



Assessment of Serum Nerve Growth Factor in PCOS: A Case-Control Study

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Introduction

Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder with reproductive and metabolic consequences. Emerging evidence links autonomic dysfunction and altered nerve growth factor (NGF) levels to its pathophysiology. This study explores reduced heart rate variability (HRV) and increased sympathetic activity in PCOS, reflecting autonomic nervous system (ANS) dysregulation and Nerve Growth Factor (NGF)—a key regulator of sympathetic system, has been found elevated in polycystic ovaries. NGF dysregulation impacts the follicular growth and theca cell proliferation, Sympathetic nerve overactivity in ovaries, Impaired oocyte maturation and inflammation. NGF overexpression in animal models mimics PCOS features—suggesting a pivotal role in its origin and progression. It may bridge the gap between ovarian pathology, metabolic stress, and neural overactivity

Objective

To evaluate serum nerve growth factor (NGF) levels in women with Polycystic ovarian syndrome (PCOS) compared to age- and BMI-matched controls and to investigate associations with markers of insulin resistance, lipid profile, heart rate variability (HRV), and anthropometric parameters.

Methods

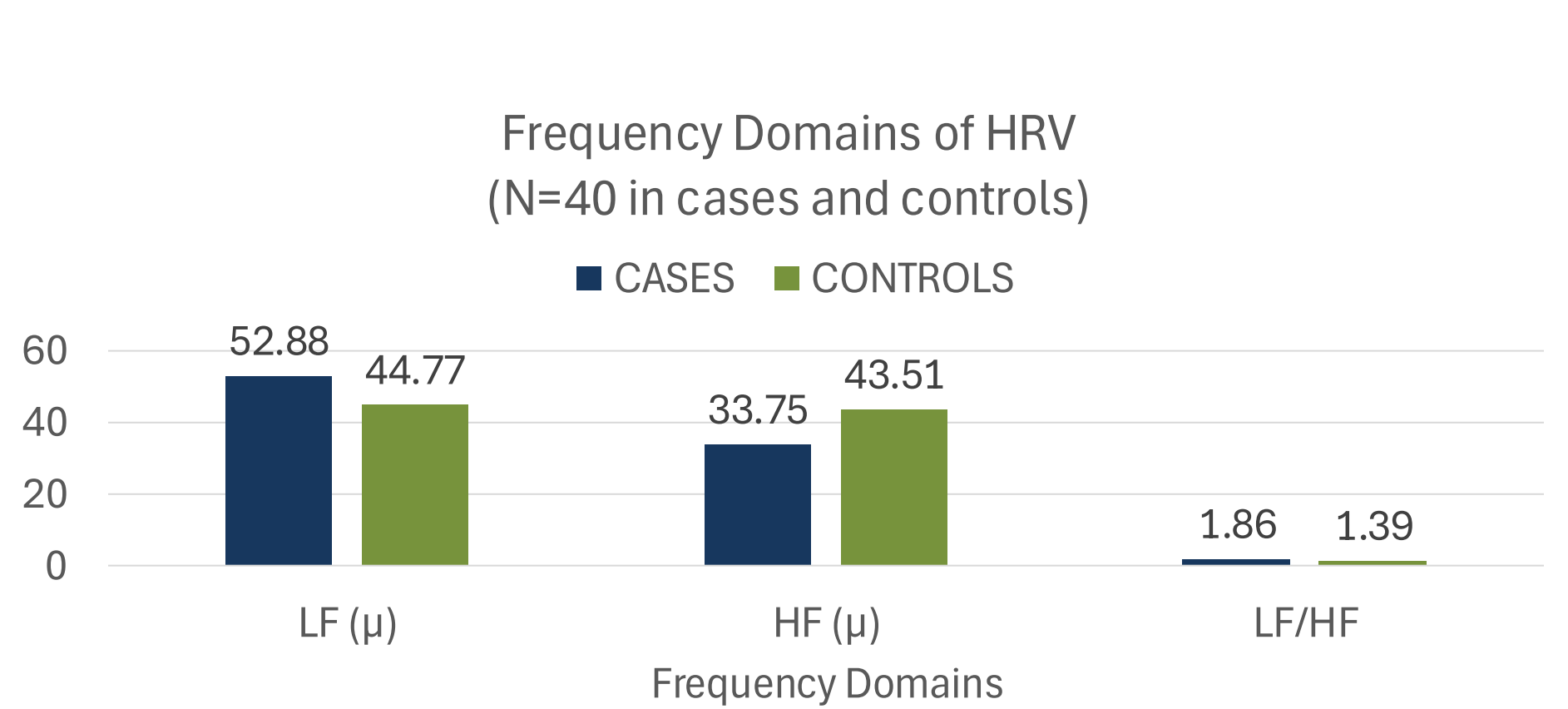
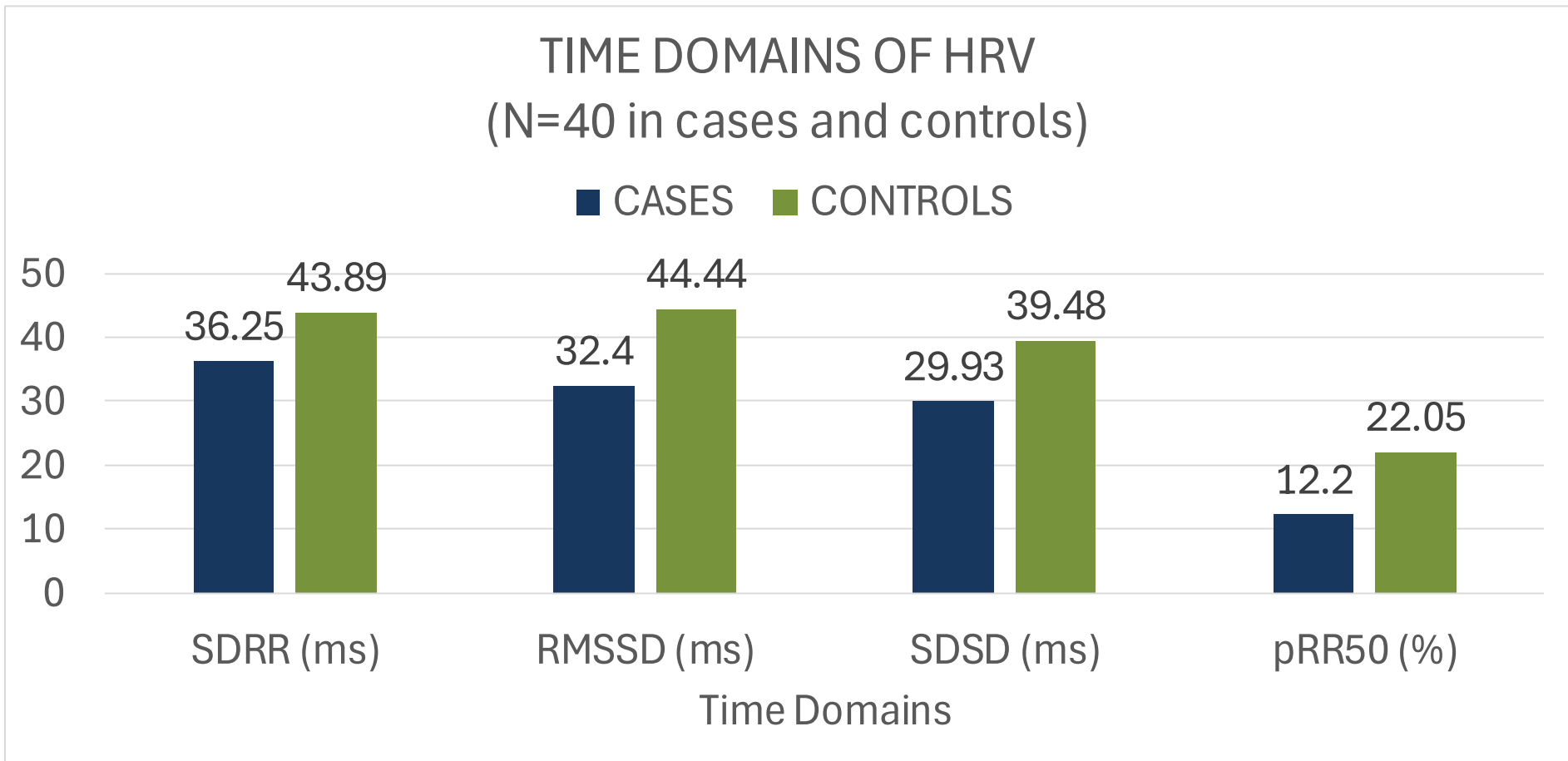
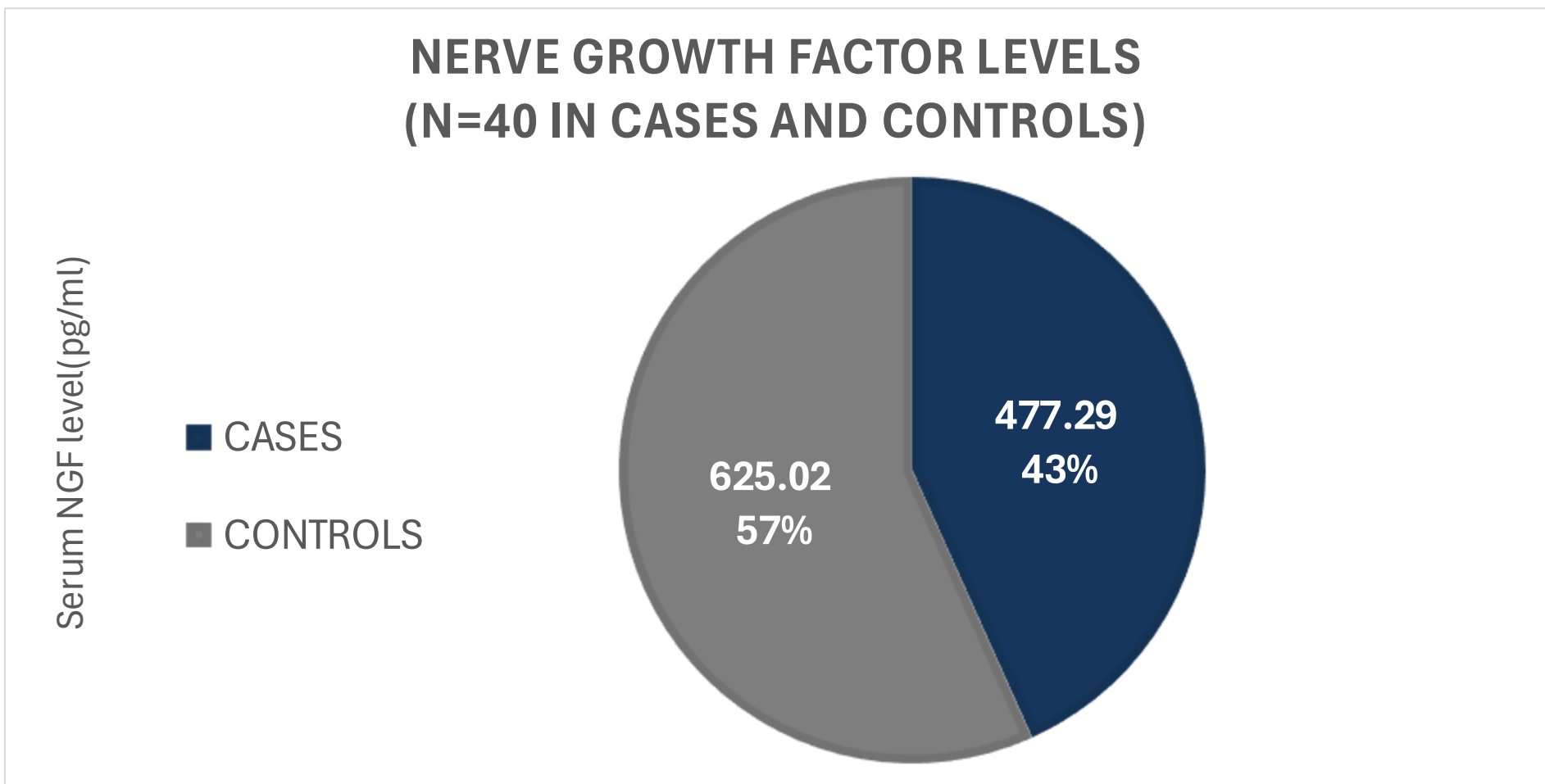
- ❖ Observational case control study
- ❖ **Participants** - 40 cases (Diagnosed by Rotterdam Criteria) - 40 controls (Disease free, Age and BMI matched)
- ❖ S.NGF measured using ELISA kit
- ❖ Fasting insulin & glucose (HOMA-IR & QUICKI calculated)
- ❖ Lipid profile, DHEA-S measured
- ❖ HRV calculated by indices derived from statistical operation of RR interval (time domain) and spectral analysis (frequency domain) of array of RR interval using Lab chart pro 8 software used on ECG (5 minutes recording)
- ❖ **Statistical Analysis**
 - Performed using SPSS 20.0
 - Independent t-tests for group comparisons
 - Pearson's correlation for evaluating associations
 - $p < 0.05$ was considered statistically significant

