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ASSOCIATION BETWEEN VISCERAL FAT, LIPID PEROXIDATION, AND ANTIOXIDANT STATUS IN PREDIABETIC INDIVIDUALS

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Abstract

Background: Prediabetes, which is often linked to central adiposity and oxidative stress, is a high-risk state for the development of type 2 diabetes and cardiovascular disease. This study aimed to assess the relationship between oxidative stress indicators and visceral adiposity in prediabetic individuals in comparison to normoglycemic controls.

Methods: A cross-sectional case-control study was carried out on 96 people with prediabetes and 96 controls who were matched for age and sex. Malondialdehyde [MDA], total antioxidant status [TAOS], and redox ratio [RR] were biochemical indicators of oxidative stress, and anthropometric measures (height, weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, and visceral fat percentage) were examined. Pearson's correlation was used to evaluate the relationships between visceral fat and biochemical markers, and independent two-sample t-tests were used to examine differences between groups.

Results: Participants with prediabetes had significantly higher visceral fat percentage ($t = –13.39$, $p < 0.0001$), waist circumference ($t = –3.29$, $p = 0.0012$), waist-to-hip ratio ($t = –3.06$, $p = 0.0025$), and BMI ($t = –3.95$, $p < 0.001$) than controls. The prediabetic group had significantly lower TAOS ($t = 39.82$, $p < 0.0001$) and higher MDA ($t = –10.71$, $p < 0.0001$) and RR ($t = 51.89$, $p < 0.0001$), according to biochemical tests. Visceral fat had a negative correlation with TAOS ($r = –0.676$, $p < 0.001$) and RR ($r = –0.683$, $p < 0.001$) and a positive correlation with MDA ($r = 0.590$, $p < 0.001$).

Conclusion: The manifestations of prediabetes include increased lipid peroxidation, decreased antioxidant defense, and increased visceral adiposity. A major molecular element in the progression from prediabetes to overt diabetes is central obesity, as seen by the substantial associations found between visceral fat and redox imbalance. Effective preventive measures could include focusing on oxidative stress reduction and visceral fat reduction.

Keywords: Prediabetes, Visceral adiposity, Oxidative stress, Malondialdehyde, Antioxidant status, Redox ratio

Introduction

An intermediate condition between normoglycemia and type 2 diabetes mellitus (T2DM), prediabetes is defined by poor glucose control. Given that one-third of persons globally are expected to develop prediabetes or diabetes at some point in their lives, it is becoming more widely acknowledged as a significant global health burden [1,2]. Even before the onset of diabetes, those with prediabetes have a higher propensity for cardiovascular disease (CVD) and are at an increased risk of developing type 2 diabetes [3].

Central obesity, especially visceral adiposity, is becoming recognized as a key cause of insulin resistance and cardiometabolic dysfunction [4,5]. Visceral adipose tissue, in contrast to subcutaneous fat, is metabolically active and releases adipokines, free fatty acids, and pro-inflammatory cytokines that worsen endothelial dysfunction, oxidative stress, and systemic inflammation [6,7]. According to recent research, the low-grade chronic inflammatory state of prediabetes is largely caused by mediators produced from visceral fat, such as adhesion molecules (ICAM-1, VCAM-1), interleukins (IL-1, IL-6), and tumor necrosis factor-alpha (TNF-α) [8,9].

Another characteristic of prediabetes is oxidative stress, which is characterized by an imbalance between the generation of reactive oxygen species (ROS) and antioxidant defenses [10,11]. Reduced antioxidant capacity and elevated lipid peroxidation products, like malondialdehyde (MDA), lead to vascular damage, decreased insulin signaling, and β-cell failure [12,13]. Importantly, there is growing evidence that visceral fat is a significant cause of oxidative stress, which connects obesity to problems with metabolism and the heart [14,15].

Despite these discoveries, little is known about the complex interactions among oxidative stress, inflammatory markers, and visceral fat storage in prediabetic people from a variety of demographics. Recognizing early pathophysiological alterations and possible intervention targets prior to the development of overt diabetes requires an understanding of these relationships. Investigating anthropometric, inflammatory, and oxidative stress profiles in prediabetic people in comparison to healthy controls was the goal of the current study. In particular, we assessed (i) variations in biochemical markers and adiposity indices, (ii) oxidative stress and antioxidant defense levels, and (iii) associations between inflammatory mediators, visceral fat, and redox imbalance. Our research highlights the relevance of visceral adiposity, oxidative stress, and inflammation as early predictors of cardiometabolic risk in prediabetes and offers new insights into the molecular relationships among these factors.

