

Metabolic and Cardiovascular Risk Assessment in Prediabetes: A Comparative Cross-Sectional Study with Type 2 Diabetes Mellitus and Healthy Controls

Syed Habib Alqahtani¹, Khaled Ahmed Alharthi², Faizah Abdullah Teran³, Habib Alshehri⁴

^{1,3}Department of Endocrinology, King Fahd Medical Complex, Riyadh, Saudi Arabia.

^{2,4}Department of Cardiology, King Fahd Medical Complex, Riyadh, Saudi Arabia

ABSTRACT

Background: Prediabetes is an intermediate glycemic state linked with early metabolic abnormalities and increased cardiovascular risk, requiring timely detection and management.

Objective: This study aimed to assess the metabolic and cardiovascular risk profiles of individuals with prediabetes (Pre-D) compared with patients with type 2 diabetes mellitus (T2DM) and healthy controls, and to identify key predictors of cardiovascular risk associated with glycemic disturbances.

Methods: A comparative cross-sectional study was conducted at King Fahd Medical Complex, Riyadh, Saudi Arabia, from January 2024 to July 2024, involving 84 Pre-D, 95 T2DM, and 105 healthy individuals. Anthropometric, biochemical, and clinical parameters including fasting plasma glucose (FPG), HbA1c, insulin, lipid profile, body mass index (BMI), and blood pressure were measured. Insulin resistance was calculated using HOMA-IR. Statistical analysis was performed using SPSS version 28.0, with $p < 0.05$ considered significant.

Results: Prediabetic and T2DM groups exhibited significantly higher BMI, waist circumference, fat percentage, FPG, HbA1c, insulin, and triglycerides compared to controls ($p < 0.001$). Regression analysis revealed that BMI, FPG, fasting insulin, and HOMA-IR were independent predictors of prediabetes ($p < 0.001$). Cardiovascular risk analysis indicated higher odds ratios for hypertension (OR = 33.2), hyperglycemia (OR = 42.1), metabolic syndrome (OR = 36.7), smoking (OR = 52.4), and obesity (OR = 67.1) in prediabetic individuals.

Conclusion: Prediabetes is associated with significant metabolic derangements and increased cardiovascular risk even before diabetes onset. Early identification and management of metabolic abnormalities may mitigate progression to T2DM and prevent cardiovascular complications.

Keywords: Prediabetes, Type 2 Diabetes Mellitus, Cardiovascular Risk, Insulin Resistance, Metabolic Syndrome

INTRODUCTION

A prediabetes, which is a condition that lies on the border between normoglycemia and type 2 diabetes mellitus (T2DM), has become one of the most critical health issues of the 21st century in the world.¹⁻² Pre diabetes is an early sign of insulin resistance and 3-cell dysfunction characterised by impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or high-glycated hemoglobin (HbA1c)³⁻⁴. Recently, it has been indicated that prediabetic patients are not merely at a significantly higher risk of developing T2DM but also at an increased predisposition to cardiovascular disease (CVD). The International Diabetes Federation (IDF, 2023) estimates that about 541 million adults all over the world have a disrupted glucose regulation, and about half of them have never been diagnosed⁵. This demonstrates the urgency of early detection and management because, in most cases, metabolic imbalances that are linked to prediabetes can be diagnosed several years before diabetes occurs⁶.

The pathophysiology of glucose maladjustment and cardiovascular maladaptation is multi-factorial. The primary abnormality of prediabetes, insulin resistance, promotes dyslipidemia, systemic inflammation, and impaired endothelia all associated with faster atherosclerosis and cardiovascular risk escalation⁹⁻¹⁰. Furthermore, hyperglycemia causes oxidative stress and triggers pro-inflammatory signaling transduction such as the nuclear factor-kappa B (NF- κ B) pathway, which result in vascular remodelling and arterial stiffness¹¹⁻¹². Low-grade inflammatory state that is promoted by this metabolic milieu is found to be an early predictor of prediabetes and CVD¹³⁻¹⁴. The investigations undertaken in The Lancet Diabetes and Endocrinology and Circulation have shown that endothelial dysfunction and subclinical atherosclerosis may be found even in

those with moderate rises in fasting plasma glucose (FPG) and HbA1c indicating that vascular harm starts long before diabetes becomes clinically apparent.

