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Original Research Article

A Cross-Sectional Observational Study: Effect of Insulin Resistance on Autonomic Functions of Obese Non Diabetic Healthy Males

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Abstract:

Obesity is recognized as a key contributor to insulin resistance and further lead to other non-communicable disease. This study is designed to test the relation of insulin resistance with deranged autonomic functions in obese males.

The present study is cross-sectional observational study on 70 obese males. Obese males are divided into two groups non-insulin resistant (HOMA-IR<2.5) and insulin resistant group (HOMA-IR> 2.5). Anthropometric parameters, Cardiovascular parameters, HRV (heart rate variability) and BRS (baroreflex sensitivity) were measured in these 70 males. Insulin resistant subjects showed increased resting HR (rate (78 ± 6 BPM vs. 72 ± 5 BPM; p<0.001) and elevated resting systolic and diastolic blood pressure suggesting increased sympathetic activity and reduced vagal tone. Spectral analysis of HRV showed significantly reduced low-frequency (LF) power (400.1 ± 130.2 ms² vs. 550.1 ± 150.1 ms²; p<0.001) and high-frequency (HF) power (300.2 ± 100.1 ms² vs. 400.1 ± 120.3 ms²; p=0.0003) in the IR group, indicating impaired autonomic modulation. Moreover, normalized LF (LFnu) was higher in the IR group (65.1 ± 7.2%) compared to the NIR group (60.2 ± 5.1%; p=0.0016), while HFnu was significantly lower (35.1 ± 7.3% vs. 40.2 ± 5.1%; p=0.0012. Time-domain indices such as SDNN and RMSSD were also significantly lower in the IR group (SDNN: 40.2 ± 8.2 ms vs. 50.1 ± 10.2 ms; RMSSD: 35.3 ± 7.1 ms vs. 45.2 ± 9.1 ms; both p<0.001), indicating reduced parasympathetic activity and overall variability All BRS indices—namely BRS(+) slope (7.1 ± 1.5 vs. 10.1 ± 2.2;) BRS (-) slope (6.1 ± 1.4 vs 9.2 ± 2.1) BRS Sequence All (6.5 ± 1.6 vs. 9.5 ± 2.0)were significantly reduced in the IR group.

Thus, significant inverse associations between HOMA-IR and autonomic indices highlight insulin resistance as a key contributor to autonomic dysfunction in obesity.

Keywords: HRV (heart rate variability), BRS (baroreflex sensitivity), HOMA-IR.

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Introduction

Obesity is now recognized as a key contributor to the increasing burden of noncommunicable diseases including type 2 diabetes mellitus, hypertension, and cardiovascular diseases [1,2]. Abdominal obesity, is a core component of metabolic syndrome and significantly elevates the risk of insulin resistance (IR), type 2 diabetes, dyslipidemia, hypertension, and NAFLD [3]. IR is characterized by the reduced ability of peripheral tissues, such as muscle, liver, and adipose tissue, to respond effectively to insulin, resulting in compensatory hyperinsulinemia to maintain glucose homeostasis [4]. Insulin resistance serves as an early biomarker of increased cardiovascular risk. It is linked with accelerated atherosclerosis, hypertension, myocardial dysfunction, and heart failure. Based on metabolic profiles, obese populations are broadly classified into two phenotypes: metabolically healthy obese (MHO), who maintain insulin sensitivity and a relatively lower cardiovascular risk, and metabolically unhealthy obese (MUO), characterized by pronounced insulin resistance and higher risk of cardiometabolic complications [5,6]. This dichotomy suggests that insulin resistance, rather than obesity per se, may be a superior indicator of cardiovascular risk. South Asians, including Indians, display a higher predisposition to insulin resistance even at lower BMI thresholds compared to Western populations, emphasizing the limitations of BMI as a sole risk assessment tool in this demographic [7,8] The autonomic nervous system (ANS) plays a vital role in maintaining homeostasis by regulating involuntary physiological functions. Obesity contributes to significant alterations in ANS function, particularly

