EVALUATION OF SERUM IRISIN WITH LIPID PROFILE IN TYPE-2 DIABETIC PATIENTS IN SULAIMANI

Fenk Bakir Maarouf [a], Mohammed O. Mohammed [b], Nazaneen Akbar Omer [a], and Beston Faiek Nore [a, c]

Submitted: 26/5/2018; Accepted: 12/8/2018; Published 15/10/2018

ABSTRACT

Background

Obesity has become one of the most growing global risk factor for many diseases and metabolic disorders, including Type -2 Diabetes Mellitus (T2DM). Irisin is a recently discovered myokine hormone and has a primary structure of 112 amino acids. It is expressed and secreted by muscles in response to physical activities that control obesity and delay insulin resistance. Several studies show decrease in Irisin levels in a number of metabolic disorders, but the Irisin status is unknown in diabetic patients in our region.

Objectives

To evaluate the level of serum Irisin with serum lipid profile in T2DM patients.

Patients and Methods

This study was carried out on 256 individuals, 156 T2DM patients (study group) and 100 non-diabetic individuals (control group) in Sulaimani diabetic centre. The serum level of irisin, glucose, urea, creatinine, lipid profile, and glycated hemoglobin were determined using biochemical and immunological methods. Statistical analysis was performed using STATA 14 software.

Results

The mean serum Irisin level was significantly higher ($P<0.01$) in the control group compared to T2DM (3.34±1.48 vs. 1.82±1.44) respectively. The body mass index (BMI) was significantly higher in T2DM patients (31.06 ±5.3) compared to the control (28.55±3.9). The levels of total cholesterol, triglyceride (TG) and low-density lipoprotein (LDL) were significantly higher in T2DM, while high-density lipoprotein (HDL) was lower in T2DM compared to the control. The Atherogenic Index of plasma (AIP) was significantly higher inT2DM (1.9±0.44) compared to the control (1.2±0.59). There was a significant inverse association ($p<0.001$) between AIP and serum Irisin in both groups.

Conclusions

Serum Irisin was significantly lower in T2DM compared to non-diabetic control. There was a significant inverse correlation between serum Irisin and AIP in both groups. However, there was no significant correlation between serum Irisin with age, gender and BMI in both groups.

Keywords: *Irisin, T2DM, BMI, Obesity, Atherogenic Index, Lipid profile.*

---

[a] Department of Biochemistry, College of Medicine, University of Sulaimani.
Correspondence: fenk.maarouf@univsul.edu.iq
[b] Department of Medicine, College of Medicine, University of Sulaimani.
[c] Department of Health, Kurdistan Institution for Strategic Studies and Scientific Research, Sulaimani.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder commonly presents with episodes of hyperglycemia and glucose intolerance as a result of lack of circulating insulin (type 1 DM) or defective insulin action (T2DM), or both [1]. Dyslipidemia is one of the major risk factors for cardiovascular disease in DM. The characteristic features of diabetic dyslipidemia are a high plasma TG, low HDL cholesterol and increased concentration of small dense LDL-cholesterol particles. Lipid changes associated with DM are explained by increasing free fatty acid flux secondary to insulin resistance [2].

Irisin is a novel myokine hormone, synthesized through proteolytic cleavage of the gene product Fndc5 (Fibronectin type III domain-containing protein 5) and released into the extracellular milieu [3, 4]. Irisin expression induced by exercise and by the peroxisome proliferator-activated receptor gamma co activator 1α (PGC1α). Irisin enhances the browning of subcutaneous adipocytes and regulates the thermogenesis by elevating the level of uncoupling protein 1 (UCP1)[5].

Recently, irisin has gained great interest as a potential new target to mitigate obesity and its associated disorders, such as T2DM. It has been found that moderate increases in circulating Irisin level accelerates energy expenditure, protects against diet-induced weight gain and mollify insulin resistance [6]. Age and skeletal muscle mass are the essential predictors of the circulating Irisin level with young male athletes having Irisin levels several folds higher than those in middle-aged obese women [7]. The circulating Irisin is significantly lower in individuals with T2DM compared with control subject [8, 9].