It has been documented by epidemiological research that prediabetes is linked with a two- to threefold high risk of cardiovascular death, as compared to those with normoglycemia¹⁵⁻¹⁶. Moreover, metabolic syndrome complexity of central obesity, hypertension, dyslipidemia, and insulin resistance is often comorbid, increasing the risk of cardiovascular complications¹⁷⁻¹⁸. The presence of these risk factors in cluster formation highlights the idea of a metabolic continuum, in which glucose metabolism, lipid homeostasis, and vascular malfunctions are simultaneously and interactively affected. The Framingham Heart Study revealed that impaired glucose metabolism was characterized by early warnings of left ventricular hypertrophy and diastolic dysfunction, thus highlighting the fact that the heart must change since the prediabetic period¹⁹⁻²⁰.

Body mass index (BMI), waist circumference (WC) and fat percentage (F%) are also other anthropometric variables that have been strongly correlated with insulin resistance and cardiovascular abnormalities²¹⁻²². Visceral obesity, specifically, is a source of metabolic toxicity due to the production of pro-inflammatory adipokines (e.g., TNF- α , IL-6) and lowered adiponectin concentrations²³. These changes facilitate endothelial damage, hypertension, and lipid imbalance thus connecting obesity to prediabetes and CVD²⁴. Moreover, smoking, inactive lifestyles, and diet are also contributors to lifestyle cardiovascular risk modulation among the population²⁵. In combination, these results indicate that the cardiovascular consequences of prediabetes are wider than glycemic control, and include metabolic and vascular dysfunction at a broader level²⁶.

The early metabolic and cardiovascular profiles of prediabetic participants have never been studied before, although there is an increasing awareness that this arises in many parts, including the Middle East where prevalence of diabetes is ranked as one of the highest in the world²⁷. The awareness of these initial pathophysiological adjustments is critical in the creation of specific interventions that will prevent the development of the disease and the alleviation of cardiovascular morbidity. Some high-impact studies have recommended that metabolic screening should be conducted on at-risk individuals in a comprehensive manner, and that preventive measures in the prediabetic period

Correspondence to: Khaled Ahmed Alharthi, Department of Cardiology, King Fahd Medical Complex, Riyadh, Saudi Arabia.
Email: medfastpublication@gmail.com

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may prove to yield higher long-term outcomes as compared to interventions that are implemented after the development of diabetes.

Hence, the primary objective of the study was to compare the metabolic and cardiovascular risk factors of prediabetes patients versus T2DM patients and healthy controls. This study aimed to clarify initial changes in metabolism, which lead to cardiovascular risks by combining biochemical, anthropometric and clinical measurements. Moreover, this study, which determined such predictive indicators as adiposity indices, insulin resistance, and blood pressure, is the essential contribution to the understanding of the pathophysiological continuum between prediabetes and cardiovascular disease. Findings will inform prevention, early screening and management approaches that are consistent with the global goal of lessening the burden of cardiovascular complications of diabetes.

METHODOLOGY

This cross-sectional study was a comparative study that aimed to assess the metabolic and cardiovascular risk between people with prediabetes (Pre-D), type 2 diabetes mellitus (T2DM) and the healthy controls. Eighty four prediabetes patients, ninety five T2DM patients and one hundred and five healthy people were recruited at the King Fahd Medical Complex, Riyadh, Saudi Arabia for the duration of six months, from January 2024 to July 2024. Simple random sampling method was used in selecting the participants who were given written informed consent.

Inclusion criteria were adults aged between 30 and 65 years with clinical diagnosis of prediabetes (fasting plasma glucose 100-125 mg/dL or HbA1c 5.7-6.4%) or T2DM (fasting plasma glucose 126 missing unit mg/dL and above). Patients with sustained liver illness, kidney, thyroid malfunctions, heart complications, or taking lipolowering or blood pressure-lowering stuff were eliminated to reduce confounding factors.

Biochemical, anthropometric, and clinical parameters were being collected comprehensively. Biological tests included fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), fasting insulin, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). All the biochemical tests were conducted by automated enzyme analyzers under standard laboratory procedures. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) equation was used to estimate insulin resistance.