Materials and Methods

Study Design and Setting

This observational, cross-sectional study was carried out at the Index Medical College and Research Center's Department of Biochemistry in Indore, Madhya Pradesh, India. Investigating the relationship between visceral adiposity and oxidative stress, particularly lipid peroxidation, in people with prediabetes was the main goal. In order to minimize participant burden and allow for a thorough investigation of statistical connections, a cross-sectional design was chosen to facilitate the efficient assessment of exposures and outcomes at a single time point. Using standardized equipment such as automated ELISA readers, microplate spectrophotometers, and calibrated anthropometric instruments, all biochemical tests were carried out in a facility approved by the National Accreditation Board for Testing and Calibration Laboratories (NABL).

Ethical Considerations

In compliance with the Declaration of Helsinki (2013 revision) and the Indian Council of Medical Research (ICMR) National Ethical Guidelines (2017), ethical approval was acquired from the Institutional Ethics Committee (IEC), Index Medical College and Research Center (Ref. MU/Research/EC/Ph.D/2022/353). Before registration, all participants provided written informed consent in either Hindi or English, depending on their preferred language. The study's goals, the voluntary nature of participation, confidentiality protocols, and any possible minor risks like venipuncture discomfort were explained to the participants. Both the subject and a study team member

recorded their consent. Participants received assurances that there would be no consequences if they chose to leave at any time.

Study Population and Recruitment

The study included 192 adults, 96 of whom had prediabetes and 96 of whom were age- and sex-matched normoglycemic controls. Through community-based screening camps and the General Medicine outpatient department, participants were gathered. Adults of either sex between the ages of 18 and 35 who met the American Diabetes Association's (ADA) criteria for prediabetes, fasting plasma glucose (FPG) of 100–125 mg/dL and/or HbA1c of 5.7–6.4%, were eligible. Type 2 diabetes mellitus with a prior diagnosis, use of anti-inflammatory or antioxidant medications, pregnancy or lactation, acute or chronic autoimmune or inflammatory disorders, cancer, cardiovascular disease, other endocrine disorders, or refusal to give informed consent were among the exclusion criteria. In order to minimize confounding variables and guarantee the inclusion of metabolically active individuals at an early stage of illness progression, these criteria were implemented.

Anthropometric and Visceral Fat Assessment

Body mass index (BMI), height, weight, hip and waist circumferences, and waist circumference were all standardized anthropometric measurements. The WHR, or waist-to-hip ratio, was computed. A calibrated digital scale was used to measure weight to the nearest 0.1 kg, and a wall-mounted stadiometer was used to measure height to the nearest 0.1 cm. Hip circumference at the greatest gluteal prominence and waist circumference halfway between the iliac crest and lower costal margin were measured. Trained personnel performed each measurement twice, and mean results were employed to reduce inter-observer variability.

A validated, FDA-approved multi-frequency bioelectrical impedance analysis (BIA) instrument (OMRON HBF-701 Body Composition Monitor) was used to detect visceral fat percentage (VF%). Before the test, participants were told to fast for the whole night, refrain from drinking or caffeine for 12 hours, and refrain from strenuous exercise for 24 hours. With verified connections to imaging modalities like CT and MRI, BIA uses proprietary algorithms and bioelectrical impedance to quantify visceral adipose tissue.

Biochemical Sample Collection and Analysis

After an overnight fast of 10–12 hours, fasting venous blood samples (8–10 mL) were taken between 8:00 and 10:00 AM. Fluoride, EDTA, and plain vacutainer tubes were used to collect the samples. Centrifugation at 3000 rpm for 10 minutes at 4°C was used to separate the plasma and serum, which were then aliquoted and kept at -80°C until analysis. In order to reduce the deterioration of redox-sensitive analytes, all experiments were conducted within 30 days.

Malondialdehyde (MDA), a persistent byproduct of the oxidation of polyunsaturated fatty acids, was measured using the thiobarbituric acid reactive substances (TBARS) assay to quantify lipid peroxidation. Spectrophotometric measurements of absorbance were made at 532 nm, and the findings were reported in mmol/L. The Trolox Equivalent Antioxidant Capacity (TEAC) assay was used to measure total antioxidant status (TAS), which is expressed in μmol/L and is based on the suppression of ABTS radical production. An integrated indicator of the burden of oxidative stress was the redox ratio (RER), which was computed as MDA: TAS.

