

Association of Cardiac Autonomic Dysfunction with Insulin Resistance and Systemic Inflammation in Women with Polycystic Ovary Syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is associated with insulin resistance (IR), chronic low-grade inflammation, and increased cardiovascular risk. Cardiac autonomic dysfunction may contribute to this risk, but the independent effects of IR and inflammation remain unclear. Our study examined the associations of IR and inflammatory markers with cardiac autonomic dysfunction in women with PCOS.

Materials and Methods: A cross-sectional observational study included 150 women with PCOS (aged 18-30 years), diagnosed per the revised Rotterdam criteria. Participants were stratified by BMI into Normal weight (BMI <23.0 kg/m², n=50), Overweight (BMI 23.0-24.9 kg/m², n=12), and Obese (BMI ≥25.0 kg/m², n=88) groups. Autonomic function was assessed using COMPASS-31, heart rate variability, and Ewing's battery. Biochemical parameters included fasting glucose, fasting insulin, HOMA-IR, CRP, and IL-6.

Results: The mean age of participants was 22.74 (SD 3.62) years. COMPASS-31 scores and LF/HF ratio increased significantly across BMI groups, while RMSSD, pNN50, and HF% decreased (all p<0.001). HOMA-IR, CRP, and IL-6 showed positive correlations with COMPASS-31 score (r=0.342-0.378; all p<0.001) and LF/HF ratio (r=0.676-0.714; all p<0.001). After adjustment for BMI, HOMA-IR (β=0.334, p=0.003), CRP (β=0.231, p=0.004), and IL-6 (β=0.169, p=0.036) remained independent predictors of LF/HF ratio, whereas BMI was not significant (p=0.095).

Conclusion: IR and systemic inflammation were associated with cardiac autonomic dysfunction in women with PCOS, independent of BMI. Early assessment of metabolic and inflammatory markers may help identify women at increased cardiovascular risk.

Keywords: PMOS; PCOD; Prediabetes; HOMA-IR; Cardiovascular diseases; Cardiovascular Autonomic Dysfunction (CVAD)

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is recognized as the most prevalent endocrine disorder affecting women of reproductive age [1, 2]. In adults, PCOS is diagnosed based on hyperandrogenism, ovulatory or menstrual dysfunction, and polycystic ovarian morphology[3]. The prevalence of PCOS varies according to the diagnostic criteria applied. A recent meta-analysis estimated prevalence rates of 12.1% using the Rotterdam criteria, 7.9% using the NIH criteria, 12.7% using the AE-PCOS criteria, and 7.8% based on self-reported diagnosis. Across WHO regions, the South-East Asia Region had an

estimated prevalence of 14.3%, highlighting the substantial regional burden[4].

In India, the pooled prevalence of PCOS is estimated at 11.33%, with rates of approximately 10% using the Rotterdam and AE-PCOS criteria and 5.8% using the NIH criteria.[5]. Beyond its reproductive manifestations, PCOS is a complex multisystem disorder associated with diverse clinical consequences. It include infertility and adverse pregnancy outcomes, psychological disorders such as anxiety and depression, dermatological manifestations including acne and hirsutism, and metabolic and cardiovascular abnormalities, particularly IR, T2DM, and

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an increased risk of cardiovascular disease[6]. Growing evidence further suggests that cardiac autonomic dysfunction (CAD) may represent an important mechanism linking PCOS to its increased cardiometabolic risk[7]. Cardiac autonomic dysfunction in women with PCOS is characterised by sympathetic predominance and reduced parasympathetic activity.[8] This imbalance is reflected by impaired heart rate variability and abnormal responses on Ewing's cardiovascular autonomic function tests.[9, 10]

The autonomic nervous system regulates cardiovascular homeostasis through modulation of heart rate, blood pressure, and peripheral vascular tone. Disruption of this balance in PCOS manifests as sustained sympathetic hyperactivity, which contributes independently to endothelial dysfunction, hypertension, and early atherosclerosis[10]. Importantly, insulin resistance a hallmark of PCOS present in up to 70% of affected women - is a potent driver of sympathetic overactivation through multiple mechanisms. Hyperinsulinemia stimulates central sympathetic outflow via hypothalamic pathways, activates the renin-angiotensin-aldosterone system, and promotes norepinephrine release from sympathetic nerve terminals, all of which sustain a chronically elevated sympathetic tone[11, 12].

