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AUTONOMIC DYSFUNCTION AND METABOLIC DYSFUNCTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: A COMPARATIVE STUDY

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOS) is an endocrine disorder affecting women during their reproductive years, often involving metabolic and autonomic irregularities. This study aimed to evaluate and compare autonomic function and insulin resistance in women with PCOS versus healthy controls, also examining the influence of Body Mass Index (BMI).

Methods: A comparative cross-sectional study was conducted on 100 female participants aged 18-30 years, divided into healthy controls and PCOS based on Rotterdam criteria. Autonomic function was assessed via Heart Rate Variability (HRV). Metabolic health was evaluated through fasting blood sugar, fasting insulin and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Data was stratified by BMI categories to determine the impact of adiposity on these physiological markers.

Result: Women with PCOS shows significant autonomic imbalance, characterized by reduce parasympathetic activity (decreased Percentage of Successive NN Intervals that differ by more than 50ms (pNN50) and (HF) High Frequency) and sympathetic dominance (increased LF/HF ratio) compared to controls ($p<0.001$). Metabolically, PCOS group showed higher fasting insulin (17.1±2.6 vs. 6.9 ± 1.3) and HOMA-IR (4.5±0.9 vs. 1.5 ±0.4) indicating increased insulin resistance. BMI has a direct relation with the severity of insulin resistance and sympathetic reactivity.

Conclusion: The findings suggest that PCOS is a multisystem condition defined by a self-perpetuating cycle of sympathetic over activity and insulin resistance. Since this distribution persist even in non-obese patient but worsen with weight gain, early screening of cardiovascular and metabolic risk helps to prevent long-term complications.

KEYWORDS: Autonomic Dysfunction, Body Mass Index (BMI), Fasting Blood Sugar (FBS), High Frequency (HF), Heart Rate Variability (HRV), HOMA-IR, Insulin Fasting, Low Frequency (LF), PCOS.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is the most frequently encountered endocrine disorder affecting women during their reproductive years. The reported prevalence varying 6% to 20% based on the diagnostic Rotterdam criteria [1]. The condition is primarily characterized by hyperandrogenism, menstrual irregularities due to ovulatory dysfunction, and polycystic ovarian morphology [2]. Although PCOS is traditionally considered a reproductive disorder, growing evidence indicates that it is also associated with significant metabolic and autonomic function disturbances [1].

Insulin resistance is one of the key metabolic abnormalities seen in PCOS, which affects nearly 50-70% of women with the disorder, even in the absence of obesity [4]. Reduce insulin sensitivity leads to compensatory hyperinsulinemia, which further stimulates ovarian androgen production and interferes with normal follicular development and ovulation. Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) is commonly used to detect insulin resistance[3]. Increased HOMA-IR values in women with PCOS have been strongly linked with a higher risk of type 2 diabetes mellitus, metabolic syndrome, and future cardiovascular complications [4].

In recent years, many researchers have increasingly focused on the involvement of the autonomic nervous system (ANS) in the underlying pathophysiology of PCOS. The ANS plays a major role in maintaining cardiovascular and metabolic homeostasis through the regulation of sympathetic and parasympathetic activity [5]. Several studies have demonstrated that women with PCOS tend to exhibit autonomic imbalance, characterized by increased sympathetic activity along with reduced parasympathetic tone [6, 7]. Such disturbance in autonomic regulation may contribute to the progression of hypertension, metabolic abnormalities, and cardiovascular risk associated with PCOS [8].

Heart rate variability (HRV) has developed a reliable and noninvasive method for evaluating autonomic function by evaluating the fluctuations in the intervals between consecutive heartbeats. HRV assessment includes both time domain and frequency domain parameters, which provide insight into sympathetic and parasympathetic nervous

system activity [9]. Understanding the relationship between autonomic dysfunction and insulin resistance in PCOS is clinically important, as early identification of these abnormalities may help in risk assessment, timely intervention and prevention of long term cardio metabolic complication [10, 11].
Furthermore, comparative evaluation of autonomic function (HRV) and insulin resistance in women with PCOS may provide deeper insight into the complex mechanisms involved in the disorder. Such findings could support the development of newer therapeutic approaches and encourage further research into alternative strategies for improving metabolic and cardiovascular health in women affected by PCOS.
In the present study HRV parameters and HOMA-IR is used to evaluate and compare autonomic function and insulin resistance in women with PCOS and healthy controls. Additionally it will also evaluate the correlation between autonomic dysfunction and insulin resistance, which may provide insights into the underlying pathophysiology mechanisms and potential therapeutic targets.

