RESEARCH PAPER

TO STUDY CORRELATION BETWEEN HEART RATE VARIABILITY AND INTERLEUKIN 6 IN CLASS 2 AND CLASS 3 OBESE INDIVIDUALS

Dr. Mitesh Sutariya[1], Dr. Rajesh J. Khyalappa[2]

[1]Junior Resident, Department of General Medicine, D.Y. Patil Medical College, Kolhapur, Maharashtra, India, D. Y Patil Education Society (Deemed to be University) Kolhapur

[2]Dean and Professor, Department of General Medicine, D.Y. Patil Medical College, Kolhapur, Maharashtra, India, D.Y Patil Education Society (Deemed to be University) Kolhapur

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ABSTRACT

Background: Obesity is a major global health concern associated with chronic low-grade inflammation, autonomic nervous system dysfunction, and increased cardiovascular risk. Interleukin-6 (IL-6), a pro-inflammatory cytokine secreted by adipose tissue, plays a crucial role in obesity-related metabolic and cardiovascular abnormalities. Heart Rate Variability (HRV) is a non-invasive marker of autonomic nervous system activity and provides insight into cardiovascular regulation. The relationship between inflammatory markers and autonomic dysfunction in severe obesity remains inadequately explored.

Objectives: To evaluate the correlation between serum IL-6 levels and HRV parameters in individuals with WHO Class II and Class III obesity and to assess the impact of obesity severity on inflammatory and autonomic function.

Methods: This cross-sectional observational study was conducted among adults with Class II obesity (BMI 35–<40 kg/m²) and Class III obesity (BMI ≥40 kg/m²) attending the outpatient and inpatient departments of a tertiary care teaching hospital. Anthropometric measurements, serum IL-6 levels, and HRV parameters were assessed. IL-6 was measured using enzyme-linked immunosorbent assay (ELISA). HRV analysis included time-domain parameters (SDNN, RMSSD, pNN50) and frequency-domain parameters (LF, HF, VLF, LF/HF ratio). Correlation and regression analyses were performed to evaluate associations among study variables.

Results: BMI demonstrated a strong positive correlation with IL-6 ($r = 0.725$, $p < 0.001$) and a negative correlation with SDNN ($r = -0.41$). Class III obese individuals exhibited significantly higher IL-6 levels and lower SDNN values compared to Class II obese individuals, indicating greater inflammatory burden and autonomic dysfunction. IL-6 showed an inverse relationship with HRV indices, particularly SDNN, suggesting that increasing systemic inflammation is associated with reduced cardiac autonomic regulation. Frequency-domain parameters showed less consistent associations with obesity severity.

Conclusion: Severe obesity is associated with elevated systemic inflammation and impaired autonomic function. Serum IL-6 levels correlate inversely with HRV, particularly SDNN, supporting the link between inflammatory activation and autonomic dysregulation. Combined assessment of IL-6 and HRV may serve as a useful approach for identifying obese individuals at increased cardiometabolic risk.

Keywords: Obesity; Interleukin-6; Heart Rate Variability; SDNN; Autonomic Dysfunction; Inflammation; Cardiometabolic Risk.

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INTRODUCTION

Obesity has become an international public health crisis in the modern era. Adipose tissue accumulates excessively and negatively characterises this condition affects metabolic, cardiovascular, and endocrine functions. The global prevalence of Due to urbanization, bad eating habits, and sedentary lifestyles, obesity has surged in recent decades. Obesity is now understood to be more than just being overweight; it is a complicated metabolic disorder involving endocrine, inflammatory, and autonomic nervous system dysregulation. Particularly, individuals with severe obesity, categorized as more levels Obesity falls into two categories: class II (BMI 35–39.9 kg/m²) and class III (BMI 40 kg/m²). or more) are characterized by metabolic abnormalities and cardiovascular risk factors when compared with individuals having mild or moderate obesity [2].

One of the key mechanisms underlying systemic inflammation that persists over time and is associated with obesity. In recent years, adipokines and cytokines—a class of bioactive compounds released by fat cells—have gained recognition as an active endocrine organ. When fat accumulates in the body, it goes through a series of structural and functional changes characterized by infiltration of inflammatory macrophages and increased

Author for Correspondence: Dr. Mitesh Sutariya

generation of cytokines that promote inflammation [3]. The significance of interleukin-6 (IL-6) in both inflammation and metabolic control has led to much research into this inflammatory mediator. A wide variety of Inflammatory cytokine Endothelial cells, fibroblasts, adipocytes, macrophages, and several other cell types release IL-6. T lymphocytes. In immunological reactions, it plays a role, inflammation, and metabolic regulation by influencing glucose pathways for glucose, lipid, and insulin signalling [4].

Nearly 25% of the circulating IL-6 originates from obesity-related elevations in circulating IL-6 levels are mostly attributable to fat tissue. Interconnected with high blood pressure, diabetes, insulin resistance, and metabolic syndrome IL-6 secretion by adipose tissue which in turn leads to systemic inflammation [5]. Research demonstrates that people who are overweight show doubled IL-6 expression in their subcutaneous fat tissues which proves that obesity increases their production of IL-6 and their activation of inflammatory pathways. The research demonstrates that higher IL-6 levels indicate an increased risk of death and disability from cardiovascular disease which highlights the importance of inflammatory markers for studying obesity-related health issues.