In parallel, the chronic low-grade inflammatory state characteristic of PCOS reflected in elevated circulating levels of CRP and interleukin-6 (IL-6) - contributes to autonomic dysfunction through neuroimmune pathways. Proinflammatory cytokines, particularly IL-6, activate the hypothalamic-pituitary-adrenal (HPA) axis and disrupt vagal anti-inflammatory reflex arcs, promoting sustained sympathovagal imbalance[13]. CRP, an acute-phase reactant produced primarily in the liver in response to IL-6, also independently correlates with reduced HRV and increased cardiovascular risk[14].

Several tools are now available for assessing autonomic function in PCOS. Ewing's battery of tests, comprising both parasympathetic (deep breathing/E:I ratio, 30:15 ratio, Valsalva maneuver, standing-to-lying ratio) and sympathetic (cold pressor test, isometric handgrip test, orthostatic blood pressure response) assessments, remains the gold standard for clinical autonomic evaluation[15]. HRV analysis provides objective, quantitative measures of sympathovagal balance. The Composite Autonomic Symptom Score-31 (COMPASS-31) is a validated, patient-reported instrument covering six autonomic domains, recently validated for use in PCOS, and offers a complementary subjective assessment of autonomic symptom burden[15].

Despite growing evidence of autonomic dysfunction in PCOS, few studies have systematically examined the independent contributions of insulin resistance and inflammation - as distinct from obesity per to the degree of cardiac autonomic impairment across different BMI phenotypes. The present study was designed to address this evidence gap through three specific objectives: (i) to compare cardiac autonomic function parameters across

BMI-defined groups (normal weight, overweight, and obese) in a cohort of women with PCOS; (ii) to examine the correlations between insulin resistance (HOMA-IR), systemic inflammation (CRP, IL-6), and cardiac autonomic function indices; and (iii) to determine whether HOMA-IR, CRP, and IL-6 serve as independent predictors of autonomic dysfunction after adjusting for BMI.

MATERIALS AND METHODS

Study design and Setting

A cross-sectional observational study was conducted in the Department of Physiology, Faculty of Medical and Health Sciences, SGT University, Gurugram, Haryana, India, in collaboration with the Department of Gynecology and Obstetrics.

Study Population

Women diagnosed with PCOS per the revised Rotterdam criteria (2003)[16] aged 18-30 years, were recruited from the Gynecology and Obstetrics outpatient department. A total of 150 women were enrolled and stratified by BMI using revised Asian-Indian consensus cut-offs into three groups: (i) Normal weight (BMI <23.0 kg/m², n=50); (ii) Overweight (BMI 23.0-24.9 kg/m², n=12); and (iii) Obese (BMI ≥25.0 kg/m², n=88) [17].

Exclusion criteria: Pregnancy or lactation, thyroid disease, pre-existing diabetes mellitus, Cushing syndrome, any acute inflammatory illness, use of hormonal contraceptives or hypoglycemic drugs within the preceding three months, and any known neurological or cardiac condition.

Anthropometric assessment: Height and weight were measured using standard techniques; BMI was calculated as weight (kg)/height (m)². Waist circumference was measured at the umbilicus and hip circumference at the widest gluteal point; waist-hip ratio (WHR) was calculated. Blood pressure and resting pulse rate were recorded after five minutes of seated rest.

Biochemical assessment: Fasting venous blood samples were collected on day 2-3 of the menstrual cycle, after ≥12 hours of fasting (no caffeine/alcohol for 12 hours prior). Fasting plasma glucose, fasting serum insulin, CRP (latex-enhanced turbidimetry), and IL-6 (ELISA) were estimated. HOMA-IR was calculated as: Fasting insulin (μIU/mL) × Fasting glucose (mg/dL) / 405. HOMA-IR >2.5 was considered indicative of insulin resistance.