Up to our knowledge, the correlations of human serum irisin alterations with human metabolic disorders have not been performed thoroughly, especially in our locality. In this study, we have assessed the correlation of serum irisin levels together with the lipid in T2DM patients and non-diabetic individuals.

PATIENTS AND METHODS

This is a case control study, conducted in the Sulaimani Diabetic centre from January 2016 to August 2016, included; 156 T2DM patients and 100 non-diabetic controls. Ethical approval was obtained from the ethical committee at the College of Medicine, University of Sulaimani, a written consent was obtained from all participants.

Inclusion criteria involved patients whom were diagnosed as T2DM and their ages were above 35 years, however Individuals with renal impairment, thyroid dysfunction, pregnant and postpartum females were excluded from this study.

Blood samples were obtained from all the participants for measuring serum irisin, glucose, urea, creatinine and lipid profile, the biochemical tests were measured by Cobas C-311/ Roche diagnostic, Germany.

Serum irisin was measured by ELISA using biotin double antibody sandwich technology, according to the manufacturer's recommendations (Shanghai LIZA Zak Co./China.

Atherogenic index of plasma (AIP) was calculated according to the formula = log(TG/HDL-C) [10, 11].

Statistical analysis was performed using STATA software 14. $P \leq 0.05$ was considered statistically significant.

RESULTS

The age distribution and gender in both groups presented in Table 1.

The mean age, gender distribution, serum urea and serum creatinine were comparable in both groups. The BMI of Diabetics (31.1± 5.3) was significantly higher ($p< 0.01$) than control (28.5± 3.9). More than half (57.7 %) of diabetics and 38% of the controls had BMI ≥ 30. The fasting blood glucose (FBG) level was significantly higher in the T2DM patients (177.6±68.6) compared to the control group (90.7±5.0), Table 2 and Figure 1.

The mean BMI of Females (31.1±5.4) was significantly ($p<0.01$) higher than that of Males (28.9± 4.2) in all participants.

The HbA1c in diabetics ranged between 6.1-15.7%, with mean of 9.67 ±2.2. Most of the patients (81.4%) had glycated hemoglobin above 7.5%, there was no significant difference regarding HbA1c and genders ($P= 0.55$).

The total serum Cholesterol, TG and LDL were significantly higher, while HDL-C was significantly lower in diabetics compared to control.The atherogenic index of plasma was significantly higher among diabetics compared to the control (Table 3).

The AIP of the participants with normal BMI was

(1.42± 0.42) which was significantly lower than AIP in obese (1.75 ± 0.52), (Table 4).

In all samples, Irisin hormone level ranged between 0.5 -26.5µg/dl, the mean serum irisin in diabetics was (1.82 ± 1.44)which was significantly lower than the mean serum irisin in controls (3.34 ± 1.48),(Table 5).

There was no significant difference (p= 0.724) in the mean serum irisin between male and female in both studied groups, Table 6.

There was no significant association between irisin with age (correlation coefficient (r: -0.0007), and BMI (r: -0.036) in both groups. However, the serum Irisin level was negatively associated with AIP (p<0.01).

Table 1. The distribution of age and gender among studied Groups.

Groups	No.	Age (Year) (Mean± SD)	Gender (Male/Female)
T2DM	156	53.5± 9.67	71/85
Controls	100	53.7 ± 8.69	48/52

Table 2. The characteristics and the laboratory data of the studied groups.