through enhanced sympathetic activity and reduced parasympathetic tone, leading to what is termed ―sympathovagal imbalance‖ (SVI) [9]. Heart rate variability (HRV) is a widely used non-invasive metric to assess cardiac autonomic regulation by measuring the variability in time intervals between successive heartbeats [10]. High HRV indicates a healthy balance between sympathetic and parasympathetic activity, while reduced HRV reflects impaired parasympathetic tone and/or excessive sympathetic dominance—a hallmark of autonomic dysfunction. Obese individual exhibit significantly lower HRV compared to lean controls, even in the absence of overt cardiovascular disease [11,12]. Importantly, insulin resistance has been independently associated with reduced HRV, suggesting that metabolic disturbances intrinsic to obesity, rather than increased adiposity per se, drive autonomic imbalance [13]. This reduction in HRV is linked to increased cardiovascular risk, including arrhythmias, sudden cardiac death, and overall mortality [14]. In diabetes, baroreflex sensitivity (BRS) is markedly diminished due to autonomic nerve damage, endothelial dysfunction, and impaired central processing of baroreceptor signals [15]. Reduced BRS leads to an inability to rapidly adjust heart rate and vascular tone in response to blood pressure fluctuations, predisposing patients to orthostatic hypotension, syncope, and greater blood pressure variability [16]. Assessment of HRV and BRS provides important diagnostic and prognostic information in diabetic patients [17]. Given these considerations, our study aims to explore the impact of insulin resistance on autonomic function—specifically HRV and BRS—in young Indian adults who are overweight or obese. By comparing individuals with similar BMI but differing insulin sensitivity, we seek to delineate the cardiovascular risk posed by insulin resistance independent of obesity severity. Understanding these relationships could facilitate early identification of high-risk individuals and guide preventive strategies to reduce the burden of cardiovascular diseases in this vulnerable population.

Material and Methods

This is a hospital based single centre cross sectional observational study which was conducted in the Upgraded Department of Physiology in collaboration with the Endocrinology Department, S.M.S Medical College and Attached Hospital, Jaipur, Rajasthan in obese males from August 2023 to October 2024. The study protocol was approved by the Research and Ethic committee of SMS Medical College, Jaipur, Rajasthan, India.

Sample size calculation: Sample size was calculated at 80% study power and 0.05% α error, assuming minimum detectable mean difference 4.74 ms/mm Hg among insulin resistance in obese and non-insulin resistant obese individuals as per results of seed article. [18] At standard deviation of 6.88 ms/mm Hg BRS, minimum sample size was 33 patients in each group was calculated which was round off to 35 patients in each group.

Inclusion Criteria:

- Male individuals aged between 20 to 40 with BMI≥25kg/m2 and given informed written consent.
- For non-insulin resistance group - HOMA-IR <2.5
- For Insulin resistance group -HOMA-IR ≥2.5

Exclusion Criteria

- Subjects on any medication.
- History of smoking and/or alcoholism,
- Subjects suffering from any acute and chronic illness.
- Those performing regular athletic activities, body building exercise and yoga were also excluded

A convenient sampling technique was employed for the selection of the study sample. This method ensures that every eligible subject meeting the predefined inclusion and exclusion criteria is recruited for participation.

Digital weighing machine was used to measure the body weight of participants with precision. Along with weight measurement, a wall-mounted stadiometer was used to measure the height of each participant in a standardized manner, For the assessment of blood pressure variability and baroreflex sensitivity (BRS), Human Non-Invasive Blood Pressure (NIBP) System, Model ML 283, manufactured by AD Instruments, Australia was used. For analysis of heart rate variability (HRV) and baroreflex sensitivity (BRS), LabChart 8 software, developed by AD Instruments, Australia was used. Additionally, Nevrokard software analysis (version 6.2.0) was employed for a detailed and sophisticated analysis of BRS parameters. BMI was calculated by the data of weight and height. Fasting blood glucose (FBG) and serum insulin were measured from fasting blood samples to calculate IR. The HOMA-IR index was derived using the following formula:

(HOMA-IR = FBG (mMol) × Insulin (μIU/l)/22.5) [,19,20]

The 70 participants, based on the BMI classification of the WHO for Asian population and HOMA-IR values, were divided into following two groups:

1. Obese NIR group: Participants having BMI 25 kg/m2 or above and HOMA-IR <2.5 (n=35);
2. Obese IR group: Participants having BMI 25 kg/m2 or above and HOMA-IR ≥2.5 (n=35).

Study Procedure: Before conducting the test, the procedure was explained in detail to all participants to ensure their understanding and cooperation. The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated for each participant to classify them based on their insulin resistance status. To minimize variability and ensure standardized conditions, all participants were instructed to follow specific pre-assessment guidelines. They were advised to:

- Refrain from consuming caffeine, alcohol, or smoking at least 12 hours prior to the Test and have adequate sleep.
- Report to the Neurophysiology Laboratory between 08:00 AM and 11:00 AM for the physiological recordings.

Before the actual testing, each participant was given a 10-minute resting period in a quiet, temperature-controlled environment to allow for acclimatization to the experimental conditions.

