

Original Article

Study on Cardiac Autonomic Nerve Function Status by Heart Rate Variability in Patients with Gastro-esophageal Reflux Disease

Mamataj S¹, Motaleb M², Azim SF³, Hossain MI⁴

Abstract

Background: Gastro-esophageal reflux disease (GERD) has been associated with autonomic nervous dysfunction along with reduced Heart Rate Variability. **Objective:** To observe cardiac autonomic nerve function status by heart rate variability analysis in patients with Gastro-esophageal reflux disease (GERD). **Methods:** This cross sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1st January, 2017 to 31st December, 2017. For this, total 30 male and female diagnosed GERD patients from the Out Patient Department (OPD) of Gastroenterology, BSMMU aged 20-35 years were included in the study group. Total power Low Frequency power (LF) and High Frequency power (HF) of HRV parameters were recorded. Thirty ages, BMI matched healthy subject also included as control. For statistical analysis, unpaired t-test was done as applicable. **Results:** Total power Low Frequency power (LF) and High frequency power (HF) were significantly lower in GERD patients in comparison to that of healthy subjects. The total power is the indicator of variability of the total cardiac autonomic nerve activities. LF power has represents sympathetic modulation on the heart and HF power is a marker of parasympathetic nerve activity on heart. **Conclusion:** This study concluded that autonomic dysfunction occurs in GERD patients which are characterized by decreased sympathetic & parasympathetic activity.

Key words: Heart rate variability, Gastro-esophageal reflux disease (GERD).

Introduction: Gastro-esophageal reflux disease (GERD) is a widely prevalent gastrointestinal disorder around the world including Asia.¹ The prevalence rate was 6.3% in urban and 4.8% in rural community of Bangladesh and the male and female percentage of this disorder was 4.41% and 6.73%.² Gastro-esophageal reflux disease (GERD) is one of the most common diseases of upper part of the gastrointestinal tract.³ The reflux of gastric material into esophagus causes symptoms, tissue damage or both, the resulting condition is called Gastro-esophageal reflux disease (GERD). Reflux causes esophagitis, esophageal stricture and columnar epithelial metaplasia.⁴ Gastro-oesophageal reflux disease develops when the esophageal mucosa is exposed to gastro-duodenal contents for prolonged periods. It occurs due to reduced tone of lower esophageal sphincter,

increasing intra-abdominal pressure and frequent episodes of inappropriate sphincter relaxation.⁵

GERD is multi-factorial in origin. Motor abnormalities, such as transient lower esophageal sphincter relaxations (TLESR), impaired esophageal acid clearance and delayed gastric emptying contribute to pathophysiology of GERD.⁶ The typical symptoms of GERD are heart burn and regurgitation.⁷ Neural dysfunction is the cause of abnormal motility in reflux disease. The vagus has a major influence on esophageal peristalsis, lower esophageal function and gastric motility.⁸ Heart rate variability (HRV) test are non-invasive methods of evaluating the integrity and functional state of the autonomic nervous system. HRV is beat to beat variation in heart rate (i.e. in R-R interval) under resting conditions.

1. Dr. Sukrana Mamataj, Assistant Professor, Physiology, Ahsania Mission Medical College

2. Dr. Mahin Motaleb, Assistant Professor, Anatomy, Ahsania Mission Medical College

3. Dr. Sabrina Fahmida Azim, Associate Professor, Physiology, Kumudini Women's Medical College

4. Dr. Mohammed Iqbal Hossain, Associate professor, Department of Pharmacology & Therapeutics, Abdul Malek Ukil Medical College, Noakhali

Correspondence : Dr. Sukrana Mamataj, Assistant Professor, Physiology, Ahsania Mission Medical College

E-mail: dr.sukranamamataj@gmail.com, Mobile: 01717758667

The parameters were recorded by a eight (8) active channels, Power Lab. Usually, time domain and frequency domain methods are used for HRV measurement.⁹

In frequency domain method, Power Spectral Density (PSD) analyzes the information of total power (variance) which distributes as a function of frequency. Low frequency (LF, frequency range 0.04-0.15 Hz) and high frequency (HF, frequency range 0.16-0.4 Hz) are the components of total power (frequency range 0.0-0.4 Hz) in a spectrum of 2-5 minutes recording. For duration of recording of ECG taskforce has recommended a 5 minutes recording (short term) used in spectral analysis. The LF component is an indicator of sympathetic modulation, but few researchers also propose it is contributed by a parameter both sympathetic and vagal influences.⁹ Some researcher were studied LF, HF, TP values were significantly lower in GERD patients in comparison to that of healthy control.¹⁰ Some researchers were observed decreased sympathetic function in GERD patients as compared to that of control.¹¹ On the contrary, Some researchers were observed HF and found no significant changes in GERD patients as compared to that of healthy control.¹² Therefore, this study has been designed to investigate the autonomic nerve function status in GERD patients.

