department of Physiology, Government Medical College, Shivpuri, Madhya Pradesh, India, [3]Department of Physiology, Sri Siddhartha Medical College, Tumkur, Karnataka, India

Correspondence to: Arbind Kumar Choudhary, E-mail: arbindchoudhary111@gmail.com

Received: July 10, 2018; **Accepted:** July 27, 2018

ABSTRACT

Background: Under normal circumstances, change in heart rate variability (HRV) in pregnancy projecting alterations within the regulation of the autonomic nervous system (ANS). Many previous works have shown an impact of gestation on the role of ANS in control of heart rate in the western country; however, it is poorly understood in Indian population, but then again a definitive this study is beneficial in relating to the influence on maternal autonomic cardiovascular control in some aspects of physiology in normal pregnancy. **Aims and Objective:** The aim of our study was to analyze the cardiac autonomic control throughout different stage of pregnancy with HRV. **Materials and Methods:** This study (n = 200) comprised normal non-pregnant and pregnant participants in the age of 20–30 years old, were divided randomly into Group 0 (n = 50) - control group comprised non-pregnant, healthy women. Study group (n = 150) classified into three subgroups; Group 1 (n = 50) - participants in their first trimester, Group 2 (n = 50) - participants in their second trimester, and Group 3 (n = 50) - participants in their third trimester. The electrocardiographic R-wave-R-wave interval HRV was measured on a beat-to-beat basis with the help of an electrocardiogram machine (BPL Cardiart 1087/MK-V) for 5 min. **Result:** Mean RR interval was decreased significantly in the 3rd trimester of pregnant study group when compared to non-pregnant control groups. Root of the mean of the sum of the squares of differences, NN50, and pNN50 were increased significantly in the first trimester of the pregnant study group when compared with non-pregnant control groups. Low frequency (LF) and LF (nu) significantly decreased, high frequency (HF) and HF (nu) significantly increased in the 1st trimester and significantly altered in 2nd trimester as well as 3rd trimester as vice versa. LF/HF ratio was significantly decreased in the 1st trimester and significantly increased in the 2nd trimester as well as 3rd trimester of pregnant study group when compared to non-pregnant control groups. **Conclusion:** The cardiac autonomic nervous activity in pregnancy showed a higher parasympathetic dominance in the 1st trimeste r and decreased gradually in 2nd trimester as well as 3rd trimester, and there was a lower sympathetic activity in the 1st trimester and increased gradually in the 2nd trimester as well as 3rd trimester. These changes throughout normal pregnancy may have an advantage in the initial identification of abnormal physiological function.

KEY WORDS: Heart Rate Variability; Pregnancy; Sympathovagal balance; Low/High Frequency

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2018.8.0723327072018	

INTRODUCTION

Pregnancy is a physiological condition that induces several physiological changes, particularly, in hemodynamic and cardiovascular domains.[1] To maintain the homeostasis, these changes can bring about alterations in cardiac autonomic function. Normal maternity ends up in hemodynamic changes,