Autonomic function assessment was performed in the follicular phase of the menstrual cycle, on a separate visit. Participants were instructed to fast for at least 4 hours and abstain from caffeinated beverages for 12 hours before testing. All tests were conducted in a quiet, temperature-controlled room after 10-15 minutes of supine rest.

COMPASS-31 questionnaire: Each participant completed the COMPASS-31 questionnaire, a validated 31-item self-assessment tool covering six autonomic domains: orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, and pupillomotor. Total scores

range from 0 to 100, with higher scores indicating greater autonomic dysfunction. A score >20 was classified as abnormal.

Ewing's battery of tests: Parasympathetic function tests included: (i) Deep breathing test (E:I ratio) -ratio of maximum RR interval during expiration to minimum RR interval during inspiration at 6 breaths/minute (normal ≥ 1.21 , abnormal ≤ 1.10); (ii) Lying-to-standing test (30:15 ratio) -ratio of RR interval at beat 30 to beat 15 after standing (normal ≥ 1.04 , abnormal ≤ 1.0); (iii) Valsalva maneuver -ratio of longest post-maneuver RR to shortest during maneuver (normal ≥ 1.45 , abnormal ≤ 1.2); (iv) Standing-to-lying ratio (S/L ratio; normal ≥ 1.01 , abnormal < 1.01). Sympathetic function tests included: (i) Cold pressor test - Δ DBP after hand immersion in cold water (4-6°C) for 1 minute (normal increase ≥ 10 mmHg); (ii) Isometric handgrip test - Δ DBP after sustained 30% maximal voluntary contraction (normal increase ≥ 10 mmHg); (iii) Orthostatic BP response - fall in SBP on standing (normal fall < 20 mmHg).

Heart rate variability analysis: HRV was recorded for 10 minutes using the PowerLab AD Instrument (AD Instruments, Australia) in the supine position. Time-domain variables analyzed: SDNN (standard deviation of NN intervals), RMSSD (root mean square of successive differences), pNN50 (proportion of successive NN intervals differing by > 50 ms). Frequency-domain variables: LF power (%), HF power (%), and LF/HF ratio. Elevated LF/HF > 2 was considered abnormal, indicating sympathovagal imbalance.

Statistical analysis: All analyses were performed using IBM SPSS Statistics, version 21.0 (IBM Corp., Armonk,

NY, USA). Data are expressed as mean $\pm$ SD. One-way ANOVA compared continuous variables across three BMI groups. Pearson correlation coefficients examined associations between biochemical exposures and autonomic function parameters. Multiple linear regression was performed with COMPASS-31 and LF/HF ratio as dependent variables and HOMA-IR, CRP, IL-6, and BMI as independent predictors. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 150 women with PCOS were included in the study, with a mean age of 22.74 ± 3.62 years. According to BMI classification, 50 (33.3%) were of normal weight, 12 (8.0%) were overweight, and 88 (58.7%) were obese. As shown in Table 1, COMPASS-31 scores differed significantly across BMI groups, increasing from 13.12 ± 4.42 in the normal-weight group to 19.75 ± 5.61 in the overweight group and 19.01 ± 7.32 in the obese group ($p < 0.001$). HRV analysis showed significantly higher LF/HF ratio and LF% with increasing BMI, whereas HF%, RMSSD, and pNN50 decreased significantly (all $p < 0.001$). No significant difference was observed in SDNN among the three groups ($p = 0.316$). Among the parasympathetic function tests, E:I ratio and the Valsalva maneuver showed significant differences across BMI categories. For sympathetic function, both the cold pressor test (Δ DBP) and sustained handgrip test were significantly different between the groups. Metabolic and inflammatory markers, including fasting glucose, fasting insulin, HOMA-IR, C-reactive protein (CRP), and interleukin-6 (IL-6), increased significantly with higher BMI (all $p < 0.001$), with the highest values observed in the overweight and obese groups. (Table 1)