Results

Serum NGF Levels- Significantly ↓ PCOS cases
Heart Rate Variability (HRV)-
Frequency Domain: ↑ LF, ↓ HF, ↑ LF/HF ratio
Time Domain: (SDRR, RMSSD, SDSD, pRR50) ↓ PCOS.
Metabolic Parameters-
Higher BMI and WHR in PCOS group
Dyslipidemia: ↑ cholesterol, LDL, TG; ↓ HDL
Insulin resistance markers (HOMA-IR, QUICKI) were worse in PCOS, though not statistically significant.
Correlations with NGF:
Strong negative correlation with BMI ($r = -0.863$), WHR ($r = -0.573$)

PARAMETERS	Cases (n=40) Mean ± SD	Controls (n=40) Mean ± SD	p-value*	Cases Correlation Coefficient (with S.NGF)	Controls Correlation Coefficient (with S.NGF)
BIOCHEMICAL					
QUICKI	0.34 ± 0.03	0.35 ± 0.02	0.464	0.479	-0.208
HOMA-IR	2.77 ± 1.71	2.24 ± 1.18	0.112	-0.489	0.335
Serum DHEA-S (µg/dl)	226.65 ± 36.71	129.23 ± 42.43	<0.001	0.216	-0.161
ANTHROPOMETRIC					
Waist Hip ratio	0.86 ± 0.05	0.84 ± 0.28	0.03	-0.573	-0.537
BMI (kg/m ²)	25.51 ± 4.01	23.04 ± 3.29	0.004	-0.863	-0.932

LIPID PROFILE	Cases (n=40) Mean ± SD	Controls (n=40) Mean ± SD	p-value*
Total Cholestrol (mg/dl)	163.58 ± 38.51	136.93 ± 34.28	0.002
HDL-C (mg/dl)	43.35 ± 11.73	51.35 ± 10.51	0.032
LDL-C (mg/dl)	103.58 ± 36.80	88.33 ± 24.49	0.002
TG (mg/dl)	147.88 ± 58.98	115.93 ± 37.61	0.005



Discussion

Our study found significantly lower serum NGF levels in PCOS patients compared to healthy controls, aligning with Zangeneh et al. (2015), who also reported reduced NGF alongside elevated inflammatory markers in PCOS. While Dissen et al. (2009) demonstrated increased intra-ovarian NGF leading to PCOS-like morphology in animal models, our findings highlight a paradox—high local but low systemic NGF in PCOS.
Ovarian NGF ↑:
In PCOS, studies (including animal models) show increased NGF expression locally in the ovary, particularly in the theca cells and stromal tissues. This is associated with Increased sympathetic innervation of the ovaries, excess androgen production, disrupted follicular development and anovulation
Serum NGF ↓:
Despite ovarian overexpression, serum NGF is paradoxically lower in PCOS. This may be due to-
❖ Reduced systemic production from other tissues (e.g., immune or adipose) due to metabolic stress or chronic inflammation
❖ Increased tissue binding or sequestration of NGF at target sites like the ovary, leading to reduced free (measurable) circulating levels
❖ Altered NGF receptor signaling, where more NGF is locally consumed but less is released into the bloodstream

Additionally, our results mirror studies by Yildirim et al. (2006) and Saranya et al. (2013), which showed increased sympathetic tone and reduced HRV in PCOS women. We further established strong negative correlations between NGF and BMI, WHR, and HRV, strengthening the theory that NGF reflects both metabolic and autonomic imbalance. Uniquely, our study fills a critical gap by analyzing these correlations in the Indian population, suggesting NGF as a promising biomarker for early risk assessment in PCOS.

Study	Design	Findings	Relevance
Dissen et al., 2009	Experimental (Transgenic mice)	↑ Ovarian NGF linked to cystic changes	Suggests mechanistic role of NGF in PCOS pathogenesis; aligns with current study hypothesis
Zangeneh et al., 2015	Cross-sectional (Iraq) – 85 PCOS vs 86 controls	↓ Serum NGF and IL-17A; ↑ inflammatory cytokines	lower serum NGF in PCOS, possibly due to inflammation
Saranya et al., 2013	Case-control (India) – 31 PCOS vs 30 controls	PCOS patients had reduced HRV, increased LF/HF ratio, and altered sympathovagal balance	Corroborates our findings of autonomic dysfunction in PCOS via HRV analysis.
Yildirim et al., 2006	Case-control (Turkey) 30 PCOS vs. 30 controls	Alterations in sympathetic & parasympathetic components of HRV	Confirms autonomic imbalance observed in current study

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Photograph showing the recording of Lead II ECG in subject for HRV analysis

Conclusion

This study demonstrated that serum Nerve Growth Factor (NGF) levels are significantly lower in women with PCOS compared to age- and BMI-matched healthy controls. The reduced NGF levels showed strong negative correlations with BMI, WHR, HRV indices, and clinical markers of hyperandrogenism, indicating its potential role in the metabolic and autonomic dysfunction associated with PCOS. Our findings are in agreement with prior research suggesting autonomic imbalance and sympathetic overactivity in PCOS. This study uniquely contributes to Indian data by integrating NGF with clinical, biochemical, and autonomic parameters. NGF may serve as a promising biomarker for early diagnosis and risk stratification in PCOS. However, larger multi-centric studies are needed to confirm these findings and explore NGF as a therapeutic target.

Take Home Message

Nerve Growth Factor (NGF) may be the missing link connecting the neuroendocrine, metabolic, and autonomic disturbances in PCOS. Significantly lower serum NGF levels in PCOS women reflect deeper systemic dysfunction—beyond just reproductive symptoms.

Assessing NGF alongside HRV, BMI, and insulin resistance could enhance early detection, risk prediction, and open doors for novel therapeutic strategies

IT'S TIME TO THINK BEYOND HORMONES