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Original Research Article

To Investigate Autonomic Function in Individuals Newly Diagnosed with Rheumatoid Arthritis by using Heart Rate Variability as a Diagnostic Tool: An Observational Study

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Abstract

Aim: To investigate autonomic function in individuals newly diagnosed with rheumatoid arthritis by using heart rate variability as a diagnostic tool.

Materials and Methods: This study was done in the Department of Physiology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India for one year. This study was designed to investigate autonomic function in newly diagnosed rheumatoid arthritis (RA) individuals using heart rate variability (HRV) as a tool. The study employed a cross-sectional design and included 50 patients newly diagnosed with rheumatoid arthritis. The inclusion criteria were as follows: patients newly diagnosed with rheumatoid arthritis as per the 2010 ACR/EULAR classification criteria, aged between 18 and 65 years, and with no prior treatment for RA. Exclusion criteria included a history of cardiovascular disease, current or past use of medications affecting the autonomic nervous system, other autoimmune or inflammatory diseases, diabetes mellitus, pregnancy, and smoking or alcohol use.

Results: The correlation between HRV parameters and the DAS28 score, which measures RA disease activity. A significant negative correlation was observed between SDNN and DAS28 ($r = -0.45$, $p = 0.01$), indicating that higher disease activity is associated with lower heart rate variability. Similarly, RMSSD showed a significant negative correlation with DAS28 ($r = -0.38$, $p = 0.02$), further supporting the link between increased disease activity and reduced parasympathetic function. The low frequency (LF) component also negatively correlated with DAS28 ($r = -0.32$, $p = 0.04$), suggesting that as RA disease activity increases, sympathetic modulation decreases. The high frequency (HF) component had a negative correlation with DAS28 ($r = -0.28$, $p = 0.05$), though this was on the threshold of statistical significance. Conversely, the LF/HF ratio had a positive correlation with DAS28 ($r = 0.30$, $p = 0.03$), indicating that higher disease activity may shift the balance towards sympathetic dominance, albeit with reduced overall autonomic activity.

Conclusion: In conclusion, the study's results highlight the significant relationship between reduced HRV and increased RA disease activity, suggesting autonomic dysfunction in newly diagnosed RA patients. These findings underscore the importance of monitoring autonomic function in RA patients as part of their comprehensive clinical assessment and support the potential use of HRV as a non-invasive marker for evaluating disease severity and guiding therapeutic interventions.

Keywords: Rheumatoid arthritis, Heart rate , Diagnostic tool

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by persistent synovitis, systemic inflammation, and autoantibody production, primarily targeting the synovial joints. This autoimmune condition often leads to progressive joint destruction, functional disability, and decreased quality of life. Despite extensive research into its etiology and pathogenesis, the exact mechanisms driving RA remain incompletely understood. [1] One intriguing aspect of RA that has garnered attention in recent years is its impact on the autonomic nervous system (ANS). The ANS, comprising the sympathetic and parasympathetic nervous systems, regulates vital physiological functions, including heart rate, blood pressure, digestion, and respiratory rate. Dysregulation of the ANS has been implicated in various chronic diseases, including cardiovascular disorders,

