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Exploring patterns of heart rate variability in major depressive disorder: A short-term study in Jaipur, Rajasthan

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Abstract

Background: Individuals suffering from major depressive disorder (MDD) frequently have abnormal heart rate variability (HRV) patterns. They have decreased HRV, which implies that there is less variance between subsequent heartbeats. Increased sympathetic nervous system activity (The "fight or flight" reaction) and decreased parasympathetic nervous system activity (The "rest and digest" response) are related to reduce HRV. This study investigates short-term HRV patterns in individuals with major depressive disorder.

Methods: This observational study was conducted at RUHS College of Medical Sciences and Associated Hospitals, Jaipur, from July 2022 to January 2023, on a major depressive disorder population of either sex in the age group of 20-40 years. Cognitive functions were assessed using a questionnaire, and AD instruments recorded heart rate variability variables (Time & frequency domain) using a digital physiograph (MLT004/ST). Data analyses were conducted using Microsoft Excel 2019. The Pearson correlation coefficient was calculated to determine the correlation, and a significance level of $p < 0.05$ was utilized.

Results: A positive association was detected between the Hamilton D (HAM D) score and high frequency and root mean square of the successive difference between normal heartbeats, which was significant ($p < 0.05$). In contrast, a significant negative correlation was seen between the Hamilton D score, heart rate, and mini-mental status ($p < 0.05$).

Conclusion: This short-term investigation indicated different HRV patterns in MDD, defining a role in the diagnosis of depression. The detected relationships between HRV and depression severity imply that HRV monitoring could benefit the diagnosis and treatment of MDD. Further investigation is required to explore the long-term stability and clinical value of these HRV patterns.

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Highlights

What is current knowledge?

Assessment of HRV can provide valuable insights into an individual's physical and mental health by demonstrating the body's ability to handle stress and change. Higher HRV generally means the body is better prepared and resilient when faced with adversities. Many research studies were conducted solely on depression.

What is new here?

This study has the advantage of using standardized techniques to measure HRV at the first visit and test for significant depression and cognitive skills. Furthermore, since HRV was measured before the start of treatment, a more precise analysis of the relationship between depressed symptoms and HRV indices was possible. This is crucial because HRV can be pretty sensitive to outside stimuli. This study's measurement and interpretation of the results were consistent because the HRV was taken at the same site each time, and the same inspector carried out all tests.

Introduction

Depression is a prevalent but serious mood disorder (Sometimes known as a major depressive disorder or clinical depression). Severe symptoms impact mood, cognition, and day-to-day functioning, including eating, sleeping, and working (1).

In 2015, it was projected that over 300 million individuals worldwide suffered from depression, making up about 4.3% of the world's population. Major depressive disorder (DD) ranked as the third most common cause of disability in 2015, with an increasing global burden of depression. (2) The estimated prevalence of depressive episode/DD worldwide is between 3.2% and 4.7% (3,4). The higher risk associated with depression may be explained by the fact that depression is also connected to increased HR and lower HRV, both of which are established risk factors for cardiac morbidity and death (5).

This reduction in HRV often indicates an imbalance in the autonomic nervous system, with a dominance of sympathetic (Fight-or-flight) activity and a decrease in parasympathetic (Rest-and-digest) activity (6). Reduced HRV in MDD is associated with a range of clinical symptoms, including increased stress, anxiety, and a higher risk of cardiovascular problems. Researchers have identified HRV as a potential biomarker for MDD. It can be used to assess the severity of depressive symptoms and may help in predicting the risk of future depressive episodes. Abnormal HRV can be linked to specific symptoms of MDD, such as anhedonia (Loss of interest in pleasurable activities) and altered emotional regulation (7,8). The exact mechanisms underlying reduced HRV in MDD are not fully understood. Still, it is believed to be related to altered autonomic nervous system functioning, inflammation, and disruptions in the regulation of the heart rate. HRV is acknowledged as a valuable and non-invasive method for assessing how the heart's autonomic nervous system is regulated (9). The variation between successive heartbeats is referred to as HRV. The autonomic nervous system's sympathetic and parasympathetic branches work together to regulate the SA node, which regulates the heart's rhythm. HR tends to rise in response to sympathetic activity very slowly (A few seconds). Conversely, parasympathetic activity mediates quickly (0.2-0.6 s) (10) and tends to lower heart rate. In physically healthy depressed adults, HRV does not differ from that of healthy controls, according to one study by Sayar K et al. (11), while Licht et al. demonstrated a substantial correlation between depression and reduced HRV (12).