alteration (decreasing) in mean arterial blood pressure (BP) and peripheral vascular resistance, with elevating circulating volume and heart rate. However, these physiological changes do not seem to be well understood particularly during pregnancy. Initial hemodynamic changes in pregnancy are concerning changes in autonomic cardiovascular control. Alteration in the autonomic cardiovascular mechanism has play a very important etiological role in pregnancy condition elicited high BP.[2] Failure in early adaptation could lead to pregnancy-related cardiovascular complications, such as pre-eclampsia.[3] The beat-to-beat fluctuation of heart rate is called heart rate variability (HRV). The balanced of a sympathetic and parasympathetic component of the cardiac autonomic nervous system (ANS) is reveal by HRV. This HRV could be a specific non-invasive tool to quantitatively estimate the cardiac autonomic balance that determines the quantity of heart rate fluctuations around the mean heart rate.[4] Usually, time and frequency domain measures derived HRV analysis give the dynamic balance between sympathetic and parasympathetic modulation.[5] If there is a deviation from normal sympathovagal balance, elucidation of the dysfunction may lead to early detection of pregnancy-induced hypertension (PIH). Early identification of sympathovagal shift in 1st trimester will provide early diagnosis of PIH and also create standardization for HRV in pregnancy. In western countries, previous studies have been observed HRV in different trimesters of pregnancy. The low/high-frequency power ratio was reduced significantly within the 1st trimester in the supine position, and progressively increases with 2nd trimester as well as 3rd trimester.[6] HRV laterally with baroreflex sensitivity showed significant changes between pregnant and non-pregnant women, whereas variation in the BP was unaffected between those groups.[7] At rest, healthy pregnant women exhibit lower parasympathetic nervous system modulation and while during exercise have increased sympathetic nervous system modulation.[8] However, in India, the underlying regulatory mechanisms are still poorly understood in the field of study of HRV during normal pregnancy. This study has the strength to evaluate the cardiac autonomic modulation by HRV analysis throughout the trimesters (1st, 2nd, and 3rd) of human pregnancy.

MATERIALS AND METHODS

Ethical Clearance

To perform the study, ethical clearance was obtained from the research committee of "Sri Siddhartha Medical College" (SSMC), Tumkur, Karnataka, India. The study was performed in view of the declaration of Helsinki. Elaborated written consent of all the participants was taken, and therefore the purpose of the study was explained to the participants, and reassurance was given to the participants that test is hurt less.

Participants

Inclusion and exclusion criteria

All participants were examined for her general physical health. Subject's clinical history and details were taken consistent with the standard pro forma. Normal pregnant girls of age 20–30 years old and supported the subsequent criteria were recruited for the study. Informed written consent was taken from all participants within the study.

The participants were excluded with history of smoking and alcoholism, anemia, obstetric and medical complications of pregnancy, cardiorespiratory diseases, and BP more than 140/90 mm of Hg, those with normal BP but already on antihypertensive medications, fasting blood sugar (FBS) more than 110 mg/dl, and those with normal FBS but already on antidiabetic treatment, on medications affecting ANS such as Atenolol, Atropine, and Salbutamol.

Sampling Size

This study (n = 200) comprised normal non-pregnant and pregnant participants in the age of 20–30 years old, who were volunteers (students and attendants) in Tumkur. All selected participants were divided randomly into following groups: Group 0 (n = 50) - control group comprised non-pregnant, healthy women. Study group (n = 150) comprised pregnant healthy women in their first, second, and third trimester attending the OPD of OBG department of SSMC, Tumkur, for antenatal care. They were classified randomly into three subgroups:

Group 1 (n = 50) - participants in their first trimester (up to 12-week), Group 2 (n = 50) - participants in their second trimester (13–28 weeks), and Group 3 (n = 50) - participants in their third trimester (29-week onward).

Protocol

Measurement of HRV

This study involved non-invasive procedure of recording electrocardiogram (ECG) and the recording was conducted between 9.00 am and 12.00 pm in the presence of a female attendant. ECG machine (BPL Cardiart 1087/MK-V) was used to attain the analog ECG signal. Analog to digital device (national Instruments [NI]-DAQ seven. 5 USBD 6008) was used because the hardware, that regenerate the analog to digital signal and processed it to the computer with the assistance of the NI–DAQ software system. All the subjects were abstained from tea or caffeine for 4 hours before the examination. The patient was made to rest for 10-minutes and then 5 minutes ECG (lead II only) was recorded with subject respiring normally. The major peak to peak intervals were detected with HRV software (version 1.1), and further

mathematical and analytical calculations were performed to determine the mean RR, root of the mean of the sum of the squares of differences (RMSSD), standard deviation of normal to normal (SDNN), NN50, pNN50, low frequency (LF) power, high frequency (HF) power, LF nu, HF nu, and LF/HF.[9] RMSSD was the square root of the mean of the sum of the squares of differences between adjacent RR intervals. The SD of the RR-intervals (SDNN, ms), and the root mean square of the difference between successive normal intervals (RMSSD, ms). Normalized values of HF (HFnu) and LF (LF nu) bands had been intended using the formulas of nuLFLF/HFLF and nu HFHF/HFLF.