Another important physiological system affected by obesity is the ANS, which oversees control of pulse and blood pressure, and homeostasis by balancing parasympathetic and sympathetic nervous system activity. Vital metabolic processes, vascular tone, the autonomic nerve system regulates pulse and systolic blood pressure. Owing to an autonomic imbalance, parasympathetic activity decreases while sympathetic activity rises in obese people. Cardiovascular disease, arrhythmias, and high blood pressure are all exacerbated in obese people by this autonomic dysregulation [6].

People use heart rate variability (HRV) as a non-invasive method to track autonomic nervous system activities which has gained popularity among users. The measurement of HRV represents how the sinoatrial node interacts with both SANS and parasympathetic nervous systems through its assessment of heartbeat interval variations. HRV analysis provides essential data about how the heart regulates its autonomic functions and maintains its balance between sympathetic and parasympathetic systems. Researchers assess HRV parameters through various frequency indexes such as LF and LF/HF ratio and time measurement indexes which include SDNN and RMSSD and pNN50 [7]. The existence of reduced HRV indicates that autonomic dysfunction has developed while people experience systemic inflammation and metabolic disorders and cardiovascular disease.

Research shows that several obesity conditions create a direct link to decreased heart rate variability which results from disrupted cardiac autonomic regulation. Excess body fat causes two main effects which include increased sympathetic activity and reduced parasympathetic activity to create cardiovascular disease risk factors that affect people with overweight status [2,3]. Adipose tissue releases inflammatory mediators which include IL-6 that can affect autonomic nervous system function and change heart rate variability patterns. The research demonstrates that inflammatory cytokines affect neurohumoral systems which control heart automatic functions [6]. The interaction between The development of inflammation and autonomic dysfunction might be significant contributors to obesity-related cardiovascular complications.

The research indicates that existing studies show a potential link between inflammatory markers and heart rate variability. The researchers established a connection between higher IL-6 levels and lower HRV values, which indicates that systemic inflammation interferes with the body's automatic functions [6]. However, most available studies have examined these relationships in general populations or individuals with metabolic disorders, while limited data are available specifically in individuals with severe obesity.

The connection between neurotransmitters and autonomic nervous system functions, which researchers assess through HRV measurements, serves as a valuable tool for detecting cardiovascular risk in obese patients. The advanced stages of Class II and Class III obesity show higher metabolic and inflammatory disturbances than other stages of adiposity. The research team will study HRV and IL-6 levels because it will help them understand how inflammation connects to autonomic failure in these individuals. The research results will help detect cardiovascular risk at an early stage and will improve both preventive and therapeutic medical approaches.

Therefore, this study's overarching goal is to assess the relationship between class II and class III obesity and heart rate variability and interleukin-6 levels. Looking into the connection between using HRV, a non-invasive indicator of autonomic nervous system obesity-related cardiovascular risk can help shed light on its relevance inflammatory cytokines autonomic dysfunction in severely obese individuals.

MATERIALS AND METHODS

A Cross-sectional Observational study conducted at both the Outpatient and Inpatient Departments of Dr. D.Y. Patil Medical College, Hospital, and Research Institute, Kolhapur. Study was started after approval of Research & Ethics committee. All study subjects were selected according to inclusion and exclusion criteria.

Inclusion Criteria: Individuals with Class II obesity (BMI35to<40kg/m²)Individuals with ClassIIIobesity(BMI≥40kg/m²)Participants of either gender

Exclusion Criteria: Historyofbeta-blockeroranti-arrhythmicdruguseAnyacuteinfectionoruseofanti-inflammatorydrugs Symptoms of heart failure, stroke, arrhythmias, thyroid issues, severe asthma, diabetes, liver illness, kidney disease, or cerebrovascular disease Current

drug or alcohol abuse Refusal to provide informed written consent

METHODOLOGY

Patients Utilyzing measures of height and weight, individuals were categorized into two groups:

Obesity categorized asClass III (BMI 40 kg/m² and above) and Class II (BMI 35–<40 kg/m²). This study, we included participants who met all of our inclusion and exclusion criteria.

For each participant, Heart rate variability characteristics and interleukin-6 levels were measured, and the correlation between the two was investigated parameters was evaluated.

Class II and Class III obese patients visiting the outpatient and inpatient departments of the Department of General Medicine were recruited for the study. Each subject was first evaluated using a comprehensive clinical history, physical examination, and systemic evaluation as inclusion and exclusion criteria.

BMI Measurement

Metabolic rate (BMR) was determined using the formula weight/height squared. In light of BMI values, participants were classified into the appropriate obesity categories.

Interleukin-6 Measurement

The researchers collected a venous blood sample from each participant at 6:00 AM during their fasting period.

Heart Rate Variability (HRV) Analysis

The researchers conducted heart rate measurements between 8:00 and 10:00 in the morning when participants remained seated to reduce natural daily variations in their heart rate and heart rate variability. The GMS diabetic risk profile machine and KODYS 50 Hz cardiac autonomic neuropathy analyzer were used to record HRV parameters.

Frequency Domain Analysis of HRV

In the low-frequency (LF) region of 0.04-0.15 Hz and the high-frequency (HF) range of 0.15-0.40 Hz, the normalised power spectral density function was integrated to get the spectral power. As a proxy for sympathovagal balance, we determined the ratio of LF to HF abundance.