diabetes, and autoimmune diseases such as RA. [2] Autonomic dysfunction in RA patients has been increasingly recognized as a significant contributor to disease morbidity. This dysfunction can manifest as altered heart rate variability (HRV), which is a non-invasive measure of autonomic function derived from the analysis of heart rate time series. HRV reflects the balance between sympathetic and parasympathetic activity and provides insights into the overall autonomic regulation of the cardiovascular system. Reduced HRV is indicative of autonomic imbalance and has been associated with increased disease activity, systemic inflammation, and heightened cardiovascular risk in RA patients. [3] The use of HRV as a tool to assess autonomic function in RA offers several advantages. It provides a quantifiable and reproducible measure of autonomic nervous system activity, allowing for the detection of subtle changes that may not be apparent through conventional clinical assessment. Additionally, HRV analysis can be easily integrated into routine clinical practice, offering a non-invasive and cost-effective method to monitor autonomic function over time. [4] In newly diagnosed RA patients, assessing autonomic function using HRV is particularly pertinent. Early detection of autonomic dysfunction can inform therapeutic decisions, as autonomic imbalance may contribute to the persistence and exacerbation of inflammatory processes. Moreover, understanding the relationship between HRV and disease activity in the early stages of RA can provide insights into the pathophysiological mechanisms linking autonomic dysfunction and systemic inflammation. Several factors can influence HRV in RA patients, including the severity and duration of the disease, the presence of comorbid conditions such as cardiovascular disease and diabetes, and the use of medications that affect autonomic function. Therefore, a comprehensive assessment of these variables is essential when interpreting HRV data in this population. [5] The integration of HRV analysis into the clinical management of RA holds the potential to enhance patient outcomes. By identifying patients at risk of autonomic dysfunction early in the disease course, clinicians can implement targeted interventions to restore autonomic balance, reduce systemic inflammation, and mitigate the risk of cardiovascular complications. Furthermore, longitudinal HRV monitoring can provide valuable feedback on the effectiveness of therapeutic strategies, allowing for timely adjustments to treatment plans. [6]

Materials and Methods

This study was done in the Department of Physiology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India for one year. This study was designed to investigate autonomic function in newly diagnosed rheumatoid arthritis (RA) individuals using heart rate variability (HRV) as a tool. The study employed a cross-sectional design and included 50 patients newly diagnosed with rheumatoid arthritis. Ethical approval was obtained from the institutional review board, and all participants provided written informed consent prior to inclusion in the study.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: patients newly diagnosed with rheumatoid arthritis as per the 2010 ACR/EULAR classification criteria, aged between 18 and 65 years, and with no prior treatment for RA. Exclusion criteria included a history of cardiovascular disease, current or past use of medications affecting the autonomic nervous system, other autoimmune or inflammatory diseases, diabetes mellitus, pregnancy, and smoking or alcohol use.

Methodology

Participants were recruited from the rheumatology outpatient clinic of our Institution. Initial screening included a detailed medical history, physical examination, and laboratory tests to confirm the diagnosis of RA and rule out other conditions. Baseline assessments included demographic information (age, sex, body mass index), disease activity score using DAS28, laboratory parameters including ESR and CRP levels, and a detailed medical history including duration of symptoms and comorbid conditions. HRV was measured using a standard 5-minute electrocardiogram (ECG) recording in a quiet, temperature-controlled room. Patients were instructed to avoid caffeine, heavy meals, and strenuous exercise for at least 24 hours before the test. Recordings were taken in a supine position after a 10-minute rest period to ensure a stable baseline.

The HRV parameters analyzed included time-domain indices (standard deviation of all NN intervals [SDNN] and root mean square of successive differences [RMSSD]) and frequency-domain indices (low frequency [LF], high frequency [HF], and the LF/HF ratio).

Statistical Analysis

Data were analyzed using SPSS software version 25.0. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as percentages. Differences between groups were assessed using the independent t-test for continuous variables and the chi-square test for categorical variables. Correlation analysis was performed to assess the relationship between HRV parameters and disease activity scores. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic Data

The demographic data presented in Table 1 show that the mean age of the participants was 45.6 years, with a standard deviation of 12.3 years. This indicates a middle-aged population with a broad age range. The gender distribution revealed a higher proportion of females (64%) compared to males (36%), which is consistent with the higher prevalence of rheumatoid arthritis (RA) in females. The mean body mass index (BMI) of the participants was 25.3 kg/m², with a standard deviation of 4.8, indicating that the average participant was within the overweight category.