Aim

To study the comparison of autonomic function and insulin resistance between women with polycystic ovary syndrome (PCOS) and healthy controls using heart rate variability (HRV) and HOMA-IR.

Objectives

1. To study the comparison of HRV between healthy and PCOS women based on BMI
2. To study the comparison of Insulin Resistance between healthy and PCOS women based on BMI
3. To study the different grading of Insulin Resistance in women with PCOS based on BMI

MATERIALS AND METHODS

After the ethical approval, the study was conducted in the Research laboratory of the Department of Physiology, in collaboration with Gynecology department. A cross sectional study include 100 female participants with the age group 18-30 years, divided into two groups i.e healthy controls and women diagnosed with PCOS on the revised Rotterdam criteria, according to which any two of the following three criteria should be fulfilled for a case to be PCOS. (1)oligo-
/anovulation, (2) clinical or biochemical hyperandrogenism, and (3) polycystic ovaries, after exclusion of other etiologies.
The inclusion and exclusion criteria are presented in Table 1.
Detailed history and demographic data was taken. Anthropometric measurements, including height and weight, were obtained using a stadiometer and weighing scale, and BMI by age and height according to revised Indian guidelines was calculated.
Heart Rate Variability (HRV) was recorded during the follicular phase using PowerLab AD Instruments for 10 minutes. Both time-domain and frequency-domain parameters were analysed.
Participants were asked to fast for 12 hours and avoid caffeine and alcohol before the assessment. Fasting blood samples were collected and Insulin resistance was also assessed using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), calculated as:
HOMA-IR = (Fasting insulin µlU/mL × Fasting glucose mg/dL) / 405

Table 1: List of inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Women aged 18–30 years	Pregnancy
Confirmed PCOS according to Rotterdam criteria	Lactation
Irregular menstrual cycles.	Thyroid disorders,
	Diabetes mellitus
	Cushing syndrome
	Acute inflammatory conditions,
	Use of hormonal contraception or hypoglycemic drugs.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0 after obtaining ethical clearance. Data were expressed as mean ± standard deviation, and comparisons between groups were performed using Independent t-test. A p-value
<0.005 was considered statistically significant.

Result and Observation

Table 2: Comparison of HRV Parameters between Normal and PCOS Groups

HRV	**Group**	**Mean± Std. Deviation**	**P-value**

SDNN (ms)	Normal Group	66.2±28.3	0.160
	PCOS Group	60.2±37.2	
RMSSD (ms)	Normal Group	58.4±38.4	0.035
	PCOS Group	44.2±28.8	
pNN50 (%)	Normal Group	26.1±20.9	**<0.001****
	PCOS Group	11.2±5.5	
LF (Power %)	Normal Group	26.7±7.9	**<0.001****
	PCOS Group	80.5±9.5	
HF (Power %)	Normal Group	34.9±15.3	**<0.001****
	PCOS Group	17.4±5.9	
LH/HF ratio	Normal Group	0.9±0.5	**<0.001****
	PCOS Group	5.2±1.8	

Used Independent T-testp<0.001= statistically highly significant**

Abbreviations: Heart Rate Variability (HRV), Standard Deviation of all NN intervals (SDNN), Root Mean Square of Successive Differences (RMSSD), Percentage of successive Normal to Normal intervals that differ by more than 50 ms (pNN50), Low Frequency (LF), High Frequency (HF).

Table 2 illustrates the comparison of heart rate variability (HRV) parameters between normal healthy women and women with PCOS. Compared to the normal group, women with PCOS exhibited a significantly lower pNN50 (11.2±5.5 vs. 26.1±20.9), elevated LF (80.5±9.5 vs. 26.7±7.9), reduced HF (17.4±5.9 vs. 34.9±15.3) and increased LF/HF (5.2±1.8 vs. 0.9±0.5). These difference were statistically highly significant ($p<0.001$) which indicate sympathetic dominance with reduced parasympathetic activity in women with PCOS.

Table 3: Comparison of Fasting Blood Sugar, Fasting Insulin, and HOMA-IR between Normal and PCOS Groups

Variable	Group	Mean± Std. Deviation	P-value
Fasting Blood Sugar (mg/dl)	Normal Group	86.2±5.6	0.803
	PCOS Group	105.9±5.6	
Fasting Insulin (µIU/ml)	Normal Group	6.9±1.3	**<0.001****
	PCOS Group	17.1±2.6	
HOMA-IR	Normal Group	1.5±0.4	**<0.001****
	PCOS Group	4.5±0.9	

Used Independent T-test p<0.001= statistically highly significant**

Abbreviations: HOMA-IR = Homeostatic Model Assessment for Insulin Resistance

Table 3 illustrates the comparison of metabolic parameters between normal healthy women and women with PCOS. The PCOS group showed markedly higher metabolic values showing statistically significant difference in fasting insulin (17.1 ± 2.6 vs 6.9 ± 1.3 µIU/ml, $p < 0.001$) and HOMA-IR (4.5 ± 0.9 vs 1.5 ± 0.4, $p < 0.001$) indicating pronounced insulin resistance.