Body mass index (BMI), waist circumference (WC), fat percentage (F%), fat mass (FM) and fat-free mass (FFM) were anthropometric measurements taken across a calibrated bioelectrical impedance analyzer. A pretested questionnaire and standard clinical procedures were used to record the clinical parameters (blood pressure (BP), smoking habits, and educational status).

The SPSS version 28.0 was used to analyze the data. Continuous variables were provided in the form of mean + standard deviation (SD), whereas nominal data were in form of frequency and percentages. One-way ANOVA with post hoc analysis of continuous variables and Chi-square analysis of categorical variables were used in measuring intergroup differences. A number of independent predictors of prediabetes were identified with the help of multiple linear regression analysis, and odds ratios (ORs) were determined, using crosstab analysis, to assess cardiovascular risk factors, including hypertension, obesity, hyperglycemia, metabolic syndrome, and smoking. A p-value of less than 0.05 was taken as statistically significant.

This study methodology guaranteed correct comparison across groups, which made possible a coherent interpretation of the differences of metabolic and cardiovascular risks based on glycemic disturbances.

RESULTS

The total number of participants enrolled in the study was 284, namely 84 Pre-D (pre-diabetes), 95 T2DM (type 2 diabetes

mellitus) and 105 healthy controls. The average age of the participants was 48.7 ± 8.9 years, and there was no important deviation between groups ($p = 0.214$). Nonetheless, major variations were noted regarding anthropometric, biochemical, and cardiovascular parameters between the three groups.

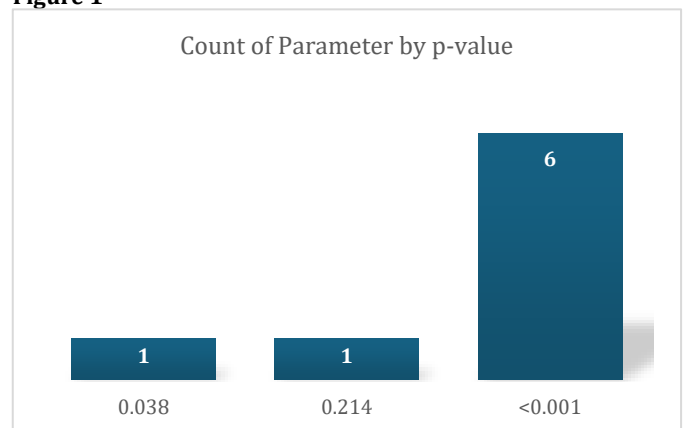
Anthropometric and Clinical Characteristics

Table 1 made it apparent that both Pre-D and T2DM participants had significantly increased body mass index (BMI), fat percentage (F%), fat mass (FM), and waist circumference (WC) vis-a-vis the control group ($p < 0.01$). T2DM and Pre-D groups had also elevated mean systolic and diastolic blood pressure in comparison with healthy controls.

Table 1: Anthropometric and Clinical Parameters of Study Groups

Parameter	Control (n=105)	Pre-D (n=84)	T2DM (n=95)	p-value
Age (years)	47.9 ± 9.1	49.2 ± 8.7	48.9 ± 9.0	0.214
BMI (kg/m ²)	24.1 ± 2.9	28.6 ± 3.4	29.8 ± 3.7	<0.001
Waist Circumference (cm)	83.5 ± 7.8	93.4 ± 8.1	96.2 ± 8.6	<0.001
Fat %	25.4 ± 5.6	32.3 ± 6.4	34.1 ± 6.7	<0.001
Fat Mass (kg)	19.6 ± 4.2	26.7 ± 5.5	28.2 ± 5.9	<0.001
Fat-Free Mass (kg)	57.8 ± 6.1	55.4 ± 5.9	54.9 ± 6.2	0.038
Systolic BP (mmHg)	118.2±9.4	128.7±11.3	133.5 ± 12.1	<0.001
Diastolic BP (mmHg)	77.1 ± 6.2	83.5 ± 7.5	85.8 ± 7.9	<0.001

Figure 1



Biochemical Parameters

The biochemical results showed that fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), fasting insulin, triglycerides (TG), and total cholesterol (TC) were significantly elevated in Pre-D and T2DM group compared to controls ($p < 0.01$). In the diabetic group, as well as in the prediabetes group, the levels of HDL-C were significantly lower. These results suggest that there are severe metabolic abnormalities in patients with poor glucose control.