Variables	T2DM (n=156)	Control (n=100)	P value
Female, No. (%)	85 (54%)	52(52%)	0.56
Male, No. (%)	71(46%)	48(48%)	0.69
Age (Mean ± SD),year	53.5 ± 9.67	53.7 ± 8.69	0.88
Family age history of T2DM	109 (69.9%)	11 (11%)	<0.01
BMI (kg/ m2)	31.1± 5.3	28.5± 3.9	<0.01
FBG (mg/dL)	177.6± 68.6	90.7±5.0	<0.01
Serum urea (mg/dL)	24.2±5.8	26.1±7.4	0.15
Serum creatinine,(mg/dL)	0.84± 0.1	0.81± 0.2	0.14
HbA1c %	9.67 ± 2.2	5.1± 0.4	<0.01

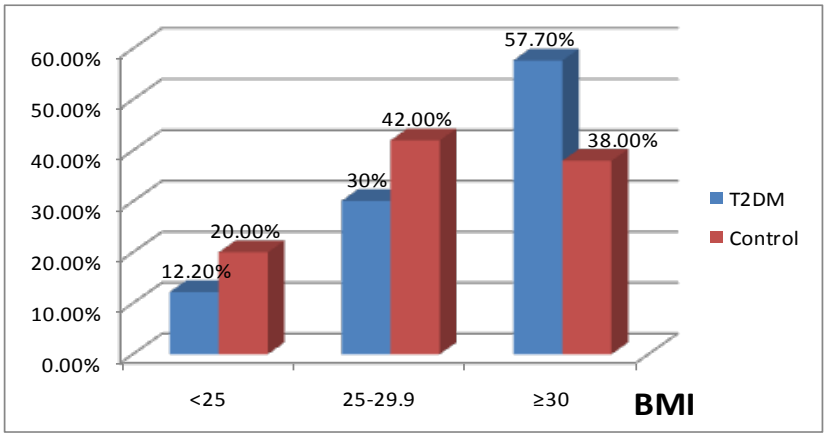

Figure 1. Body mass index is classified among the studied groups as normal (<25), overweight (25-29.9) and obese (≥ 30).

Table 3. The biochemical parameter analysis among the studied groups. (A) Lipid profile and (B) Atherogenic index of plasma (AIP).

(A) Lipid profile

Serum Lipid Profile (mg/dL)	T2DM Mean± SD	Control Mean± SD	P value
T.Cholestrol	198.7±55.8	172.2± 35.4	<0.01
TG	236±84.2	152.9± 78.1	<0.01
HDL-C	34.8± 5.3	42.3±10.4	<0.01
LDL-C	131.1±49.3	99.3± 29.1	<0.01

(B) AIP

Groups	AIP (Mean±SD)	95% Confidence Interval (µg/dl)		P value
T2DM	1.9± 0.44	1.79	1.93	< 0.01
Control	1.2± 0.59	1.07	1.31	

Table 4. Atherogenic index of plasma in normal, overweight and obese participants using ANOVA.

BMI	No.	AIP* (Mean±SD)	95 % Confidence Interval (µg/dl)		P valu ANOVA
Up to 24.9	39	1.42± 0.42*	1.36	1.54	<0.01
25- 29.9	89	1.47 ± 0.57	1.35	1.60	
30 and over	128	1.75 ± 0.52*	1.64	1.86	
Total	256	1.60±0.60	1.53	1.67	

Table 5. Serum Irisin level in diabetic and control groups.

Serum Irisin	T2DM	Control	P value
M.±SD µg/dl	1.82 ± 1.44	3.34 ± 1.48	<0.01
95 % C.I	1.59- 2.05	2.25- 4.43	

Table 6. Correlation of serum Irisin with gender in all participants.

S. Irisin	Male (No. 119)	Female (No. 137)	Total (No. 256)
Mean± SD (µg/dl)	2.334±3.146	2.497±4.091	2.421±3.676
P value		0.724	

DISCUSSION

Since Irisin's discovery in 2012, it has attracted great attention for its suggested role of the browning of white adipose tissue and therefore increasing energy expenditure by enhanced thermogenesis, and its potential use as a new therapy option in obesity and diabetes mellitus [12].

The mean age of recruited patients was 53.5 ± 9.67years, this is comparable to another study which showed that T2DM is the disease of middle age and elderly people [13].The family history of diabetes was significantly higher among diabetic group than control, this could be explained by the fact that genetic factors play an important role in the pathogenesis of T2DM [14].