Statistical Analysis

Analysis of the data was carried out with IBM SPSS Statistics version 27.0. For continuous variables, mean ± standard deviation (SD) was used. Independent-sample t-tests were used to compare the groups of participants with prediabetes with those without. Using Pearson's correlation coefficient (r), relationships between visceral fat % and oxidative stress indicators (MDA, TAS, and RER) were evaluated. At $p < 0.05$, statistical significance was established.

Results

Anthropometric Parameters

Height (cm)

The prediabetic group's mean height was 160.60 ± 6.95 cm, while the control group's was 163.97 ± 7.31 cm. A significant difference between the groups was found using a two-sample t-test (pooled variance) with t(190) = 3.27 and p = 0.0013. 3.37 cm was the mean difference (95% CI: 1.36–5.38). The test power was high (1–β = 0.93), and the effect size was moderate (Cohen's d = 0.47). The F-test revealed that the variances were equal (p = 0.624). With a moderate effect size, control subjects were noticeably taller than prediabetic participants (Table 1).

Weight (kg)

The prediabetic group weighed 63.97 ± 7.31 kg on average, while the control group weighed 62.00 ± 2.30 kg. According to a two-sample t-test with pooled variance, prediabetic subjects were on average 1.97 kg heavier (95% CI: –3.51 to –0.43), indicating a significant difference (t(190) = –2.52, p = 0.0126). With a strong test power (1–β = 0.93), the observed effect size was moderate (Cohen's d = 0.36). However, Table 1 shows that the equality of variances assumption was broken (F-test, p < 0.001) (Table 1).

BMI (kg/m²)

The prediabetic group's mean BMI was 24.79 ± 2.30 kg/m2, while the control group's was 23.04 ± 3.68 kg/m². There was a significant difference, t(190) = –3.95, p < 0.001, according to a two-sample t-test (pooled variance), with prediabetic subjects having a higher BMI by 1.75 kg/m² (95% CI: –2.62 to –0.88). With excellent statistical power (1–β = 0.93), the observed effect size was moderate (Cohen's d = 0.57). There was a violation of the premise of equal variances (F-test, p = 0.000007). With a moderate effect size, persons with prediabetes had a substantially higher BMI than controls (Table 1).

Waist circumference (cm)

Both the prediabetic and control groups had mean waist circumferences of 81.11 ± 5.09 cm and 78.77 ± 4.76 cm, respectively. Participants with prediabetes had a 2.34 cm greater waist circumference (95% CI: –3.73 to –0.95), according to a two-sample t-test (pooled variance) that showed a significant difference (t(190) = –3.29, p = 0.0012). The measured effect size had excellent statistical power (1–β = 0.93) and was modest (Cohen's d = 0.47). Using the F-test, the assumption of equal variances was satisfied (p = 0.515). Compared to controls, patients with prediabetes had a moderately larger waist circumference (Table 1).

Hip circumference (cm)

In the prediabetic group, the mean hip circumference was 90.60 ± 6.41 cm, while in the control group, it was 89.96 ± 6.99 cm. No significant difference between groups was found using a two-sample t-test (pooled variance) with t(190) = –0.66 and p = 0.509. The average variation was -0.64 cm (95% CI: -2.54 to 1.26). Although test power was high (1–β = 0.93), the effect magnitude was small (Cohen's d = 0.10). According to the F-test, p = 0.40, the premise of equal variances was satisfied. There was no significant distinction in hip circumference between the control and prediabetic groups, and the effect size was negligible (Table 1).

Table 1. Comparison of Anthropometric Parameters Between Prediabetic and Control Groups

Parameter	Prediabetic (Mean ± SD)	Control (Mean ± SD)	t-statistic	p-value	Mean Difference (95% CI)	Cohen's d	Interpretation
Height (cm)	160.60 ± 6.95	163.97 ± 7.31	3.27	0.0013	3.37 (1.36–5.38)	0.47 (moderate)	Controls taller than prediabetics
Weight (kg)	63.97 ± 7.31	62.00 ± 2.30	–2.52	0.0126	–1.97 (–3.51 to –0.43)	0.36 (moderate)	Prediabetics heavier

