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Research Article

Interplay of adiponectin and resistin in type 2 diabetes: Implications for insulin resistance and atherosclerosis

Rawan Abudalo[1], Abdelrahim Alqudah[1], Esam Qnais[2], Rabaa Y. Athamneh[3], Muna Oqal[4], Roaa Alnajjar[5]

1 *Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, The Hashemite University, Zarqa, Jordan*
2 *Department of Biology and Biotechnology, Faculty of Science, The Hashemite University, Zarqa, Jordan*
3 *Department of Medical Laboratory Sciences, Faculty of Allied Science, Zarqa University, Zarqa, Jordan*
4 *Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, The Hashemite University, Zarqa, University*
5 *Faculty of pharmaceutical sciences, Jordan University, Amman, Jordan*

Corresponding author: Abdelrahim Alqudah (abdelrahim@hu.edu.jo)

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Abstract

Aim: The study aims to investigate the association between type 2 diabetes and adipokines, particularly resistin and adiponectin, in insulin resistance. It also explores the potential of the resistin to adiponectin ratio as an indicator for these conditions

Methods: This research involved 198 participants, including 100 patients with type 2 diabetes and 98 controls. It focused on measuring various biochemical parameters like HbA1c, fasting plasma glucose, lipid profiles (low-density lipoprotein, oxidized low-density lipoprotein, triglyceride, total cholesterol), and adipokines (resistin and adiponectin). The study utilized the Homeostasis Model Assessment of Insulin Resistance and Triglyceride-Glucose index to evaluate insulin resistance.

Results: Type 2 diabetic patients exhibited higher levels of HbA1c, fasting plasma glucose, lipid profiles, and resistin, but lower adiponectin levels compared to controls. Adiponectin showed a negative correlation with insulin resistance, while resistin demonstrated a positive correlation. Both adipokines significantly related to atherogenic markers, with adiponectin offering protection against atherosclerosis and resistin augmenting it.

Conclusion: The findings underscore the complex roles of resistin and adiponectin in the pathophysiology of type 2 diabetes, insulin resistance. The resistin to adiponectin ratio could be a useful biomarker for insulin resistance. These insights suggest potential therapeutic strategies for treating diabetes and preventing its complications.

Keywords

type 2 diabetes, adiponectin, resistin, insulin resistance, HOMA-IR, TyG index, lipid profile

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PENSOFT

Introduction

Type 2 diabetes (T2D) is a global epidemic characterized primarily by hyperglycemia resulting from impaired insulin action and secretion (American Diabetes American Diabetes Association 2018). One of the pivotal mechanisms underlying the development of T2D is insulin resistance, wherein cells fail to respond efficiently to insulin, culminating in elevated blood glucose levels (Kahn 2003).

This impaired glucose metabolism and insulin resistance not only derange metabolic homeostasis but also has profound implications for cardiovascular health. The chronically elevated glucose levels in T2D patients can trigger endothelial dysfunction, a sentinel event in the initiation of atherosclerotic vascular disease(Hsueh and Quiñones 2003). Furthermore, insulin resistance has been directly linked to dyslipidemia, systemic inflammation, and hypertension, each of which can accelerate the progression of atherosclerosis and culminate in a broad spectrum of cardiovascular diseases (CVDs) (Bornfeldt and Tabas 2011).

Atherosclerosis is a primary factor leading to macrovascular disease in diabetic patients due to the constriction of blood vessel walls, especially the arterioles (Katakami 2018). This condition is multifaceted. Crucially, there's substantial evidence highlighting inflammation's role in the onset of atherosclerosis and the resulting vascular complications in diabetes (Blaschke et al. 2006). Elevated levels of certain biomarkers have been found, suggesting a potential for predicting atherosclerosis and related heart diseases in those with diabetes. Yet, few clinical studies have delved into the relationship and physiological effects of these inflammatory biomarkers in the context of diabetes and atherosclerosis. For instance, the pro-inflammatory biomarker CD36, found on macrophage membranes, interacts with oxidized LDL (Park 2014). This interaction boosts the creation of foam cells, marking the onset of atherosclerosis.

