ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Correlation of irisin with lipid profile in type 2 diabetes mellitus

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Submission: 27-11-2024 Revision: 04-01-2025 Publication: 01-02-2025

ABSTRACT

Background: Irisin, a novel adipo-myokine, improves insulin sensitivity by browning of white adipose tissue and also promotes pancreatic β-cell proliferation. Irisin was seen to have great therapeutic potential in treating type 2 diabetes mellitus (T2DM) patients. **Aims and Objectives:** Our study aimed to estimate the levels of serum irisin, lipid profile, and fasting blood sugar (FBS) in T2DM cases and healthy controls and to find any correlation among them. **Materials and Methods:** We conducted a case–control study on 40 T2DM patients and 40 healthy controls. Enzyme-linked immunosorbent assay was employed for the estimation of serum irisin level, estimation of FBS by glucose oxidase-phenol 4 amino phenazone method (GOD/PAP), and lipid profile by enzymatic colorimetric method. **Results:** Irisin was found to be lesser (P = 0.00) in T2DM cases (14.5 ± 8.6 ng/mL) as compared to controls (28.4 ± 3.9 ng/mL). In T2DM cases, serum irisin was inversely correlated with FBS levels (r = −0.32, P = 0.04), FBS was correlated directly with total cholesterol (T-Chol) (r = 0.216, P = 0.180), triglyceride (TG) (r = 0.289, P = 0.071), and low-density lipoprotein (LDL) (r = 0.325, P = 0.041) and negatively correlated (r = −0.269, P = 0.094) with high-density lipoprotein (HDL) levels. Whereas irisin levels showed negative correlation with T-Chol (r = −0.294, P = 0.066), TGs (r = −0.237, P = 0.140), and LDL (r = −0.341, P = 0.031) and positive correlation with HDL (r = 0.238, P = 0.139) levels. **Conclusion:** Our study showed that the level of serum irisin was decreased in T2DM patients significantly when compared with controls. Irisin improves lipid profile and FBS levels in T2DM cases, hence it may be essential as an adjunctive therapeutic target in the management of T2DM.

Key words: Diabetes; Irisin; Lipid profile

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i2.4342

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Irisin is a peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α)-dependent myokine which is released mainly by skeletal muscle. Certain tissues, such as adipose tissue, liver, brain, heart, stomach, and subcutaneous gland also secrete irisin in low concentration.[1] The predecessor of irisin, fibronectin type III domain containing 5 (FNDC5), undergoes proteolytic cleavage and releases irisis.[2] Irisin is known to be expressed and secreted in response to exercise, and also it improves insulin resistance by reducing obesity through the browning of white adipose tissue.[3] Brown adipose tissues affect body metabolism through its role in thermogenesis by its action on uncoupling protein 1 (UCP1). Enhancing thermogenesis may improve glucose tolerance, reduce fat mass, lower body weight, and increase insulin sensitivity.[4,5]

Irisin is also known to have its effect on several complications of obesity including dyslipidemia, metabolic syndrome, and type 2 diabetes mellitus (T2DM).[6] Furthermore, irisin through its effect on the expression of UCP1 increases the expenditure of energy and consumption of lipid reserves thereby, contributing to metabolic diseases.[7] Dyslipidemia in diabetes is characterized by raised total cholesterol (T-Chol), triglyceride (TG), high-density lipoprotein (HDL), and normal or increased low-density lipoprotein

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(LDL).[8] Diabetic patients often have risk factors for cardiovascular diseases as they exhibit an atherogenic lipid profile.[9] However, various studies have shown inconsistent relations between irisin and dyslipidemia. Therefore, this study was taken up to find out the association between them by measuring the lipid profile, serum irisin, and fasting blood sugar (FBS) levels in patients with T2DM and healthy individuals.

Aims and objectives

1. To estimate the level of serum irisin, fasting blood sugar and lipid profile in T2DM cases and healthy controls
2. To compare and find any correlation among them.

MATERIALS AND METHODS

With permission from the Regional Institute of Medical Sciences Ethical Board, the case–control study was carried out in the Biochemistry and Medicine Departments in Imphal, Manipur. It was conducted from October 2019 to September 2021. The study population comprised 40 T2DM patients and 40 healthy controls.