Clinical and Laboratory Parameters

Table 2 outlines the clinical and laboratory parameters of the participants. The mean Disease Activity Score (DAS28) was 4.5, with a standard deviation of 1.2, suggesting moderate disease activity among the cohort. The erythrocyte sedimentation rate (ESR), a marker of inflammation, had a mean value of 28.6 mm/hr with a standard deviation of 15.4, indicating elevated inflammatory activity. Similarly, the mean C-reactive protein (CRP) level was 15.3 mg/L (SD 8.6), further supporting the presence of active inflammation in these newly diagnosed RA patients. The average duration of symptoms before diagnosis was 6.2 months, with a standard deviation of 3.4 months, highlighting a relatively short duration from symptom onset to diagnosis. Additionally, 20% of the participants had comorbid conditions, which could influence both disease progression and treatment outcomes.

Heart Rate Variability (HRV) Parameters

Table 3 presents the HRV parameters, which were used to assess autonomic function. The mean standard deviation of all NN intervals (SDNN) was 35.4 ms (SD 10.2), which is below the normal range of 50-100 ms, indicating reduced overall heart rate variability and potential autonomic dysfunction. The root mean square of successive differences (RMSSD) had a mean of 25.6 ms (SD 8.7), which falls within the normal range of 20-50 ms but is on the lower end, suggesting decreased parasympathetic activity. The low frequency (LF) component had a mean value of 150 ms² (SD 50), and the high frequency (HF) component had a mean of 120 ms² (SD 45), both of which are significantly below their respective normal ranges (500-1500 ms² for LF and 300-1000 ms² for HF). These values indicate a reduction in both sympathetic and parasympathetic modulation of heart rate. The LF/HF ratio was 1.25 (SD 0.5), which falls within the normal range of 1-2, suggesting a balanced but overall reduced autonomic activity.

Correlation Between HRV Parameters and Disease Activity (DAS28)

Table 4 details the correlation between HRV parameters and the DAS28 score, which measures RA disease activity. A significant negative correlation was observed between SDNN and DAS28 ($r = -0.45$, $p = 0.01$), indicating that higher disease activity is associated with lower heart rate variability. Similarly, RMSSD showed a significant negative correlation with DAS28 ($r = -0.38$, $p = 0.02$), further supporting the link between increased disease activity and reduced parasympathetic function. The low frequency (LF) component also negatively correlated with DAS28 ($r = -0.32$, $p = 0.04$), suggesting that as RA disease activity increases, sympathetic modulation decreases. The high frequency (HF) component had a negative correlation with DAS28 ($r = -0.28$, $p = 0.05$), though this was on the threshold of statistical significance. Conversely, the LF/HF ratio had a positive correlation with DAS28 ($r = 0.30$, $p = 0.03$), indicating that higher disease activity may shift the balance towards sympathetic dominance, albeit with reduced overall autonomic activity.

Results

The results of this study are presented in the following tables, which include demographic data, clinical and laboratory parameters, and heart rate variability (HRV) measures.

Table 1: Demographic Data

Variable	Mean ± SD / Frequency (%)
Age (years)	45.6 ± 12.3
Male (%)	18 (36%)
Female (%)	32 (64%)
Body Mass Index (kg/m²)	25.3 ± 4.8

Table 2: Clinical and Laboratory Parameters

Parameter	Mean ± SD / Frequency (%)
Disease Activity Score (DAS28)	4.5 ± 1.2
Erythrocyte Sedimentation Rate (ESR, mm/hr)	28.6 ± 15.4
C-Reactive Protein (CRP, mg/L)	15.3 ± 8.6

Duration of Symptoms (months)	6.2 ± 3.4
Comorbid Conditions (%)	10 (20%)

Table 3: Heart Rate Variability (HRV) Parameters

HRV Parameter	Mean ± SD	Normal Range
SDNN (ms)	35.4 ± 10.2	50-100
RMSSD (ms)	25.6 ± 8.7	20-50
Low Frequency (LF, ms²)	150 ± 50	500-1500
High Frequency (HF, ms²)	120 ± 45	300-1000
LF/HF Ratio	1.25 ± 0.5	1-2

Table 4: Correlation Between HRV Parameters and Disease Activity (DAS28)

HRV Parameter	Correlation Coefficient (r)	p-value
SDNN	-0.45	0.01*
RMSSD	-0.38	0.02*
Low Frequency	-0.32	0.04*
High Frequency	-0.28	0.05
LF/HF Ratio	0.30	0.03*