In recent years, there has been a rise in interest in the effect of oxidative stress and inflammation in common metabolic disorders such as type 2 diabetes (T2D) (Holvoet et al. 2007). Individuals diagnosed with diabetes have a reduction in plasma antioxidant activity and an elevation in levels of lipid hydroperoxides which are widely known indicators of oxidative stress in vivo (Lopez et al. 2005). Oxidative stress resulting from hyperglycemia leads to the modification of low-density lipoprotein cholesterol (LDL-C) into a form known as oxidized LDL (ox-LDL) (Evans et al. 2002). Elevated levels of Oxidized LDL have been shown to exacerbate atherosclerosis and cause damage to the endothelium of the artery wall (Goyal et al. 2012). The increase in ox-LDL levels within atherosclerotic plaques also plays a significant role in the progression of atherosclerosis (Yla-Herttuala et al. 1994).

Emerging in the milieu of metabolic and cardiovascular research are adipokines, bioactive molecules secreted by adipose tissue. These molecules have a crucial role in the control of various physiological processes, such as hunger and satiety, fat distribution, inflammation, blood pressure, and endothelial function they exhibit their functions in several organs, such as adipose tissue, the brain, the liver, blood vessels, and muscles (Blüher 2014).

These molecules serve as significant regulators of glucose and lipid metabolism and are directly implicated in the pathophysiology of insulin resistance, T2D, atherosclerosis, and CVD (Ouchi et al. 2011). Adiponectin, an abundant adipokine, is often lauded for its insulin-sensitizing, anti-inflammatory, and anti-atherogenic properties (Yamauchi et al. 2002). Multiple epidemiological studies indicate that a lack of adiponectin is linked to hypertension and coronary artery disease (Iwashima et al. 2004). In addition, mounting evidence from experimental investigations suggests that adiponectin plays a vital role in the prevention of metabolic and cardiovascular disease (Shibata et al. 2012). Multiple clinical researches have shown that hypoadiponectinemia is associated with the occurrence of insulin resistance (IR) and type 2 diabetes mellitus (DM) (Tabák et al. 2009; Kishida et al. 2012). Most of these studies indicate a decrease in adiponectin levels in individuals with Type 2 diabetes mellitus even at the initial stages of the disease, such as at the time of diagnosis (Sharma et al. 2006). Several prospective studies have shown that elevated levels of circulating adiponectin are linked to a reduced risk of Type 2 DM, even after accounting for several factors that could potentially influence this association (Mather et al. 2008).

Conversely, resistin, another adipokine, has been associated with insulin resistance and pro-inflammatory pathways, promoting endothelial dysfunction and atherosclerosis (Reilly et al. 2005). High levels of resistin are observed in obese and diabetic mice (Steppan et al. 2001), whilst functional reductions in resistin protein, such as the use of anti-resistin antibodies or resistin gene knockouts, have been shown to enhance insulin sensitivity and lower levels of blood glucose, free fatty acids, and triglycerides in mouse models (Kim et al. 2004). Recent clinical studies have found a direct association between elevated levels of resistin in the bloodstream and the severity of unstable angina and worse prognostic outcomes in patients with coronary artery disease (Lubos et al. 2007). This may be explained as resistin promotes the production of endothelin, a potent vasoconstrictor in endothelial cells, as well as prothrombotic atherogenic factors (Li et al. 2007). Considering these results collectively, it may be hypothesized that adiponectin and resistin have a shared regulatory mechanism that influences the body's metabolism, including energy, glucose, and lipid homeostasis. Therefore, a new index called the resistin/adiponectin (R/A) ratio may be suggested to offer a more accurate measure of metabolic homeostasis and metabolic diseases.

