International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Research Article *DOI: 10.61336/im/26-4-42*

Evaluation of Autonomic Nervous System Activity in Patients with Metabolic Syndrome

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Received: **January 10, 2026**
Revised: **February 16, 2026**
Accepted: **March 09, 2026**
Published: **April 13, 2026**

Abstract

Background: Metabolic syndrome is associated with an increased risk of cardiovascular morbidity and mortality, with autonomic nervous system dysfunction proposed as an underlying mechanism. The present study aimed to evaluate autonomic function in patients with metabolic syndrome. ***Material and Methods:*** This cross-sectional study included 110 participants (55 cases with metabolic syndrome and 55 age- and sex-matched controls). Anthropometric parameters, blood pressure, and biochemical markers were assessed. Autonomic function was evaluated using heart rate variability (HRV) analysis and standard cardiovascular reflex tests. Statistical analysis was performed using appropriate parametric tests, with $p < 0.05$ considered significant. ***Results:*** No significant difference in age or gender distribution was observed between groups. Cases showed significantly higher body mass index, waist circumference, systolic and diastolic blood pressure ($p < 0.01$). Fasting blood glucose and triglyceride levels were significantly elevated, while HDL cholesterol was reduced in cases ($p < 0.01$). HRV analysis revealed significantly lower SDNN (32.4 ± 8.6 vs 48.9 ± 10.2 ms) and RMSSD (21.7 ± 6.5 vs 36.8 ± 9.1 ms), higher LF (62.5 ± 10.8 vs 51.3 ± 9.7 nu), lower HF (37.2 ± 9.4 vs 48.6 ± 8.8 nu), and increased LF/HF ratio (1.82 ± 0.54 vs 1.08 ± 0.36) in cases ($p < 0.01$). Parasympathetic indices (E:I, Valsalva, 30:15 ratios) were significantly reduced, while sympathetic responses were impaired, with greater fall in systolic BP and reduced rise in diastolic BP ($p < 0.01$). LF/HF ratio showed significant positive correlation with BMI, waist circumference, fasting glucose, and triglycerides, and negative correlation with HDL. ***Conclusion:*** Metabolic syndrome is associated with significant autonomic dysfunction characterized by sympathetic predominance and reduced parasympathetic activity, correlating with the severity of metabolic abnormalities.

Keywords: Metabolic syndrome, Autonomic dysfunction, Heart rate variability, Sympathetic activity, Parasympathetic activity

INTRODUCTION

Metabolic syndrome is a cluster of interrelated cardiometabolic abnormalities, including central obesity, insulin resistance, dyslipidemia, and hypertension, which collectively increase the risk of type 2 diabetes mellitus and cardiovascular disease [1]. The global burden of metabolic syndrome has increased substantially in recent decades, making it a major public health concern due to its association with adverse cardiovascular outcomes and mortality [2].

Emerging evidence suggests that autonomic nervous system dysfunction plays a pivotal role in the pathophysiology of metabolic syndrome. Autonomic imbalance, characterized by increased sympathetic activity and reduced parasympathetic tone, has been implicated in the development of hypertension, insulin resistance, and other metabolic derangements [3]. This dysregulation contributes to cardiovascular risk by promoting hemodynamic instability, endothelial dysfunction, and altered metabolic homeostasis [3].

Heart rate variability (HRV) has been widely used as a non-invasive and reliable tool for assessing autonomic nervous system activity. It reflects the dynamic interplay between sympathetic and parasympathetic influences on the sinoatrial node [4]. Reduced HRV is considered an early marker of autonomic dysfunction and has been associated with increased cardiovascular morbidity and mortality [4].

Recent systematic reviews and meta-analyses have demonstrated that individuals with metabolic syndrome exhibit significantly reduced HRV parameters, including lower SDNN and RMSSD, indicating impaired autonomic modulation [5]. Additionally, alterations in frequency-domain indices, such as reduced high-

frequency power and altered sympathovagal balance, further support the presence of autonomic imbalance in these patients [5].

Furthermore, individual components of metabolic syndrome, particularly hyperglycemia and central obesity, have been shown to independently influence cardiac autonomic modulation, suggesting a cumulative effect of metabolic abnormalities on autonomic function [6]. Despite these observations, the extent and pattern of autonomic dysfunction in metabolic syndrome remain incompletely characterized, especially in different population settings.