Table 1. Demographic, anthropometric, cardiovascular autonomic function, and biochemical profiles of participants according to BMI category (N = 150)

Parameter	Normal weight (n = 50)	Overweight (n = 12)	Obese (n = 88)	p-value
Demographic and anthropometric characteristics				
Age (years)	22.62 ± 3.62	19.92 ± 1.32	23.59 ± 3.84	0.004*
BMI (kg/m ²)	20.46 ± 1.63	23.85 ± 0.46	29.12 ± 3.07	<0.001*
Waist circumference (cm)	80.60 ± 4.61	101.17 ± 7.03	96.47 ± 6.89	<0.001*
Hip circumference (cm)	95.21 ± 4.08	111.33 ± 6.33	109.87 ± 9.61	<0.001*
Waist-to-hip ratio	0.85 ± 0.06	0.91 ± 0.09	0.88 ± 0.08	0.023*
SBP (mmHg)	118.06 ± 5.75	113.67 ± 14.49	112.98 ± 12.82	0.089
DBP (mmHg)	75.42 ± 4.54	77.33 ± 7.40	73.64 ± 9.98	0.218
Pulse rate (bpm)	78.52 ± 4.50	87.33 ± 14.82	85.53 ± 14.08	<0.001*
Autonomic symptoms and heart rate variability parameters				
COMPASS-31 score	13.12 ± 4.42	19.75 ± 5.61	19.01 ± 7.32	<0.001*
SDNN (ms)	65.89 ± 27.83	49.25 ± 13.28	62.14 ± 38.34	0.316
RMSSD (ms)	58.26 ± 37.99	36.21 ± 12.82	45.94 ± 29.56	0.035*
pNN50 (%)	26.17 ± 20.78	10.44 ± 4.36	11.28 ± 5.54	<0.001*
LF (%)	27.10 ± 7.96	80.63 ± 8.94	80.61 ± 9.39	<0.001*
HF (%)	35.33 ± 14.91	19.12 ± 7.92	16.90 ± 5.21	<0.001*
LF/HF ratio	0.91 ± 0.45	4.91 ± 1.73	5.28 ± 1.77	<0.001*

Ewing's autonomic function tests: parasympathetic parameters				
E:I ratio	1.11 ± 0.10	1.08 ± 0.08	1.06 ± 0.05	0.014*
30:15 ratio	1.04 ± 0.17	1.01 ± 0.03	1.12 ± 0.96	0.593
Valsalva ratio	1.22 ± 0.16	1.09 ± 0.02	1.09 ± 0.02	<0.001*
S/L ratio	1.06 ± 0.10	1.77 ± 2.51	1.10 ± 0.97	0.083
Ewing's autonomic function tests: sympathetic parameters				
Cold pressor test, Δ DBP (mmHg)	12.06 ± 4.23	7.50 ± 3.78	8.41 ± 4.17	<0.001*
Handgrip test, Δ DBP (mmHg)	12.48 ± 2.24	7.92 ± 3.86	8.52 ± 4.01	<0.001*
Orthostatic test, Δ SBP (mmHg)	15.62 ± 4.81	21.75 ± 3.56	22.03 ± 2.98	<0.001*
Biochemical parameters				
Fasting glucose (mg/dL)	86.22 ± 5.53	108.58 ± 5.56	109.44 ± 6.00	<0.001*
Fasting insulin (μ IU/mL)	6.96 ± 1.34	18.96 ± 3.01	19.50 ± 3.23	<0.001*
HOMA-IR	1.50 ± 0.38	5.14 ± 1.06	5.32 ± 1.15	<0.001*
CRP (mg/L)	2.11 ± 0.62	8.61 ± 2.13	7.64 ± 1.54	<0.001*
IL-6 (pg/mL)	4.01 ± 0.41	8.60 ± 1.20	8.99 ± 1.77	<0.001*
NOTE: $p < 0.05$ was considered statistically significant. BMI, body mass index; COMPASS-31, Composite Autonomic Symptom Score-31; CRP, C-reactive protein; DBP, diastolic blood pressure; E:I, expiration-to-inspiration; HF, high frequency; HOMA-IR, homeostatic model assessment of insulin resistance; IL-6, interleukin-6; LF, low frequency; pNN50, percentage of successive normal-to-normal intervals differing by more than 50 ms; RMSSD, root mean square of successive differences; SBP, systolic blood pressure; SDNN, standard deviation of normal-to-normal intervals; S/L, standing-to-lying; Δ, change.				