Therefore, this study aimed to demonstrate the status of heart rate variability parameters in a group with major depressive disorder at a specialized care facility.

Methods

Study design and participants: This observational study spanned six months and involved the enrollment of 90 patients aged 20-40 years diagnosed with major depressive disorder (MDD) as per ICD-10 criteria (13) at the outpatient psychiatric department. Exclusion criteria included psychiatric illnesses, including schizophrenia or schizoaffective disorder and bipolar disorder. Besides, those with organic disorders such as dementia, epilepsy, cerebrovascular diseases, history of electroconvulsive therapy in the last three months, musculoskeletal disorders such as kyphosis, scoliosis, and chronic diseases such as hypertension, diabetes, and chronic renal disease were excluded.

Ethics and consent: The study protocol was approved by Institutional Ethical Number RUHS-CMS/Ethics Comm./2022/70. Before enrollment, all participants were provided with a participation information sheet, and written informed consent was obtained.

Data collection: The Hamilton Rating Scale for Depression (14) was used to assess major depressive disorders after recruitment from the psychiatry department.

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- Sociodemographic detail was recorded according to the modified Kuppuswamy Scale 2021(Sex, marital status, geographical area, socioeconomic status) (15).
- Cognitive functions were assessed using the MMSE (Mini-Mental Status Examination) (16) questionnaire.
- Autonomic functions were assessed by heart rate variability indices (17), including:

➢ Time domain (RMSSD: Root Mean Square of the Successive Difference between normal heartbeats, PNN50: Percentage of number of pairs of NN that is longer than 50, SDNN: Standard Deviation of NN interval)

➢ Frequency domain parameters (LF: Low Frequency, HF: High Frequency, LF/HF: Low-Frequency/High-Frequency ratio) were recorded using a digital physiograph (MLT004/ST) by AD instruments (The electrocardiogram or ECG) which can be recorded for five minutes to determine HRV. The ECG extracted intervals between successive beats or R-R intervals. Rather than using the ECG, the peripheral pulse was used in this experiment to make capturing a signal for analysis easier. A peripheral pulse occurs during each normal cardiac cycle. Therefore, the pulse's peak-to-peak interval corresponded to the R-R interval from an ECG recording. This technique involves studying and showing the various frequency components of the N-N intervals.

Statistical analysis: All analyses were conducted using Microsoft Excel 2019 and analyzed using SPSS 21.

➢ Descriptive statistics were calculated for all variables and presented as mean and standard deviation.

➢ Pearson's or Spearman's correlations were used to examine relationships between MMSE, HRV measures, and depression severity scores.

Results

Figure 1 depicts the distribution of participants by demographic variable, highlighting the dominance of specific categories. It demonstrates that most participants were from rural areas, aged 20-30, married, and belonged to the upper middle class. Furthermore, males were slightly more prevalent (45) compared to females (40).

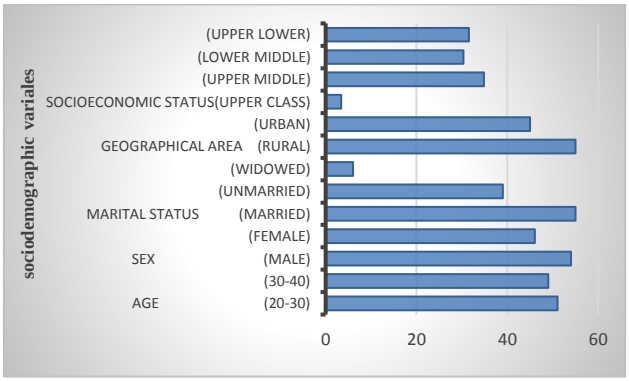

Figure 1. Frequency distribution of participants according to sociodemographic variables