Understanding the complex interplay between adipokines, insulin resistance, T2D, and atherosclerosis could unravel new diagnostic and therapeutic avenues for managing metabolic and cardiovascular diseases.

Thus, this study aims to dissect the correlation between adiponectin, resistin, and the adiponectin-to-resistin ratio concerning parameters of glucose metabolism, and lipid profiles in patients with T2D. By exploring these

connections, we aspire to provide insights that could be instrumental in devising novel strategies for risk prediction and management in T2D and associated CVD.

Methodology

Study design and participants

This study was a case-control study as indicated by different previous reports (Al-Azzam et al. 2013; Babiikir Eltahir et al. 2020). Between April and July 2021, individuals with Type 2 Diabetes (T2D) and healthy individuals were directed to the Endocrinology Department at Prince Hamzah Hospital. Before joining the study, they were thoroughly briefed and provided their consent for a blood sample collection. The study included 100 people with T2D, and 98 were also included as controls who were matched for age and sex.

without any health concerns. The participants were eligible if they were diagnosed with T2D at least six months before the study, lived in Jordan, were older than 18, and were on a sulphonylurea derivative as an oral hypoglycemic drug, and diet treatment. Their casual physical activity ranged from simple household chores to brief post-meal walks, aiding in their energy burn and weight control. Those with Type 1 diabetes or Individuals with cancer, kidney failure, severe liver damage, inflammatory conditions, or those taking insulin, biguanide, thiazolidinedione, or cholesterol-lowering medications were not included in the research.

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of the Hashemite University (IRB number: 11/7/2020/2021).

Clinical and biochemical assessments

The diagnosis of T2D followed the criteria set by the American Diabetes Association (Anon n.d.), which hinges on a fasting blood glucose (FBG) level of 126 mg/dl or higher after refraining from eating for at least 8 hours. The control group was verified to be free of diabetes by checking the FBG levels on two distinct occasions. Body mass index (BMI) was determined by dividing their self-stated weight (in kg) by the square of their self-stated height (in meters). After resting for 10 minutes, trained nurses measured blood pressure three times from the right arm. Blood was drawn from a peripheral vein into tubes containing heparin. After gentle mixing, these samples were centrifuged at 3,000 rpm at a temperature of 4 °C for a quarter of an hour. Subsequently, the plasma was extracted and preserved at a temperature of -80 °C for later assessments.

Measurement of fasting blood glucose, HbA1c, insulin, HOMA-IR and TyG index

HbA1c levels were determined using a kit from Wondfo (China, catalog number: W207). Blood glucose concentrations were evaluated with a colorimetric detection kit by Biolabo (France, catalog number: 80009), all in line with the guidance provided by the respective manufacturers. Insulin was also measured using a commercially available kit (MBS761338, Mybiosource, USA) according to the manufacturer's instructions.

To assess insulin resistance, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and triglyceride–glucose (TyG) index were calculated. HOMA-IR was calculated using Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using a standard formula based on fasting glucose and insulin levels.

HOMA-IR = (Fasting glucose (mg/dL) × Fasting insulin (μIU/mL)/405 (Yoon et al. 2016).

TyG index was calculated using a standard formula based on fasting triglyceride and glucose levels.

TyG index = ln [fasting TG (mg/dL) × fasting glucose (mg/dL)/2] (Lee et al. 2021).

Analysis of lipid profile

Total cholesterol, low-density lipoproteins (LDL), and, high-density lipoproteins (HDL) were assessed using specific kits from Biolabo (France, catalog numbers: 80106, 90816, and 86516, respectively), following the guidelines provided by the manufacturer. Triglyceride (TG) levels were determined using a kit from Linear Chemicals (Spain, catalog number: 1155005), also in compliance with the manufacturer's directions. Oxidized LDL (ox-LDL) was measured using a commercially available kit (MBS168574, MyBioSource, USA) according to the manufacturer's instructions.