Discussion

The demographic data analysis showed a mean age of 45.6 years with a broad age range, indicating a middle-aged population. The gender distribution revealed a higher proportion of females (64%) compared to males (36%), which aligns with the known higher prevalence of rheumatoid arthritis (RA) in females. This gender disparity is well-documented in the literature, with studies such as Gabriel and Michaud (2009) highlighting that RA is more common in women, potentially due to hormonal and genetic factors. The mean body mass index (BMI) of the participants was 25.3 kg/m², suggesting that the average participant was overweight. This is significant because obesity is a known risk factor for both the development and progression of RA (Crowson et al., 2013). [7,8]

The clinical and laboratory parameters revealed a mean Disease Activity Score (DAS28) of 4.5, suggesting moderate disease activity among the cohort. Elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, with means of 28.6 mm/hr and 15.3 mg/L respectively, indicate active inflammation, which is consistent with newly diagnosed RA patients. Studies by Smolen et al. (2016) and Aletaha et al. (2010) have shown that higher DAS28 scores correlate with increased disease activity and inflammation markers, underscoring the importance of these parameters in assessing RA severity. The average duration of symptoms before diagnosis was 6.2 months, highlighting the often rapid progression of RA symptoms leading to diagnosis. The presence of comorbid conditions in 20% of the participants is also notable, as comorbidities can influence disease progression and treatment outcomes (Dougados et al., 2014). [9-11]

The HRV parameters indicated reduced autonomic function in the study population. The mean standard deviation of all NN intervals (SDNN) was 35.4 ms, below the normal range of 50-100 ms, indicating reduced overall heart rate variability. This finding aligns with studies by Evrengül et al. (2004) and Ewing et al. (1991), which reported decreased HRV in RA patients, suggesting autonomic dysfunction. The root mean square of successive differences (RMSSD) had a mean of 25.6 ms, which is within the normal range but on the lower end, indicating decreased parasympathetic activity. The low frequency (LF) and high frequency (HF) components were significantly below their respective normal ranges, reflecting impaired autonomic modulation of heart rate. These findings are consistent with studies by Panoulas et al. (2008) and Piha (1991), which have also documented reduced HRV in RA patients, indicating both sympathetic and parasympathetic dysregulation. The LF/HF ratio of 1.25 suggests a balanced but overall diminished autonomic function. [12-15]

The correlation analysis revealed significant negative correlations between DAS28 and HRV parameters (SDNN, RMSSD, LF, and HF), indicating that higher disease activity is associated with lower heart rate variability. Specifically, SDNN and RMSSD showed significant negative correlations with DAS28 ($r = -0.45$, $p = 0.01$ and $r = -0.38$, $p = 0.02$, respectively), supporting the link between increased disease activity and reduced autonomic function. These findings are corroborated by studies by Evrengül et al. (2004) and Laitinen et al. (1999), which also reported decreased HRV with higher RA disease activity. [12,16] The LF component also negatively correlated with DAS28 ($r = -0.32$, $p = 0.04$), suggesting that as RA disease activity increases, sympathetic modulation

decreases. The HF component had a negative correlation with DAS28 ($r = -0.28$, $p = 0.05$), though this was on the threshold of statistical significance. The LF/HF ratio had a positive correlation with DAS28 ($r = 0.30$, $p = 0.03$), indicating that higher disease activity may shift the balance towards sympathetic dominance, albeit with reduced overall autonomic activity. This pattern is consistent with findings from studies by Panoulas et al. (2008) and Piha (1991), which demonstrated altered autonomic balance in RA patients with higher disease activity.

Conclusion

In conclusion, the study's results highlight the significant relationship between reduced HRV and increased RA disease activity, suggesting autonomic dysfunction in newly diagnosed RA patients. These findings underscore the importance of monitoring autonomic function in RA patients as part of their comprehensive clinical assessment and support the potential use of HRV as a non-invasive marker for evaluating disease severity and guiding therapeutic interventions.

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