Assessment of Baroreceptor Sensitivity (BRS) and Heart Rate Variability (HRV): The spontaneous baroreflex sensitivity and heart rate variability (HRV) test was conducted using continuous plethysmographic arterial measurements. The test was performed using a Finometer, which records spontaneous changes in systolic blood pressure (SBP) and R-R intervals through a sensor placed on the middle finger. Participants were in a supine position, and the measurements were recorded for 10 minutes during spontaneous breathing.

The recorded signals were processed using Beatscope Easy software (NEVROKARD) to calculate baroreceptor sensitivity (BRS) and HRV indices.

Observations and Result

Table 1: Comparison of Anthropometric Parameters Between Obese NIR and Obese IR Groups

Arthrometric Parameters	Obese NIR (HOMA-IR<2.5, n=35)	Obese IR (HOMA-IR ≥2.5, n=35)	P-value
Weight (kg)	85.1 ± 10.1	88.1 ± 11.3	0.2457
Height (cm)	170.3 ± 5.2	171.2 ± 6.1	0.5088
Waist Circumference (cm)	98.1 ± 8.2	102.1 ± 9.2	0.0590
BMI (kg/m²)	27.5 ± 3.9	29.2 ± 4.1	0.08

Table 2: Comparison of cardiovascular parameters between Obese NIR and Obese IR Groups

Cardiovascular Parameter	Obese NIR (HOMA IR <2.5), N=35	Obese IR (HOMA IR >2.5), N=35	P value
Resting heart rate (BPM)	72±5.1	78 ±6	<0.001
Resting SBP (mmHg)	120 ± 10	130±12	0.0004
Resting DBP (mm Hg)	80.1±8.2	85.1±9.1	0.0184

Table 3: Comparison of HRV parameters between Obese NIR and Obese IR Groups

HRV Parameter	Obese NIR (HOMA IR <2.5), N=35	Obese IR (HOMA IR >2.5), N=35	P value
LF Power (ms²)	550.1±150.1	400.1±130.2	<0.001
HF Power (ms²)	400.1±120.3	300.2±100.1	0.0003
LFnu (%)	60.2±5.1	65.1±7.2	0.0016
HFnu (%)	40.2±5.1	35.1±7.3	0.0012
SDNN (ms)	50.1±10.2	40.2±8.2	<0.001
RMSSD (ms)	45.2±9.1	35.3±7.1	<0.001

Table 4: Comparison of Baroreflex Sensitivity (BRS) Parameters between Obese NIR and Obese IR Groups

BRS Parameter	Obese NIR (HOMA IR <2.5), N=35	Obese IR (HOMA IR >2.5), N=35	P value
BRS (+) Slope	10.1 ± 2.2	7.1 ± 1.5	<0.001
BRS (-) Slope	9.2 ± 2.1	6.1 ± 1.4	<0.001
BRS Sequence All	9.5 ± 2.0	6.5 ± 1.6	<0.001

Discussion

This cross-sectional study was conducted from August 2023 to October 2024 in the Upgraded Department of Physiology in collaboration with the Endocrinology Department, S.M.S. Medical College and Attached Hospital, Jaipur, Rajasthan, to investigate metabolic parameters in obese males. A total of 70 participants were categorized based on insulin resistance status using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) into two groups. The mean age of the obese

non-insulin-resistant (NIR) group (HOMA-IR <2.5; n=35) was 42.5 ± 8.3 years, while that of the insulin-resistant (IR) group (HOMA-IR ≥2.5; n=35) was 43.2 ± 7.1 years, with no statistically significant difference (p=0.706). The mean BMI of the insulin-resistant (IR) group (HOMA-IR ≥ 2.5) was 29.2 ± 4.1 kg/m², and of non-insulin-resistant (NIR) group (HOMA-IR < 2.5), was 27.5 ± 3.9 kg/m² (p=0.08), showing no statistically difference. The finding of no significant statistically difference of age and BMI between both groups shows that both groups were age and BMI matched. This is necessary as HRV and BRS parameters are affected by age and BMI. [21]