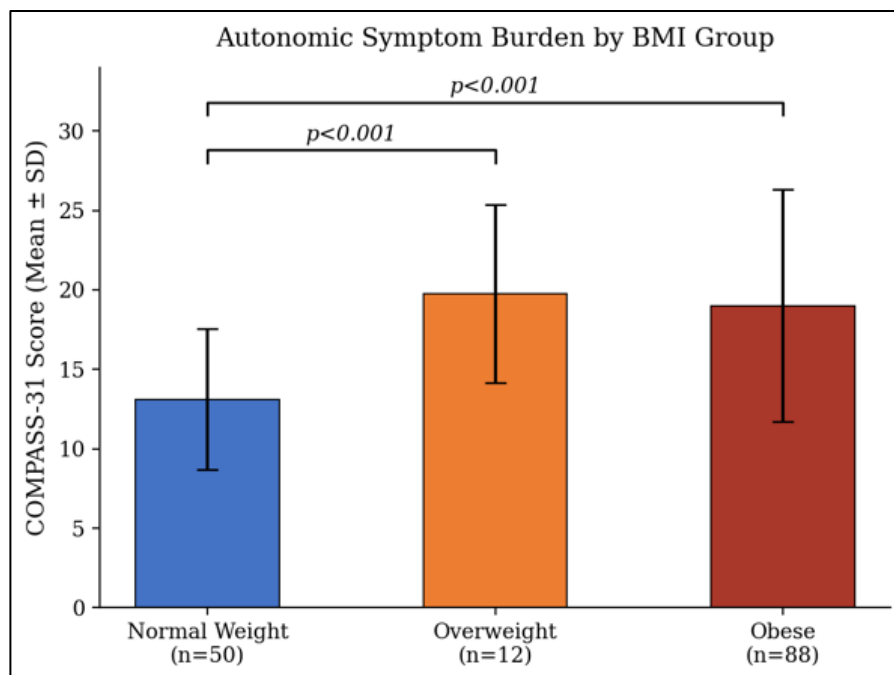


Figure 1: COMPASS-31 score (mean ± SD) across BMI groups in PCOS women.