The mean HbA1c of diabetics was 9.67 ± 2.2 % (more than 80% of the diabetic patients in this study had their HbA1c above 7.5%), this indicates a poor glycemic control during that period. This result is similar to studies in Malaysia and other developing countries which showed that only 20.4% of diabetics achieved the target control. This result could be explained by regional diet style, lack of physical activities, and lack of knowledge on protection measures toward diabetes. Conversely, the better glycemic control in Japan and Germany might be due to the higher literacy rate, and better knowledge about the disease [15].

In the present study, it was found that the total cholesterol, TG and LDL were significantly higher, while HDL was significantly lower in diabetics compared to control, which is similar to Hachem and Nooradian study [16]. These changes are resulted from increased free fatty acid flux secondary to insulin resistance and aggravated by increased inflammatory Adipokines [17, 18].A similar pattern of altered plasma lipid profiles was observed in the UK Prospective Diabetes Study [2, 19].

The mean AIP was significantly higher in T2DM compared to control , this result is in agreement with Tan and Rajab studies [19, 20] .The AIP was significantly ($p < 0.01$) associated with BMI, which also proved by Niroumand study [21].

In this study, the mean serum irisin level in diabetics, control group were (1.82 ± 1.44 and 3.34 ± 1.48 µg/dl) respectively, with significant difference ($P< 0.01$). In other studies, a significant lower serum irisin level was found in newly diagnosed and untreated T2DM as compared to BMI matched control [8, 9, 22],the lower circulating irisin in T2DM may be due to lower PGC-1α activity in skeletal muscles which consequently leads to decreased UCP1-in brown adipocytes [23, 24].

In the present work, it was found that about 88% of T2DM has BMI above normal with lower mean serum Irisin. In another study a significant negative correlation between body fat mass ($r= - 0.47$, $P < 0.05$) with circulating Irisin levels [25]. Irisin level was inversely associated with AIP, this finding is supported by another study that found a negative correlation of serum Irisin with the TG contents in the liver and liver enzymes in obese adults [26].

In conclusion, the mean serum irisin concentration was significantly lower in T2DM than control. There was no significant correlation between serum Irisin with gender, age and BMI in both groups. Serum irisin was negatively associated with AIP. Serum total Cholesterol, TG and LDL were significantly higher, but HDL-C was lower, in diabetic group compared to control. AIP was significantly higher among diabetics compared to control group, and significantly correlated with BMI in both groups.

Acknowledgements

We are grateful to the staff members of Diabetic Center, and Directorate General Health Laboratory-2, for their help in collecting the samples. Thanks to Dr. Saman Hussein and Dr.Baraa Ramzi for their support.

Conflict of interest

The authors declare no competing financial interests.

REFERENCES

1. Piero MN. Diabetes mellitus – a devastating metabolic disorder. Asian J Biomed Pharm Sci. 2015;4(40):1–7.

2. Mooradian A. Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab [Internet]. 2009;5(3):150–9. Available from: http://www.nature.com/nrendo/journal/v5/n3/full/ncpendmet1066.html

3. Ferrer-Martínez A, Ruiz-Lozano P, Chien KR. Mouse PeP: A novel peroxisomal protein linked to myoblast differentiation and development. Dev Dyn. 2002;224(2):154–67.

4. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012;481(7382):463–8.

5. Hwang Y-C, Jeon WS, Park C-Y, Youn B-S. The ratio of skeletal muscle mass to visceral fat area is a main determinant linking circulating irisin to metabolic phenotype. Cardiovasc Diabetol [Internet]. BioMed Central; 2016;15(1):9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26790404%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4719696

6. Chen J, Huang Y, Gusdon AM, Qu S. Irisin: a new molecular marker and target in metabolic disorder. Lipids Health Dis. 2015;14:2.

7. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. Metabolism. 2012;61(12):1725–38.

8. Choi YK, Kim MK, Bae KH, Seo HA, Jeong JY, Lee WK, et al. Serum irisin levels in new-onset type 2 diabetes. Diabetes Res Clin Pract. 2013;100(1):96–101.