Time Domain Analysis of HRV

While the research was underway, domain analysis of HRV was computed using R-R intervals. So that we can do the math, we needed 100 consecutive regular R-R intervals. We omitted extrasystoles when the change was more than 25% from the previous period.

RESULT

Age Statistics

The researchers discovered that their subjects had a broad age range because they used Pearson's correlation analysis to examine the relationship between IL-6 levels and HRV measurements. The researchers established their statistical significance threshold at p-values which fell below 0.05. The median age of the participants reached 39 years because their ages extended from 24 to 75 years. The research findings demonstrate that the study group contained participants of all adult age ranges, while most subjects showed concentration in the early middle age group.

Gender Frequency

The total number of participants in the study was 45, which included 26 male participants and 19 female participants. The study results showed that more males than females participated in the research. The gender distribution shows representation of both sexes, with males constituting the larger share of the enrolled obese individuals who completed the study.

Weight Statistics

The subjects' average weight was 106.25 kg and their standard deviation was 12.95 kg which showed that body weight among subjects experienced some variation. The median weight was 106 kg which was very close to the mean. The minimum recorded weight was 83 kg and the maximum was 137 kg which showed that participants had a wide range of body weights.

Table 1: BMI Stats

Variable	Mean	SD	Median	Min	Max

Height Statistics

The average height of participants in the study measured 1.67 meters with a standard deviation of 1.67 meters which showed low height variance among participants. The median height of the study group recorded 1.67 meters which equaled the average height of the group. The study group showed a narrow height range between their minimum height of 1.53 meters and maximum height of 1.79 meters.

BMI Statistics

The subjects had an average body mass index of 37.96 kg/m² which showed a standard deviation of 2.69 kg/m² because most measurements fell between the severe obesity boundary. The median BMI was 37.03 kg/m². BMI values ranged from 35 kg/m² to 45.92 kg/m² which verified that the study included participants from both Class II and Class III obesity categories.

BMI	37.96	2.69	37.03	35	45.92

Obese Class Frequency
The research sample included 45 study participants who had 36 members with obesity class II and nine members with obesity class III. The research sample showed a dominant presence of Class II obese individuals. The sample showed 80.0% of its members with Class II obesity while Class III obesity accounted for 20.0% of the sample.

RR Interval Statistics
The mean RR interval displayed a value of 722.29 milliseconds which showed standard deviation of 39.32 milliseconds. The measurement showed actual fluctuations in RR interval values that reached moderate levels of variability. The median value of 721 milliseconds showed a close approximation to the average value. The study participants showed measurable variations in their cardiac cycle durations through their RR intervals which ranged from 583.75 milliseconds to 845.75 milliseconds.

Table 2: RR Interval Stats

Variable	Mean	SD	Median	Min	Max
AVERAGE RR INTERVAL MEAN RR	722.29	39.32	721	583.75	845.75

Heart Rate Statistics
The average heart rate reached 83.32 beats per minute which showed a standard deviation of 4.69 beats per minute that demonstrated low participant variability. Heart rates ranged from 83.22 to 84.22 beats per minute. The study group exhibited a heart rate range that extended from 70.94 beats per minute to 102.78 beats per minute which represented their most conservative estimate and highest recorded rate.

Table 3: Heart Rate Stats

Variable	Mean	SD	Median	Min	Max
AVERAGE HR NN	83.32	4.69	83.22	70.94	102.78

SDNN Summary
The mean SDNN value was 30.92 ms with a standard deviation of 7.87 ms, which showed that SDNN values had moderate dispersion. The median SDNN was 29.3 ms. The studied obese participants showed substantial differences in their heart rate variability because their SDNN values ranged between 15.33 ms and 51.85 ms.

RMSSD Summary

The mean RMSSD value reached 37.4 milliseconds with an 8.34 milliseconds standard deviation, which showed that participants displayed moderate variation in their results. The median RMSSD was 38 ms, which was close to the mean. The values ranged from 20.83 ms to 65.44 ms, showing a noticeable spread in short-term heart rate variability within the study population.

HF Power Statistics
The average HF power in the study reached 81.3 ms^2 while the standard deviation measured 58.57 ms^2 which demonstrated significant variation between HF power measurements. The median HF power was 70.75 ms^2. The minimum value recorded was 20.63 ms^2, while the maximum was 204.6 ms^2, showing a wide distribution of parasympathetic-related spectral power among participants.

LF Power Statistics
The mean LF power was 133.96 ms^2 with a standard deviation of 121.16 ms^2, which showed that LF values had substantial variation. The median LF power was 99.06 ms^2. The LF power ranged from 21.91 ms^2 to 601.64 ms^2, which showed that obese study participants had a wide range of low-frequency spectral power.

VLF Statistics
The average VLF power value for the study group measured 218.81 ms^2 with a standard deviation of 118.31 ms^2 which showed significant fluctuations in VLF measurements. The median VLF power value reached 197.3 ms^2. The study participants showed a range of very low frequency power values which extended from 43.3 ms^2 to 522.16 ms^2 as their minimum and maximum VLF power measurements.

