



RESEARCH ARTICLE

Assessment of Heart Rate Variability and Autonomic Function in Patients with Major Depressive Disorder: A Comparative Study with Healthy Controls

Virinchi Sharma¹, Vishnu Gade², Kurukuntlasubramanyam³

ABSTRACT

Background: Major depressive disorder (MDD) is a common psychiatric disorder associated not only with psychological symptoms but also with disturbances in cardiovascular and autonomic regulation. Heart rate variability (HRV) is a non-invasive physiological marker that provides information regarding cardiac autonomic modulation. Reduced HRV, particularly reduced vagally mediated components, has been reported in patients with depression and may partly explain the increased cardiovascular risk associated with MDD. The present study was undertaken to assess HRV and autonomic function in patients with MDD and compare the findings with healthy controls.

Materials and Methods: A comparative cross-sectional study was conducted among 120 adults, comprising 60 patients diagnosed with MDD and 60 age- and sex-matched healthy controls. Participants underwent standardized cardiovascular autonomic assessment and short-term resting ECG recording for HRV analysis. Time-domain parameters including SDNN and RMSSD and frequency-domain parameters including low-frequency (LF), high-frequency (HF) power and LF/HF ratio were assessed. Heart rate and blood pressure were also recorded. Independent-samples t-test and repeated-measures analysis were used for comparison. A p value <0.05 was considered statistically significant.

Results: Patients with MDD had significantly higher resting heart rate and significantly lower SDNN, RMSSD and HF-HRV compared with healthy controls. The LF/HF ratio was significantly higher in the MDD group. Conventional autonomic tests also demonstrated significantly reduced parasympathetic function in patients with MDD. The differences in HRV and autonomic function between the groups were statistically significant, with p values <0.001 for most parameters.

Conclusion: Patients with MDD demonstrated significant alteration of cardiac autonomic function characterized predominantly by reduced parasympathetic modulation and relative sympathovagal imbalance. HRV assessment may provide a useful non-invasive physiological measure for identifying autonomic dysregulation in patients with MDD.

Keywords: Major depressive disorder; heart rate variability; autonomic function; parasympathetic activity; sympathetic activity; SDNN; RMSSD; LF/HF ratio.

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INTRODUCTION

Major depressive disorder (MDD) is a prevalent psychiatric disorder characterized by persistent depressed mood, anhedonia, cognitive disturbances and changes in sleep, appetite and psychomotor activity. In addition to psychological manifestations, MDD is associated with substantial physical morbidity, particularly cardiovascular morbidity. The relationship between depression and cardiovascular disease has stimulated increasing interest in the physiological mechanisms linking depressive illness with altered cardiovascular regulation. [1]

The autonomic nervous system plays an important role in maintaining cardiovascular homeostasis by continuously regulating heart rate, vascular tone and cardiac function. Heart rate variability (HRV), defined as the variation in successive cardiac cycle lengths, provides a non-invasive method for assessing cardiac autonomic modulation.

Standardized time-domain and frequency-domain measures of HRV have been established for physiological and clinical assessment of autonomic function. [2]

A growing body of evidence indicates that patients with MDD exhibit reduced HRV compared with healthy individuals. Reduced HRV may indicate diminished parasympathetic or vagal modulation of the heart and impaired autonomic flexibility. A meta-analysis of studies involving patients with major depression without cardiovascular disease found significantly lower HRV in depressed patients compared with healthy controls, with reductions particularly evident in high-frequency and other vagally related measures. [3]

Large population-based studies have further demonstrated an association between MDD and altered

¹Associate Professor, Department of Psychiatry, CMR Institute of Medical sciences, Medchal, Telangana, India

²Professor, Department of Psychiatry, Arundathi Institute of Medical sciences, Dundigal, Hyderabad, Telangana, India

³Assistant professor, Department of Physiology, Surabhi Institute of medical sciences, Siddipet, Telangana, India

Corresponding Author: Virinchisharma, Associate Professor, Department of Psychiatry, CMR Institute of Medical sciences, Medchal, Telangana, India E-mail: dr.virinchisharma@gmail.com

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cardiac autonomic regulation. In the Netherlands Study of Depression and Anxiety, patients with current MDD demonstrated differences in several measures of cardiac autonomic control compared with healthy controls. [4] More recent systematic evidence has similarly shown that most studies comparing drug-free MDD patients with healthy controls report reduced HRV, particularly parameters predominantly reflecting parasympathetic activity. [5]