Measurement of serum resistin and adiponectin

Serum concentrations of resistin and adiponectin were determined using commercially available ELISA kits (Mybiosource, USA, MBS355429, and MBS2024009, respectively) as per the manufacturer's guidelines. The absorbance readings were taken at 450 nm using the ELx800 Microplate Reader by BioTek Instruments, located in Winooski, VT, USA. For every patient, the Resistin/Adiponectin (R/A) ratio was computed by dividing the resistin serum concentration (given in ng/ml) by the adiponectin serum concentration (expressed in ng/ml).

Statistical analysis

The demographic and clinical characteristics were summarized using means and standard deviations for continuous variables and frequencies for categorical variables. T-tests were used to compare the means between the T2D patients and the controls. P values were calculated, with values below 0.05 considered statistically significant. Pearson's correlation coefficient was used to assess the relationships between the adipokines (adiponectin, resistin, and the R/A ratio) and other metabolic and cardiac parameters. Again, p-values < 0.05 were considered to indicate a significant correlation.

Results

Clinical characteristics of type 2 diabetes patients vs. controls

As depicted in Table 1, the clinical characteristics of patients with Type 2 diabetes (T2D) were compared to controls to elucidate potential differences. A total of 100 T2D patients and 98 controls were included in this analysis.

Table 1. Clinical characteristics of the participants.

Parameter	Controls (n=98)	T2D (n=100)	*P* value
Gender (F/M, n)	52/46	51/49	
Age (years)	62.5 ± 9.4	64.0 ± 10.9	0.27
BMI (kg/m^2)	30.0 ± 2.0	29.0 ± 2.4	0.13
SBP (mm Hg)	124.2 ± 4.3	125.1 ± 2.9	0.26
DBP (mm Hg)	85.1 ± 5.2	85.5 ± 4.0	0.56
HbA1c (%)	4.9 ± 0.5	8.2 ± 1.7	0.0001
FPG (mg/dl)	83.5 ± 9.2	189 ± 44.7	0.0001
LDL (ng/ml)	42.4 ± 9.9	122.7 ± 9.1	0.0001
ox-LDL (pg/ml)	2466.4 ± 483.7	2931.7 ± 830.1	0.0001
TG (mmol/L)	1.8 ± 0.3	2.84 ± 0.2	0.001
T. Cholesterol (mmol/L)	4.6 ± 0.3	6.1 ± 0.4	0.007
HDL (ng/ml)	4421.3 ± 789.2	3286 ± 749.3	0.0001
Insulin (μU/ml)	4.1 ± 1.6	5.1 ± 1.3	0.0001
HOMA-IR	0.85 ± 0.3	2.4 ± 0.9	0.0001
TyG index	4.3	4.9	0.009
Adiponectin (ng/ml)	4.3 ± 1.6	0.6 ± 0.03	0.0001
Resistin (ng/ml)	7.5 ± 1.4	12.5 ± 1.2	0.0001
R/A ratio	1.8 ± 0.8	45.0 ± 15.1	0.0001

The gender distribution was comparable between the two groups, with females and males comprising 53% and 47% of the control group, respectively, and 51% and 49% of the T2D group (p=0.09). Similarly, age did not differ significantly between the groups (62.5 ± 9.4 years for controls and 64.0 ± 10.9 years for T2D patients; p=0.27) as individuals between groups were gender and age-matched to remove the impact of those variables.

Key metabolic parameters highlighted some stark differences between the groups. The HbA1c was markedly elevated in the T2D group (8.2 ± 1.7%) compared to controls (4.9 ± 0.5%) with a significant p-value of 0.0001. Fasting plasma glucose (FPG) in T2D patients was more than double that of controls (189 ± 44.7 mg/dl vs. 83.5 ± 9.2 mg/dl; p=0.0001).

Lipid profile was notably different between the groups. LDL levels in T2D patients were almost three times higher than in controls (122.7 ± 9.1 ng/ml vs. 42.4 ± 9.9 ng/ml; p=0.0001). On the contrary, HDL was found to be significantly lower in T2D patients when compared to controls (3286 ± 749.3 ng/ml vs. 4421.3 ± 789.2 ng/ml; p=0.0001), suggesting that dysregulation of lipoprotein metabolism and dyslipidemia associated with diabetes.

