Assessing the impact of body mass index on insulin resistance and metabolic risk factors in pre-diabetic individuals: A comprehensive cross-sectional study

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ABSTRACT

Background: Insulin resistance plays a crucial role in the onset of type 2 diabetes, with body mass index (BMI) being a significant determinant. **Aims and Objectives:** This study examines the link between BMI and insulin resistance in pre-diabetic individuals to inform strategies for early diabetes intervention. **Materials and Methods:** This cross-sectional study involved 100 pre-diabetic participants. Data on demographic characteristics, BMI, insulin resistance (measured by the Homeostatic Model Assessment for Insulin Resistance, HOMA-IR), lipid profiles, and blood pressure (BP) were collected. Participants were categorized into normal weight, overweight, and obese groups to explore the relationship between BMI and insulin resistance and its impact on metabolic and cardiovascular health. **Results:** The average participant age was 45.8 years (SD = 12.3), with a slight majority being female (52%) and an average BMI of 28.4 kg/m² (SD = 4.5). A significant positive correlation (r = 0.64, P < 0.001) between BMI and the HOMA-IR index highlighted the association between increased BMI and insulin resistance. Obese individuals had a notably higher HOMA-IR index (3.5 ± 1.3) compared to those overweight (2.5 ± 1.0) and of normal weight (1.9 ± 0.8). In addition, the study found worsening lipid profiles and increased BP with higher BMI categories. Gender did not significantly affect insulin resistance, whereas a slight increase in HOMA-IR with age was noted (r = 0.23, P = 0.02). **Conclusion:** The findings highlight the strong correlation between higher BMI and increased insulin resistance in pre-diabetics. They emphasize the importance of managing body weight to mitigate the risk of diabetes and cardiovascular diseases.

Key words: Insulin resistance; Body mass index; Pre-diabetes; Diabetes prevention; Early intervention

INTRODUCTION

The escalating prevalence of type 2 diabetes globally presents a significant public health challenge, with insulin resistance serving as a cornerstone in its pathophysiology.[1,2] Insulin resistance, a condition characterized by the diminished effectiveness of insulin in lowering blood glucose levels, often precedes the onset of type 2 diabetes.[3]

Pre-diabetes, a state of impaired glucose tolerance not yet reaching the threshold for diabetes, offers a critical window for intervention to prevent the progression to full-blown diabetes.[4]

Body mass index (BMI), a widely used measure of body fat based on an individual's weight in relation to their height, has been identified as a significant predictor of

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insulin resistance.[5] The relationship between elevated BMI and increased risk of developing insulin resistance is well documented, highlighting the importance of weight management in diabetes prevention strategies.[6] However, the specific correlation between BMI and insulin resistance in pre-diabetic individuals remains an area of active research, underscoring the need for studies that can inform targeted interventions.

Aims and objectives

The aim of the study is to explore the association between BMI and insulin resistance in individuals with pre-diabetes, with the goal of identifying how excess body weight contributes to the pathogenesis of type 2 diabetes. The objectives are as follows:

To categorize pre-diabetic individuals based on BMI and analyze the correlation between BMI categories (normal weight, overweight, and obese) and insulin resistance, as measured by the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index.

To assess the impact of BMI on metabolic and cardiovascular risk factors, including lipid profiles (total cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL]), triglycerides, fasting glucose, HbA1c levels, blood pressure (BP), C-reactive protein (CRP), fasting insulin, leptin, and adiponectin levels, to understand how body weight influences these parameters in the pre-diabetic phase.

To evaluate the gender-specific responses and the influence of age on insulin resistance, utilizing HOMA-IR scores to discern any significant differences or trends that could inform personalized intervention strategies.

MATERIALS AND METHODS

Study design and setting

This investigation was designed as a cross-sectional observational study and was conducted at King George Hospital, affiliated with Andhra Medical College, Visakhapatnam.