Inclusion criteria

Age, sex, and body mass index (BMI) matched adult-diagnosed cases of T2DM and normal healthy individuals as controls.

Exclusion criteria

Pregnancy, anorexia nervosa, metabolic syndrome, chronic renal disease, coronary artery disease, type 1 diabetes, and a history of vascular illnesses were excluded.

Biochemical parameters

About 5 mL of fasting blood was drawn from the antecubital vein. Enzyme-linked immunosorbent assay method was employed for the estimation of serum irisin, FBS was estimated using glucose oxidase/phenol 4 amino phenazone method, and fasting lipid profile estimation was done by enzymatic colorimetric assay.

Statistical analysis

For data analysis, IBM: SPSS version 21.0 was employed. The independent samples t-test and the Chi-square test were employed to compare the means. To establish the correlation between the variables, Pearson's correlation was used. P<0.05 was regarded as significant.

RESULTS

In our research, the age, sex, and BMI of the two categories, that is, 40 cases and 40 controls, were matched. In comparison to the control group (86.6±9.2 mg/dL), the FBS in cases (163.6±64 mg/dL) was substantially higher (P<0.05).

Figure 1 shows that serum irisin level was significantly decreased (P=0.00) in cases of T2DM (mean=14.5±8.6 ng/mL) as compared to controls (mean=28.4±3.9 ng/mL).

Figure 2 shows that T-Chol, TG, and LDL levels were higher in cases of T2DM as compared to controls though both the values were in the normal range. The HDL value was lower than normal in T2DM cases but normal in controls.

Figure 3 shows that there is a good amount of clumping in this scattered diagram with the pattern of dots sloping from left upper to right lower side which indicates a negative correlation between serum irisin and FBS which was statistically significant (r=−0.32, P=0.04).

Table 1: This table shows that FBS is positively correlated with T-Chol, TG, and LDL and negatively correlated with HDL levels though the correlation is low and statistically significant only for the value of LDL (P=0.041).

