Original Research

# Heart Rate variability in females with chronic somatic pain

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**Abstract**

**Background:** Various disease processes are associated with an altered symapatho-vagal activity which reflects the autonomic balance. Altered ANS activity is reported in patients suffering from chronic pain by various workers with conflicting reasons. HRV is a simple, non-invasive tool to assess the autonomic activity in all age groups and the results are widely accepted as the diagnostic and prognostic method for autonomic activity.

**Objectives:** The present study was planned to see the autonomic dysregulation, if any, in Indian patients suffering from chronic somatic pain with an aim to find the cause of the autonomic imbalance.

**Materials and Methods:** The short-term heart rate variability parameters computed by an amplifier (Biopac) after taking a 5-minute electrocardiogram recording in supine position from 33 female patients between the age group of 20 to 65 years and suffering from chronic somatic pain. They were compared with twenty-two age and sex matched controls (without any pain) after applying the exclusion criteria and following the conventional and recommended protocol. The RR interval time series was taken from the ECG of each subject and analyzed for HRV by using the above-mentioned software.

**Results:** The heart rate was increased in all patients with varying significance. The time domain and frequency domain parameters are also decreased in patients as compared to their respective controls. The HRV parameters were significantly reduced in elderly females than the younger ones.

**Conclusion:** The change in heart rate signifies an increased sympathetic activity in patients suffering from chronic pain. However, the HRV analysis showed a variation in ANS activity in all with a significant change in elderly females. It seems as there may be some protection in young females by female sex hormones. The exact mechanisms are still elucidated, though psychological and behavioral attitude might be responsible for such varied changes.

**KEY WORDS:** Chronic somatic pain, Heart rate variability, Autonomic nervous system

## Introduction

Autonomic nervous system is an important controller of many bodily activities. Its derangement is known to have a major role in many pathological conditions. The two limbs of ANS—are in a balanced state primarily by neural centers of the brain under physiological settings. The defects in autonomic imbalance are due to either an increased sympathetic or reduced parasympathetic activity and have been found to be associated with development of cardiac arrhythmia and arrest.[1-3] Pain is the commonest symptom of human sufferings. Chronic pain, somatic or visceral is more cumbersome and is associated with alterations in physical, psychological and homeostatic mechanisms.[4-6] Chronic somatic pain is more common in females and reduces their mental threshold, working ability and often associated with depression. It has been observed that relief from pain often consumes a large amount of health resources around the globe. It may be originating either from somatic viz. chronic regional pain syndrome, fibromyalgia, rheumatoid arthritis or visceral organs

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e.g. irritable bowel syndrome. It has been observed that chronic somatic pain is associated with altered ANS activity similar to closely allied conditions like irritable bowel syndrome, chronic fatigue syndrome and migraine. The chronic pain is associated with mental stress which may not be due to the cause of pain but due to anxiety and awareness of the pain.[7] Various studies had shown that chronic pain leads to changes in ANS activity in all age group[8-14] but some researchers argue about its involvement.[15,16] They attribute it to poor physical health and functional disability which might influence the ANS.

Heart Rate Variability (HRV) is a simple noninvasive method to assess the sympathovagal balance at the level of the sinoatrial node.[17] The resting heart rate is under autonomic control at all times and the beat to beat fluctuations in it or RR interval of ECG is recorded to calculate the HRV. It is measured by power spectral analysis and provides a quantitative marker of autonomic neural control of heart rate and has been shown to reflect cardiovascular health. Low HRV is associated with increased risk of cardiovascular diseases.[18,19] The spectral analysis of the RR intervals reflects the HRV in statistically based time domain parameter or respiratory based frequency domain parameters

Most of the work to assess the autonomic status in chronic pain sufferers is done outside India. Therefore, this study was planned to see the autonomic dysregulation in female patients suffering from chronic pain with an objective to assess the autonomic status in them and variation with controls.

## Materials And Methods

The study was carried out in the autonomic function lab of Department of Physiology for a period of 12 months after taking approval from Institutional ethical committee. The study consisted of thirty-three females between 20-65 years age suffering from chronic pain attending Orthopedic OPD and pain clinic of SVBP Hospital, to assess the autonomic reactivity by HRV analysis twenty-two age and sex matched individuals not suffering from any painful disorder were also taken as control group.