Therefore, the present study was undertaken to evaluate autonomic nervous system activity in patients with metabolic syndrome using heart rate variability analysis and standard cardiovascular reflex tests.

MATERIALS AND METHODS

Study Design and Setting: A hospital-based cross-sectional analytical study was conducted at a tertiary care teaching hospital. Written informed consent was obtained from all participants prior to enrolment.

Study Population: The study included adult participants aged 30–60 years. Subjects were divided into two groups:

- **Group A (Cases):** Patients diagnosed with metabolic syndrome
- **Group B (Controls):** Age- and sex-matched apparently healthy individuals without metabolic syndrome

Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, requiring the presence of at least three of the following [7]:

1. Waist circumference >102 cm in males and >88 cm in females (modified cut-offs for Asian population applied: >90 cm in males, >80 cm in females)
2. Fasting plasma glucose ≥100 mg/dL or on treatment for diabetes
3. Blood pressure ≥130/85 mmHg or on antihypertensive treatment
4. Serum triglycerides ≥150 mg/dL
5. HDL cholesterol <40 mg/dL in males and <50 mg/dL in females

Sample Size Determination: The sample size was calculated based on previous studies evaluating autonomic dysfunction using heart rate variability parameters in metabolic syndrome, assuming a moderate effect size (Cohen's d = 0.6), a power of 80%, and a significance level (α) of 0.05. The minimum required sample size was estimated to be 45 subjects per group. To account for potential dropouts and incomplete data, a total of 110 participants were enrolled, comprising 55 cases and 55 controls.

Inclusion Criteria

- Individuals aged 30–60 years
- Diagnosed cases of metabolic syndrome (for Group A)
- Apparently healthy individuals without metabolic syndrome (for Group B)
- Willingness to participate in the study

Exclusion Criteria

- History of cardiovascular diseases (e.g., ischemic heart disease, arrhythmias)
- Diabetes mellitus with complications (neuropathy, nephropathy, retinopathy)
- Chronic kidney disease or liver disease
- Thyroid disorders
- Use of medications affecting autonomic function (e.g., beta-blockers, antidepressants)
- Smoking, alcohol abuse
- Pregnancy

Data Collection and Clinical Assessment: A detailed clinical history was obtained, followed by a thorough physical examination. Anthropometric parameters including height, weight, body mass index (BMI), and waist circumference were recorded using standardized techniques. Blood pressure was measured using a calibrated sphygmomanometer after 10 minutes of rest in a seated position.

Biochemical Analysis: After overnight fasting (8–12 hours), venous blood samples were collected for estimation of:

- Fasting blood glucose
- Serum triglycerides
- High-density lipoprotein (HDL) cholesterol

All biochemical parameters were analyzed using standard enzymatic methods in the central laboratory.

Assessment of Autonomic Nervous System Activity: Autonomic function was evaluated using non-invasive cardiovascular autonomic function tests:

1. Heart Rate Variability (HRV): Short-term HRV analysis was performed using a computerized ECG recording system under standardized resting conditions. Time-domain parameters (SDNN, RMSSD) and frequency-domain parameters (LF, HF, LF/HF ratio) were assessed.

2. Parasympathetic Function Tests:

- Heart rate response to deep breathing (E:I ratio)
- Valsalva maneuver
- Immediate heart rate response to standing (30:15 ratio)

3. Sympathetic Function Tests:

- Blood pressure response to standing

- Isometric handgrip test

All tests were conducted in a quiet, temperature-controlled room, with participants instructed to avoid caffeine, heavy meals, and strenuous activity for at least 12 hours prior to testing.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent Student's t-test. The chi-square test was used for categorical data. Correlation between variables was assessed using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

RESULTS

The baseline demographic characteristics were comparable between the two groups. There was no statistically significant difference in age ($p = 0.512$) or gender distribution ($p = 0.689$) between cases and controls. However, anthropometric and hemodynamic parameters showed significant differences. Body mass index, waist circumference, systolic blood pressure, and diastolic blood pressure were significantly higher in cases compared to controls ($p < 0.01$ for all), indicating a higher burden of adiposity and cardiovascular risk factors in the metabolic syndrome group (Table 1).