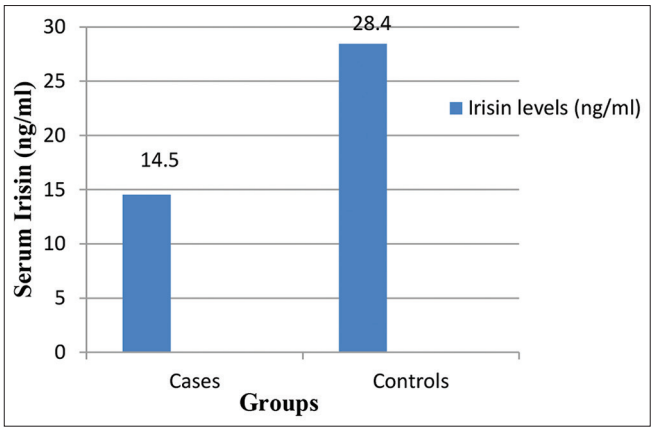

Figure 1: Serum irisin level in cases and controls

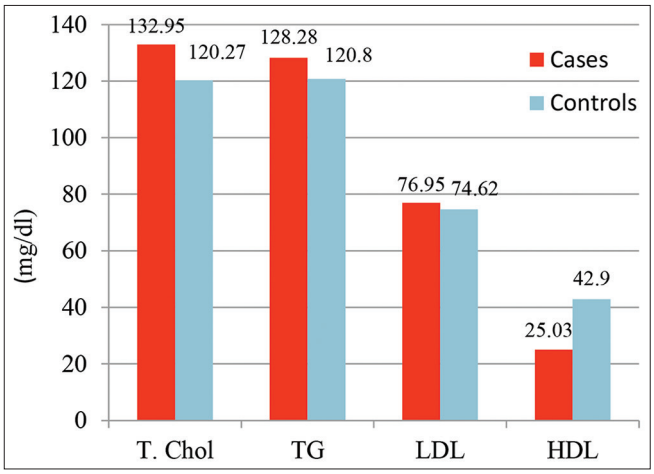

Figure 2: Graphical representation of lipid profile in cases versus controls

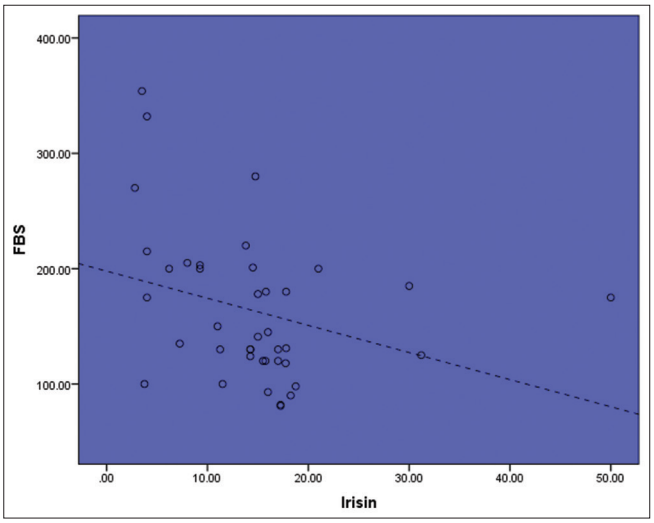

Figure 3: Correlation between serum irisin and fasting blood sugar in type 2 diabetes mellitus cases (scattered diagram)

Table 1: Correlation of fasting blood sugar with lipid profile in cases of T2DM

Lipid profile	FBS	
	r-value*	P-value
Total cholesterol	0.216	0.180
Triglyceride	0.289	0.071
LDL	0.325	0.041
HDL	−0.269	0.094

*Pearson correlation (0.2≤r ≤ 0.39: Low correlation), LDL: Low-density lipoprotein, HDL: High-density lipoprotein, T2DM: Type 2 diabetes mellitus, FBS: Fasting blood sugar

Table 2: Correlation of serum irisin with lipid profile in cases of T2DM

Lipid profile	Irisin	
	r-value*	P-value
Total cholesterol	−0.294	0.066
Triglyceride	−0.237	0.140
LDL	−0.341	0.031
HDL	0.238	0.139

*Pearson correlation (0.2≤r ≤ 0.39: Low correlation), LDL: Low-density lipoprotein, HDL: High-density lipoprotein, T2DM: Type 2 diabetes mellitus

Table 2: This table shows that irisin is negatively correlated with T-Chol, TG, and LDL and positively correlated with HDL levels though the correlation is low and statistically significant only for the value of LDL (P=0.031).

DISCUSSION

The present study found that dyslipidemia improved with higher irisin levels and worsened with higher FBS levels, though the correlation was statistically significant only with LDL levels for both associations.

In this study, the mean level of irisin in T2DM cases (14.5±8.6 ng/mL) is significantly lower than that of controls (28.4±3.9 ng/mL) as shown in Figure 1. Such similar findings were witnessed by Xuan et al., Balaban et al., and Elizondo-Montemayor et al.,[10-12] in their studies. Some researchers believe that reduced irisin levels in T2DM can be explained by lower PGC-1α activity in the muscle tissue which leads to reduced synthesis of FNDC5, ultimately lowering irisin production.[13,14] PGC-1α has also been shown to operate on white adipocytes *in vitro* and *in vivo*, promoting UCP1 expression and changing the expression of many molecules that resemble brown fat.[5] This conversion enhances thermogenesis leading to an improved sensitivity toward insulin and glucose tolerance along with the reduction in body weight in mice.[5,15] Beta cell regeneration and expression of betatrophin are stimulated by UCP-1 mediated action of irisin resulting in improved insulin sensitivity. Therefore, these findings suggested that irisin can act as a sensitive biomarker of insulin resistance.[16]

Our study has shown a better lipid profile in controls as compared to cases of T2DM as shown in Figure 2. Previous studies have reported dyslipidemia as being a risk factor in diabetes.[17] Studies published by AL-Bahrani and Yassin and Azad et al., have demonstrated an association between dyslipidemia and glycemic control in patients with type 2 diabetes.[9,18]

There is an inverse correlation between FBS and serum irisin (Figure 3) in cases of T2DM (r=−0.32, P=0.04) which is similar to the findings observed in the studies done by He et al., and Xiang et al.,[19,20] These observances suggest that insulin resistance might be an outcome of reduced serum irisin levels.