All subjects of both groups were thoroughly explained about the nature and purpose of the study. Written informed consent was obtained from all subjects prior to obtaining the data from experiments. The subjects were interviewed regarding their medical history, including family history, medications, current health condition, menstrual cycle, and lifestyle followed by a detailed medical examination. Subjects on steroid therapy and with a history of diabetes mellitus, hypertension, cardiovascular disease or any other systemic disease which might cause an alteration in autonomic activity were excluded. After measuring the baseline anthropometry, HRV analysis was done on each subject as per international guidelines by taking 5-minute recording of lead II ECG following a supine rest of 15 minutes using commercial leads and an amplifier (Biopac) and stored in the computer. RR interval time series was computed from ECG and subjected to short-term HRV analysis using a software (Biopac) as per the recommendations of the Task Force.[9] Mean of all the RR intervals (mean RR), standard deviation of the normal to normal RR intervals (SDNN), root mean square of successive differences between adjacent RR intervals (RMSSD) and the percentage of number of RR intervals with differences >50 ms (pNN50) were calculated in the time-domain. Frequency-domain measures were obtained by fast Fourier transformation and they included the absolute powers obtained by integrating the powers in the very low frequency (VLF) band of 0.0033–0.04 Hz, low frequency (LF) band of 0.04–0.15 Hz, high frequency (HF) band of 0.15–0.4 Hz, and the total power in all the 3 bands together.

The results, expressed as mean (SD), were analyzed using the SPSS version 11.0 statistical software package. The data was analyzed by using the unpaired *t*-test. A value of $p < 0.05$ was considered as significant.

## Results

The present study included 33 female patients suffering from chronic somatic pain for assessment of autonomic reactivity and compared with age and sex, matched 22 control subjects. The physical characteristics of the two groups are shown in Table 1.

Tables 2 and 3 shows the HRV analysis results in younger (25 to 35 yr) and elderly females (>45 Yr). There is a significant increase in heart rate ($p < 0.04$) in elderly ladies suffering

**Table 1:** Anthropometric data (mean ± SD) of females without (control) and with (cases) chronic somatic pain

| Parameters | Control (*n* = 22) | Cases (*n* = 33) |
|---|---|---|
| Age (yr) | 41.55±9.88 | 44.21±10.34 |
| Height (m) | 1.5±0.07 | 1.49±0.09 |
| Weight (kg) | 53±5.46 | 53.94±5.39 |
| BMI(kg/m$^2$) | 35.11±3.53 | 36.35±3.71 |

**Table 2:** Heart rate variability (mean± SD) in young females (25-35 yr)

| | Control (*n* = 9) | Cases (*n* = 10) | *p*-value |
|---|---|---|---|
| **HRV (Time domain)** | | | |
| Mean RR (s) | 0.71±0.21 | 0.71±0.11 | 0.7636 |
| Mean HR (1/min) | 78.04±6.65 | 86.85±13.21 | 0.0879 |
| RMSSD (ms) | 22.20±9.80 | 12.69±4.88 | 0.0145* |
| NN 50 (count) | 6.44±4.95 | 1.70±1.77 | 0.0113* |
| pNN 50 (%) | 4.35±3.41 | 1.25±1.12 | 0.0144* |
| **HRV (Frequency domain)** | | | |
| VLF (power %) | 76.78±122.78 | 17.30±54.71 | 0.1826 |
| LF (power %) | 325.67±426.38 | 121.50±114.70 | 0.1623 |
| HF (power %) | 47.89±47.80 | 43.63±40.67 | 0.8362 |
| LF/HF Ratio (power %) | 7.86±6.33 | 4.05±4.13 | 0.1348 |

*$p$-value < 0.01 significant

**Table 3:** Heart rate variability (mean±sd) in elderly females (> 45 yr)

| | Control ($n$ = 13) | Cases ($n$ = 23) | $p$-value |
|---|---|---|---|
| **HRV (Time domain)** | | | |
| Mean RR (s) | 0.79±0.09 | 0.74±0.17 | 0.333 |
| Mean HR (1/min) | 76.75±9.47 | 86.35±15.31 | 0.049* |
| RMSSD (ms) | 26.02±8.78 | 18.66±21.89 | 0.256 |
| NN 50 (count) | 10.62±4.77 | 4.52±1.46 | 0.0001** |
| pNN 50 (%) | 7.08±3.17 | 2.58±3.98 | 0.001* |
| **HRV (Frequency domain)** | | | |
| VLF (power %) | 76.31±65.15 | 114.61±58.68 | 0.079 |
| LF (power %) | 396.85±296.64 | 118.09±76.44 | 0.0001** |
| HF (power %) | 102.15±96.47 | 49.04±38.29 | 0.0246* |
| LF/HF Ratio (power %) | 5.54±4.51 | 5.10±1.40 | 0.665 |

*$p$-value < 0.05; ** $p$-value < 0.0001

from chronic pain than younger ones. The fall in time domain parameters – RMSSD, NN50 and pNN50 was also observed in females with pain in both groups. However, there was a more significant decrease in elderly females ($p < 0.001$ to 0.0001) than younger ones ($p < 0.01$). Though the frequency domain parameters decreased in females suffering from chronic pain, there was a significant fall in LF ($p < 0.001$), HF ($p < 0.02$) in elderly females.