Despite considerable evidence of autonomic abnormalities in depression, variations in study population, medication exposure, severity of depression, cardiovascular comorbidity and HRV methodology have contributed to inconsistent findings. Assessment of autonomic function using standardized HRV measurements in carefully selected patients without major cardiovascular or systemic disease may therefore provide clinically useful information. The present study was designed to assess resting HRV and cardiovascular autonomic function in patients with MDD and compare the findings with healthy controls. We hypothesized that patients with MDD would demonstrate reduced HRV, decreased parasympathetic activity and altered sympathovagal balance compared with healthy controls.

MATERIALS AND METHODS

Study Design

A hospital-based comparative cross-sectional study was

conducted to assess cardiac autonomic function and HRV in patients diagnosed with MDD and to compare the findings with healthy controls.

Study Setting

The study was conducted in the Department of Physiology in collaboration with the Department of Psychiatry at a tertiary-care teaching hospital in Department of Psychiatry, CMR Institute of Medical sciences, Medchal, Telangana

Study Period

The study was conducted over a period of 12 months, from January 2025 to December 2025.

Study Population and Sample Size

- A total of 120 participants were included.
- Group I: 60 patients diagnosed with MDD.
- Group II: 60 age- and sex-matched apparently healthy controls.

The sample size was determined considering an expected moderate difference in HRV parameters between the two groups, with 80% statistical power and a 5% level of significance.

Inclusion Criteria

- *MDD Group*
- Adults aged 18–55 years.
- Patients fulfilling accepted diagnostic criteria for MDD.
- Patients attending the Psychiatry outpatient/inpatient service.
- Participants willing to provide written informed consent.
- Participants able to cooperate with autonomic function testing.
- Healthy Control Group
- Adults aged 18–55 years.
- No current psychiatric illness.
- No known cardiovascular, endocrine, neurological or major systemic disease.
- No history of substance dependence.
- Not taking medications known to significantly influence autonomic function.
- Willingness to participate and provide informed consent.

Exclusion Criteria

- Participants were excluded if they had:
- Known cardiovascular disease.

- Hypertension or diabetes mellitus.
- Significant neurological or endocrine disorders.
- Substance dependence or recent substance abuse.
- Severe systemic illness.
- Pregnancy.
- Current use of beta-blockers, antiarrhythmic drugs or other drugs substantially affecting autonomic function.
- Significant arrhythmia or ECG abnormality.
- Inability to cooperate with the autonomic function tests.

Clinical Assessment

Diagnosis of MDD was established by a psychiatrist using standard diagnostic criteria. Demographic details, clinical history, duration of illness and relevant medication history were recorded.

Depressive symptom severity was assessed using a validated depression-rating scale. The score was recorded for evaluating the severity of depressive symptoms and exploring its relationship with autonomic parameters.

Preparation of Participants

Participants were instructed to avoid strenuous exercise, caffeine, nicotine and alcohol for at least 12 hours before testing. Testing was performed in the morning in a quiet, temperature-controlled laboratory.

Participants rested in the supine position for approximately 15 minutes before autonomic measurements were obtained.

Heart Rate Variability Assessment

A standard three-lead ECG was recorded continuously under controlled resting conditions.

A five-minute artifact-free ECG segment was selected for short-term HRV analysis according to established HRV measurement recommendations. [2]

Time-Domain Parameters

The following parameters were assessed

- SDNN: standard deviation of normal-to-normal intervals.
- RMSSD: root mean square of successive differences between normal-to-normal intervals.
- RMSSD was considered predominantly reflective of cardiac vagal modulation.
- Frequency-Domain Parameters
- The following spectral parameters were assessed:
- Low-frequency (LF) power.
- High-frequency (HF) power.
- LF/HF ratio.

HF power was considered predominantly related to parasympathetic cardiac modulation, while the LF/HF ratio was interpreted as an indicator of sympathovagal balance rather than a direct measure of sympathetic activity.

Cardiovascular Autonomic Function Tests

The following conventional autonomic function parameters were assessed

- Resting heart rate.
- Resting systolic blood pressure.
- Resting diastolic blood pressure.
- Deep-breathing heart-rate variability.
- Valsalva ratio.
- Heart-rate response to standing.
- All tests were performed according to standardized procedures.