Sympathovagal Statistics
The mean LF/HF ratio was 1.99 with a standard deviation of 1.68 this result showed that participants displayed significant differences in their sympathovagal balance. The median LF/HF ratio was 1.69. The values ranged from 0.3 to 9.35 which demonstrated that the study population showed a wide distribution of sympathovagal index values.

IL-6 Statistics
The mean interleukin-6 concentration with its standard deviation showed moderate variability across participants because interleukin-6 concentration measured at 34.43 pg/mL and standard deviation measured at 10.69 pg/mL. The median IL-6 value showed a measurement of 34.84 pg/mL which approached the mean value. The IL-6 levels showed a range between 14.05 pg/mL and 57.95 pg/mL which displayed high variability of inflammatory marker measurements in the studied population.

Table 4: IL-6 Stats

Variable	Mean	SD	Median	Min	Max
INTERLEUKIN 6 CONCENTRATION PG ML	34.43	10.69	34.84	14.05	57.95

STATISTICAL ANALYSIS REPORT: PART 2
Bivariate Comparison: Obese Class 2 vs. Class 3

Comparison of HRV Indices and Inflammatory Markers

Comparison of Gender Distribution by Obese Class
Class II obesity affected 17 females and 2 males, whereas Class III obesity affected 7 males and 19 females respectively. The distribution of genders among Class II and Class III obese individuals was shown by a Chi-square test p-value of 0.3266 individuals failed to demonstrate a discernible change.

Table 5: Comparison of Gender Distribution by Obese Class

Gender	2	3	P value
F	17	2	0.3266
M	19	7	

Chi-Square Test p-value: 0.3266

Comparison of BMI by Obese Class
The mean **BMI** in **Class II obesity** measured 36.84 ± 1.44 kg/m², with a median of 36.43 kg/m², compared to 42.42 ± 1.70 kg/m², with a median of 42.31 kg/m², in Class III obesity. The The statistically substantial difference ($p < 0.001$) clearly indicates that the Class III obese group had higher BMI values.

Table 6: Comparison of BMI by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	36.84	1.44	36.43	<0.001
3	9	42.42	1.70	42.31	

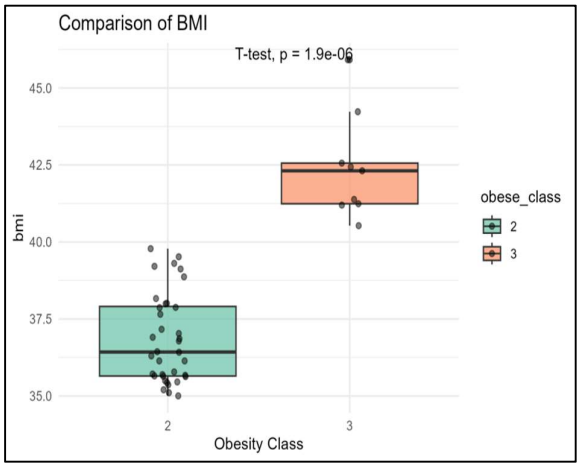


Chart 17: Boxplot Comparison of BMI

Comparison of Weight by Obese Class
The mean **weight** in **Class II obesity** was **101.75 ± 9.59 kg** with a median of **101.5 kg**, whereas in **Class III obesity** it was **124.24 ± 8.05 kg** with a median of **123.0 kg**. People in the Class III obesity category had significantly greater body weights, as shown, there is a statistically significant difference ($p < 0.001$).

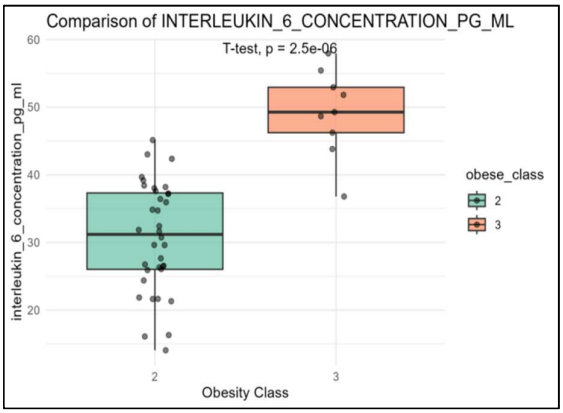
Comparison of WBC by Obese Class
The mean **WBC count** in **Class II obesity** was **7,811.67 ± 1,751.75**, with a median of **7,935**, while in **Class III obesity** it was **7,541.11 ± 1,533.42**, with a median of **7,780**. The difference neither group differed significantly from the other ($p = 0.653$), indicating that obese people had similar white blood cell counts.

The Interleukin-6 concentrations ranged from 30.74 ± 8.01 pg/mL in Class II obesity to 49.21 ± 6.41 pg/mL in Class III obesity, with a median value of 49.27 pg/mL. Significantly increased IL-6 levels were indicated as a result of the meaningful disparity ($p < 0.001$) in Class III obese individuals.