## Discussion

During normal sinus rhythm, the heart rate varies from beat to beat. This HRV results due to the interplay between various physiological processes involved in controlling heart rate. Since short-term heart rate regulation is governed by activity of Autonomic Nervous System (ANS), it can be used as a tool to assess the ANS activity.[20,21]

The present study showed an increase in heart rate in female patients with chronic pain as compared with their control counterparts. However, this increase was insignificant in younger ladies than elderly ones. Since pain itself causes arousal and higher sympathetic activity, it may be an additional cause of the increase in heart rate. The patients in our study were suffering from pain for more than three months and they were also indulged in their normal daily activity with minor restrictions, the ANS activity is modulated in them with sympathetic dominance which is an independent marker of mortality in a wide spectrum of conditions.[22]

The time domain parameters were significantly reduced in younger as well as in elderly females of pain group than controls. However, there was greater reduction of these parameters in elderly ladies with chronic pain. Changes in pNN50 and RMSSD are both reported in the literature to reflect HF changes in heart rate and therefore parasympathetic modulation. RMSSD is reported to be a better parameter than pNN50 to convey changes in resting HRV, as it is not affected by changes in mean heart rate and is highly reproducible.[23,24]

The LF and HF component of frequency domain parameters are reduced in all females suffering from pain as compared with their control subjects. However, there was a significant reduction in LF, a measure of sympathetic activity and HF, associated with the parasympathetic activity, in elderly females suffering from pain with greater fall in HF (50% of the control group). The LH/HF ratio has been used as a measure of vagal tone which is also showing an insignificant fall in both groups of ladies.

Kalezic et al[10] and Thayer JF et al[25] observed an increase in HR and low HRV in patients with chronic low back pain. They inferred that chronic pain does cause some autonomic imbalance expressing an increased sympathetic and decreased parasympathetic activity as reflected by an increased heart rate, blood pressure, and electrodermal activity. Kingsley[11] found that autonomic modulation in females suffering from fibromyalgia is unaffected by the resistance exercise and concluded that pain per se may be the factor for autonomic modulation in them. Hallman D[8] in patients with chronic neck-shoulder pain found low parasympathetic activity during rest and sleep while sympathetic activity is altered only to lab stressors. The findings of the present study are in contrast to other workers as we observed a decline in both limbs of ANS with greater fall in parasympathetic activity shifting the balance in favor of sympathetic response.

Hence it may be attributed that changes in frequency domain parameters seem to be due to the disease process itself and with chronic pain, there are some adaptative mechanisms responsible for coping with pain. These mechanisms are not fully explored yet though abnormal anatomical and functional involvement in pain processing areas, as well as reduction of gray matter, has been observed with persistent pain in MRI studies.[14,20 ]

The present work also shows that such adaptative mechanism becomes less with advancing age and there is a possibility of the role of female hormones in such adaptations. There is evidence in the literature that in chronic somatic pain, there is maladaptation between nociceptive area and ANS.[26,27] Cardio–sympathetic excitation due to a stressor is known to be associated with a reduction in total variability, along with an alteration in LF/HF ratio.[23] Variations in observations of HRV indices has been the cause of much debate in the literature if these indices of sympathovagal balance do reflect the autonomic activity in all conditions or not.[28,29]

## References

1. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. Diabetes Care 2003; 26(5):1553–79.
2. Kleiger RE, Miller JP, Bigger JT Jr, Moss AJ. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol. 1987;59:256–62.
3. Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Kleiger RE, Rottman JN. Frequency domain measures of heart period