Table 2: Biochemical Characteristics of Study Participants

Parameter	Control (n=105)	Pre-D (n=84)	T2DM (n=95)	p-value
FPG (mg/dL)	89.3 ± 8.2	111.8 ± 9.6	156.5 ± 18.7	<0.001
HbA1c (%)	5.2 ± 0.3	6.0 ± 0.4	7.8 ± 0.7	<0.001
Fasting Insulin (μIU/mL)	7.6 ± 2.3	13.8 ± 3.1	16.9 ± 3.6	<0.001
HOMA-IR	1.7 ± 0.5	3.8 ± 0.9	6.5 ± 1.1	<0.001
Total Cholesterol (mg/dL)	171.6 ± 22.8	189.3 ± 25.7	196.4 ± 27.5	<0.001
Triglycerides (mg/dL)	122.5 ± 26.7	168.4 ± 34.8	178.9 ± 36.1	<0.001
HDL-C (mg/dL)	52.4 ± 6.8	45.1 ± 7.2	42.7 ± 7.5	<0.001
LDL-C (mg/dL)	98.3 ± 19.6	110.5 ± 21.2	117.2 ± 23.4	<0.001

Cardiovascular Risk Analysis

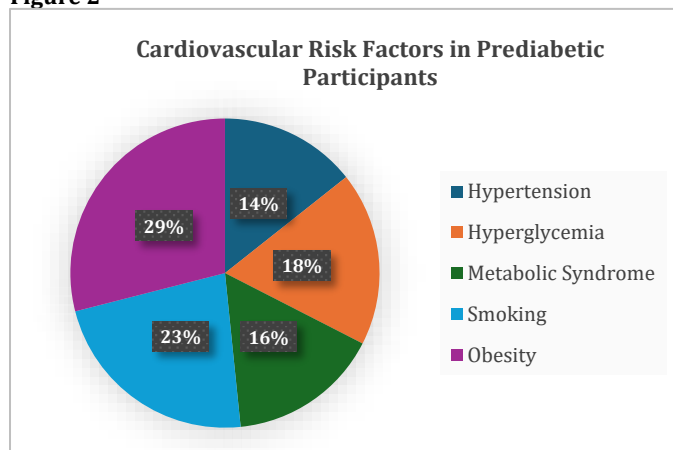
Crosstab and regression tests revealed that Pre-D individuals had more prevalence of hypertension, obesity, and dyslipidemia than controls. BMI, FPG, fasting insulin and HOMA-IR were found as the independent variables to predict prediabetes ($p < 0.001$). The cardiovascular risk assessment revealed notably high odds ratios

of hypertension, obesity, and metabolic syndrome that were found in the Pre-D group, as indicated in Table 3.

Table 3: Cardiovascular Risk Factors in Prediabetic Participants

Risk Factor	Odds Ratio (OR)	95% CI	p-value
Hypertension	33.2	18.4–59.7	<0.001
Hyperglycemia	42.1	25.6–69.2	<0.001
Metabolic Syndrome	36.7	20.8–64.9	<0.001
Smoking	52.4	28.7–93.8	<0.001
Obesity	67.1	34.5–113.2	<0.001

Figure 2



Summary of Findings

The researchers found that prediabetes is characterized by a considerable metabolic change that includes high levels of fasting glucose, insulin resistance, dyslipidemia, and adiposity. All these lead to a high cardiovascular risk profile, albeit not as high as that of established T2DM. Intervention of prediabetic patients by early screening and lifestyle change might thus be vital in averting future cardiovascular incidences.