Table 1 depicts correlations between HAM-D (Hamilton Depression Rating Scale) scores and physiological and cognitive measures. The Mini-Mental State Examination (MMSE) scores and HAM-D scores have a perfect negative association ($r = -1.00$, $p < 0.001$), which suggests that with an increase in depression severity, cognitive performance decreases as assessed by the MMSE. Similarly, there was a strong negative correlation between HAM-D scores and the following variables: LF ($r = -0.99$, $p < 0.001$), SDNN ($r = -0.99$, $p < 0.01$), RMSSD ($r = -0.93$, $p < 0.01$), and mean heart rate ($r = -0.99$, $p < 0.001$). These results indicate that lower heart rate variability, as seen by lower RMSSD, SDNN, and LF values, as well as a lower mean heart rate, are linked to higher depression scores. On the other hand, there was a highly significant and negative correlation ($r = -1.00$, $p < 0.001$) between HAM-D scores and HF (High-frequency power), which highlights the effect of depression on autonomic nervous system function.

Table 1. Association of HAM-D with cognitive and heart rate variability parameters

Outcome measure	r	P-value	Strength of correlation
Cognitive parameters			
MMSE	-1.00	< 0.001	Strong
Heart rate variability			
RMSSD	- 0.93	< 0.05	Strong
SDNN	- 0.99	< 0.001	Strong
LF	- 0.99	< 0.001	Strong
HF	- 1.00	< 0.001	Strong

Figure 2 shows the correlation analysis between HAMD, MMSE, and heart rate variability parameters (RMSSD): Root Mean Square of the Successive Difference between normal heartbeats, PNN50: Percentage of the number of pairs of NN that is longer than 50, SDNN: Standard Deviation of NN interval, LF: Low Frequency, HF: High Frequency, Mean Heart Rate (mean HR).

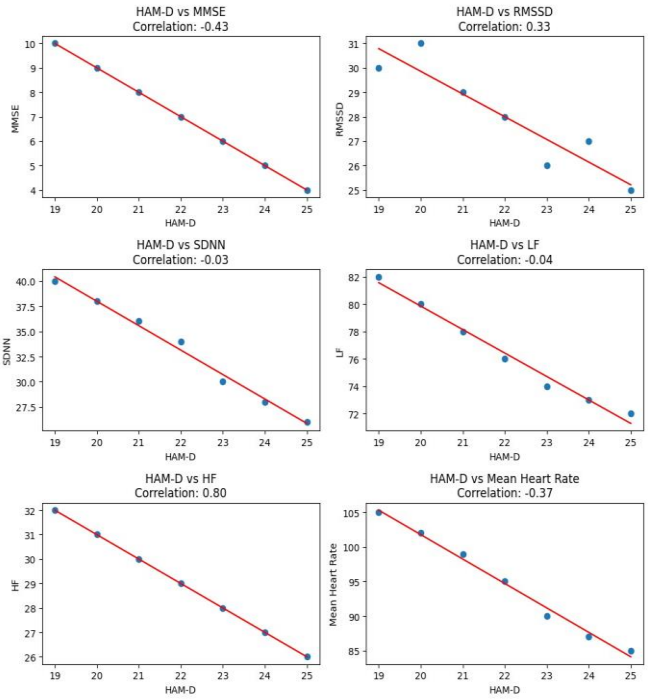

Figure 2. Scatter plots comparing Hamilton Depression Rating Scale (HAM-D) scores with MMSE and various heart rate variability (HRV) measures in patients with major depressive disorder

Discussion

This study examined the relationships between depression severity, as measured by the Hamilton Depression Rating Scale (HAM-D), and various heart rate variability (HRV) parameters in patients with major depressive disorder (MDD).

The most notable observation was a significant positive connection between HAM-D scores and high-frequency (HF) power ($r = 0.80$). This finding contradicts the common notion that depression is related to decreased HF power, which is often interpreted as decreased parasympathetic activity (18). Kemp et al. (2010) observed that patients with major depressive disorder (MDD) exhibited lower HF power compared to healthy controls in a meta-analysis (19). Our findings indicate that in our sample, parasympathetic activity increased with depression severity, which is consistent with the findings of the study conducted by Singla et al. (20).