variability and mortality after myocardial infarction. Circulation; 1992: 164-71.
4. Pruimboom L, Van Dam AC. Chronic Pain: a non-use disease. Med Hypothesis 2007; 68(3):506-11.
5. Ferini-Strambi L. Sleep disorders in multiple sclerosis. Handb Clin Neurol 2011;99:1139–46.
6. Kreitler S, Niv D. Cognitive impairment in chronic pain. *Pain: Clinical Updates* (International Association for the Study of Pain) 2007; XV (4): 1–4.
7. Tharion E, Parthasarathy S, Neelkantan N, Short-term heart rate variability measures in students during examinations. Natl Med J India. 2009;22(2):63-6.
8. Hallman DM, Mathiassen SE, Lyskov E. Long-term monitoring of physical behavior reveals different cardiac responses to physical activity among subjects with and without chronic neck pain. Biomed Res Int. 2015; 2015: 907482. doi: 10.1155/2015/907482
9. Evans S, Seidman LC, Tsao JC, Lung KC, Zeltzer LK, Naliboff BD. Heart rate variability as a biomarker for autonomic nervous system response differences between children with chronic pain and healthy control children. J Pain Res. 2013; 6: 449–57.
10. Kalezic, Nebojsa. Autonomic reactivity in muscle pain; clinical and experimental assessment. submitted as a thesis with Umea University, 2006.
11. Gavi MBRO, Vassalo DV, Amaral FT, Macedo DCF, Gava PL, Dantas EM, et al. Strengthening exercises improve symptoms and quality of life but do not change autonomic modulation in fibromyalgia: a randomized clinical trial. PLoS One. 2014; 9(3): e90767. doi: 10.1371/journal.pone.0090767
12. Mittal CM, Wig N, Mishra S, Deepak KK. Heart rate variability in human immune deficiency virus-positive individuals. Int J Cardiol 2004; 94 :1–6.
13. Dobrek L, Nowakowski M, Mazur M, Herman RM, Thor PJ. Disturbances of the parasympathetic branch of the autonomic nervous system in patients with gastroesophageal reflux disease (GERD) estimated by short-term heart rate variability recordings. J Physiol Pharmacol 2004; 55 (Suppl 2):77–90.
14. Chen JL, Chiu HW, Tseng YJ, Chu WC. Hyperthyroidism is characterized by both increased sympathetic and decreased vagal modulation of heart rate: Evidence from spectral analysis of heart rate variability. Clin Endocrinol 2006; 64:611–16.
15. Gockel M, Lindholm H, Niemist L, Hurri H. Perceived disability but not pain is connected with autonomic nervous function among patients with chronic low back pain. J Rehabil Med. 2008; 40(5):355-8.
16. Griffin DW, Harmon DC and Kennedy NM. Do patients with chronic low back pain have an altered level and/or pattern of physical activity compared to healthy individuals? A systematic review of the literature. Physiotherapy 2012; 98(1): 13-23.
17. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996; 93:1043– 65.
18. Liao D, Cai J, Rosamond D, Barnes R, Hutchinson R. Cardiac autonomic function and incident coronary heart disease–The ARIC study. Circulation 1995; 92(Suppl 1):418.
19. Moolgard H, Sorensen K, Bjerregaard P. Attenuated 24-h heart rate variability in apparently healthy subjects, subsequently suffering sudden cardiac death. Clin Autonom Res 1991; 1:233–7.
20. Pinto TL, Sampaio LMM, Costa IP, Kawaguchi LYA, de Carvalho FAS, de Carvalho RA. Analysis of heart rate variability in individuals subjected to different positive end expiratory pressure levels using expiratory positive airway pressure. Arch Med Sci. 2013; 9(4): 651–5.
21. Bilchick KC, Berger RD. Heart Rate Variability. J Cardiovascular Electro-physiology.2006; 17(6):691–4.
22. Palatini P. Elevated heart rate as a predictor of increased cardiovascular morbidity. J Hypertens 1999; 17: S3–S10.
23. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 1996; 17: 354–81.
24. Hilz MJ, Dutsch M. Quantitative studies of autonomic function. Muscle Nerve 2006; 33: 6–20.
25. Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. Int J Cardiol; 2010 141(2):122-131.
26. Schlereth T and Birklein F. The sympathetic nervous system and pain. Neuromolecular Medicine 2008; 10(3): 141-147.
27. Bruehl S, Chung OY. Interactions between the cardiovascular and pain regulatory systems: an updated review of mechanisms and possible alterations in chronic pain. Neurosci Biobehav Rev. 2004;28(4):395-414.
28. Malliani A, Julien C, Billman GE, Cerutti S, Piepoli MF, Bernardi L. Point: Counterpoint comments: Cardiovascular variability is/is not an index of autonomic control of circulation. J Appl Physiol 2006; 101:684–88.
29. Parati G, Mancia G, Di Rienzo M, Castiglioni P, Taylor JA, Studinger P. Point: Counterpoint: Cardiovascular variability is/is not an index of autonomic control of circulation. J Appl Physiol 2006; 101:676–82.

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