Table 7: Comparison of Interleukin-6 Concentration by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	30.74	8.01	31.18	<0.001
3	9	49.21	6.41	49.27	

Chart 20: Boxplot Comparison of INTERLEUKIN_6_CONCENTRATION_PG_ML



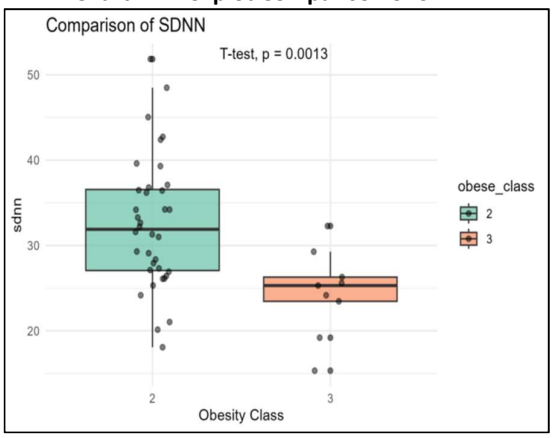
Comparison of SDNN by Obese Class

The mean **SDNN** in **Class II obesity** was **32.52 ± 7.68 ms** with a median of **31.90 ms**, whereas in **Class III obesity** it was **24.55 ± 5.02 ms** with a median of **25.31 ms**. The difference was **statistically significant (p = 0.0013)**, indicating lower SDNN values in individuals with Class III obesity.

Table 8: Comparison of SDNN by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	32.52	7.68	31.90	0.0013
3	9	24.55	5.02	25.31	

Chart 21: Boxplot Comparison of SDNN



Comparison of RMSSD by Obese Class

The mean **RMSSD** in **Class II obesity** was **38.02 ± 8.67 ms** with a median of **38.04 ms**, while in **Class III obesity** it was **34.93 ± 6.72 ms** with a median of **34.60 ms**. With a p-value of just 0.2639, we can rule out any statistical significance for the difference, indicating comparable RMSSD values between the two obesity classes.

Table 9: Comparison of RMSSD by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	38.02	8.67	38.04	0.2639
3	9	34.93	6.72	34.60	

Comparison of HF by Obese Class

The mean **HF power** in **Class II obesity** was **80.20 ± 59.42 ms²** with a median of **70.53 ms²**, whereas in **Class III obesity** it was **85.72 ± 58.26 ms²** with a median of **70.75 ms²**. The difference is not statistically significant (p = 0.8043). showing similar HF power values across both obese classes.

Table 10: Comparison of HF by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	80.20	59.42	70.53	0.8043
3	9	85.72	58.26	70.75	

Comparison of LF by Obese Class

The mean **LF power** in **Class II obesity** was **130.7 ± 124.22 ms²** with a median of **84.53 ms²**, while in **Class III obesity** it was **147.0 ± 113.98 ms²** with a median of **124.30 ms²**. With a p-value of just 0.7123, Statistical analysis did not reveal any discernible variation in LF power among categories.

Table 11: Comparison of LF by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	130.7	124.22	84.53	0.7123
3	9	147.0	113.98	124.30	

Comparison of VLF Power by Obese Class

The mean **VLF power** in **Class II obesity** was **206.47 ± 120.86 ms²** with a median of **171.09 ms²**, whereas in **Class III obesity** it was **268.17 ± 98.23 ms²** with a median of **266.01 ms²**. At p = 0.1297, the disparity did not reach statistical significance, indicating comparable VLF power values between the two obesity classes.

Table 12: Comparison of VLF POWER by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	206.47	120.86	171.09	0.1297
3	9	268.17	98.23	266.01	

Comparison of LF/HF Ratio by Obese Class

The mean **LF/HF ratio** in **Class II obesity** was **1.89 ± 1.33** with a median of **1.74**, while in **Class III obesity** it was **2.39 ± 2.73** with a median of **1.49**. A statistical analysis revealed the sympathovagal ratio did not vary significantly across the groups (p = 0.612), hence there was no need to draw any conclusions two obesity classes.

Table 13: Comparison of LF_HF_RATIO by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	1.89	1.33	1.74	0.612
3	9	2.39	2.73	1.49	

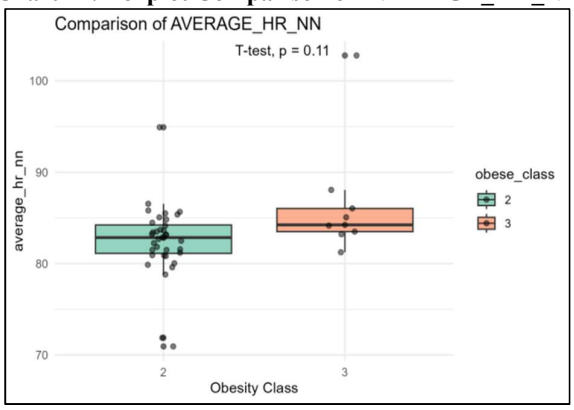
Comparison of Average Heart Rate by Obese Class

The mean **average heart rate (AVERAGE_HR_NN)** in **Class II obesity** was **82.52 ± 3.88 beats/minute** with a median of **82.86**, whereas in **Class III obesity** it was **86.48 ± 6.40 beats/minute** with a median of **84.25**. No statistical significance was found (p = 0.1076), indicating comparable heart rate values across both groups.