Statistical Analysis

The statistical software (SPSS 15.0,) was used for the analysis of the data. To find the significance of study parameters between groups of patients, Analysis of variance (ANOVA) was used. *Post-hoc* Tukey test has been used to find the pairwise significance level at $P \leq 0.05$.

RESULTS

In the present study, there was not any significant distinction in age between the non-pregnant control groups and pregnant study group [Figure 1].

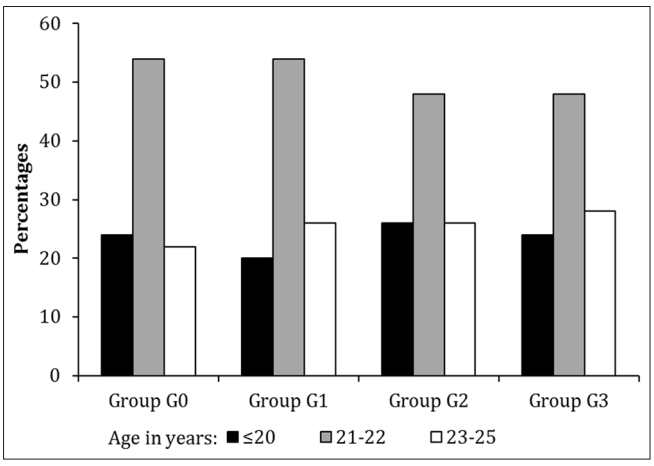

Figure 1: Age (years) distribution among controls and study group

Comparison of Heart Rate in Trimesters of Pregnancy

The summarized data with mean ± SD are presented in Table 1: Mean heart rate was found to be gradually increasing from 1st trimester to 3rd trimester in pregnant study group when compare to non-pregnant control groups.

Comparison of Time Domain Parameters in Trimesters of Pregnancy

The summarized data with mean ± SD are presented in Table 1: We observed that mean RR interval was decreased significantly in the 3rd trimester of pregnant study group when compare to non-pregnant control groups. Although mean RR interval reduced gradually in the 1st and 2nd trimester of the pregnant study group, it was an insignificant decrease when compared to non-pregnant control groups. In time domain: The SDNN was comparable among non-pregnant control groups and pregnant study group. Although RMSSD, NN50, and pNN50 were increased significantly in the first trimester of the pregnant study group, when compared with non-pregnant control groups. Then, there RMSSD, NN50, and pNN50 decreased gradually in the 2nd trimester and 3rd trimester; however, this decrease was comparable when compared with control groups.

Comparison of Frequency Domain Parameters in Trimesters of Pregnancy

The summarized data with mean ± SD are presented in Table 2: LF and LF NU power significantly decreased in the 1st trimester and significantly increased in 2nd trimester as well as 3rd trimester of pregnant study group when compare to non-pregnant control groups. HF and HF nu power increased significantly in the 1st trimester, and significantly decreased in the 2nd trimester as well as 3rd trimester of pregnant study group when compared to non-pregnant control groups. LF/HF ratio was significantly decreased in the 1st trimester, and significantly increased in the 2nd trimester as well as 3rd trimester of pregnant study group when compared to non-pregnant control groups.

DISCUSSION

In our study, we observed that RR interval was gradually increasing from 1st trimester to 2nd trimester along with