Methods

This cross sectional study was carried out in the year 2017 at the Department of Physiology, Sir Salimullah Medical college & Mitford Hospital (SSMCH) to observe cardiac autonomic nerve function status by Heart rate variability in patients with Gastro-esophageal reflux disease.

For this, total Thirty (30) diagnosed GERD patients age ranged from 20-35 years were included in this study. They were selected on the basis of inclusion and exclusion criteria from the Out Patient Department (OPD) of Gastro-enterology, Sir Salimullah Medical College and Mitford Hospital and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

Inclusion criteria for study group are diagnosed patients with Gastro-esophageal reflux disease, age ranged from 20 to 35 years of both male and female

and exclusion criteria are history of any heart disease, hypertension, upper gastrointestinal haemorrhage, previous gastric surgery, diabetes mellitus, chronic renal failure, psychic disorders, pregnancy, habit of smoking, alcoholism & drugs which alters autonomic nerve function.

In addition to this, thirty (30) apparently healthy age and BMI matched individuals were selected from personal contact as control. All subjects were belonged to middle socio-economic status.

After proper counseling the aim, objectives, risk and procedure of the study were explained in details to the subjects. They were encouraged for voluntary participation and they were allowed to withdraw themselves from the study even after participation whenever they like. Only positive respondents were recruited as research participants. The ethical permission was taken from the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College. Written Informed consent was taken from the participants. Detailed history about personal, family, medical and occupation of the participants were taken and thorough physical examination of all participants were done and recorded in a prefixed questionnaire. Detail of the procedure of HRV test was explained to the participants and preparation was done for the procedure.

All the subjects were requested to be present at the Department of Physiology (BSMMU) between 8am to 10 am on fasting state, a day before the HRV recording. Then, blood was collected for biochemical test and ECG was done.

After enrollment the subject were advised to follow some instruction in the previous night of HRV test day. They were advised to finish their meal by 9:00 pm on previous day, to remain free from any type of stress, not to take sedative hypnotic medication. They were requested to take light breakfast without tea and coffee and to attend the autonomic nerve function test laboratory in the Department of Physiology, BSMMU between 9:00 am to 11:00 am on the test day. A thorough physical examinations including pulse, BP, height, weight were measured and BMI was calculated. The subject was advised to take rest for 15-20 minutes in controlled laboratory environment. During this period the subject was not

allowed to talk, eat or drink, to perform physical or mental activity, even sleep. ECG was recorded on lead II for 5 minutes by data acquisition device Power Lab 8/35 (AD instrument, Australia). HRV recording was analyzed by Lab chart software.

Data were expressed as mean \pm SD (Standard Deviation). The Statistical analysis was done by using Statistical Package of Social Science (SPSS) for Windows version 22. Unpaired “t” test was used to compare the data as applicable. p value ≤ 0.05 was considered as statistically significant.

Result

In this study, all GERD patients were similar to healthy control by age, BMI. There was no statistical significant difference of SBP & DBP was observed.

In this study, The mean value of LF power, HF power & TP were significantly ($p < 0.05$) lower in GERD patients than that of control and the difference was statistically highly significant ($p < 0.001$).

Table I: Age and BMI of the subjects in both groups (N=60)

Parameters	Control (n=30)	Study (GERD) group (n=30)
Age (years)	26.70 \pm 3.77 (20 - 35)	27.43 \pm 4.76 (20 - 35)
BMI (Kg/m ²)	21.44 \pm 1.26 (19.30 - 23.90)	21.26 \pm 1.01 (18.70 - 22.90)

Data were expressed as mean \pm SD. Figure in parenthesis indicate ranges. The Statistical analysis was done by unpaired “t” test. n = total number of subjects, BMI= Body mass index.