This study's weak positive connection between HAM-D scores and RMSSD ($r = 0.33$) is consistent with the HF power finding, as both are considered measures of parasympathetic activity. However, it contradicts prior research that reported lower RMSSD in depression (21). The absence of association between HAM-D and SDNN ($r = -0.03$) shows that depression severity may not have significantly affected the overall HRV in our population, contrary to some earlier studies (22).

Interestingly, no significant association was found between HAM-D ratings and low-frequency (LF) power ($r = -0.04$). This contradicts previous research that reported lower LF power in depression (19). The lack of a relationship in our study might suggest that depression severity did not systematically affect our group's sympathetic component of HRV.

The moderate negative correlation ($r = -0.43$) between HAM-D and MMSE scores supports the previously documented link between depression and cognitive function (23). This conclusion is consistent with the expanding body of research indicating a bidirectional link between depression and cognitive decline (24).

The slight negative correlation between HAM-D ratings and mean heart rate ($r = -0.37$) was entirely unexpected, given that depression has frequently been linked to increased heart rate (25). This conclusion may reflect the complicated interplay between depression and autonomic regulation, which could be altered by medication or concomitant diseases. In contrast, there is evidence indicating that there is no difference in HRV between individuals with depression and healthy individuals (26).

Heart rate variability (HRV) in major depression is caused by various interconnected systems, including the autonomic nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, neurotransmitter imbalances, inflammation, and behavioral variables. Depression is frequently characterized by an overactive sympathetic nervous system and diminished parasympathetic

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(Vagal) tone, resulting in lower HF HRV. Dysregulation of the HPA axis causes high-stress hormones such as cortisol, further suppressing parasympathetic function. Neurotransmitter abnormalities, particularly those involving serotonin, norepinephrine, and GABA, contribute to autonomic dysregulation. Genetic and epigenetic factors can make a person more susceptible to depression and autonomic dysfunction, which in turn can further decrease heart rate variability (HRV) (27). However, as stated by Porges et al., the vagus nerve regulates heart rate by slowing it down via its influence on the heart pacemaker. This modulation is essential for maintaining a healthy autonomic nervous system. Low vagal tone, which is common in depression, reduces HRV and increases the risk of heart disease. The vagus nerve regulates heart rate, which is crucial for mental and physical well-being (28).

This study had significant limitations. Multiple investigations have demonstrated that antidepressants influence HRV indicators (12,26), while this study provided no information regarding the medications the patients used. This can be considered a significant study limitation since medication use by patients could have influenced the outcomes. Moreover, there was no healthy control group in this study. Furthermore, we excluded cardiac diseases such as ischemic heart disease and myocardial infarction as they can be confounding factors.

The use of standardized tools to screen for comorbid depression in participants, together with the administration of psychological test scales and HRV measures at the initial visit, can be considered as the advantages of this study. Additionally, since HRV was measured before treatment, a more precise analysis of the correlation between depression symptoms and HRV indices was possible. This can be crucial as HRV can be pretty sensitive to environmental factors. To ensure consistency in measurement and result interpretation, the same inspector conducted all tests and measured HRV at the same place throughout the study. To the best of our knowledge, research on the connection between depression and HRV is still sparse. This study's clinical implications include the potential use of the findings as significant biomarkers for the assessment and management of individuals with depression at an earlier age.

Conclusion

In this study, we discovered a positive correlation between greater feelings of depression and increased parasympathetic activation. We found a significant negative connection between HAM-D scores, heart rate, and Mini-Mental State Examination (MMSE) scores, suggesting that severe depressive symptoms are associated with lower heart rates and poorer cognitive function. These findings show the complex and multidimensional links between depressive symptoms, autonomic function, and cognitive performance, emphasizing the need for a comprehensive approach to understanding and treating major depression. HRV can be considered an essential potential biomarker to assess cardiovascular health in the early stages of life.

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Ethical statement

Institutional Ethical approval was obtained from the Institutional Ethics Committee (RUHS-CMS/Ethics Comm./2022/70). Each participant provided informed consent to participate in the study.

Conflicts of interest

There are no conflicts of interest.

Author contributions

SS analyzed and interpreted the data regarding subjects. NS also interpreted the data and was a significant contributor to the manuscript. SK drafted the work or substantively revised it. All authors read and approved the final manuscript.

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