Biochemical analysis revealed that cases had significantly elevated fasting blood glucose and triglyceride levels, along with significantly reduced HDL cholesterol levels when compared to controls ($p < 0.01$ for all parameters), consistent with the metabolic derangements characteristic of metabolic syndrome (Table 2).

Assessment of autonomic function using heart rate variability demonstrated a significant reduction in time-domain parameters among cases. Both SDNN and RMSSD were markedly lower in the metabolic syndrome group ($p < 0.01$), indicating reduced overall heart rate variability and diminished parasympathetic activity. In the frequency domain, cases exhibited significantly higher low-frequency (LF) values and lower high-frequency (HF) values compared to controls ($p < 0.01$). Consequently, the LF/HF ratio was significantly elevated in cases, suggesting a shift towards sympathetic dominance (Table 3).

Parasympathetic function tests further supported these findings. The E:I ratio, Valsalva ratio, and 30:15 ratio were all significantly reduced in cases compared to controls ($p < 0.01$), indicating impaired vagal modulation in individuals with metabolic syndrome (Table 4).

Evaluation of sympathetic function revealed a significantly greater fall in systolic blood pressure upon standing in cases compared to controls ($p < 0.01$), reflecting impaired sympathetic vasoconstrictor response. Additionally, the rise in diastolic blood pressure during isometric handgrip was significantly attenuated in cases ($p < 0.01$), further indicating reduced sympathetic reactivity (Table 5).

Correlation analysis demonstrated that the LF/HF ratio showed a moderate positive correlation with body mass index ($r = 0.42$, $p = 0.002$), waist circumference ($r = 0.48$, $p < 0.01$), fasting blood glucose ($r = 0.36$, $p = 0.007$), and triglyceride levels ($r = 0.39$, $p = 0.004$). In contrast, a significant negative correlation was observed with HDL cholesterol levels ($r = -0.41$, $p = 0.003$). These findings suggest that worsening metabolic parameters are associated with increased sympathetic predominance (Table 6).

Table 1: Baseline Demographic and Anthropometric Characteristics of Study Participants

Parameter	Cases (n=55)	Controls (n=55)	p-value
Age (years)	46.8 ± 7.2	45.9 ± 6.8	0.512
Male/Female (n)	32/23	30/25	0.689
BMI (kg/m²)	29.6 ± 3.4	23.8 ± 2.9	<0.01
Waist Circumference (cm)	98.4 ± 8.1	82.7 ± 6.5	<0.01
Systolic BP (mmHg)	138.6 ± 12.4	118.2 ± 9.6	<0.01
Diastolic BP (mmHg)	88.9 ± 8.7	76.5 ± 6.8	<0.01

Table 2: Biochemical Parameters in Cases and Controls

Parameter	Cases (n=55)	Controls (n=55)	p-value
Fasting Blood Glucose (mg/dL)	112.3 ± 18.6	89.7 ± 10.4	<0.01
Triglycerides (mg/dL)	178.5 ± 35.2	121.6 ± 28.9	<0.01
HDL Cholesterol (mg/dL)	38.6 ± 6.1	49.8 ± 7.3	<0.01

Table 3: Heart Rate Variability (HRV) Parameters

Parameter	Cases (n=55)	Controls (n=55)	p-value
SDNN (ms)	32.4 ± 8.6	48.9 ± 10.2	<0.01
RMSSD (ms)	21.7 ± 6.5	36.8 ± 9.1	<0.01
LF (nu)	62.5 ± 10.8	51.3 ± 9.7	<0.01
HF (nu)	37.2 ± 9.4	48.6 ± 8.8	<0.01
LF/HF Ratio	1.82 ± 0.54	1.08 ± 0.36	<0.01

Table 4: Parasympathetic Function Tests

Parameter	Cases (n=55)	Controls (n=55)	p-value
E:I Ratio	1.12 ± 0.08	1.28 ± 0.10	<0.01
Valsalva Ratio	1.28 ± 0.12	1.52 ± 0.14	<0.01
30:15 Ratio	1.05 ± 0.07	1.21 ± 0.09	<0.01