Study period

The study spanned from January 2023 to December 2023, encompassing both data collection and analysis phases within this timeframe.

Participants

The study cohort consisted of 100 individuals identified as pre-diabetic based on fasting glucose levels and/or HbA1c criteria according to the American Diabetes Association guidelines.

Inclusion criteria

Adults aged 18 years and above.

Confirmed pre-diabetes diagnosis based on fasting glucose levels and/or HbA1c criteria according to the American Diabetes Association guidelines.

Exclusion criteria

- Individuals who have been previously diagnosed with diabetes
- Pregnant women
- Individuals diagnosed with significant metabolic or endocrine disorders other than pre-diabetes.

Data collection

Participants underwent a comprehensive baseline evaluation that included demographic information (age, gender), body measurements (weight, height), and the calculation of BMI. BMI was categorized according to the World Health Organization's classifications: normal weight (BMI <25 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI ≥30 kg/m²).

Laboratory measurements

Fasting blood samples were collected to evaluate insulin resistance using the HOMA-IR, as well as to assess comprehensive lipid profiles (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), fasting blood glucose, and HbA1c levels. Laboratory analyses were conducted utilizing the AU480 Beckman Coulter autoanalyzer for high precision and reliability in measuring glucose, HbA1c, and lipid profiles within a clinical biochemistry laboratory setting.

Additional parameters, including CRP, fasting insulin, leptin, and adiponectin levels, were also measured to provide a more comprehensive assessment of metabolic health.

Statistical analysis

Descriptive statistics were utilized to summarize the demographic and clinical characteristics of the participants. The relationship between BMI and HOMA-IR was examined using Pearson's correlation coefficient. ANOVA was conducted to compare mean HOMA-IR values across different BMI categories, followed by *post-hoc* analyses to identify specific group differences. $P<0.05$ was considered statistically significant for all tests.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee, Andhra Medical College, Visakhapatnam. Informed consent was obtained from all participants before their inclusion in the study, ensuring confidentiality and

compliance with ethical standards for research involving human subjects.

RESULTS

In this cross-sectional observational study, we assessed the demographic and general characteristics of 100 participants, delineating the correlation between BMI and insulin resistance among pre-diabetic individuals. The cohort comprised an almost equal distribution of genders, with 52% females, and exhibited a mean age of 45.8 years (SD=12.3 years) and a mean BMI of 28.4 kg/m² (SD=4.5 kg/m²) (Table 1, Figure 1).

BMI categories and insulin resistance

Analysis of BMI categories (Table 2) indicated a progressive increase in the HOMA-IR index correlating with BMI status. Specifically, individuals classified as normal weight (n=25) had a mean HOMA-IR index of 1.9 (SD=0.8), those overweight (n=45) reported a mean HOMA-IR of 2.5 (SD=1.0), and obese participants (n=30) presented with a mean HOMA-IR of 3.5 (SD=1.3), highlighting a significant upward trend in insulin resistance with increasing BMI (Figure 2).
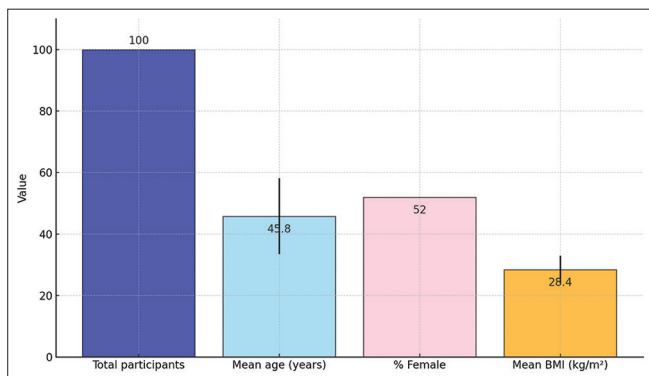