The oxidized LDL (ox-LDL), was significantly elevated in the T2D group (2931.7 ± 830.1 pg/ml) in comparison to the control group (2466.4 ± 483.7 pg/ml; p=0.0001). Similarly, the total cholesterol, triglycerides, insulin levels, HOMA-IR, and TyG (markers of insulin resistance) were also significantly higher in the T2D group.

Adiponectin, which is often decreased in diabetic conditions, was markedly lower in T2D patients (0.6 ± 0.03 ng/ml) compared to controls (4.3 ± 1.6 ng/ml; p=0.0001) while resistin, another adipokine, was elevated in the T2D group (12.5 ± 1.2 ng/ml) compared to controls (7.5 ± 1.4 ng/ml; p=0.0001). The resistin to adiponectin ratio (R/A ratio), an emerging marker of metabolic syndrome and insulin resistance, showed an exceedingly elevated value in T2D patients (45.0 ± 15.1) as opposed to controls (1.8 ± 0.8; p=0.0001).

Correlation between adipokines and HOMA-IR and TyG index in T2D

A correlation analysis was performed to understand the relationship between HOMA-IR, a well-established marker of insulin resistance, and adipokine-related parameters (Table 2).

Table 2. Pearson's correlation for serum adiponectin, resistin, and R/A ratio with HOMA-IR in T2D.

Parameter	HOMA-IR		TyG index	
	R	*P* value	R	*P* value
R/A	0.69	0.0001	0.53	0.006
Resistin	0.34	0.001	0.42	0.003
Adiponectin	-0.89	0.0001	-0.77	0.004

A robust positive correlation was observed between the R/A (Resistin/Adiponectin) ratio and HOMA-IR, with a correlation coefficient *r*=0.69 (p=0.0001). Similarly, a positive correlation was documented between R/A (Resistin/Adiponectin) ratio and the TyG index, with a correlation coefficient r=0.53 (p=0.006). This indicates that as the R/A ratio increases, there is a corresponding rise in HOMA-IR TyG index values.

Resistin showed a moderate positive correlation with HOMA-IR. The correlation coefficient was found to be 0.34, and the association was statistically significant with a p-value of 0.001. Similarly, resistin showed a positive correlation with the TyG index with a coefficient of 0.42 and this association was statistically significant with a p-value of 0.003. This result implies that higher levels of resistin are associated with increased insulin resistance. In contrast, adiponectin demonstrated a strong negative correlation with HOMA-IR and TyG index, with a correlation coefficient *r*=−0.89 and -0.77 (p=0.0001, 0.004, respectively).This inverse relationship suggests that as adiponectin levels decrease, there is a marked increase in HOMA-IR and TyG index values, indicating an enhancement in insulin resistance.

Correlations between adipokines and metabolic parameters in T2D

To unravel the relationship between the adipokines (Adiponectin and Resistin), as well as their ratio (R/A) and various metabolic parameters, a detailed correlation analysis was carried out (Table 3).

Adiponectin demonstrated a strong negative correlation with HbA1c (*r*=−0.87, p=0.0001). As adiponectin levels de-

Table 3. Pearson's correlation for serum adiponectin, resistin, and R/A ratio with various parameters in T2D.

Parameter	Adiponectin		Resistin		R/A	
	r	*P* value	r	*P* value	r	*P* value
HbA1c	-0.87	0.0001	0.78	0.0001	0.69	0.0001
LDL	-0.87	0.0001	0.88	0.0001	0.77	0.0001
ox-LDL	-0.97	0.0001	0.74	0.0001	0.66	0.0001
TG	-0.94	0.0001	0.58	0.001	0.65	0.001
T. Cholesterol	-0.30	0.01	0.49	0.001	0.49	0.001
HDL	0.88	0.0001	-0.74	0.0001	-0.71	0.0001

crease, HbA1c values tend to increase, suggesting potential glycemic control disruptions. On the other hand, Resistin positively correlated with HbA1c (r=0.78, p=0.0001), implying higher resistin levels might be associated with poor glycemic control. Moreover, a positive correlation between R/A ratio and HbA1c (r=0.69, p=0.0001) was observed.

