**International Journal of Medical and Pharmaceutical Research**

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

# Autonomic Function Assessment in Normotensive Offspring of Hypertensive Parents

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*Received: 16-01-2026*
*Accepted: 10-02-2026*
*Available online: 25-02-2026*



## ABSTRACT

**Background**: Hypertension is a multifactorial disorder with strong familial predisposition. Autonomic nervous system imbalance has been implicated as an early mechanism in the pathogenesis of essential hypertension. Normotensive offspring of hypertensive parents may exhibit subclinical autonomic alterations before the development of sustained elevation in blood pressure.
**Aim**: To assess autonomic function in normotensive offspring of hypertensive parents and compare the findings with offspring of normotensive parents.
**Materials and Methods:** This cross-sectional comparative study included 100 healthy individuals aged 18–25 years, divided into two groups: 50 normotensive offspring of hypertensive parents (study group) and 50 normotensive offspring of normotensive parents (control group). Autonomic function was evaluated using heart rate variability (HRV) analysis and standardized cardiovascular reflex tests, including deep breathing test (E:I ratio), Valsalva maneuver, 30:15 ratio, isometric handgrip test, and cold pressor test. Statistical analysis was performed using appropriate parametric and non-parametric tests, with $p < 0.05$ considered significant.
**Results**: The study group demonstrated significantly higher resting heart rate, reduced HRV indices (SDNN, RMSSD, HF power), and elevated LF/HF ratio compared to controls ($p < 0.05$). Parasympathetic function tests showed reduced E:I ratio, Valsalva ratio, and 30:15 ratio in the study group. Sympathetic reactivity was significantly increased, as evidenced by exaggerated blood pressure responses to isometric handgrip and cold pressor tests.
**Conclusion**: Normotensive offspring of hypertensive parents exhibit early autonomic dysfunction characterized by sympathetic predominance and reduced parasympathetic activity. These alterations may represent early markers of future hypertension and highlight the importance of preventive strategies in high-risk individuals.

***Keywords:*** Autonomic dysfunction; Hypertension; Offspring; Heart rate variability; Sympathovagal imbalance; Cardiovascular reflex tests.

## INTRODUCTION

Hypertension is a major non-communicable disease and a leading contributor to global cardiovascular morbidity and mortality. It is strongly associated with coronary artery disease, stroke, heart failure, and chronic kidney disease. According to global epidemiological estimates, more than one billion adults are affected worldwide, and the burden continues to increase, particularly in low- and middle-income countries undergoing rapid lifestyle transitions[1]. Despite improvements in therapeutic strategies, the prevalence of hypertension remains high, emphasizing the importance of identifying individuals at increased risk before the development of sustained elevation of blood pressure.

Essential hypertension constitutes nearly 90–95% of all hypertensive cases and results from a multifactorial interaction between genetic predisposition and environmental influences[2]. Familial clustering of hypertension has been consistently demonstrated, and individuals with one or both hypertensive parents have a significantly higher probability of developing hypertension later in life[3]. Studies indicate that normotensive offspring of hypertensive parents exhibit early physiological alterations even when their resting blood pressure falls within the normal range. These subclinical changes may represent the initial stage in the progression toward overt hypertension.

Among the various mechanisms implicated in the pathogenesis of essential hypertension, dysregulation of the autonomic nervous system (ANS) has gained considerable attention. The ANS plays a central role in cardiovascular homeostasis by modulating heart rate, myocardial contractility, and vascular tone through balanced sympathetic and parasympathetic activity. Persistent sympathetic overactivity can increase cardiac output, enhance peripheral vascular resistance, promote renal sodium retention, and induce vascular remodeling—all of which contribute to sustained blood pressure elevation[4]. In contrast, adequate parasympathetic (vagal) activity exerts protective cardiovascular effects by maintaining heart rate variability and modulating baroreflex sensitivity.

Emerging evidence suggests that autonomic imbalance, characterized by sympathetic predominance and vagal withdrawal, may precede the clinical onset of hypertension[5]. Normotensive individuals with a positive family history often demonstrate exaggerated cardiovascular responses to stress and reduced baroreceptor sensitivity compared to those without such history. These findings support the hypothesis that inherited differences in neural cardiovascular regulation may contribute to future hypertensive risk.