BMI (kg/m²)	24.79 ± 2.30	23.04 ± 3.68	–3.95	<0.001	–1.75 (–2.62 to –0.88)	0.57 (moderate)	Prediabetics had higher BMI
Waist circumference (cm)	81.11 ± 5.09	78.77 ± 4.76	–3.29	0.0012	–2.34 (–3.73 to –0.95)	0.47 (moderate)	Prediabetics had a larger waist
Hip circumference (cm)	90.60 ± 6.41	89.96 ± 6.99	–0.66	0.509	–0.64 (–2.54 to 1.26)	0.10 (negligible)	No significant difference
Waist-to-Hip Ratio (WHR)	0.89 ± 0.04	0.87 ± 0.05	–3.06	0.0025	–0.02 (–0.035 to –0.005)	0.44 (moderate)	Prediabetics had higher WHR
Visceral fat (%)	12.30 ± 2.53	7.84 ± 2.06	–13.39	<0.0001	–4.46 (–5.47 to –3.45)	1.93 (very large)	Prediabetics had markedly higher visceral fat

Waist-to-Hip Ratio (WHR)

The control group's mean WHR was 0.87 ± 0.05, while the prediabetic group's was 0.89 ± 0.04. There was a significant difference, t(190) = –3.06, p = 0.0025, according to a two-sample t-test (pooled variance), with prediabetic subjects having a higher WHR by 0.02 units (95% CI: –0.035 to –0.005). There was a modest effect size (Cohen's d = 0.44) and a significant test power (1–β = 0.93). The equality of variances assumption, however, was broken (F-test, p = 0.031). Participants with prediabetes had a somewhat large effect size and a considerably higher WHR than controls (Table 1).

Visceral fat (%)

Between the prediabetic and control groups, the mean visceral fat percentage was 12.30 ± 2.53% and 7.84 ± 2.06%, respectively. Participants with prediabetes had a 4.46% (95% CI: –5.47 to –3.45) higher visceral fat, according to a two-sample t-test (pooled variance) that showed a very significant difference (t(190) = –13.39, p < 0.0001). High test power (1–β = 0.93) and a very big effect size (Cohen's d = 1.93) indicated a significant magnitude of difference. There was a breach of the equal variance assumption (F-test, p = 0.047). Participants with prediabetes had visceral fat that was significantly higher than that of controls, with a very large effect size (Table 1).

Biochemical parameters

Malondialdehyde (MDA, mmol/L)

In the control group, the mean MDA concentration was 2.22 ± 0.53 mmol/L, while in the prediabetic group, it was 3.25 ± 0.62 mmol/L. There was a highly significant difference, t(190) = –10.71, p < 0.0001, according to a two-sample t-test (pooled variance), with prediabetic subjects having higher MDA levels by 1.03 mmol/L (95% CI: –1.41 to –0.65). A high test power (1–β = 0.93) and a very big effect size (Cohen's d = 1.55) indicated a significant magnitude of difference. (F-test, p < 0.001) The assumption of equal variances was broken. MDA levels were significantly greater in prediabetic subjects than in controls, with a very large effect size, indicating elevated oxidative stress (Figure 1A).

Total Antioxidant Status (TAOS, µmol/L)

The control group's mean TAOS level was 4.76 ± 0.41 µmol/L, while the prediabetic group's was 1.85 ± 0.32 µmol/L. A highly significant difference was found using a two-sample t-test: t(190) = 39.82, p < 0.0001. Controls had a greater antioxidant status by 2.91 µmol/L (95% CI: 2.63 to 3.19). Both the test power (1–β = 0.93) and the effect magnitude (Cohen's d = 5.75) were very high. There was a breach of the equal variance assumption (F-test, p = 0.0019). As a result of decreased antioxidant defense in the prediabetic state, control participants' TAOS levels were significantly greater than those of prediabetic persons, with a very large effect size (Figure 1B).

Redox Ratio (RR)

Between the prediabetic and control groups, the mean RR was 4.18 ± 0.36 and 1.45 ± 0.28, respectively. A highly significant difference was found using a two-sample t-test: t(190) = 51.89, p < 0.0001, with prediabetic subjects exhibiting a higher RR by 2.73 (95% CI: 2.64 to 2.82). There was a strong test power (1–β = 0.93), and the effect size was quite large (Cohen's d = 7.49). The F-test

revealed that the assumption of equal variances was broken ($p < 0.001$). Because of the significant redox imbalance in the prediabetic state, prediabetic individuals showed a much higher RR than controls, with a very large effect size (Figure 1C).