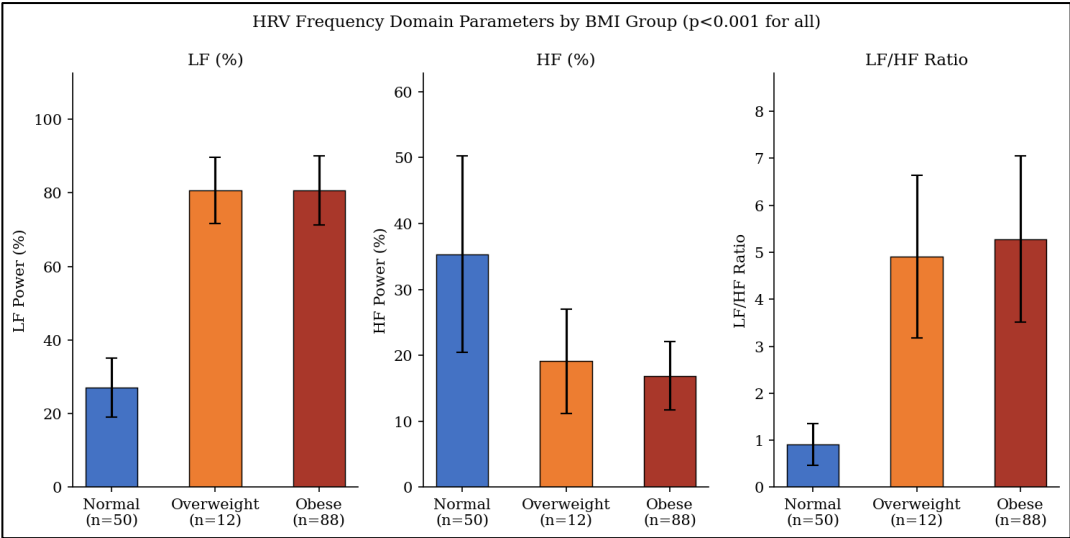


Figure 2: HRV frequency domain parameters (LF%, HF%, and LF/HF ratio) across BMI groups (p<0.001).

Table 2 shows Pearson correlation between HOMA-IR, CRP, IL-6 and autonomic function parameters across all 150 women. HOMA-IR, CRP, and IL-6 all showed strong positive correlations with COMPASS-31 score, LF/HF ratio, and LF%, and significant inverse correlations with HF%, RMSSD, and pNN50.

Table 2: Correlation of insulin resistance and inflammatory biomarkers with autonomic function measures (N = 150)

Measures	HOMA-IR <i>r</i> (<i>p</i> -value)	CRP <i>r</i> (<i>p</i> -value)	IL-6 <i>r</i> (<i>p</i> -value)
COMPASS-31 score	0.342 (<0.001)	0.371 (<0.001)	0.378 (<0.001)
Frequency-domain HRV			
LF (%)	0.823 (<0.001)	0.834 (<0.001)	0.800 (<0.001)
HF (%)	−0.567 (<0.001)	−0.567 (<0.001)	−0.555 (<0.001)
LF/HF ratio	0.703 (<0.001)	0.714 (<0.001)	0.676 (<0.001)
Time-domain HRV			
SDNN (ms)	−0.062 (0.454)	−0.009 (0.913)	−0.110 (0.180)
RMSSD (ms)	−0.168 (0.040)	−0.111 (0.177)	−0.208 (0.011)
pNN50 (%)	−0.429 (<0.001)	−0.402 (<0.001)	−0.430 (<0.001)
NOTE: Values are Pearson correlation coefficients (<i>r</i>) with corresponding two-tailed <i>p</i> -value. A <i>p</i> -value <0.05 was considered statistically significant. COMPASS-31, Composite Autonomic Symptom Score-31; CRP, C-reactive protein; HF, high frequency; HOMA-IR, homeostatic model assessment of insulin resistance; IL-6, interleukin-6; LF, low frequency; pNN50, percentage of successive normal-to-normal intervals differing by more than 50 ms; RMSSD, root mean square of successive differences; SDNN, standard deviation of normal-to-normal intervals.			

In multivariable analysis, higher HOMA-IR, CRP, and IL-6 levels were independently associated with a higher LF/HF ratio (*p* = 0.003, 0.004, and 0.036, respectively), whereas BMI was not significantly associated. None of the included predictors was significantly associated with the COMPASS-31 score. (Table 3)

Table 3. Multiple linear regression models for predictors of LF/HF ratio and COMPASS-31 score (N = 150)

Predictor	LF/HF ratio <i>B</i> (SE)	<i>p</i> -value	COMPASS-31 score <i>B</i> (SE)	<i>p</i> -value
HOMA-IR	0.334 (0.109)	0.003	0.278 (0.435)	0.523
CRP (mg/L)	0.231 (0.078)	0.004	0.380 (0.313)	0.228
IL-6 (pg/mL)	0.169 (0.080)	0.036	0.519 (0.321)	0.108
BMI (kg/m ²)	0.072 (0.043)	0.095	−0.013 (0.172)	0.938
NOTE: Values are unstandardized regression coefficients (<i>B</i>) with standard errors. Both models were adjusted for all variables shown. Model fit: LF/HF ratio, <i>R</i> ² = 0.599; COMPASS-31, <i>R</i> ² = 0.162.				