Non-invasive autonomic function tests provide practical and reliable methods for assessing cardiovascular autonomic regulation. Standardized cardiovascular reflex tests described by Ewing and Clarke evaluate parasympathetic function through heart rate responses to deep breathing, Valsalva maneuver, and postural change, while sympathetic function is assessed through blood pressure responses to isometric handgrip and cold pressor tests[6]. Additionally, heart rate variability (HRV) analysis has emerged as a sensitive tool to quantify sympathovagal balance. Reduced high-frequency (HF) power, elevated low-frequency (LF) power, and an increased LF/HF ratio indicate sympathetic dominance and reduced vagal modulation[7]. Alterations in HRV parameters have been observed in individuals at increased cardiovascular risk, including normotensive offspring of hypertensive parents.

Identifying early autonomic disturbances in genetically predisposed individuals has significant preventive implications. Detection of sympathetic overactivity at a preclinical stage allows implementation of non-pharmacological interventions such as regular physical activity, dietary modification, stress management, and weight control. Such measures may delay or prevent the transition from normotension to established hypertension.

Although autonomic dysfunction in established hypertension has been widely studied, data focusing specifically on normotensive offspring of hypertensive parents remain comparatively limited, particularly among young adults. Understanding early autonomic alterations in this population may help clarify the pathophysiological pathway linking familial predisposition to future hypertension. Therefore, the present study aims to assess autonomic function in normotensive offspring of hypertensive parents and to compare these findings with those of age- and sex-matched offspring of normotensive parents.

## MATERIALS AND METHODS:

### Study Design and Ethical Approval

This cross-sectional comparative study was conducted in the Department of Physiology at a tertiary care teaching institution over a period of 6 months. The study protocol was approved by the Institutional Ethics Committee prior to initiation. All procedures were carried out in accordance with the ethical principles of biomedical research involving human participants as outlined in the Declaration of Helsinki[8]. Written informed consent was obtained from all participants before enrollment.

### Study Population

A total of 100 apparently healthy young adults aged 18–25 years were enrolled in the study. Participants were categorized into two groups:

- **Study Group (n = 50):** Normotensive offspring of hypertensive parents (at least one parent diagnosed with essential hypertension or receiving antihypertensive therapy).
- **Control Group (n = 50):** Normotensive offspring of normotensive parents (no documented history of hypertension in either parent).

Familial predisposition has been recognized as a significant determinant of future hypertension risk[9]. Parental history was confirmed through medical records or documented treatment history wherever available.

**Inclusion Criteria**

- Age between 18 and 25 years
- Resting systolic blood pressure <120 mmHg and diastolic blood pressure <80 mmHg as per ACC/AHA guidelines[10]
- Body Mass Index (BMI) between 18.5–24.9 kg/m² according to WHO classification[11]
- Apparently healthy individuals without chronic systemic illness

**Exclusion Criteria**

- Known hypertension, diabetes mellitus, thyroid disorders, or cardiovascular disease
- Obesity (BMI ≥30 kg/m²)[11]
- History of smoking, alcohol consumption, or substance abuse
- Use of medications affecting autonomic function (e.g., beta-blockers, antidepressants)
- Acute illness within the past two weeks

**Sample Size Estimation**

Sample size calculation was based on previous studies evaluating autonomic parameters in offspring of hypertensive parents[12]. With a confidence level of 95%, statistical power of 80%, and an anticipated moderate effect size in HRV indices, the minimum required sample size was calculated as 45 per group. To compensate for potential dropouts, 50 participants were included in each group.

**Pre-Test Preparation and Standardization**

Participants were instructed to abstain from caffeine, nicotine, and heavy meals for at least 3 hours before testing. Vigorous physical activity was avoided for 24 hours prior to assessment. All autonomic function tests were conducted between 9:00 AM and 12:00 noon in a quiet, temperature-controlled laboratory (22–24°C) to minimize circadian variation in autonomic parameters[13]. Subjects rested in the supine position for 15 minutes before recordings.

**Anthropometric Measurements**

- Height was measured using a standardized stadiometer to the nearest 0.1 cm, and body weight was recorded using a calibrated digital weighing scale to the nearest 0.1 kg. BMI was calculated as:
- $BMI = Weight(kg)/Height(m)^2$
- BMI categorization followed WHO recommendations[11].

**Blood Pressure Measurement**

Blood pressure was recorded using a validated automated sphygmomanometer following standard protocol[10]. Measurements were taken after 5 minutes of seated rest. Three readings were recorded at 5-minute intervals, and the average of the last two readings was considered for analysis.

**Assessment of Autonomic Function**

Autonomic function was evaluated using standardized cardiovascular reflex tests described by Ewing and Clarke[14] and heart rate variability (HRV) analysis according to international Task Force guidelines[15].