Table 4: Comparison of Heart Rate Variability and Metabolic Parameters between Normal and PCOS Groups across BMI Categories

BMI category	Test variable	Group-Normal	Group-PCOS	P-value
		Mean± SD	Mean± SD	
(Underweight	HRV-SDNN (ms)	65.5±37.1	29±0.1	0.570
	HRV-pNN50 (%)	23.4±15.1	4.7±0.1	**<0.001****
	HRV-LF (Power %)	25.1±8.2	47.1±0.1	0.544
	HRV-HF (Power %)	21.6±8.9	27.5±0.1	0.611
	HRV-LH/HF ratio	1.18±0.113	1.7±0.1	0.273
	FBS (mg/dl)	84±6	111±0.1	0.684
	FI (µIU/ml)	6.4±1.2	19.1±0.1	0.163
Normal	HRV-SDNN (ms)	69.1±31.4	60±34.6	0.132

	HRV-pNN50 (%)	30.2±21.1	10.6±5.6	**<0.001**
	HRV-LF (Power %)	27.31±7.72	77.8±9.8	0.058
	HRV-HF (Power %)	38.8±16	19.5±6.8	**<0.001****
	HRV-LH/HF	0.852±0.455	4.6±1.9	**<0.001****
	FBS (mg/dl)	86±6	105.4±5.6	**<0.001****
	FI (µIU/ml)	7±1.4	16.9±2.4	**<0.001****
Overweight	HRV-SDNN (ms)	61.1±15.1	58.4±30.3	0.055
	HRV-pNN50 (%)	15.9±14.4	12.07±4.5	0.52
	HRV-LF (Power %)	25.74±8.91	85.7±2.6	0.44
	HRV-HF (Power %)	27.1±9.3	14.3±2.3	0.101
	HRV-LH/HF	1.053±0.475	6.2±1.1	**0.039**
	FBS-mg/dl	87±6	105.9±6.3	**0.013**
	FI µIU/ml	6.9±1.4	17.2±3.1	**0.012**
Obesity	HRV-SDNN (ms)	29.8±0.1	65.1±49.4	0.77
	HRV-pNN50 (%)	6.61±0.1	11.54±5.98	**<0.001****
	HRV-LF (Power %)	19.1±0.1	81.9±7.3	0.69
	HRV-HF (Power %)	21.3±0.1	16.5±5.3	0.34
	HRV-LH/HF	0.89±0.1	5.5±1.9	**<0.001****
	FBS (mg/dl)	86±0.1	106.5±5.4	**<0.001****
	FI (µIU/ml)	6.7±0.1	17.3±2.5	**<0.001****

Used Independent T-test p<0.001= statistically highly significant**

Abbreviations: Heart Rate Variability (HRV), Standard Deviation of all NN intervals (SDNN), Percentage of successive Normal to Normal intervals that differ by more than 50 ms (pNN50), Low Frequency (LF), High Frequency (HF), Fasting Blood Sugar (FBS), Fasting Insulin (FI)

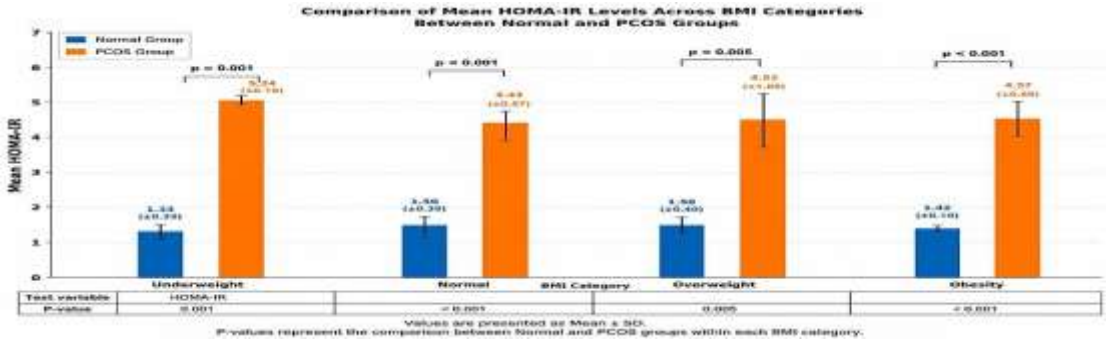
Table 4 illustrates that women with PCOS have significant autonomic and metabolic alterations across BMI groups. In underweight group pNN50 is significantly reduced (p<0.001). In the normal BMI group, significant reductions in pNN50 and HF with increased LF/HF, FBS and insulin are observed (p<0.001). In overweight group, LF/HF (p=0.039) FBS (p=0.013) and insulin (0.012) are significantly higher. In obese group pNN50, LF/HF ratio, FBS and insulin are all significantly altered (p<0.001), indicating worsening dysfunction with increasing BMI.