In our study, the IR group demonstrated a significantly higher resting heart rate (78 ± 6 BPM vs. 72 ± 5 BPM; p<0.001) significantly elevated resting systolic blood pressure (130 ± 12 mmHg vs. 120 ± 10 mmHg; p=0.0004), and significantly elevated resting diastolic blood pressure (85.1±9.1 mmHg vs 80.1±8.2mmHg; p value=0.018) suggesting increased sympathetic activity and reduced vagal tone. Spectral analysis of HRV showed significantly reduced low-frequency (LF) power (400.1 ± 130.2 ms² vs. 550.1 ± 150.1 ms²; p<0.001) and high-frequency (HF) power (300.2 ± 100.1 ms² vs. 400.1 ± 120.3 ms²; p=0.0003) in the IR group, indicating impaired autonomic modulation. Moreover, normalized LF (LFnu) was higher in the IR group (65.1 ± 7.2%) compared to the NIR group (60.2 ± 5.1%; p=0.0016), while HFnu was significantly lower (35.1 ± 7.3% vs. 40.2 ± 5.1%; p=0.0012) suggesting impaired autonomic function with sympathovagal balance tilting towards increased sympathetic activity. Time-domain indices such as SDNN and RMSSD were also significantly lower in the IR group (SDNN: 40.2 ± 8.2 ms vs. 50.1 ± 10.2 ms; RMSSD: 35.3 ± 7.1 ms vs. 45.2 ± 9.1 ms; both p<0.001), indicating reduced parasympathetic activity. These findings are consistent with previous evidence that insulin resistance is associated with sympathetic overactivity and vagal withdrawal, contributing to cardiovascular dysregulation [22] Chronic hyperinsulinemia has been shown to activate the sympathetic nervous system via central and peripheral mechanisms, leading to elevated heart rate and blood pressure, while reducing baroreflex sensitivity and parasympathetic tone [23] Reduced HRV parameters such as SDNN and RMSSD are independent predictors of cardiovascular morbidity and mortality and autonomic dysfunction, even in the absence of overt diabetes or established cardiovascular disease [24]. In the Indian context, where metabolic syndrome and insulin resistance are prevalent at lower BMI thresholds, the evaluation of HRV can serve as an important, non-invasive tool for early risk stratification.

In the present study, baroreflex sensitivity (BRS) was significantly impaired in obese individuals with insulin resistance (IR) compared to those without (NIR). All BRS indices—namely BRS (+) slope (7.1 ± 1.5 vs. 10.1 ± 2.2) BRS (-) slope (6.1 ± 1.4 vs9.2 ± 2.1); BRS sequence all (6.5 ± 1.6 vs. 9.5 ± 2.0); p<0.001)—were significantly reduced in the IR group. This reduction reflects blunted autonomic modulation of heart rate in response to blood pressure fluctuations. Baroreflex sensitivity is a critical physiological mechanism for short-term blood pressure regulation, mediated through the autonomic nervous system. Lower BRS values indicate impaired reflex control, favouring sympathetic predominance and reduced parasympathetic tone [25] in obese individuals with insulin resistance, chronic hyperinsulinemia has been shown to alter baroreceptor function through vascular stiffness, endothelial dysfunction, and autonomic dysregulation [26]. Our findings are in line with previous research showing a significant inverse relationship between insulin resistance and BRS [27]. Insulin resistance contributes to arterial stiffness and endothelial damage, which reduce the mechanical transduction of arterial wall stretch to baroreceptor afferents, thus impairing reflex sensitivity. Furthermore, sympathetic overdrive, which accompanies IR, may lead to desensitization of the baroreflex loop, creating a vicious cycle of autonomic imbalance and metabolic derangement. Lowered BRS has been identified as an early marker of cardiovascular risk, even in asymptomatic obese individuals, and has been associated with increased incidence of arrhythmias, sudden cardiac death, and progression to overt hypertension [28]. Importantly, our study shows that BRS reduction is evident even in relatively young or normotensive obese individuals with IR, underlining the subclinical cardiovascular dysregulation linked to metabolic status. This supports the notion that assessing BRS along with HRV can provide a more comprehensive picture of autonomic cardiovascular control and early risk in insulin-resistant individuals. Interventions such as aerobic exercise, weight loss, and insulin sensitizers have shown promise in improving BRS and HRV, thereby reducing long-term cardiovascular risk [29]

Conclusion

This study demonstrates that obese individuals with insulin resistance (IR) exhibit significantly impaired autonomic function, as evidenced by reduced heart rate variability (HRV) and baroreflex sensitivity (BRS), compared to their non-insulin resistant (NIR) counterparts. These changes are accompanied by higher resting heart rate and blood pressure, and early signs of cardiovascular dysregulation. The significant inverse associations between HOMA-IR and autonomic indices

highlight insulin resistance as a key contributor to autonomic dysfunction in obesity. These findings underscore the need for early identification and management of IR to prevent cardiovascular and metabolic complications, with HRV and BRS serving as valuable non-invasive markers for risk assessment.

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