Table II: Blood pressure of the subjects in both groups (N=60)

Parameters	Control (n=30)	Study group (GERD) (n=30)	p value
Systolic BP (mm of Hg)	115.00 \pm 5.09 (110 - 120)	116.33 \pm 4.90 (110 - 120)	0.305 ^{ns}
Diastolic BP (mm of Hg)	76.00 \pm 4.98 (70 - 80)	76.50 \pm 4.76 (70 - 80)	0.693 ^{ns}

Results were expressed as mean \pm SD. For statistical analysis, Unpaired t test was performed to compare both groups. Figure in parenthesis indicate ranges. ns = not significant.

Table III: Frequency domain measures of HRV of the subjects in both groups (N=60)

Parameters	Group A (n=30)	Group B (n=30)	p value
TP (μs^2)	1773.12 \pm 707.22 (912.7 - 3871.0)	1318.02 \pm 757.35 (167.10 - 2272.0)	<0.001***
LF Power (μs^2)	655.78 \pm 355.76 (197.1 - 1523.0)	308.08 \pm 184.63 (25.86 - 799.0)	<0.001***
HF Power (μs^2)	524.71 \pm 398.96 (114.4 - 1771.0)	96.76 \pm 59.88 (27.03 - 253.2)	<0.001***

Results were expressed as mean \pm SD. For statistical analysis, Unpaired t test was performed to compare both groups. Figure in parenthesis indicate ranges. TP= Total power, LF = Low frequency power, HF = High frequency power.

In this study, the mean value of TP, LF power & HF power were significantly ($p < 0.001$) lower in GERD patients than that of control group, n = total number of subjects.

*** = significant at $p < 0.001$, ns = not significant.

The total power is the indicator of variability of the total cardiac autonomic nerve activities. LF power has represents sympathetic modulation on the heart and HF power is a marker of parasympathetic nerve activity on heart.

Discussion

The study was undertaken to observe autonomic nerve function status in gastroesophageal reflux disease (GERD) patients by analysis of heart rate variability (HRV). In order to assess cardiac autonomic nerve function status, 30 diagnosed GERD patients, age ranged from 20 to 35 years were selected. HRV of all subjects were assessed. HRV data were also obtained from age and BMI matched 30 apparently healthy subjects and their data were normally distributed. Among HRV indices, LF power and represent sympathetic activity while HF power represent parasympathetic activity and Total power represent overall heart rate variability.⁹

In addition to HRV, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also recorded which are the marker for end organ response of cardiovascular autonomic activity.

In the present study all the subjects of both groups were age and BMI matched and they were normotensive, non-diabetic and having normal kidney function.

In the study, Systolic blood pressure (SBP) and diastolic blood pressure (DBP) during rest were measured both in control group and GERD patients to observe their basal status. Both SBP and DBP of control group and GERD patients were within normal range. No significant difference was observed between them. Similar type of findings were reported by some other researchers in GERD patients.¹⁰ (Subhashini. S. 2011; Teena Sogan, Manisha Sankhla and Keerti Mathur, 2016).

On the contrary, some researchers found significantly higher systolic blood pressure in GERD patients than that of healthy control. These researchers also found higher diastolic blood pressure in GERD patients as compared to that of healthy control but the result was not statistically significant.¹¹ (Milovanovic et al. 2015). This discrepancy might be due to geographical or ethnic factors, large population diversity and laboratory assessment method (long term, 24 hours analysis of HRV).

HRV parameters- (Frequency domain):Total power: In this study, total power was significantly lower in GERD patients than that of control group which is in agreement with others.¹⁴

LF power:In this study, the value of LF power was significantly lower in GERD patients in comparison to that of control group. Some researchers observed similar results.¹⁵ On the contrary, some researchers observed LF power in reflux positive patients was significantly higher as compared to that of reflux negative patients.¹³

HF power: In this study, the values of mean HF power and HF norm were significantly lower in GERD patients as compared to that of control group. Similar findings were also reported by several researchers.¹⁴ On the contrary, some researchers found significantly higher value of HF power in GERD patients than that of healthy control.¹⁵ This discrepancy might be due to anatomical and/or functional alteration of the esophagus.

Conclusion

In this study, the mean value of TP, LF power & HF power were significantly lower in GERD patients than that of control group. The total power is the indicator of variability of the total cardiac autonomic nerve activities. LF power has represents sympathetic modulation on the heart and HF power is a marker of parasympathetic nerve activity on heart. From this study it can be concluded that, autonomic dysfunction occurs in GERD patients which is characterized by decreased sympathetic & parasympathetic activity

Acknowledgement

The authors acknowledge the contribution of Professor Dr. Mahmuda Begum, Head of the Department, Department of Physiology, Sir Salimullah Medical College (SSMC), for her cordial guidance and details instructions for this research. The authors express their gratitude to the other faculty members, medical officers and the support staffs of the Department of Physiology & Gastroenterology of SSMC & Mitford Hospital & BSMMU for providing various help during this study without which this study would not be possible.