Statistical Analysis

- Data were entered into statistical software and analyzed using appropriate descriptive and inferential statistical tests.
- Continuous variables were expressed as mean $\pm$ standard deviation (SD). Categorical variables were expressed as frequencies and percentages.
- The independent-samples t-test was used to compare continuous variables between MDD patients and controls. The chi-square test was used for categorical variables.
- Pearson correlation analysis was used to assess the relationship between depression severity and selected HRV parameters.
- A p value <0.05 was considered statistically significant, while $p < 0.001$ was considered highly statistically significant.

RESULTS

Table 1: Comparison of demographic characteristics between MDD patients and healthy controls

Parameter	MDD group (n=60)	Healthy controls (n=60)	p value
Age (years)	37.2 $\pm$ 8.6	36.5 $\pm$ 8.1	0.64
Male/Female	28/32	30/30	0.72
BMI (kg/m ²)	24.8 $\pm$ 3.2	24.3 $\pm$ 2.9	0.38
SBP (mmHg)	124.6 $\pm$ 9.8	121.7 $\pm$ 9.2	0.10
DBP (mmHg)	79.1 $\pm$ 7.0	76.8 $\pm$ 6.5	0.07

Table 2: Comparison of resting cardiovascular and HRV parameters

Parameter	MDD group	Healthy controls	p value
Heart rate (beats/min)	84.3 ± 8.9	75.6 ± 7.2	<0.001
SDNN (ms)	31.7 ± 8.4	40.8 ± 9.5	<0.001
RMSSD (ms)	22.9 ± 6.8	32.4 ± 7.9	<0.001
LF power (ms ²)	421 ± 128	449 ± 135	0.24
HF power (ms ²)	272 ± 98	386 ± 121	<0.001
LF/HF ratio	1.86 ± 0.59	1.38 ± 0.47	<0.001

A total of 120 participants were included in the final analysis. The MDD and healthy control groups were comparable in terms of age, sex and BMI.

Interpretation

There was no statistically significant difference between the two groups with respect to age, sex, BMI or resting blood pressure, indicating adequate baseline comparability.

Interpretation

Patients with MDD had significantly higher resting heart rate and LF/HF ratio and significantly lower SDNN, RMSSD and HF power compared with controls. These findings indicate reduced vagally mediated cardiac modulation and altered sympathovagal regulation.

Table 3: Comparison of conventional autonomic function parameters

Autonomic parameter	MDD group	Healthy controls	p value
Valsalva ratio	1.38 ± 0.18	1.55 ± 0.20	<0.001
Deep-breathing E:I ratio	1.19 ± 0.09	1.31 ± 0.11	<0.001
30:15 ratio	1.09 ± 0.07	1.17 ± 0.08	<0.001
Resting HR (beats/min)	84.3 ± 8.9	75.6 ± 7.2	<0.001
Postural SBP fall (mmHg)	7.8 ± 4.6	5.1 ± 3.8	0.001

Table 4: Comparison of frequency-domain HRV parameters

Parameter	Correlation coefficient (r)	p value
SDNN	-0.42	0.001
RMSSD	-0.46	<0.001
HF power	-0.39	0.002
LF/HF ratio	+0.44	<0.001
Resting heart rate	+0.35	0.006

Table 5: Association between depression severity and HRV parameters in MDD patients

Parameter	MDD group	Healthy controls	Mean difference	p value
LF power (ms ²)	421 ± 128	449 ± 135	-28	0.24
HF power (ms ²)	272 ± 98	386 ± 121	-114	<0.001
LF normalized units	58.6 ± 9.1	51.8 ± 8.3	6.8	<0.001
HF normalized units	31.5 ± 7.8	38.7 ± 8.1	-7.2	<0.001
LF/HF ratio	1.86 ± 0.59	1.38 ± 0.47	0.48	<0.001

Interpretation

Patients with MDD demonstrated significantly lower Valsalva ratio, deep-breathing E:I ratio and 30:15 ratio compared with healthy controls, suggesting reduced parasympathetic cardiovascular function.

Interpretation

The MDD group showed significantly lower HF power and HF normalized units and significantly higher LF normalized units and LF/HF ratio. This pattern suggests reduced parasympathetic modulation and relative alteration of sympathovagal balance.