Table 5: BMI-wise Comparison of HOMA-IR between Normal and PCOS Groups

BMI category	Test variable	Group-Normal	Group-PCOS	P-value
		Mean± SD	Mean± SD	
Underweight	HOMA-IR	1.33±0.33	5.24±0.1	**0.001**
Normal	HOMA-IR	1.5±0.39	4.43±0.87	**<0.001****
Overweight	HOMA-IR	1.5±0.4	4.53±1.09	**0.005**
Obesity	HOMA-IR	1.42±0.1	4.57±0.89	**<0.001****

Used Independent T-test p<0.001= statistically highly significant**

Table 5 shows that women with PCOS have significantly higher HOMA-IR across all BMI categories, indicating increased insulin resistance.



Figures I: BMI-wise Comparison of HOMA-IR between Normal and PCOS Groups Table 6: Grading of

Insulin Resistance in PCOS Women on the basis of BMI

Insulin Resistance (n=50)	Normal weight	Overweight	Obese
Mild	6	3	10
Moderate	3	6	12
Severe	3	1	6

Table 6 shows the distribution of insulin resistance severity among PCOS women across BMI categories. Overall out of 50 women with PCOS In obese women, the highest number of cases was observed in obese, with moderate insulin resistance (12), followed by mild (10) and severe (6). This indicates that the severity and prevalence of insulin resistance increase with higher BMI in PCOS women.

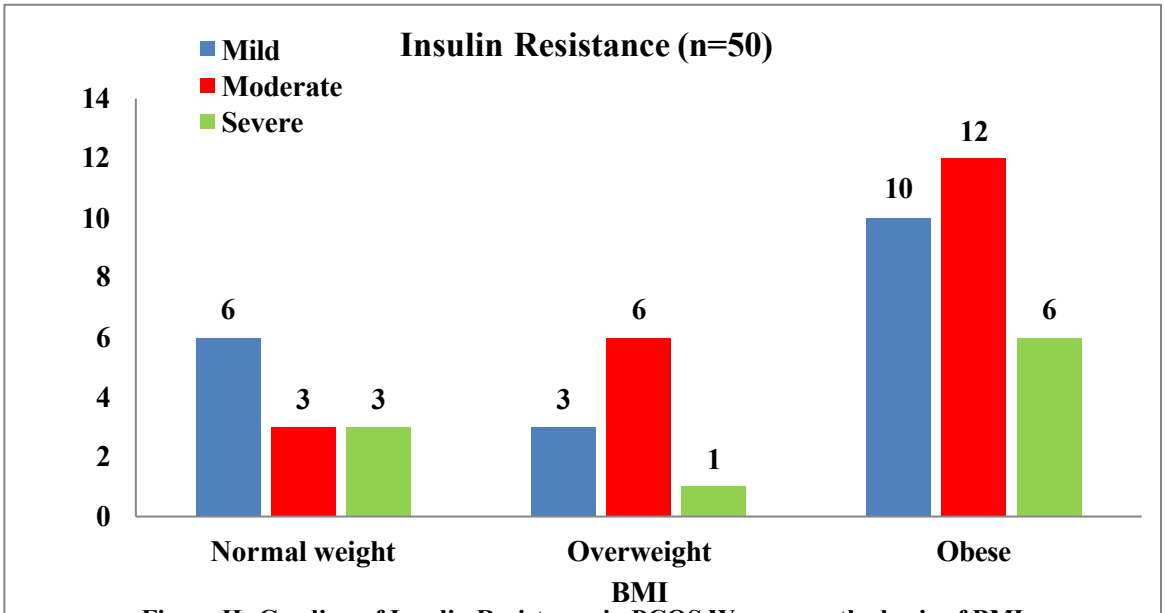


Figure II: Grading of Insulin Resistance in PCOS Women on the basis of BMI

DISCUSSION

The present study demonstrates significant alterations in both autonomic and metabolic disturbances in women with PCOS compared to healthy controls. The observed changes in HRV parameters indices of insulin resistance indicate that PCOS is a multisystem disorder including neuroendocrine, metabolic and cardiovascular deregulations rather than being limited to reproductive abnormalities [12, 13].