Table 14: Comparison of AVERAGE HR NN by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	82.52	3.88	82.86	0.1076
3	9	86.48	6.40	84.25	

Chart 27: Boxplot Comparison of AVERAGE_HR_NN



Comparison of Average RR Interval by Obese Class

The mean **average RR interval** in **Class II obesity** was **729.78 ± 35.25 ms** with a median of **724.95 ms**, while in **Class III obesity** it was **692.36 ± 42.54 ms** with a median of **705.31 ms**. The difference was **statistically significant (p = 0.0331)**, showing lower RR interval values in Class III obesity.

Table 15: Comparison of AVERAGE RR INTERVAL MEAN RR by Obese Class

Obese Class	N	Mean	SD	Median	P Value
2	36	729.78	35.25	724.95	0.0331
3	9	692.36	42.54	705.31	

STATISTICAL ANALYSIS REPORT: PART 3

Correlation Analysis: IL-6 vs. HRV and Anthropometrics

Evaluating the Relationship between Inflammation and Autonomic Function

Correlation Analysis between BMI and IL-6

The concentration of interleukin-6 was positively correlated with body mass index, with a correlation coefficient of **r = 0.725**. This association had a substantial statistical impact (p < 0.001). Body mass index (BMI) was shown to be correlated with higher IL-6 levels among the obese individuals included in the study.

Table 16: Correlation Analysis between BMI and IL-6

Parameter A	Parameter B	Correlation Coefficient r	P Value	Significance
BMI	INTERLEUKIN_6_CONCENTRATION_PG_ML	0.725	<0.001	Significant

Correlation Analysis between IL-6 and SDNN

The correlation coefficient between SDNN and interleukin-6 concentration was -0.474, indicating a moderate negative association. With a p-value of 0.001, this correlation was quite strong. Lower SDNN was related with greater IL-6 levels, according to the results values in the study population.

Table 17: Correlation Analysis between IL-6 and SDNN

Parameter A	Parameter B	Correlation Coefficient r	P Value	Significance
INTERLEUKIN6 CONCENTRATION PG ML	SDNN	-0.474	0.001	Significant

Correlation Analysis between IL-6 and RMSSD

The correlation coefficient between interleukin-6 levels and RMSSD was -0.109. This indicates a modest negative association. At p = 0.4775, it was not deemed statistically significant. It seems from the data that IL-6 levels did not

show any meaningful linear relationship with RMSSD in the study population.

Correlation Analysis between IL-6 and HF Power
A correlation value of r = -0.02 indicated a modest negative relationship between HF power and interleukin-6 levels. We were unable to determine if this association was statistically significant (p = 0.8952). In the obese population, IL-6 levels were not significantly related to HF power included in the study.

Table 18: Correlation Analysis between IL-6 and HF Power

Parameter A	Parameter B	Correlation Coefficient r	P Value	Significance
INTERLEUKIN 6 CONCENTRATION PG ML	HF	-0.02	0.8952	Not Significant

Correlation Analysis between IL-6 and LF/HF Ratio
A correlation value of r = 0.088 indicated a modest positive connection between LF/HF ratio and interleukin-6 levels. Statistical significance of this association could not be shown (p = 0.565). Statistical analysis revealed no connection between interleukin-6 (IL-6) and sympathovagal ratio in the study population.

Table 19: Correlation Analysis between IL-6 and LF/HF Ratio

Parameter A	Parameter B	Correlation Coefficient r	P Value	Significance
INTERLEUKIN_6_CONCENTRATION_PG_ML	LF_HF_RATIO	0.088	0.565	Not Significant

Correlation Analysis between Age and IL-6
A modest negative association (r = -0.163) was found between age and interleukin-6 levels. A with the results did not indicate a statistically significant connection (p=0.2852). Age did not demonstrate a statistically significant linear correlation with IL-6 levels in the study participants.

Correlation Analysis between WBC and IL-6
What is the regression coefficient linking white blood cell count to interleukin-6 concentrations was 0.052, indicating a slight positive link. The statistical significance of this link was not established (p = 0.7329). The research found no significant association between WBC values and IL-6 levels population.

Comprehensive Correlation Matrix
The correlation matrix showed the strongest positive association between **BMI and interleukin-6** with **r = 0.73**.Interleukin-6 and SDNN showed a moderately unfavourable connection (r = -0.47) and between **BMI and SDNN (r = -0.41)**. Correlations involving **age, WBC, RMSSD, and LF/HF ratio** were weak, with values ranging from **-0.24 to 0.13**.

Table 20: Comprehensive Correlation Matrix

Variable	age	BMI	WBC	SDNN	RMSSD	Lfhfratio	Interleukin 6 concentration pgml
age	1.00	-0.24	-0.11	-0.02	0.04	-0.10	-0.16
bmi	-0.24	1.00	-0.09	-0.41	-0.07	0.05	0.73
wbc	-0.11	-0.09	1.00	0.12	0.13	0.01	0.05
sdnn	-0.02	-0.41	0.12	1.00	0.36	-0.05	-0.47
rmssd	0.04	-0.07	0.13	0.36	1.00	-0.15	-0.11
lf_hf_ratio	-0.10	0.05	0.01	-0.05	-0.15	1.00	0.09
interleukin_6_concentration_pg_ml	-0.16	0.73	0.05	-0.47	-0.11	0.09	1.00

STATISTICAL ANALYSIS REPORT: PART 4
Multivariate Analysis and Predictive Modeling

Advanced Statistical Evaluation of HRV and Inflammation

Multiple Linear Regression Model for SDNN
In the multiple linear regression model, the **intercept** was **62.22 ± 19.94** with a **t-value of 3.12** and **p = 0.0033**. The regression coefficient for **interleukin-6** was **-0.2718 ± 0.1448** with **t = -1.88** and **p = 0.0677**. **BMI** showed a coefficient of **-0.5000 ± 0.5836** with **t = -0.86** and **p = 0.3966**, while **age** had a coefficient of **-0.0685 ± 0.0815** with **t = -0.84** and **p = 0.4049**.