**A. Parasympathetic Function Tests**

1**. Resting Heart Rate**

Resting heart rate was recorded from a standard Lead II ECG after 15 minutes of supine rest[14].

2. **Heart Rate Variability (HRV)**

A 5-minute resting ECG was recorded and analyzed using computerized HRV software. HRV parameters were interpreted according to the recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology[15].

**Time Domain Parameters:**

- SDNN
- RMSSD

**Frequency Domain Parameters:**

- Low Frequency (LF: 0.04–0.15 Hz)

- High Frequency (HF: 0.15–0.40 Hz)
- LF/HF ratio

HF power was considered a marker of parasympathetic modulation, whereas LF/HF ratio reflected sympathovagal balance[15].

**3. Deep Breathing Test (E:I Ratio)**

Participants performed deep breathing at six breaths per minute. The ratio of longest RR interval during expiration to shortest RR interval during inspiration (E:I ratio) was calculated[14].

**4. Valsalva Maneuver**

Participants exhaled into a mouthpiece connected to a manometer and maintained 40 mmHg pressure for 15 seconds. The Valsalva ratio was computed as:
Longest RR interval after maneuver / Shortest RR interval during maneuver[14].

**5. 30:15 Ratio (Immediate Heart Rate Response to Standing)**

The ratio of RR interval at the 30th beat to that at the 15th beat after standing from supine position was calculated[14].

**B. Sympathetic Function Tests**

**1. Isometric Handgrip Test**

Participants performed sustained handgrip at 30% of maximum voluntary contraction for 3 minutes using a handgrip dynamometer. The increase in diastolic blood pressure during the final minute was recorded[14].

**2. Cold Pressor Test**

The non-dominant hand was immersed in cold water (4–6°C) for 1 minute. Blood pressure was recorded before immersion and during the test. The maximum rise in systolic and diastolic blood pressure was noted[14].

**Statistical Analysis**

Data were analyzed using SPSS version 20.0 Continuous variables were expressed as mean ± standard deviation. After assessing normality using the Shapiro–Wilk test, normally distributed variables were compared using the independent Student's *t*-test, while non-normally distributed variables were analyzed using the Mann–Whitney *U* test. Categorical variables were presented as frequencies and percentages and analyzed using the Chi-square test. A p-value $< 0.05$ was considered statistically significant.

**RESULTS:**

A total of 100 participants were included in the study, with 50 subjects in each group. Both groups were comparable with respect to age, gender distribution, and body mass index (BMI), ensuring that differences in autonomic parameters were not influenced by baseline demographic variables.

There was no statistically significant difference between the study and control groups regarding age, BMI, resting systolic blood pressure (SBP), and diastolic blood pressure (DBP) ($p > 0.05$). However, resting heart rate was significantly higher in normotensive offspring of hypertensive parents, suggesting early autonomic imbalance as shown in table 1.

**Table 1: Comparison of Baseline Characteristics Between Groups**

| Parameter | Control Group (n=50) Mean ± SD | Study Group (n=50) Mean ± SD | p-value |
|---|---|---|---|
| Age (years) | 20.8 ± 1.9 | 21.1 ± 2.0 | 0.48 |
| BMI (kg/m²) | 22.1 ± 1.8 | 22.4 ± 2.1 | 0.36 |
| Resting SBP (mmHg) | 112.4 ± 6.2 | 114.1 ± 5.8 | 0.17 |
| Resting DBP (mmHg) | 72.6 ± 4.8 | 74.2 ± 5.1 | 0.11 |
| Resting Heart Rate (beats/min) | 72.8 ± 6.4 | 78.6 ± 7.1 | **0.001*** |

*Statistically significant

Time-domain HRV parameters showed reduced parasympathetic activity in the study group. SDNN and RMSSD values were significantly lower among offspring of hypertensive parents, indicating reduced vagal modulation as shown in table 2

**Table 2: Comparison of HRV Time Domain Parameters**

| Parameter | Control Group Mean ± SD | Study Group Mean ± SD | p-value |
|---|---|---|---|
| SDNN (ms) | 52.4 ± 10.6 | 41.8 ± 9.3 | **0.001*** |
| RMSSD (ms) | 46.2 ± 8.9 | 34.5 ± 7.6 | **0.001*** |

Frequency-domain analysis revealed significantly reduced HF power and elevated LF/HF ratio in the study group, indicating sympathetic predominance and sympathovagal imbalance. LF power was mildly increased but not statistically significant as shown in table 3.