9. Liu J-J, Wong MDS, Toy WC, Tan CSH, Liu S, Ng XW, et al. Lower circulating irisin is associated with type 2 diabetes mellitus. J Diabetes Complications [Internet]. 2013;27(4):365–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23619195

10. Kanthe PS, Patil BS, Bagali S, Deshpande A, Shaikh GB, Aithala M. Atherogenic index as a predictor of cardiovascular risk among women with different grades of obesity. Int J Collab Res Intern Med Public Heal. 2012;4(10):1767–74.

11. Dobiásová M, Frohlich J, Sedová M, Cheung MC, Brown BG. Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography. J Lipid Res. 2011;52(3):566–71.

12. Saleh BO, Majeed MJ, Oreaby GM. Irisin impact as a medication that ameliorate and hinder the development of insulin resistance associated disorders without regular exercise (experimental study). 2014;13(9):28–35.

13. CDC. Crude and Age-Adjusted Incidence of Diagnosed Diabetes per 1,000 Population Aged 18–79 Years, United States, 1980–2011. Diabetes Public Health Resource. 2014.

14. Scott RA, Langenberg C, Sharp SJ, Franks PW, Rolandsson O, Drogan D. Europe PMC Funders Group The link between Family History and risk of Type 2 Diabetes is Not Explained by Anthropometric , Lifestyle or Genetic Risk Factors : the EPIC-InterAct Study. 2014;56(1):60–9.

15. Ahmad NS, Islahudin F, Paraidathathu T. Factors associated with good glycemic control among patients with type 2 diabetes mellitus. J Diabetes Investig. 2014;5(5):563–9.

16. Hachem SB, Mooradian AD. Familial dyslipidaemias: An overview of genetics, pathophysiology and management. Vol. 66, Drugs. 2006. p. 1949–69.

17. Taskinen MR. Diabetic dyslipidaemia: From basic research to clinical practice. Vol. 46, Diabetologia. 2003. p. 733–49.

18. Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes: Prevalence, pathophysiology, and management. Drugs. 2013;73(4):327–39.

19. Rajab T. Study for Atherogenic Index of Plasma (Aip) in Patients With Type1 Diabetes Mellitus, Type2 Diabetes Mellitus, Betathalassemia. Ijcsr [Internet]. 2012;02i2:1–9. Available from: http://www.doaj.org/doaj?func=fulltext&aId=1082638

20. Tan MH, Johns D, Glazer NB. Pioglitazone reduces atherogenic index of plasma in patients with type 2 diabetes. Clin Chem. 2004;50(7):1184–8.

21. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodaee G, et al. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. Med J Islam Repub Iran. 2015;29(1):627–35.

22. Moreno-Navarrete JM, Ortega F, Serrano M, Guerra E, Pardo G, Tinahones F, et al. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J Clin Endocrinol Metab. 2013;98(4):E769-78.

23. Wu J, Bostr??m P, Sparks LM, Ye L, Choi JH, Giang AH, et al. Beige adipocytes are a distinct type of thermogenic fat cell in mouse and human. Cell. 2012;150(2):366–76.

24. Majeed MJ, Saleh O. Descriptive Consideration of Serum Irisin Levels Various Factors: Obesity, Type 2 Diabetes Mellitus, Pre-Diabetic Status, Gender, and Athletics. J Diabetes Metab [Internet]. 2014;5(12). Available from: http://www.omicsonline.org/diabetes-metabolism-abstract.php?abstract_id=36605

25. Jameel F, Thota RN, Wood LG, Plunkett B, Garg ML. Sex-dependent association between circulating irisin levels and insulin resistance in healthy adults. J Nutr Intermed Metab [Internet]. Elsevier Inc; 2015;2(3–4):86–92. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2352385915300086

26. Zhang HJ, Zhang XF, Ma ZM, Pan LL, Chen Z, Han HW, et al. Irisin is inversely associated with intrahepatic triglyceride contents in obese adults. J Hepatol. 2013;59(3):557–62.