High TG and low HDL together with elevated T-Chol were seen in T2DM patients in the research conducted by Bhowmik et al., which is similar to our observation as shown in Table 1.[8] Actions of cholesteryl ester transfer protein (CETP), regulation of lipoprotein lipase, effects of insulin on apoprotein production by the liver along with actions of insulin on muscle and adipose tissues are related to diabetic dyslipidemia.[21] Insulin resistance in hypertriglyceridemia is mainly caused by the elevated release of very low-density lipoprotein particles by the liver, reduced levels of lipoprotein lipase, and post-prandial hyperlipidemia. The current hypertriglyceridemia facilitates the transfer of TG from TG-rich lipoproteins (CETP mediated) leading to the formation of HDL-C enriched with TG. Hepatic lipase reduces the amount of total HDL by breaking down big HDL particles into smaller ones that the kidneys can eliminate more quickly.[22,23]

Dyslipidemia combined with increased blood glucose levels aggravates atherosclerosis-associated inflammation.[24]

Newly diagnosed asymptomatic T2DM patients have also demonstrated a large extent of coronary artery calcification.[25] In addition to being a significant risk factor for macrovascular problems, dyslipidemia has also been linked to microvascular problems associated with type 2 diabetes, including diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy.[26-29]

According to this study, irisin had a favorable correlation with HDL and a negative correlation with T-Chol, TG, and LDL in T2DM patients even though it is a low correlation and significant only for LDL. Similar findings were observed by Xiong et al., Zhang et al., Morelli et al., and Tang et al.[30-33]

A study done by Xiong et al. shows that FNDC5 overexpression and irisin perfusion reduced the serum T-Chol, TG, free fatty acid, and FBS levels which were elevated in mice fed with a high-fat diet, this indicates that irisin efficiently attenuates the derangement of lipid metabolism in obesity.[30]

In addition, this work has demonstrated that FNDC5/irisin enhances lipolysis and decreases hyperlipidemia through the phosphorylation of hormone-sensitive lipase (HSL) and perilipin, which serves as an HSL-protecting coat for adipocytes. Phosphorylation of perilipin exposes stored lipids to HSL leading to lipolysis.[30,34-36] Perilipin must be phosphorylated by protein kinase A to cause the translocation of HSL from the cytosol to the surface of lipid droplets and start lipolysis.[37,38] Thus, perilipin downregulation and HSL upregulation induced by irisin are partially responsible for its lipolysis-promoting effect.[30] The beneficial effect of FNDC5/irisin in increasing lipolysis by upregulation of UCP1 expression, which in turn increases the expenditure of energy which reduces the accumulation of lipids in tissues. This decreases serum lipid levels and attenuates glucose/lipid metabolic abnormalities and insulin resistance. Thus, FNDC5/irisin can be considered an effective therapeutic approach in the management of glucose/lipid metabolic disorders.[30]

Limitations of the study

The limitations of the study were restricted study duration which resulted in smaller sample size and uncertain duration of dyslipidemia.

CONCLUSION

This study showed that T2DM patients have significantly lowered levels of serum irisin when compared with controls and it also showed an inverse correlation with FBS and related with improved lipid profile. FBS level also showed an inverse relationship with better lipid profile in cases of T2DM. Irisin, secreted by muscles and adipocytes in response to exercise, is suggested to have an essential role in glucose utilization and lipid metabolism. Due to its anti-diabetic and anti-obesity properties, there is a hope that irisin can be used as an injection for treatment using recombinant DNA technology. Hence, irisin may be essential as an adjunctive therapeutic target in the management of T2DM. Moreover, exercise may be encouraged for potential prevention and a better prognosis of T2DM.

ACKNOWLEDGMENT

We would like to express our gratitude to our lab-mates and technicians who helped in our study.

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WDD- Concept, design, manuscript preparation, literature survey, preparing the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, and editing; **OPD**- Concept, design, manuscript editing, review manuscript; **UK**- Concept, design, literature survey, review manuscript and Edit; **TPS**- Concept, design, manuscript editing, review manuscript, and manuscript revision.

Work attributed to:
We would like to attribute this study to our senior faculties for their guidance and support.

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Source of Support: Nil, **Conflicts of Interest:** None declared.