Table 1: Comparison of Time domain parameters

Parameters	Group G0	Group G1	Group G2	Group G3	Overall *P* value	Significance					
						G0-G1	G0-G2	G0-G3	G1-G2	G1-G3	G2-G3
Mean RR (ms)	758.38±92.55	800.28±137.67	756.97±105.89	665.78±108.35	<0.001**	0.247	1.000	<0.001**	0.220	<0.001**	<0.001**
SDNN (ms)	17.88±10.40	23.04±15.95	18.86±9.69	19.08±11.72	0.159	0.151	0.978	0.960	0.318	0.368	1.000
RMSSD (ms)	25.23±13.11	54.22±39.48	32.46±51.46	16.29±11.59	<0.001**	<0.001**	0.704	0.545	0.008**	<0.001**	0.079+
NN50	20.72±17.61	32.66±32.21	13.68±15.64	4.04±9.22	<0.001**	<0.001**	0.894	0.383	<0.001**	<0.001**	0.101
PNN50	14.54±5.83	17.94±14.72	5.96±6.05	1.89±3.25	<0.001**	<0.001**	0.844	0.419	<0.001**	<0.001**	0.089

+Suggestive significance (P=0.05<P < 0.10), *Moderately significant (P=0.01<P ≤ 0.05), **Strongly significant (P≤0.01). RMSSD: Root of the mean of the sum of the squares of differences, SDNN: Standard deviation of normal to normal, PNN

Table 2: Comparison of frequency domain parameter

Parameters	Group G0	Group G1	Group G2	Group G3	Overall *P* value	Significance				
						G0-G1	G0-G2	G0-G3	G1-G2	G1-G3	G2-G3
LF power	781.85±249.83	407.38±127.96	1039.23±593.92	1905.64±603.65	<0.001**	<0.001**	<0.001**	<0.001**	0.041*	0.859	0.240
HF power	369.94±169.91	1335.29±1617.30	267.20±108.42	152.88±22.01	<0.001**	<0.001**	1.000	0.559	<0.001**	<0.001**	0.570
LF nu	67.08±6.08	39.97±9.60	75.22±6.06	88.51±4.69	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**
HF nu	32.92±6.08	60.03±9.60	26.78±6.06	14.49±4.69	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**
LF/HF	2.15±0.63	0.71±0.29	3.89±0.75	6.67±2.58	<0.001**	<0.001**	0.040*	<0.001**	<0.001**	<0.001**	<0.001**

+Suggestive significance (P=0.05<P < 0.10), *Moderately significant (P=0.01<P ≤ 0.05), **Strongly significant (P≤0.01). LF: Low frequency, HF: High frequency

3rd trimester. In frequency and time domain parameter, for example, RMSSD, NN50, pNN0, HF power, and HF nu were significantly increased in the 1st trimester and decreased gradually in the 2nd trimester as well as 3rd trimester. However, LF power, LF nu, and LF/HF were diminished in the 1st trimester and amplified gradually in the 2nd trimester together with 3rd trimester. The mean RR values are correlated to HF power in the frequency domain, which represents vagal response.[9] During this study, the mean RR values were increased in the 1st trimester and then gradually decreases to 3rd trimester, as per heart rate increased progressively throughout the pregnancy and reached a peak during the 3rd trimester,[10] thus suggesting that the increase in the parasympathetic activity in the first trimester. The alterations in the autonomic tone that are predominantly vagally-mediated are revealed by the SDNN values in addition to RMSSD, NN50, and pNN50 values are also considered as a measure of parasympathetic activity.[9] NN50 count is the time domain variable, which is also correlated to HF power in frequency domain. The HF component is the major supporter of the vagal response. Alteration of SDNN, RMSSD, and pNN50 values showed that an increase in the parasympathetic activity in the 1st trimester as compared to 2nd trimester as well as 3rd trimester. The sympathetic activity and parasympathetic activity are considered as a measure of LF and LF nu power values and HF and HF nu values power values, respectively. During this study, the alteration of LF and HF values thus suggesting the rise within the parasympathetic activity in the 1st trimester, as compared to 2nd trimester along with 3rd trimester. Typicallythe sympathovagal balance is revealed using LF/HF ratio.During this study, the values LF/HF ratio were significantly decreased throughout in 1st trimester as compared to 2nd trimester along with 3rd trimester, thus suggesting the alteration in the sympathovagal balance toward the parasympathetic component throughout 1st trimester in pregnant women. LF/HF values were significantly increased in 2nd trimester along with 3rd trimester, therefore suggesting sympathovagal balance toward the sympathetic component. Our finding is relating to the previous study[11] stating that commonly pregnancy is connected with noticeable changes in cardiovascular hemodynamics, that partly could also be because of modifications in autonomic control mechanisms and biphasic change in parasympathetic and sympathetic system in pregnancy from a preponderantly parasympathetic or vagal output in 1st trimester to a mostly sympathetic output in 2nd trimester along with 3rd trimester.[12]