The HRV findings presented in table 2 show a distinct pattern of sympathovagal imbalance among women with PCOS.

Although SDNN (ms) values did not differ significant between groups, parasympathetic markers such as RMSSD (ms) and pNN50 (%) were significantly reduced, suggesting decreased vagal activity. In addition, frequency domain analysis revealed elevated LF (Power%) and LF/HF ratio together with reduced HF (Power%), indicating sympathetic predominace. Similar observation have been reported in earlier studies by Celal Kilit and others, who suggest that hyperinsulinemia and excess androgen levels may alter central autonomic regulation and contribute to increased sympathetic activity in PCOS women [14, 15, 16]. Likewise, Yildirir reported reduced HF (Power%) and elevated LF (Power%) values in women with PCOS, supporting the presence of autonomic dysfunction in this condition [17].

The metabolic findings shown in table 3 further confirm the presence of insulin resistance in PCOS subjects. Although fasting blood glucose levels were not significantly different, fasting insulin and HOMA-IR values were markedly higher in the PCOS group. This suggests that compensatory hyperinsulinemaia develops before the onset of overt hyperglycemia, which is a characteristic feature of insulin resistance states [18, 19]. Elevated HOMA-IR values in PCOS women indicate significant insulin resistance, which is known to aggravate hyperandrogenism and impair normal ovarian function, thereby playing a central role in the pathophysiology of PCOS [20, 21, 22].

The BMI based analysis in table 4 provides further understanding of how obesity influences autonomic and metabolic abnormalities in PCOS. Significant reduction in parasympathetic indicators such as pNN50 (%) and HF (Power %) were observed even among normal weight and underweight PCOS women. However, with increasing BMI, there was a progressive rise in LF/HF ratio along with worsening metabolic parameters, indicating that obesity intensifies both sympathetic over activity and insulin resistance [13, 21, 23]. Overweight and obese women with PCOS showed significant higher fasting glucose and insulin levels, reflecting metabolic impairment [24]. These findings suggest that autonomic is an inherent component of PCOS and is not solely attributable to obesity, since similar autonomic alterations have also been reported in lean PCOS women [25, 26]. Nevertheless, obesity appears to further aggravate autonomic imbalance and metabolic dysregulation, making the abnormalities more severe in obese PCOS subjects [24]. Elevated HOMA-IR across all BMI categories as shown in table 5 and fig. I highlights that insulin resistance is a core defect in PCOS. Even underweight PCOS women demonstrated significantly elevated HOMA-IR values supporting findings by Moghetti et. al indicating that insulin resistance can occur independently of adiposity, although its severity tends to increase with higher BMI. This observation is clinically important because it emphasizes the need for routine metabolic screening in all women with PCOS, irrespective of body weight [27, 28, 29].

In table 6 and fig.II the grading of insulin resistance demonstrates a gradual increase in severity with rising BMI. Mild insulin resistance was more commonly observed in normal weight women with PCOS, whereas moderate to severe insulin resistance predominated in overweight and obese PCOS subjects, suggesting a dose dependent relationship between adiposity and metabolic dysfunction [30]. Increased visceral fat accumulation, chronic low

grade inflammation and progressive impairment in insulin signaling pathways may explain this association. Previous studies have also reported a positive correlation between BMI and the severity of insulin resistance in women with PCOS [28, 29].

Overall, the findings of the present study indicate a close association between autonomic dysfunction and insulin resistance in PCOS. Increased sympathetic activity may contribute to insulin resistance by reducing skeleton muscle blood flow and impairing glucose uptake, whereas hyperinsulinemia may further stimulate sympathetic centers, thereby creating a self-perpetuating cycle [27]. The coexistence of autonomic imbalance and metabolic dysfunction may substantially increase the future risk of cardiovascular and metabolic complications in women with PCOS.

Limitations: The present study has certain limitations. Having a small sample size may limit the generalization of the findings. Lifestyle and hormonal factors that may influence autonomic and metabolic functions were not comprehensively assessed

CONCLUSION

The present study shows that women with Polycystic Ovary Syndrome have significant autonomic imbalance and insulin resistance compared to healthy controls. Reduced parasympathetic activity with increased sympathetic dominance, along with elevated fasting insulin and HOMA-IR levels, suggests that PCOS is associated with both metabolic and autonomic dysfunction. The findings highlight the importance of early metabolic and autonomic assessment in women with PCOS to reduce the future risk of cardiovascular and metabolic complications and to improve overall management of the disorder.

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