Table 21: Multiple Linear Regression Model for SDNN

Predictor	Estimate (B)	Std. Error	t-value	P-Value
(Intercept)	62.22193482	19.93631679	3.1210346	0.00329674
Interleukin 6 concentration pgml	-0.27182213	0.14483311	-1.8767954	0.06767518
BMI	-0.49995600	0.58360323	-0.8566711	0.39660624
age	-0.06854541	0.08145494	-0.8415132	0.40494210

Model Fit: R-Squared = 0.248, Adjusted R-Squared = 0.193, F-statistic: 4.5 ($p < 0.001$)

DISCUSSION

AgeNataraj et al. studied a younger overweight population with a mean age of 22.53 ± 1.58 years and reported less pronounced obesity-related HRV impairment compared with the present cohort [7].

The present middle-aged cohort likely reflects longer exposure to oxidative stress, neurohumoral dysregulation, and adipose tissue inflammation, supporting an established obesity-related cardiometabolic state.

Although age did not significantly predict SDNN in regression analysis (B = −0.0685, p = 0.4049), the age profile provides important clinical context for the findings.

Gender distribution Laudisio et al. reported a significant association between IL-6 and heart rate among women with high BMI (B = 4.16, 95% CI: 1.40–6.91; p = 0.003), suggesting sex-specific inflammatory–cardiac interactions [8].

The present findings suggest that higher IL-6 and lower SDNN in Class III obesity were more closely related to obesity severity than gender distribution.

Weight Nataraj et al. studied younger overweight adults with lower adiposity (BMI: 27.38 ± 1.51 kg/m²) and less severe metabolic characteristics than the present cohort [7].

The findings indicate that increasing body weight in severe obesity reflects biological dysregulation beyond body size alone and may contribute to impaired autonomic control and inflammatory activation.

Body mass index BMI showed a negative correlation with SDNN (r = −0.41), while IL-6 showed a strong positive correlation with BMI (r = 0.725, p < 0.001), indicating worsening autonomic dysfunction and inflammation with increasing adiposity.

Sindhu et al. reported a strong positive correlation between BMI and IL-6R expression (r = 0.80, P < 0.0001) and a moderate correlation with IL-6 expression (r = 0.58, P = 0.008), supporting the present findings [9].

Tacoy et al. found no BMI-related HRV differences in systolic heart failure patients, suggesting that obesity-related autonomic impairment may be more directly observed in non-heart failure populations [10].The present findings suggest that increasing BMI in severe obesity is associated with higher IL-6 levels and lower SDNN, supporting BMI as a marker of systemic inflammation and autonomic impairment.

White blood cell count Al-Rashed et al. linked inflammatory leukocyte markers with immune activation in obesity, contributing tocardiometabolic dysfunction [11].

The present findings suggest that IL-6 is a more sensitive marker of low-grade systemic inflammation in severe obesity than total WBC count.

Interleukin- 6IL-6 showed a strong positive correlation with BMI (r = 0.725, p < 0.001), indicating increasing inflammatory burden with obesity severity.

Sindhu et al. reported significantly higher adipose tissue IL-6 expression in obese individuals (127.0 ± 15.91 vs 86.69 ± 5.25; P = 0.03) and higher IL-6 mRNA expression (16.60 ± 2.214-fold vs 9.376 ± 1.656-fold; P = 0.0108), supporting the present findings [9].

IL-6 clearly differentiated Class II and Class III obesity, unlike WBC count, supporting the role of IL-6 as a key mediator linking obesity with cardiovascular and metabolic risk as proposed by Yudkin et al. [12].

RR interval Laudisio et al. reported a significant association between IL-6 and heart rate in individuals aged ≥85 years (B = 1.42; 95% CI: 0.43–2.42; p = 0.005), with stronger effects among women with higher BMI, indirectly supporting the present RR interval findings [71].

Al-Rashed et al. reported that obese individuals with elevated resting heart rate had a more pronounced pro-inflammatory profile [11].

The present findings suggest that Class III obesity is associated with greater autonomic strain and reduced cardiac autonomic regulation, complementing the observed IL-6 and SDNN changes.

Heart rate Laudisio et al. reported a significant positive association between IL-6 and heart rate in women with higher BMI (B = 4.16; 95% CI: 1.40–6.91; p = 0.003), supporting the trend observed in the present study [8].

Although not statistically significant, the higher heart rate in Class III obesity paralleled shorter RR interval, lower SDNN, and higher IL-6, suggesting increasing autonomic strain with worsening obesity severity.

HF power von Känel et al. reported lower HF power with higher IL-6 levels (β = −0.36, p = 0.002), while Parish et al. found reduced HF in obese adolescents, supporting obesity-related autonomic dysfunction [13,12].