Previous studies investigating HRV in resting conditions reported a reduced HF component of HRV[8,13] during the 2nd trimester as well as with 3rd trimester in normotensive pregnant women. Beginning pregnancy condition was related with increased parasympathetic reactivity whereas in later pregnancy was related with increased sympathetic reactivity.[6,14,15] In Indian population, there was decreased sympathetic and parasympathetic nervous activity in the second trimester of pregnancy when compared to controls.

[16] The reasons for the shift of sympathovagal balance in pregnancy may be because of increase in blood volume increasing substantially throughout pregnancy that starts as early as the 6th weeks of gestation and increases rapidly till mid-pregnancy, there forth it continues to expand at a slower rate.[6] This increase of blood volume might increase cardiac output during initial pregnancy. The variations in blood volume and hemodynamics might cut back the amount of workload of the heart and subsequently shift the ANS into a condition of lower sympathetic along with greater vagal modulation. As gestational age will increase any extra-aortocaval compression caused by the enlarging gravid uterus further compromises blood vessel come back to the heart (venous return) and flow rate (cardiac output), leading to a shift in autonomic nervous activity toward sympathetic and lower vagal modulation within the 3rd trimester of pregnancy.[6] The other reason for the shift may be decreased in systemic arterial pressure that begins throughout the 1st trimester and reaches the lowest point in mid-pregnancy. The decline in systemic vascular resistance is perhaps caused by gestational hormones, increased circulating prostaglandins level, augmented heat production by the growing fetus, and expansion of a low-resistance circulation within the pregnant uterus.[17] Conversely, a number of the previous studies reported, decreased HRV; however, there was no consensus on the alterations in autonomic nervous activity throughout pregnancy, According to them, there was an arranging of autonomic tone in normal pregnancy, which will be understood as a shift of autonomic balance toward a relative vagal predominance throughout normal pregnancy or Inadequate stratification of gestational stages may be the foremost reason behind this discrepancy.[18] A similar trend of change in different trimesters in absolute powers of spectral HRV was observed, but they failed to mention concerning normalized spectral powers and LF/HF power ratios in their study.[19]

Strength and Limitation of the Study

Strength: It is helpful to incorporate the cardiovascular HRV as screening tests in pregnancy because it measures sympathovagal balance and produces data on baroreflex sensitivity in an exceedingly specific and non-invasive manner. The tests are suggested for learning the regulation of the cardiovascular system in mother throughout the duration of pregnancy.

Limitation: However, to assign a statistical significance to the current observation a much larger range of samples need to be studied. The baroreflex sensitivity has been not performed due to lack of research funding.

CONCLUSION

The cardiac autonomic nervous activity in pregnancy showed a better parasympathetic dominance within the 1st trimester and attenuated bit by bit in the 2nd trimester along with 3rd trimester, and there was a lower sympathetic activity within the 1st trimester and raised gradually in the 2nd trimester as well as 3rd trimester. Although the accurate mechanisms for HRV change during trimester of pregnancy remain unclear until now. Additional studies are required to stipulate these changes. Characterizing and understanding such changes throughout pregnancy may gain an advantage in early identification of abnormal physiological function and establish patients in danger for adverse responses.

ACKNOWLEDGMENTS

We gratefully acknowledge the SSMC, Tumkur, Karnataka, India, for provided that financial support.