DISCUSSION

The present study examined cardiac autonomic function across BMI-defined phenotypes in 150 women with PCOS and demonstrated three principal findings. First,

sympathovagal imbalance-characterized by an elevated LF/HF ratio, reduced HF power, and diminished parasympathetic indices (RMSSD, pNN50) was markedly pronounced in overweight and obese PCOS women,

although autonomic symptoms (COMPASS-31) were already elevated across all BMI strata. Second, insulin resistance (HOMA-IR) and systemic inflammation (CRP, IL-6) exhibited strong, graded correlations with autonomic dysfunction indices. Third, and most importantly, multiple linear regression revealed that HOMA-IR,

CRP, and IL-6 were independent predictors of the LF/HF ratio after adjustment for BMI, whereas BMI itself lost significance. These findings suggest that autonomic impairment in PCOS is driven more by underlying metabolic and inflammatory milieu than by adiposity. Our HRV findings are consistent with the established literature on autonomic dysfunction in PCOS. In a recent meta-analysis of 17 studies, Mirzohreh et al.[18] reported significant reductions in SDNN, pNN50, and HF power alongside increased LF/HF ratio and LFnu in women with PCOS compared with controls, with subgroup analyses confirming these abnormalities across normal-weight, overweight, and obese categories. Similarly, Yildirim et al.[19], using 24-hour Holter monitoring, demonstrated reduced HF and elevated LF/HF ratio in young PCOS women, while Ji et al. [20] observed lower SDNN, RMSSD, and HF power in a retrospective cohort. The magnitude of sympathovagal shift in our study-LF/HF ratio rising from 0.91 in normal-weight to approximately 5.0 in overweight/obese groups-exceeds the thresholds reported in many prior studies and underscores the severity of autonomic dysregulation in Asian-Indian women with PCOS, a population known to manifest metabolic complications at lower BMI cut-offs. Notably, SDNN did not differ across BMI groups in our cohort, a finding that aligns with Hashim et al.[21], who reported reduced SDNN in PCOS but noted considerable inter-study variability, likely reflecting differences in recording duration and sample characteristics.

The application of Ewing's battery and the COMPASS-31 questionnaire alongside HRV strengthens the robustness of our assessment. Shrivastava et al.[10] were among the first to utilize this exact trio of autonomic evaluations in PCOS, reporting elevated COMPASS-31 scores and impaired parasympathetic function tests similar to our observations. Our finding that the COMPASS-31 score increased from 13.1 in normal-weight to approximately 19 in overweight/obese PCOS women mirrors their results and validates the use of patient-reported autonomic symptom burden as a clinically relevant endpoint. The significant deterioration in E:I ratio and Valsalva maneuver across BMI groups, together with blunted sympathetic responses on cold pressor and handgrip tests, confirms that both parasympathetic withdrawal and sympathetic dysfunction characterize the PCOS autonomic phenotype, as previously described by Saranya et al.[22] and Özkeçeci et al. [23].

In our regression model, HOMA-IR emerged as the strongest independent predictor of LF/HF ratio ($\beta = 0.334$, $p = 0.003$), suggesting that insulin resistance may be a major determinant of sympathetic predominance in women with PCOS. This interpretation is supported by

evidence that insulin resistance is highly prevalent across PCOS phenotypes. Rahmatnezhad et al. [24] reported insulin resistance in 74.4% of an Iranian PCOS cohort, with the greatest prevalence observed in phenotype B (91.9%). Furthermore, Szkodziak et al. [25] proposed a "vicious cycle" model in which insulin resistance, compensatory hyperinsulinemia, androgen excess, and reduced SHBG reinforce one another, contributing to persistent metabolic and autonomic dysregulation in PCOS.