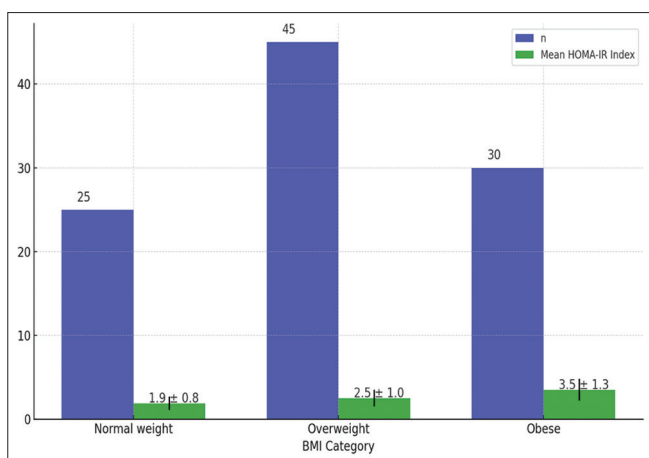**Figure 1:** Demographic and general characteristics

Figure 2: Body mass index categories and homeostatic model assessment for insulin resistance index

Comprehensive metabolic and cardiovascular risk profile

Our evaluation extended to a comprehensive metabolic and cardiovascular risk profile across BMI categories (Table 3). Key findings included:

A marked increase in total cholesterol, LDL ("bad" cholesterol), and triglycerides with higher BMI categories, whereas HDL ("good" cholesterol) demonstrated an inverse relationship. Notably, obese individuals exhibited significantly higher total cholesterol (220±40 mg/dL), LDL (150±35 mg/dL), and triglycerides (180±60 mg/dL), coupled with lower HDL (45±7 mg/dL) levels.

Elevated fasting glucose and HbA1c percentages were observed alongside increasing BMI, with obese participants showing fasting glucose levels at 110±15 mg/dL and HbA1c at 6.0±0.5%.

Table 1: Demographic and general characteristics

Characteristic	Value
Total participants	100
Mean age (years)	45.8±12.3
% Female	52%
Mean BMI (kg/m²)	28.4±4.5

BMI: Body mass index

Table 2: BMI categories and HOMA-IR index

BMI category	n	% of Total	Mean HOMA-IR index
Normal weight	25	25	1.9±0.8
Overweight	45	45	2.5±1.0
Obese	30	30	3.5±1.3

BMI: Body mass index, HOMA-IR: Homeostatic model assessment for insulin resistance

Table 3: Comprehensive metabolic and cardiovascular risk profile by BMI category

Parameter	Normal	Overweight	Obese
Total cholesterol (mg/dL)	185±30	200±35	220±40
LDL (mg/dL)	110±25	130±30	150±35
HDL (mg/dL)	55±10	50±8	45±7
Triglycerides (mg/dL)	130±45	150±50	180±60
Fasting glucose (mg/dL)	90±10	100±12	110±15
HbA1c (%)	5.5±0.5	5.7±0.5	6.0±0.5
Systolic BP (mmHg)	120±7	125±8	130±10
Diastolic BP (mmHg)	85±5	88±6	92±7
Insulin resistance (HOMA-IR)	1.5±0.5	2.0±0.7	2.5±1.0
C-reactive protein (mg/L)	2±1	3±1.5	4±2
Fasting insulin (µU/mL)	8±2	10±3	12±4
Leptin (ng/mL)	6±1	8±2	10±3
Adiponectin (µg/mL)	10±2	8±2	6±1.5

BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, HOMA-IR: Homeostatic model assessment for insulin resistance, BP: Blood pressure

Table 4: Gender and age analysis	
Parameter	**Value**
HOMA-IR for Males	2.8±1.3
HOMA-IR for Females	2.6±1.1
Correlation of Age with HOMA-IR	r=0.23, P=0.02

HOMA-IR: Homeostatic model assessment for insulin resistance

Systolic and diastolic BPs were significantly higher in the obese group, indicating the cardiovascular risks associated with a higher BMI.