Source of funding: Self-funding.

Financial support and sponsorship: No financial fund was taken from the any organization.

Conflict of Interest: There are no conflict of interest.

References:

1. Hunt, R. et al. 2017, 'World Gastroenterology Organization Global Guidelines: GERD Global Perspective On Gastroesophageal Reflux Disease', *Journal of Clinical Gastroenterology*, vol. 51, no. 6, pp. 467-78.
2. Shaha, M., Perveen, I., Alamgir, M.J., Masud, M.H. and Rahman, M.H. 2012, 'Prevalence and risk factors for gastro-esophageal reflux disease in the North-Eastern part of Bangladesh', *Bangladesh Med. Res. Coun. Bull*, no. 38, pp. 108-13.

3. Dobrek, L., Nowakowski, M., Mazur, M., Herman, R. M. and Thor, P. J. 2004, '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', *Journal of physiology and pharmacology*, vol. 55, no. 2, pp. 77-90.
4. Barrett, K.E., Barman, S.M., Boitano, S. and Brooks, H.L. 2012, 'Autonomic nervous system' Ganong's Review of Medical Physiology, 24th ed.; India (NewDelhi): Tata McGraw-Hill., New York, Chapter 13,; pp. 255-267.
5. Penman, I.D. and Less, C.W. 2014, 'Alimentary tract and pancreatic disease' In: Walker, B.R., Colledge, N.R., Ralston, S.H. and Penman, I.D. (eds.), *Davidson's Principles & Practice of Medicine*, 22nd ed., Elsevier limited, London, pp. 865.
6. Giorgi, F.D., Palmiero, M., Esposito, I., Moska, F. and Cuomo, R. 2006 'Pathophysiology of gastro-oesophageal reflux disease', *Italian ACTA*, pp. 241-46.
7. Kumar, P. and Clark. M. 2009, 'Gastro intestinal disease' In: *Clinical Medicine*, 7th ed., Elsevier limited, London, pp. 251.
8. Cunningham, K. M., Horowitz, M., Riddell, P.S., Maddern, G.J., Myers, J.C., Holloway, R.H., Wishart, J.W. and Jamieson, G.G. 1991, 'Relations among autonomic nerve dysfunction, oesophageal motility, and gastric emptying in gastro-oesophageal reflux disease', *Gastroenterology Unit, Royal Adelaide, South Australia*, no. 32, pp. 1436-40.
9. 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, no. 17, pp. 354-58.
10. Dobrek, L., Nowakowski, M., Mazur, M., Herman, R. M. and Thor, P. J. 2004, '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', *Journal of physiology and pharmacology*, vol. 55, no. 2, pp. 77-90.
11. Campo, S.M.A., Capria, A., Antonucci, F., Martino, G., Ciamei, A., Rossini, P.M., Bologna, E. and Cannata, D. 2001, 'Decreased sympathetic inhibition in gastroesophageal reflux disease', *Clinical Autonomic research*, vol. 11, pp. 45-51.
12. Nowak, J. K., Lazniak, A., Lisowska, Z., Bobkowski, W., Walkowiak, J. 2017, 'Gastroesophageal reflux is not associated with short-term variability of parasympathetic activity in children' *Elsevier Advance in Medical Sci.*, vol. 62, pp. 103-9.
13. Subhashini, S. 2011, 'Heart rate variability and 24 hour pH analysis in patients symptomatic for acid peptic disease' *The Tamil Nadu DR. M.G.R. Medical University*.
14. Milovanovic, B., Filipovic, B., Mutavdzin, S., Zdravkovic, M., Gligorijevic, T., Paunovic, J. and Arsic, Marina. 2015, 'Cardiac autonomic dysfunction in patients with gastroesophageal reflux disease', *World Journal of Gastroenterology*, vol. 21, pp. 6982-89.
15. Marra, L., Ciccaglione, A.F., Sepe, A., Tavani, R., Cocciolillo, S., Berardino, M.D., Giacomo, C.D., Vecchione, V., Grossi, L and Marzio, L. 2017, 'The influence of acid reflux on the Heart Rate Variability (HRV) in patients with and without gastroesophageal reflux disease (GERD)', vol. 152, pp. 131.