**Table 3: Comparison of HRV Frequency Domain Parameters**

| Parameter | Control Group Mean ± SD | Study Group Mean ± SD | p-value |
|---|---|---|---|
| LF Power ($ms^2$) | 580 ± 140 | 640 ± 155 | 0.07 |
| HF Power ($ms^2$) | 620 ± 150 | 420 ± 120 | **0.001*** |
| LF/HF Ratio | 0.94 ± 0.28 | 1.82 ± 0.45 | **0.001*** |

Cardiovascular reflex tests assessing parasympathetic function (E:I ratio, Valsalva ratio, and 30:15 ratio) were significantly reduced in the study group, suggesting decreased vagal tone as shown in table 4.

**Table 4: Comparison of Parasympathetic Function Tests**

| Parameter | Control Group Mean ± SD | Study Group Mean ± SD | p-value |
|---|---|---|---|
| E:I Ratio | 1.32 ± 0.12 | 1.18 ± 0.10 | **0.001*** |
| Valsalva Ratio | 1.56 ± 0.18 | 1.38 ± 0.15 | **0.002*** |
| 30:15 Ratio | 1.21 ± 0.09 | 1.12 ± 0.08 | **0.001*** |

Blood pressure response to isometric handgrip and cold pressor test was significantly exaggerated in the study group. The rise in diastolic blood pressure during handgrip and both systolic and diastolic pressures during cold pressor test were higher among offspring of hypertensive parents, indicating heightened sympathetic reactivity as shown in table 5.

**Table 5: Comparison of Sympathetic Function Tests**

| Parameter | Control Group Mean ± SD | Study Group Mean ± SD | p-value |
|---|---|---|---|
| Rise in DBP during Handgrip (mmHg) | 14.2 ± 3.6 | 20.8 ± 4.2 | **0.001*** |
| Rise in SBP during CPT (mmHg) | 12.4 ± 4.1 | 19.6 ± 5.0 | **0.001*** |
| Rise in DBP during CPT (mmHg) | 10.8 ± 3.8 | 17.9 ± 4.6 | **0.001*** |

**DISCUSSION:**

The present study evaluated autonomic function in normotensive offspring of hypertensive parents and demonstrated significant autonomic imbalance characterized by increased sympathetic activity and reduced parasympathetic modulation. Although resting blood pressure values were within normal limits in both groups, offspring of hypertensive parents exhibited higher resting heart rate, altered heart rate variability indices, diminished parasympathetic reflex responses, and exaggerated sympathetic reactivity. These findings support the concept that autonomic dysregulation precedes the clinical onset of hypertension.

Resting heart rate was significantly higher in the study group, suggesting enhanced basal sympathetic tone or reduced vagal influence. Elevated resting heart rate has been recognized as an early marker of cardiovascular risk and is associated with increased sympathetic nervous system activity[16]. Previous studies have reported similar findings in normotensive individuals with positive family history of hypertension, indicating that autonomic imbalance may be inherited or genetically influenced[17].

Heart rate variability (HRV) analysis in the present study revealed significantly reduced SDNN and RMSSD values in offspring of hypertensive parents. These parameters reflect overall variability and short-term vagal modulation of heart rate, respectively. Reduced HRV is considered a marker of impaired autonomic regulation and has been associated with increased cardiovascular risk[18]. Frequency-domain analysis further demonstrated reduced high-frequency (HF) power and significantly elevated LF/HF ratio, indicating sympathovagal imbalance with sympathetic predominance. Similar

observations were reported by other investigators who documented reduced parasympathetic activity and increased sympathetic dominance in young normotensive offspring of hypertensive individuals[19].

The parasympathetic cardiovascular reflex tests (E:I ratio, Valsalva ratio, and 30:15 ratio) were significantly lower in the study group, indicating reduced vagal tone. These tests primarily assess cardiac parasympathetic integrity through baroreceptor-mediated reflex pathways. Impaired parasympathetic function may reduce the buffering capacity of the cardiovascular system against stress-induced blood pressure fluctuations[20]. Early vagal withdrawal may therefore represent a crucial mechanism in the progression toward sustained hypertension.

Sympathetic function tests in the present study revealed exaggerated blood pressure response to isometric handgrip and cold pressor tests among offspring of hypertensive parents. The isometric handgrip test increases blood pressure through sustained muscle contraction and activation of sympathetic efferents, while the cold pressor test stimulates sympathetic outflow via nociceptive pathways[21]. Heightened pressor response in the study group suggests hyper-reactive sympathetic vasomotor control. Similar exaggerated sympathetic responses have been documented in normotensive individuals with familial predisposition to hypertension[22].