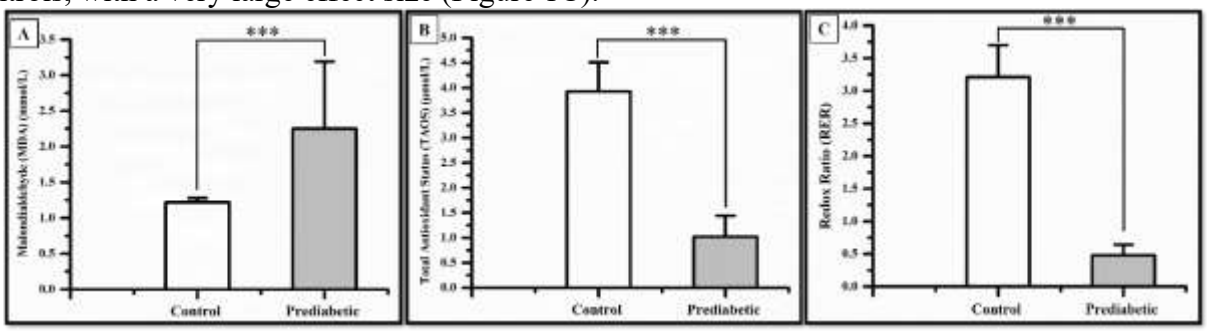

Figure 1. Comparison of oxidative stress parameters between prediabetic and control groups.

Bar plots represent mean ± SD values for (A) Malondialdehyde (MDA, mmol/L), (B) Total Antioxidant Status (TAOS, µmol/L), and (C) Redox Ratio (RR). Independent two-sample t-tests revealed highly significant differences for all parameters ($p < 0.0001$). Prediabetic individuals demonstrated markedly elevated MDA and RR, indicating enhanced lipid peroxidation and redox imbalance, while TAOS levels were significantly lower compared to controls, reflecting impaired antioxidant defense. Error bars denote standard deviation. Statistical significance is indicated by superscripted stars (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$).

Correlation between visceral fat and oxidative stress parameters

In prediabetic people, the correlation analysis (Table 5) showed clear relationships between visceral fat percentage and lipid peroxidation indicators. Visceral fat and MDA showed a substantial positive connection ($r = 0.590$, $p < 0.001$) (Figure 2A), indicating that lipid peroxidation is significantly higher as adiposity rises. In contrast, there were significant negative correlations between visceral fat and TAOS ($r = –0.676$, $p < 0.001$) (Figure 2B).and Figure 2B's redox ratio ($r = -0.683$, $p < 0.001$) (Figure 2C). These coefficients demonstrate the robustness of these correlations by representing substantial effect sizes based on Cohen's criteria. All together, the results show that increased oxidative stress, weakened antioxidant defenses, and disturbance of the redox balance are associated with increased visceral fat storage. The development of central obesity and the transition from prediabetes to overt metabolic and cardiovascular problems may be significantly influenced by this interaction.

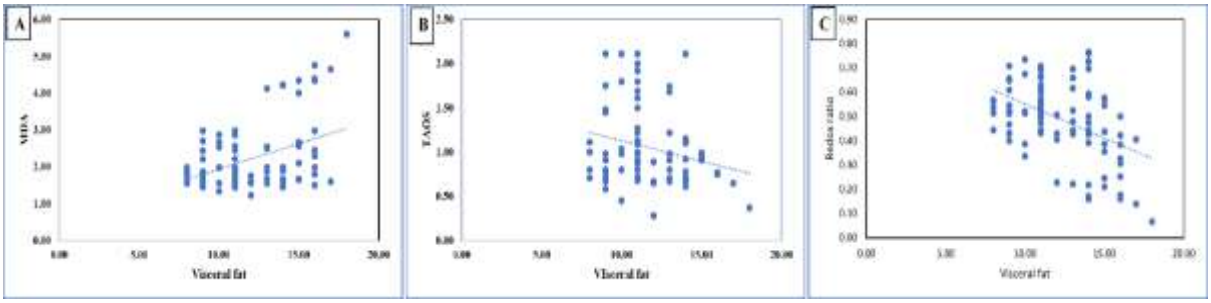

Figure 2. Correlation between visceral fat and oxidative stress parameters in prediabetic individuals.