Interpretation

Increasing depression severity was significantly associated with lower SDNN, RMSSD and HF power and higher LF/HF ratio and resting heart rate. This suggests that greater depressive symptom burden may be associated with greater autonomic dysregulation.

DISCUSSION

The present study demonstrated significant alterations in cardiac autonomic function among patients with MDD compared with healthy controls. Patients with MDD had higher resting heart rate and lower SDNN, RMSSD and HF-HRV, together with a higher LF/HF ratio. These findings are consistent with earlier research demonstrating reduced HRV in depression and suggest impaired cardiac autonomic flexibility. [6]

A major finding was the significant reduction in RMSSD and HF power among patients with MDD. These parameters predominantly reflect vagally mediated cardiac modulation, and their reduction suggests decreased parasympathetic influence on the heart. A meta-analysis involving unmedicated adults with major depression found significantly lower HRV compared with healthy controls, supporting the presence of reduced autonomic cardiac regulation in depression. [7]

The present findings are also consistent with studies using conventional autonomic tests. Patients with major depression have previously been shown to exhibit lower Valsalva ratio and other indices of parasympathetic function together with increased sympathovagal balance compared with healthy controls. [8] The reduction in Valsalva ratio, deep-breathing response and 30:15 ratio observed in our study further supports impaired parasympathetic cardiovascular function in MDD.

The significantly higher LF/HF ratio observed in the MDD group suggests altered sympathovagal regulation. However, LF/HF should not be interpreted as a direct measure of sympathetic activity because the components of HRV are influenced by multiple physiological mechanisms. The findings are better interpreted as evidence of altered autonomic balance characterized predominantly by reduced vagal modulation. A large population-based investigation also demonstrated an association between MDD and altered cardiac autonomic control after consideration of relevant clinical and lifestyle factors. [9]

An additional finding was the significant negative correlation between depression severity and SDNN, RMSSD and HF power. Conversely, depression severity showed a positive correlation with resting heart rate and LF/HF ratio. This suggests that autonomic dysregulation may increase with increasing depressive symptom burden. Previous meta-analytic evidence has similarly demonstrated an inverse relationship between depression severity and HRV, suggesting that autonomic abnormalities may be related to the clinical severity of depressive illness. [10]

The physiological mechanisms underlying reduced HRV in MDD are likely multifactorial. Altered hypothalamic-pituitary-adrenal axis activity, chronic stress, inflammation, impaired central autonomic regulation and behavioral factors may contribute to changes in cardiac autonomic control. Reduced parasympathetic activity may also represent one pathway linking depression with increased cardiovascular risk. Overall, the findings support the concept that MDD is associated with measurable physiological alterations extending beyond psychological symptoms.

LIMITATIONS OF THE STUDY

- The cross-sectional design prevents determination of a causal relationship between MDD and autonomic dysfunction.
- The study was conducted at a single centre, which may limit generalizability.
- The sample size was relatively modest.
- HRV was assessed using short-term recordings rather than 24-hour Holter monitoring.
- Anxiety symptoms, sleep quality and physical activity may have influenced autonomic measurements.
- Different clinical subtypes and durations of MDD were not analyzed separately.
- Although medication-related confounding was minimized, treatment history may still influence autonomic parameters.
- The study did not include longitudinal follow-up to determine whether autonomic abnormalities improve after treatment of depression.

CONCLUSION

Patients with major depressive disorder demonstrated significant impairment of cardiac autonomic function compared with healthy controls. The principal abnormalities included increased resting heart rate, reduced SDNN, RMSSD and HF-HRV, and increased LF/HF ratio. Conventional autonomic function tests also demonstrated reduced parasympathetic cardiovascular activity. Furthermore, greater depression severity was associated with greater autonomic dysregulation. HRV assessment may therefore serve as a useful non-invasive physiological tool for evaluating autonomic abnormalities in patients with MDD. Longitudinal studies are required to determine whether successful treatment of depression leads to normalization of autonomic function.

ETHICAL CLEARANCE

The study protocol was reviewed and approved by the Institutional Ethics Committee before commencement.

Written informed consent was obtained from all participants after explaining the objectives, procedures, possible risks and benefits of the study. Confidentiality of participant information was maintained throughout the study.

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