Table 5: Sympathetic Function Tests

Parameter	Cases (n=55)	Controls (n=55)	p-value
Fall in SBP on Standing (mmHg)	14.8 ± 5.2	8.6 ± 3.9	<0.01
Rise in DBP during Handgrip (mmHg)	10.4 ± 3.6	16.9 ± 4.2	<0.01

Table 6: Correlation of LF/HF Ratio with Selected Parameters in Cases

Variable	Correlation Coefficient (r)	p-value
BMI	+0.42	0.002
Waist Circumference	+0.48	<0.01
Fasting Blood Glucose	+0.36	0.007
Triglycerides	+0.39	0.004
HDL Cholesterol	−0.41	0.003

DISCUSSION

The present study demonstrates significant autonomic dysfunction in individuals with metabolic syndrome, characterized by reduced parasympathetic activity and relative sympathetic predominance. These findings are consistent with the growing body of evidence indicating that metabolic syndrome is closely associated with alterations in autonomic regulation, particularly affecting cardiovascular control mechanisms [8].

In the current study, HRV parameters such as SDNN and RMSSD were significantly reduced in cases compared to controls, indicating diminished vagal tone. Similar observations have been reported in recent systematic reviews, which have demonstrated that individuals with metabolic syndrome exhibit significantly lower time-domain HRV indices, reflecting impaired parasympathetic modulation [9]. Additionally, the observed increase in LF and LF/HF ratio along with reduced HF further supports a shift toward sympathetic dominance, which has been widely recognized as a hallmark of autonomic imbalance in metabolic disorders [8].

The impairment in parasympathetic function tests, including E:I ratio, Valsalva ratio, and 30:15 ratio, in the present study is in agreement with previous research demonstrating reduced vagal responsiveness in metabolic syndrome. This reduction in cardiovagal activity may contribute to increased cardiovascular risk by diminishing the heart's ability to adapt to physiological stress [10]. Furthermore, sympathetic dysfunction observed in this study, as evidenced by altered blood pressure responses, aligns with findings suggesting that metabolic syndrome affects both branches of the autonomic nervous system rather than isolated pathways [8].

The positive correlation of LF/HF ratio with anthropometric and biochemical parameters such as BMI, waist circumference, fasting glucose, and triglycerides, along with its negative correlation with HDL cholesterol, indicates that worsening metabolic profile is associated with greater autonomic imbalance. Similar associations have been documented in recent studies, where hyperglycemia and central obesity were identified as key contributors to impaired autonomic modulation [11]. These findings support the concept that metabolic syndrome components exert a cumulative adverse effect on autonomic function.

The pathophysiological mechanisms underlying these observations may involve chronic low-grade inflammation, insulin resistance, and neurohumoral activation, which collectively promote increased sympathetic outflow and reduced parasympathetic activity. Increased sympathetic activity has also been implicated in myocardial remodeling and progression toward cardiovascular complications, further

highlighting the clinical relevance of autonomic dysfunction in metabolic syndrome [12].

Moreover, autonomic dysfunction has been linked to other cardiovascular abnormalities such as arterial stiffness and impaired heart rate recovery, suggesting that HRV alterations may serve as an early indicator of subclinical cardiovascular damage [13]. Therefore, assessment of autonomic function using HRV and reflex tests may provide valuable insights into cardiovascular risk stratification in these patients.

Despite these findings, the cross-sectional design of the study limits causal inference. Additionally, factors such as lifestyle variations and unmeasured confounders may influence autonomic parameters. Future longitudinal studies are warranted to establish causal relationships and to evaluate the impact of therapeutic interventions on autonomic function.

CONCLUSION

The present study demonstrates that individuals with metabolic syndrome exhibit significant autonomic imbalance characterized by reduced parasympathetic activity and relative sympathetic predominance. This is evidenced by diminished heart rate variability, impaired parasympathetic function test responses, and altered sympathetic reactivity. Furthermore, the observed correlations between autonomic indices and metabolic parameters such as adiposity, dysglycemia, and dyslipidemia indicate that the severity of metabolic derangements is closely associated with the degree of autonomic dysfunction. These findings highlight the importance of early assessment of autonomic function in patients with metabolic syndrome, as it may serve as a useful marker for cardiovascular risk stratification and guide preventive interventions.

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