Regarding the correlation with lipid profile measures, Adiponectin and Resistin showed strong negative and positive correlations respectively (r=−0.87 and r=0.88, both p=0.0001) with atherogenic LDL. The R/A ratio also displayed a positive correlation with LDL (r=0.77, p=0.0001). However, cardioprotective HDL demonstrated a strong positive correlation with Adiponectin (r=0.88, p=0.0001) and negative correlations with Resistin and the R/A ratio (r=−0.74 and r=−0.71 respectively, both p=0.0001). Furthermore, Adiponectin and Resistin correlated negatively and positively with TG respectively (r=−0.94 and r=0.58, both p=0.001). The R/A ratio also exhibited a positive correlation with TG (r=0.65, p=0.001) while a mild negative correlation was observed between cholesterol and adiponectin (r=−0.30, p=0.01) and moderate positive correlations with Resistin and the R/A ratio (r=0.49 for both, p=0.001). The results provide evidence to support the hypothesis that adiponectin may exert its beneficial effects on cardiovascular disease (CVD) by lowering lipoproteins, such as LDL, TG, and total cholesterol in contrast to resistin.

In a similar pattern, Adiponectin demonstrated a substantial negative correlation with ox-LDL (r=−0.97, p=0.0001), while Resistin showed a positive one (r=0.74, p=0.0001). The R/A ratio displayed a positive correlation with ox-LDL as well (r=0.66, p=0.0001). Thereby, resistin significantly increases lipid peroxidation in contrast to adiponectin.

Discussion

Type 2 diabetes (T2D) is a multifaceted metabolic disorder. The present study aimed to investigate the clinical characteristics of patients with T2D and controls and then delve deeper into the relationship between insulin resistance (quantified by HOMA-IR and TyG index) and specific adipokines, particularly adiponectin and resistin.

Consistent with established literature, our cohort of T2D patients showed significant differences in several metabolic and cardiovascular parameters compared to controls (American Diabetes Association 2018). Remarkably, HbA1c, FPG, LDL, ox-LDL, TG, and T. Cholesterol were substantially elevated in the T2D group which is consistent with a previous study that found that more than 90% of type 2 diabetic patients in Jordan had dyslipidemia of some kind. Specifically, hypercholesterolemia (77.2%), low HDL (83.9%), high LDL-c (91.5%), and hypertriglyceridemia (83.1%) were all present in this population (Nazik et al. 2008). As well as, the levels of resistin were substantially elevated in the T2D group, while adiponectin levels significantly diminished. Several studies have reported that individuals diagnosed with type 2 diabetes mellitus exhibited reduced concentrations of adiponectin in their bloodstream (Babiikir Eltahir et al. 2020). Meanwhile, a positive correlation between resistin levels and insulin resistance was established in type 2 diabetes and obese individuals (Siddiqui et al. 2020).

The aberration in these parameters aligns with the recognized pathophysiological alterations associated with T2D (Kahn 2003). Elevated HbA1c and FPG confirm chronic hyperglycemia in T2D patients, while the dyslipidemic profile, marked by heightened LDL, ox-LDL, and TG levels, underscores the heightened cardiovascular risk in this group (Lambie et al. 2021).