REFERENCES

1. Voss A, Baumert M, Baier V, Stepan H, Walther T, Faber R. Autonomic cardiovascular control in pregnancies with abnormal uterine perfusion. Am J Hypertens 2006;19:306-12.
2. Panja S, Bhowmick K, Annamalai N, Gudi S. A study of cardiovascular autonomic function in normal pregnancy. Al Ameen J Med Sci 2013;6:170-5.
3. Rang S, Wolf H, Montfrans GA, Karemaker JM. Non–invasive assessment of autonomic cardiovascular control in normal human pregnancy and pregnancy-associated hypertensive disorders: A review. J Hypertens 2002;20:2111-9.
4. Karim N, Hasan JA, Ali SS. Heart rate variability-a review. J Basic Appl Sci 2011;7:71-7.
5. Pagani M. Heart rate variability and pregnancy. J Hypertens 2002;20:2125-6.
6. Kuo C, Chen G, Yang M, Lo H, Tsai Y. Biphasic changes in autonomic nervous activity during pregnancy. Br J Anaesth 2000;84:323-9.
7. Voss A, Malberg H, Schumann A, Wessel N, Walther T, Stepan H, *et al.* Baroreflex sensitivity, heart rate, and blood pressure variability in normal pregnancy. Am J Hypertens 2000;13:1218-25.
8. Avery N, Wolfe L, Amara C, Davies G, McGrath M. Effects of human pregnancy on cardiac autonomic function above and below the ventilatory threshold. J Appl Physiol 2001;90:321-8.
9. Camm A, Malik M, Bigger J, Breithardt G, Cerutti S, Cohen R, *et al*. Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European society of cardiology and the North American society of pacing and electrophysiology. Circulation 1996;93:1043-65.
10. Kole S, Shenoy J, Shivakumar J, Suvarna P, Prasannakumar J. Variations in electrical activity of the heart as the pregnancy progresses. Natl J Physiol Pharm Pharmacol 2014;4:187.
11. Blake MJ, Martin A, Manktelow BN, Armstrong C, Halligan AW, Panerai RB, *et al*. Changes in baroreceptor sensitivity for heart rate during normotensive pregnancy and the puerperium. Clin Sci 2000;98:259-68.
12. Clark SL, Cotton DB, Lee W, Bishop C, Hill T, Southwick J, *et al*. Central hemodynamic assessment of normal term pregnancy. Am J Obstetr Gynecol 1989;161:1439-42.
13. Baumert M, Walther T, Hopfe J, Stepan H, Faber R, Voss A. Joint symbolic dynamic analysis of beat-to-beat interactions

of heart rate and systolic blood pressure in normal pregnancy. Med Biol Eng Computing 2002;40:241-5.
14. Ekholm EM, Erkkola RU. Autonomic cardiovascular control in pregnancy. Eur J Obstetr Gynecol Reprod Biol 1996;64:29-36.
15. Kuo CD, Chen GY, Yang MJ, Tsai YS. The effect of position on autonomic nervous activity in late pregnancy. Anaesthesia 1997;52:1161-5.
16. Athani KB. A comparative study of cardiovascular autonomic function tests between second trimester pregnant women and non-pregnant women. Natl J Physiol Pharm Pharmacol 2018;8:785-9.
17. Gerber J, Payne N, Murphy R, Nies A. Prostacyclin produced by the pregnant uterus in the dog may act as a circulating vasodepressor substance. J Clin Invest 1981;67:632-6.
18. Speranza G, Verlato G, Albiero A. Autonomic changes during pregnancy: Assessment by spectral heart rate variability analysis. J Electrocardiol 1998;31:101-9.
19. Eneroth-Grimfors E, Westgren M, Ericson M, Ihrman-Sandahl C, Lindblad LE. Autonomic cardiovascular control in normal and pre-eclamptic pregnancy. Acta Obstetr Gynecol Scand 1994;73:680-4.

How to cite this article: Alam T, Choudhary AK, Kumaran DS. Maternal heart rate variability during different trimesters of pregnancy. Natl J Physiol Pharm Pharmacol 2018;8(11):1475-1480.

Source of Support: Nil, **Conflict of Interest:** None declared.