Scatterplots depict the associations of visceral fat percentage with (A) malondialdehyde (MDA, mmol/L), (B) total antioxidant status (TAOS, µmol/L), and (C) redox ratio (RER). Visceral fat showed a strong positive correlation with MDA ($r = 0.590$, $p < 0.001$), indicating elevated lipid peroxidation with higher adiposity. In contrast, significant negative correlations were observed with TAOS ($r = –0.676$, $p < 0.001$) and RER ($r = –0.683$, $p < 0.001$), suggesting impaired antioxidant defense and disrupted redox balance in individuals with greater visceral fat accumulation.

Discussion

The current investigation highlights the interaction between central obesity, oxidative stress, and compromised antioxidant defense by revealing notable anthropometric and biochemical abnormalities between prediabetic individuals and healthy controls. Despite being somewhat lower in height than controls, prediabetic subjects had significantly higher body weight, BMI, waist circumference, waist-to-hip ratio, and visceral fat. These results are in line with past research showing that central adiposity, not total obesity, is a key factor in the onset of prediabetes and the development of type 2 diabetes (T2DM) [4,16]. Specifically, visceral adipose tissue is metabolically active and closely linked to inflammation, insulin resistance, and cardiovascular risk [5,6]. In identifying those at risk, recent research has highlighted the superiority of indicators, including the visceral adiposity index, cardiometabolic index, and lipid accumulation product, over conventional measurements like BMI [17]. Increases in waist circumference and BMI are linearly linked to an increased risk of diabetes, according to extensive meta-analyses [18]. These results highlight how crucial central adiposity evaluation is as a prediabetes screening method.

According to biochemical tests, prediabetic people had significantly lower total antioxidant status (TAOS), which indicated compromised antioxidant defense, and significantly higher malondialdehyde (MDA) levels, which indicated enhanced lipid peroxidation. This pattern is consistent with data showing oxidative damage leads to β-cell malfunction and insulin resistance and occurs before overt hyperglycemia [10,11,19]. A significant difference between pro-oxidant and antioxidant systems, a defining feature of prediabetes that accelerates vascular problems and leads to endothelial dysfunction, is highlighted by the raised redox ratio (RR) found in our study. [12,13]. Mechanistically, this ifference is caused by a combination of advanced glycation end product synthesis, polyol and protein kinase C pathway activation, and hyperglycemia-induced overproduction of reactive oxygen species (ROS) [20,21].

The substantial correlation between oxidative stress indicators and visceral adiposity is one of the study's main conclusions. Visceral fat had a negative connection with TAOS and RR and a positive correlation with MDA, suggesting that oxidative imbalance is directly caused by fat accumulation. This association is supported by earlier research: Compared to subcutaneous fat, visceral fat mass has a stronger correlation with markers of systemic oxidative stress, such as oxidized LDL and urine isoprostanes [14,15,22]. Mechanistically, pro-inflammatory cytokines, adipokines, and free fatty acids released by visceral adipose depots encourage mitochondrial dysfunction and ROS overproduction [7,23]. These results highlight the function of visceral adiposity as a cause of oxidative damage as well as a sign of metabolic inefficiency.

When taken as a whole, our findings emphasise visceral adiposity as a key factor in prediabetic oxidative stress and redox imbalance. By increasing the risk of cardiovascular disease (CVD), endothelial damage, and β-cell dysfunction, this interaction speeds up the transition from prediabetes to type 2 diabetes [3]. Therefore, targeted therapies that reduce visceral fat by medication, lifestyle changes, and maybe antioxidant supplements may have two advantages: they may help mitigate oxidative damage and metabolic dysregulation.

Conclusion

This study emphasizes how visceral adiposity plays a critical role in promoting oxidative stress and weakening antioxidant defenses in people with prediabetes. A clear redox imbalance was highlighted by the prediabetic patients' increased central adiposity, increased lipid peroxidation, and decreased total antioxidant status as compared to normoglycemic controls. Strong associations between oxidative stress indicators and visceral fat further imply that visceral adipose tissue actively contributes to vascular dysfunction, oxidative damage, and systemic inflammation in addition to serving as an energy store. These results shed light on the mechanisms by which central adiposity raises the risk of cardiometabolic disease and accelerates the transition from prediabetes to type 2 diabetes. Early identification and targeted reduction of visceral fat, along with strategies to restore redox homeostasis, may offer dual benefits in mitigating metabolic dysregulation and preventing long-term complications. Future longitudinal and interventional studies are warranted to validate

these associations and evaluate the therapeutic potential of visceral fat reduction and antioxidant-based interventions in delaying or reversing prediabetes progression.

Conflict of interest: The Authors declare no conflict of interest**.**

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