Resistin and adiponectin have emerged as vital links in the interplay between metabolism and inflammation. The adipokine adiponectin, generally deemed to have insulin-sensitizing properties, showed a strong negative correlation with HOMA-IR, supporting its protective role against insulin resistance (Myeong et al. 2006). This observation complements previous findings that tout adiponectin as a negative regulator of inflammation and a mediator of glucose regulation (Fantuzzi 2005). In contrast, resistin displayed a positive correlation with HOMA-IR, highlighting its role in exacerbating insulin resistance (Askin et al. 2022). It has been proposed that resistin acts on liver and muscle cells, inhibiting the effects of insulin, and thereby promoting insulin resistance (Gu et al. 2023).

Another focal point was the understanding of how these adipokines relate to atherosclerosis, a prime mediator of cardiovascular complications in T2D (Gasbarrino et al. 2023b). Elevated LDL, TG, and total cholesterol levels are known to promote atherosclerosis (Mushenkova et al. 2021). Our findings suggest that adiponectin is inversely associated with these atherogenic markers, while resistin shares a direct relationship. Adiponectin, through its anti-inflammatory and anti-atherogenic properties, can inhibit the transformation of macrophages to foam cells, a crucial step in atherosclerotic plaque formation (Gasbarrino et al. 2023a). Conversely, resistin's pro-inflammatory actions might fuel atherosclerosis progression (Dos Santos et al. 2021).

The role of oxidized low-density lipoprotein (LDL) as a marker of oxidative stress in the progression of atherosclerosis has been proposed to be substantial, and there exists a correlation between atherosclerotic problems with both diabetes and obesity. Limited research has been conducted on the association between oxidized low-density lipoprotein (Ox-LDL) and adipokines, with a notable absence of studies specifically examining their correlation with resistin and adiponectin. In this study, we formulated a

hypothesis regarding a potential correlation between adipokines and Oxidized LDL in an in vivo setting. The findings of our study indicate a positive correlation between concentrations of Ox-LDL and resistin (Xu et al. 2006) whilst Ox-LDL has an inverse correlation with adiponectin (Basati et al. 2011).

Elevated levels of resistin and decreased levels of adiponectin are both associated with detrimental outcomes in cardiovascular health. Resistin, an adipokine, is not just an indicator of adiposity but has been correlated with increased inflammation, endothelial dysfunction, and atherosclerotic progression, which are critical factors in the onset and progression of cardiovascular disease (Reilly et al. 2005; Tarkhnishvili et al. 2022). In contrast, adiponectin, another adipokine, often acts in a protective capacity for the cardiovascular system. Lower adiponectin concentrations have been linked to an elevated risk of hypertension, coronary artery disease, and other cardiovascular complications. This protective adipokine is known to inhibit vascular inflammation and atherosclerotic plaque formation, suggesting its critical role in maintaining cardiovascular health (Shibata et al. 2005; Zhou et al. 2021). Thus, imbalances in resistin and adiponectin levels can serve as significant indicators and potentially modifiable risk factors for cardiovascular disease.

The R/A ratio, representing the resistin to adiponectin balance, has been proposed as a better marker for insulin resistance and atherosclerosis than each adipokine alone (Norata et al. 2007). Our results corroborate this, as the R/A ratio exhibited strong positive correlations with several markers of insulin resistance and atherosclerosis.

Conclusion

Our findings amplify the intricate roles of resistin and adiponectin in modulating insulin resistance, atherosclerosis, and cardiovascular function in T2D patients. The R/A ratio stands out as a potential diagnostic and prognostic tool. Future studies should focus on mechanistic pathways of adipokines as diagnostic and therapeutic targets.

Author contributions

Conceptualization, A.A. and R.A.D.; methodology, E.Q. and R.Y.A.; software, M.O.; validation, A.A. and E.Q.; formal analysis, R.A.N.; investigation, A.A.; resources, E.Q.; data curation, M.O.; writing—original draft preparation, A.A.; writing—review and editing, R.A.D.; visualization, E.Q.; supervision, R.A.D.; project administration, R.A.D.; funding acquisition, R.A.D. All authors have read and agreed to the published version of the manuscript.

All participants provided a consent form prior to joining the study.

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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