Additional markers such as insulin resistance (HOMA-IR), CRP, fasting insulin, leptin, and adiponectin levels varied significantly across BMI categories, underscoring the multifactorial risk profile associated with obesity.

Gender and age analysis

Gender-specific analysis (Table 4) revealed that the mean HOMA-IR for males was 2.8±1.3, slightly higher than for females at 2.6±1.1. Moreover, a statistically significant correlation was found between age and HOMA-IR (r=0.23, P=0.02), suggesting that insulin resistance modestly increases with age among pre-diabetic individuals.

DISCUSSION

The findings of our cross-sectional observational study conducted at King George Hospital, affiliated with Andhra Medical College, Visakhapatnam, contribute valuable insights into the relationship between BMI and insulin resistance among pre-diabetic individuals. Our results, drawn from a cohort of 100 pre-diabetic participants, underscore a significant positive correlation between BMI and the HOMA-IR index, supporting the notion that elevated BMI is a crucial factor in driving increased insulin resistance.[7]

The observed correlation coefficient (r=0.64, P<0.001) between BMI and HOMA-IR indexes not only indicates a robust association but also emphasizes the pivotal role of obesity management in halting the progression of insulin resistance. This correlation is particularly noteworthy in the context of pre-diabetes, a stage that presents a strategic opportunity for intervention to prevent the transition to type 2 diabetes.[8] The gradient in mean HOMA-IR values across BMI categories, spanning from normal weight to obese, further underscores the linear relationship between adiposity and insulin resistance.[8]

Our study findings are consistent with existing literature,[9-14] which suggests that adipose tissue, especially visceral fat, contributes to systemic inflammation and the release of adipokines, exacerbating insulin resistance. The significant disparities in HOMA-IR values among BMI categories,

supported by ANOVA and *post hoc* analyses, underscore the significance of weight management in ameliorating insulin resistance.

In addition, the findings related to lipid profiles and BP elaborate on the multifaceted impact of obesity, demonstrating how increased BMI correlates with unfavorable lipid profiles and elevated BP, thereby compounding the risk of cardiovascular diseases in pre-diabetic populations.[15]

Remarkably, our study found no substantial gender disparity in HOMA-IR values, indicating that the association between BMI and insulin resistance is consistent across genders in pre-diabetic individuals. However, the weak correlation between age and HOMA-IR suggests a modest increase in insulin resistance with aging, suggesting that while age plays a role, it is not as significant as BMI in influencing insulin resistance.[16]

Limitations of the study

It is important to acknowledge the limitations of our study, including its cross-sectional design, which precludes the establishment of causality between BMI and insulin resistance. In addition, the sample size of 100 pre-diabetic individuals, while informative, may not fully represent the broader pre-diabetic population, potentially limiting the generalizability of the findings. Furthermore, relying on HOMA-IR as a surrogate marker for insulin resistance, while widely accepted, may not capture the complete complexity of the insulin resistance syndrome.

CONCLUSION

Our study highlights the urgent need for targeted interventions focusing on weight reduction and lifestyle modifications in pre-diabetic individuals. By addressing obesity as a modifiable risk factor, it is possible to significantly mitigate insulin resistance, thereby delaying or preventing the onset of type 2 diabetes.

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REFERENCES

1. Tang ML, Zhou YQ, Song AQ, Wang JL, Wan YP and Xu RY. The relationship between body mass index and incident diabetes mellitus in Chinese aged population: A cohort study. J Diabetes Res. 2021;2021:5581349.
https://doi.org/10.1155/2021/5581349

2. Yang S, Shi X, Liu W, Wang Z, Li R, Xu X, et al. Association between triglyceride glucose-body mass index and heart failure in subjects with diabetes mellitus or prediabetes mellitus: A cross-sectional study. Front Endocrinol (Lausanne). 2023;14:1294909.