Unlike SDNN, HF power did not significantly distinguish obesity classes, suggesting that total HRV measures may better reflect obesity-related autonomic impairment in the present cohort.

LF power von Känel et al. reported an inverse association between IL-6 and LF power (β = −0.31, p = 0.007), supporting inflammation-related autonomic impairment [13].

In the present study, LF power did not significantly distinguish obesity classes, suggesting it may be a less stable marker of obesity-related autonomic dysfunction than SDNN, which showed clearer association with obesity severity and IL-6.

VLF power Previous studies mainly focused on IL-6, LF, HF, and overall HRV rather than VLF [68,73]. The present findings suggest that VLF is a less reliable standalone marker of obesity-related autonomic dysfunction than IL-6, RR interval, and SDNN.

LF/HF ratio von Känel et al. reported inverse associations of IL-6 with LF and HF but did not identify LF/HF ratio as a sensitive inflammatory marker [13].

The present findings suggest that LF/HF ratio was not a useful discriminator of obesity severity, while SDNN and RR interval provided clearer evidence of autonomic dysfunction [68,73].

Correlation between BMI and IL-6 Yudkin et al. identified IL-6 as a key mediator linking obesity with metabolic and cardiovascular risk [12], while Mendham et al. reported transient exercise-related IL-6 elevation rather than chronic obesity-related inflammation [15].

The present findings support BMI–IL-6 correlation as an important indicator of progressive inflammatory dysregulation in severe obesity.

Correlation between IL-6 and SDNN
von Känel et al. reported inverse associations between IL-6 and HRV indices, including LF (β = −0.31, p = 0.007) and HF (β = −0.36, p = 0.002), consistent with the present findings [13].

Parish et al. also reported reduced HRV with obesity-related inflammation in adolescents [14].

Unlike HF, RMSSD, and LF/HF ratio, SDNN showed a clearer association with IL-6, suggesting that total autonomic variability better reflects obesity-related inflammatory burden in severe obesity.

Regression analysis
Hoffmann et al. reported that body composition, inflammation, and physical activity influenced HRV, with moderate exercise associated with lower IL-6 (p = 0.003) [16], while Yudkin et al. identified IL-6 as a mediator between metabolic and inflammatory pathways [12].

The present findings suggest that autonomic dysfunction in severe obesity is multifactorial, involving obesity, inflammation, and age-related influences, although larger studies are needed to confirm the independent effect of IL-6.

Correlation between IL-6 and RMSSD
von Känel et al. reported an inverse association between IL-6 and HF power (β = −0.36, p = 0.002), supporting inflammation-related parasympathetic impairment [13], while Parish et al. reported reduced autonomic modulation in obese adolescents [14].

Compared with RMSSD, SDNN showed a stronger association with IL-6, suggesting that obesity-related inflammatory autonomic dysfunction may be better reflected by overall HRV reduction rather than isolated parasympathetic impairment.

Correlation between IL-6 and HF power
von Känel et al. reported a significant inverse association between IL-6 and HF power, while Parish et al. reported lower HF levels in obese adolescents, supporting obesity-related vagal dysfunction [13,14].

In contrast, the present study found HF power to be less informative than SDNN and RR interval for detecting obesity-related autonomic dysfunction, likely due to variability and small sample size.

Correlation between IL-6 and LF/HF ratio
von Känel et al. reported stronger associations of inflammation with LF and HF components than with ratio-based measures [13], while Tacoy et al. observed that HRV changes may not consistently parallel BMI or inflammation [10].

Despite higher IL-6 levels in Class III obesity (49.21 ± 6.41 pg/mL vs 30.74 ± 8.01 pg/mL) and lower SDNN, LF/HF ratio remained unchanged, suggesting SDNN is a more useful marker of obesity-related autonomic dysfunction than LF/HF ratio.

Comparison of Class II and Class III obesity distribution
Sindhu et al. similarly reported stronger IL-6 pathway activation with increasing adiposity [9].

The present class-wise analysis suggests that increasing obesity severity is associated with progressive

inflammatory and autonomic dysfunction, improving risk stratification beyond broad obesity categorization.

Overall inflammatory-autonomic pattern

Yudkin et al. identified IL-6 as a key mediator of obesity-related cardiovascular risk [67], while Hoffmann et al. reported associations between inflammation, body composition, physical activity, and HRV [16].

The present findings suggest that Class III obesity represents a more advanced inflammatory–autonomic phenotype, with IL-6 and SDNN serving as useful markers of elevated risk across severe obesity.

CONCLUSION

Severe obesity is associated with increased systemic inflammation and impaired cardiac autonomic function, indicating an interconnected inflammatory–autonomic disturbance.

Progression from Class II to Class III obesity is accompanied by worsening inflammatory status and reduced global heart rate variability, suggesting increasing autonomic dysfunction with greater obesity severity.

Serum IL-6 levels show an inverse relationship with autonomic function, supporting the association between higher inflammation and reduced heart rate variability in obese individuals.

Global HRV measures, particularly SDNN, appear to be more useful indicators of autonomic dysfunction in severe obesity than isolated spectral HRV parameters.

Combined assessment of inflammatory markers and heart rate variability may help identify obese individuals at increased cardiometabolic risk and support obesity as a multisystem disorder involving inflammatory and neurocardiac dysregulation.

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