The pathophysiological basis of these findings may involve genetic factors influencing central sympathetic regulation, altered baroreceptor sensitivity, enhanced vascular responsiveness to catecholamines, and early endothelial dysfunction[23]. Increased sympathetic tone can lead to structural vascular changes, increased peripheral resistance, and progressive elevation of blood pressure over time. Reduced parasympathetic activity further diminishes cardioprotective effects, thereby amplifying cardiovascular risk.

Importantly, these autonomic alterations were observed despite normal resting blood pressure values, indicating that autonomic dysfunction may be an early subclinical marker rather than a consequence of established hypertension. Identification of such early changes provides a window of opportunity for preventive interventions. Regular physical activity, weight management, stress reduction, and dietary modification have been shown to improve autonomic balance and reduce sympathetic overactivity[24].

The findings of this study are consistent with the hypothesis that essential hypertension may originate from inherited abnormalities in neural cardiovascular regulation. Longitudinal follow-up of such high-risk individuals may help determine whether these autonomic changes predict future development of sustained hypertension.

## CONCLUSION:

Normotensive offspring of hypertensive parents exhibit significant autonomic imbalance despite having normal blood pressure. Reduced heart rate variability and exaggerated sympathetic responses indicate early sympathovagal dysregulation in this high-risk group. These findings suggest that autonomic dysfunction may precede the development of clinical hypertension. Early identification and lifestyle interventions may help delay or prevent future hypertension.

## REFERENCES:


1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005;365(9455):217–223.
2. Carretero OA, Oparil S. Essential hypertension. Circulation. 2000;101(3):329–335.
3. Ehret GB, Caulfield MJ. Genes for blood pressure: an opportunity to understand hypertension. Eur Heart J. 2013;34(13):951–961.
4. Grassi G, Seravalle G, Quarti-Trevano F. The sympathetic nervous system and hypertension. Circ Res. 2015;116(6):976–990.
5. Pal GK, Adithan C, Ananthanarayanan PH, et al. Sympathovagal imbalance in offspring of hypertensive parents. Indian J Physiol Pharmacol. 2001;45(4):449–454.
6. Ewing DJ, Clarke BF. Diagnosis and management of autonomic neuropathy. Br Med J. 1982;285:916–918.
7. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996;93(5):1043–1065.
8. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–2194.
9. Ehret GB, Caulfield MJ. Genes for blood pressure: an opportunity to understand hypertension. Eur Heart J. 2013;34(13):951–961.
10. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA guideline for prevention, detection, evaluation, and management of high blood pressure in adults. Hypertension. 2018;71(6):e13–e115.
11. World Health Organization. Obesity: preventing and managing the global epidemic. WHO Technical Report Series 894. Geneva: WHO; 2000.

12. Pal GK, Adithan C, Ananthanarayanan PH, et al. Sympathovagal imbalance in offspring of hypertensive parents. Indian J Physiol Pharmacol. 2001;45(4):449–454.
13. Malik M. Heart rate variability: standards of measurement and interpretation. Ann Noninvasive Electrocardiol. 1996;1(2):151–181.
14. Ewing DJ, Clarke BF. Diagnosis and management of autonomic neuropathy. Br Med J. 1982;285:916–918.
15. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996;93(5):1043–1065.
16. Palatini P. Elevated heart rate as a predictor of increased cardiovascular morbidity. J Hypertens. 1999;17(3):S3–S10.
17. Wu JS, Lu FH, Yang YC, et al. Sympathetic hyperactivity in normotensive offspring of hypertensive parents. Am J Hypertens. 2008;21(3):347–352.
18. Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance and heart rate variability to cardiovascular disease risk factors. Int J Cardiol. 2010;141(2):122–131.
19. Pavithran P, Madanmohan, Mithun R, et al. Heart rate variability in offspring of hypertensive parents. Indian J Physiol Pharmacol. 2008;52(1):45–52.
20. Goldstein DS. The autonomic nervous system in health and disease. New York: Marcel Dekker; 2001.
21. Victor RG, Mark AL. The sympathetic nervous system in human hypertension. N Engl J Med. 2000;342(6):435–447.
22. Grassi G, Seravalle G, Dell'Oro R, et al. Sympathetic nerve traffic and hypertension. Hypertension. 1998;31(1):1–7.
23. Esler M. The sympathetic system and hypertension. Am J Hypertens. 2000;13(6 Pt 2):99S–105S.
24. Carter JB, Banister EW, Blaber AP. Effect of endurance exercise on autonomic control of heart rate. Sports Med. 2003;33(1):33–46.