https://doi.org/10.3389/fendo.2023.1294909

3. Wen J, Cai X, Zhang J, Jiang J, Li W, Liu G, et al. Relation of adipose tissue insulin resistance to prediabetes. Endocrine. 2020;68(1):93-102.

https://doi.10.1007/s12020-020-02186-8

4. Rahmanian K, Shojaei M, Jahromi AS and Madani A. The association between pre-diabetes with body mass index and marital status in an Iranian urban population. Glob J Health Sci. 2015;8(4):95-101.

https://doi.org/10.5539/gjhs.v8n4p95

5. Haghighatdoost F, Amini M, Feizi A and Iraj B. Are body mass index and waist circumference significant predictors of diabetes and prediabetes risk: Results from a population based cohort study. World J Diabetes. 2017;8(7):365-373.

https://doi.org/10.4239/wjd.v8.i7.365

6. Andes LJ, Cheng YJ, Rolka DB, Gregg EW and Imperatore G. Prevalence of prediabetes among adolescents and young adults in the United States, 2005-2016. JAMA Pediatr. 2020;174(2):e194498.

https://doi.org/10.1001/jamapediatrics.2019.4498

7. Caporaso NE, Jones RR, Stolzenberg-Solomon RZ, Medgyesi DN, Kahle LL and Graubard BI. Insulin resistance in healthy U.S. adults: Findings from the national health and nutrition examination survey (NHANES). Cancer Epidemiol Biomarkers Prev. 2020;29(1):157-168.

https://doi.org/10.1158/1055-9965.EPI-19-0206

8. Cheng YH, Tsao YC, Tzeng IS, Chuang HH, Li WC, Tung TH, et al. Body mass index and waist circumference are better predictors of insulin resistance than total body fat percentage in middle-aged and elderly Taiwanese. Medicine (Baltimore). 2017;96(39):e8126.

https://doi.org/10.1097/MD.0000000000008126

9. Srikanthan P and Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. J Clin Endocrinol Metab. 2011;96(9):2898-2903.

https://doi.org/10.1210/jc.2011-0435

10. Tabák AG, Herder C, Rathmann W, Brunner EJ and Kivimäki M. Prediabetes: A high-risk state for diabetes development. Lancet. 2012;379(9833):2279-2790.

https://doi.org/10.1016/S0140-6736(12)60283-9

11. Chai Y, Liu Y, Yang R, Kuang M, Qiu J and Zou Y. Association of body mass index with risk of prediabetes in Chinese adults: A population-based cohort study. J Diabetes Investig. 2022;13(7):1235-1244.

https://doi.org/10.1111/jdi.13783

12. Miao Z, Alvarez M, Ko A, Bhagat Y, Rahmani E, Jew B, et al. The causal effect of obesity on prediabetes and insulin resistance reveals the important role of adipose tissue in insulin resistance. PLoS Genet. 2020;16(9):e1009018.

https://doi.org/10.1371/journal.pgen.1009018

13. Helliwell R, Warnes H, Kietsiriroje N, Campbell M, Birch R, Pearson SM, et al. Body mass index, estimated glucose disposal rate and vascular complications in type 1 diabetes: Beyond glycated haemoglobin. Diabet Med. 2021;38(5):e14529.

https://doi.org/10.1111/dme.14529

14. Freeman AM, Acevedo LA and Pennings N. Insulin resistance. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507839 [Last accessed on 2023 Aug 17].

15. US Preventive Services Task Force. Screening for prediabetes and type 2 diabetes: Us preventive services task force recommendation statement. JAMA. 2021;326(8):736-743.

https://doi.org/10.1001/jama.2021.12531

16. Han Y, Hu H, Li Q, Deng Z and Liu D. Triglyceride glucose-body mass index and the risk of progression to diabetes from prediabetes: A 5-year cohort study in Chinese adults. Front Public Health. 2023;11:1028461.

https://doi.org/10.3389/fpubh.2023.1028461

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