Equally significant was the independent contribution of inflammatory biomarkers to autonomic dysfunction. In our study, both CRP and IL-6 were independent predictors of LF/HF ratio after mutual adjustment and BMI control. This is consistent with Zeb et al., [26] who reported a strong correlation ($r = 0.67$) between IL-6 and HOMA-IR in PCOS, and with the comprehensive meta-analysis by Bansal et al.[27], which confirmed significantly elevated IL-6 in PCOS (pooled mean difference 0.72, $p < 0.0001$) across 94 inflammatory marker studies. The earlier systematic review by Escobar-Morreale et al. [28] established that CRP, IL-6, and TNF- α are chronically elevated in PCOS, while Kumari et al.[29] demonstrated that visceral adiposity-rather than generalized obesity-was the key determinant of adipokine and inflammatory alterations in this population. Proinflammatory cytokines, particularly IL-6, disrupt vagal anti-inflammatory reflex arcs and activate the hypothalamic-pituitary-adrenal axis, thereby promoting sustained sympathovagal imbalance. Our regression data suggest that this neuroimmune pathway operates independently of adiposity, as BMI was not a significant predictor of LF/HF ratio once inflammatory markers were included in the model.

The observation that BMI lost statistical significance in the multivariate model ($p = 0.095$) while metabolic and inflammatory variables retained independent predictive power carries important pathophysiological implications. It suggests that the autonomic consequences of excess weight in PCOS are largely mediated by attendant insulin resistance and low-grade inflammation rather than by mechanical or mass-related effects of adiposity alone. This finding resonates with the recent BMI-stratified phenotyping literature; the 2026 gut microbiota study in *Frontiers in Endocrinology* [30] demonstrated distinct metabolic and inflammatory signatures between obese and non-obese PCOS, with the obese phenotype characterized by more severe IR and inflammatory profiles. Similarly, Ribeiro et al.[31] found that LF/HF ratio in overweight PCOS correlated more strongly with androgen levels than with BMI, further supporting the primacy of endocrine-metabolic factors over anthropometric measures in determining autonomic tone.

LIMITATIONS

A few limitations should be considered. The cross-sectional design precludes causal inference regarding the relationships between metabolic, inflammatory, and autonomic parameters. The small overweight subgroup ($n = 12$) may have limited the statistical power of between-

group comparisons. The absence of a healthy control group also restricts assessment of whether autonomic abnormalities in women with normal-weight PCOS differ from those in women without PCOS. In addition, hormonal and lipid parameters were not evaluated, although they may influence autonomic function. Although autonomic testing was performed during the follicular phase to improve consistency, irregular menstrual cycles in women with PCOS may have introduced residual variability related to cycle phase. Future longitudinal studies should include healthy controls, larger and more balanced BMI subgroups, and comprehensive hormonal and lipid profiling. Interventional studies are also needed to determine whether insulin-sensitising or anti-inflammatory therapies improve autonomic function in women with PCOS.

CONCLUSION

CAD is more pronounced in women with PCOS who are overweight or obese. Compared with women with normal-weight PCOS, these participants had greater autonomic symptom burden, reduced parasympathetic modulation, and increased sympathetic predominance, as indicated by altered heart rate variability and Ewing's autonomic function tests. Our findings demonstrated that higher fasting glucose, fasting insulin, HOMA-IR, CRP, and IL-6 levels, reflects greater metabolic and inflammatory disturbances.

HOMA-IR, CRP, and IL-6 were significantly associated with the LF/HF ratio and remained independent predictors of sympathovagal imbalance, whereas BMI was not independently associated. This suggests that IR and systemic inflammation may contribute more directly to autonomic dysfunction than body size alone. In contrast, none of the evaluated predictors was independently associated with the COMPASS-31 score, indicating that objective autonomic abnormalities may not consistently correspond with self-reported symptoms.

Autonomic assessment may provide additional value in the cardiometabolic evaluation of women with PCOS, particularly those with insulin resistance or elevated inflammatory markers. Longitudinal and interventional studies are required to clarify the temporal relationships among obesity, insulin resistance, inflammation, and autonomic dysfunction and to determine whether lifestyle modification, weight reduction, or insulin-sensitising therapies can improve autonomic function.

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