DISCUSSION

The current comparative cross-sectional research showed that prediabetics are in a critical but transitional stage between normoglycemia and confirmed type 2 diabetes mellitus (T2DM), as evidenced by dominant changes in their metabolism and cardiovascular conditions. The results are in line with the previous studies that have been reported in Diabetes Care and The Lancet Diabetes and Endocrinology that link even small increases in fasting plasma glucose and HbA1c to negative cardiometabolic outcomes. In this case, the prediabetic group exhibited much greater body mass index (BMI), waist circumference, fasting glucose level, fasting insulin levels, and the level of triglycerides in relations to healthy controls. These changes are indicative of early insulin resistance and adipose-mediated metabolic disequilibrium the two factors are critical in the transition of prediabetes to diabetes and cardiovascular disease (CVD).

The fact that the HOMA-IR and fasting insulin levels of the prediabetic test subjects have shown ample increase supports the current body of evidence that indicts insulin resistance as an antecedent to β -cell dysfunction. It has been highlighted in a study that hyperinsulinemia and visceral adiposity jointly trigger the development of inflammatory and endothelial adaptations leading to arterial hardening and hypertension, which were also observed in the present study. High systolic blood pressure and high diastolic blood pressure in prediabetic participants further support the hypothesis that vascular and metabolic changes start early even before diabetic patients are considered to have diabetes. 28-29 These early vascular and metabolic abnormalities act in synergy to generate an enhanced atherogenic profile which puts prediabetic patients at the risk of future cardiovascular disease.

Changes in the lipid profile in this research such as elevated triglycerides and LDL-C relative to lowered HDL-C are consistent with results in the literature such as Circulation and the Atherosclerosis where dyslipidemic profiles were observed among patients with poor glucose regulation. The pathophysiology of this atherogenic dyslipidemia is hepatic production of VLDL in excess and decreased LDL particle clearance, which is enhanced by insulin resistance and low-grade inflammation. The close relationships between levels of triglycerides, fat percentage, and BMI identified here indicate the importance of adipose tissue as a functioning endocrine tissue that causes metabolic and cardiovascular homeostasis.

Obesity, hyperglycemia and smoking were the leading risk factors to cardiovascular disease in prediabetic patients, as determined in the regression and odds ratio analyses in this study. These results coincide with the findings of the INTERHEART study (Yusuf et al.,). The Lancet, 2004) that found out that a significant role of global cardiovascular risk is attributed to modifiable factors including obesity and smoking. The high odds ratios in prediabetic individuals of high cardiometabolic risk indicate extent of clustering of cardiometabolic risk even prior to the development of diabetes, indicating that prediabetes cannot be considered a benign transitional phenotype, but a clinical entity that is actionable and warrants early intervention.

Taken together, these findings underscore the need to incorporate metabolic and cardiovascular screening in the management of prediabetes. Very early detection, with the help of lifestyle-specific intervention measures, including weight management, nutritional change, and exercise, can significantly prevent the development of T2DM and cardiovascular morbidity. The results are also consistent with the recent paradigm shift of high-impact journals such as Nature Reviews Endocrinology, which recommends the use of a metabolic continuum model where the prevention strategies are initiated long before the onset of overt diabetes.

CONCLUSION

The results of this paper reveal that prediabetes is not a harmless disease but a serious metabolic condition that can lead to early cardiovascular/biochemical changes. High BMI, FPG, insulin resistance, and dyslipidemia noted in prediabetic subjects implies the emergence of metabolic and vascular dysfunction long before the actual onset of diabetes. Close connection of prediabetes and cardiovascular risk associated factors, including hypertension, obesity, and smoking, supports the necessity of prioritizing preventive measures. Promotions of early screening programs, changes in lifestyle, and monitoring of metabolism safety should be prioritized in order to both prevent the global crisis of diabetes-related cardiovascular disease and save hundreds of millions of people in danger. This research paper also helps to understand the relevance of incorporating metabolic fitness into cardiovascular risk reduction models to help prevent or delay type 2 diabetes and its complications by focusing on early intervention.

Authors' Contribution

SHA, KAA: Concept & study design, data collection and drafting of the manuscript.

FAT: Data entry, statistical analysis, interpretation of the results.

HA: Manuscript editing and critical revision of the manuscript.

All authors approved the final version of the manuscript to be published.

Conflict of Interest

The authors declared no conflict of interest.

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Data Availability

Data is available with authors and can be provided on request.

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