Association of irisin hormone with some physiological and inflammatory parameters of type 1 diabetic mellitus (TIDM) patients in Thi-Qar province, Iraq

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Abstract. The current study aimed to verify of irisin concentration in TIDM and to scan the association the irisin value with the physiological inflammatory parameters. The study included 60 individuals diagnosed in newly onset TIDM and 35 healthy individuals as a control group. IL-6 and C-reactive protein (CRP) concentration was calculated. Serum irisin level in addition to inflammatory factors were evaluated by ELISA kit. The results explained a significant increased at (P ≤ 0.05) in level of fasting blood sugar (FBS), HbA1C and irisin level in type I patients compared with the control group, (7.95±2.02 vs 94±0.47 mmol/dl, 6.91±1.09 vs 28±0.56 mmol/dl, 33.38±7.9 ng/ml vs 27.24±4.50 ng/ml respectively). So the results showed significantly decreased of BMI, C-peptide, Insulin and HOMO-IR level (P ≤ 0.05) in GI contrast with control grouping (19.04±0.71 vs 22.62±1.19, 0.21±0.02 vs 6.11±0.50, 0.19±0.04 vs 24.99±0.73, 0.06±0.02 vs 5.49±0.53 respectively). Investigation of lipid profile the results explained there was non-significant decreased of cholesterol (P ≤ 0.05) in GI contrast with group's control, but there was significant decreased of Tg and HDL levels in GI contrast with group's control on the other hand the results showed a significant increase (P ≤ 0.05) of LDL level in GI compared with control group (3.78±0.46 vs 3.96±0.46, 1.55±0.21 vs 1.62±0.37, 1.02±0.15 vs 1.52±0.37, 2.45±0.58 vs 2.11±0.45 respectively). The results of inflammatory parameters explained there was a significant increased (P ≤ 0.05) of IL-6 and CRP levels in patients compared with control group (21.0±5.25 vs 12.79±0.93, 3.14±1.16 vs 2.37±0.69 respectively) (Table 1). In TIDM grouped, irisin in value showed negative association with (HbA1c) value (r = -0.353, P<0.001), glucose (r=-0.290) and HOMO-IR (r= -0.232), cholesterol (r=-0.133), Tg, (r= -0.071) and LDL (r= -0.163). So the correlation analysis explained a positive correlation with insulin level (r= 0.055), C.peptide (r= 0.105), HDL (r= 0.229), BMI (r= 0.115), IL-6 (r= 0.067), and CRP (r= 0.171).

1 Introduction

Diabetes mellitus (DM) is the continual disease common characterize by hyperglycemia resulting from defects in insulin secretion and/or activity (W. H. O., 1999). Its frequency elevate regularly every year. The universal commonness of diabetes, amongst adults were 6.4%, affecting 285 million patients in [26], and is probable to augment to 7.7% (ie, 439 million individuals) in [26].

[5] identified the irisin, an energetic metabolism-related myokine. Its secretion involves the increase of peroxisome proliferator-activated receptor-gamma coactivator 1 alpha (PGC1 alpha) in the muscle, inducted by exercise, promoting the expression and proteolysis cleavage of Fndc5, a type 1 membrane protein fibronectin type III domain-containing protein 5, with release the irisin fragment for the blood flow [5].

This hormone promotes a browning process on the white adipose tissue, a encoding for the thermo genesis in the tissue cells, through the increase of the mitochondrial uncoupling protein 1 (UCP1) [5].
The final effect of the hormonal signal promoted by the irisin is an enlarge on the physical energy spending, with the decrease of the obesity and development on the insulin resistance caused by diet [5]. Some new studies have shown that the irisin values were lesser in patients in TIIDM when contrast to non-diabetics [2], perhaps for a lacking expression of PGC1 alpha in the muscle[20]. This variation also found on other forms of diabetes, like the type 1 diabetes mellitus (TIDM) [8],and gestational diabetes mellitus (GDM) [7]. In addition, amplified levels of irisin are also linked with other metabolic parameters such as BMI, 2 h plasma glucose after OGGT "(oral glucose tolerance test)", HbA1c and triglycerides [6].

Numerous studies have addressed the relationship between low of serum irisin levels and insulin resistance or diabetes.[31], and others explained a negative correlation with fasting glucose in blood and HbA1c [30]. Our study as well showed elevated of irisin levels in the non-obese type I diabetic.

2 Material and Methods

2.1 Subjects

The aim population of this study was 60 males individuals who are already diagnosed as new onset TIDM which referred to the Nasiriyah Endocrine and Diabetes Centre in Thi-Qar province, Iraq during February 2018-August 2018. The patients are diagnosed as newly onset by the consultant medical staff, according to checked clinical examination and biochemical analysis. Another group of 40 healthy individuals represented as a control group. The history was obtained from each patient including ages, BMI, medications, other disease, any other chronic disease and medical history.

2.1.1 Blood collection

About (5 mL) of fasting venous blood of TIDM patients and controls divided to two parts the first part about (2ml) putting in tube with anticoagglutination (EDTA tube) this used to determination of HbA1C test, and the second part about (3ml) to obtain of serum putting it in empty disposable tubes then centrifuge to separate it in the centrifuge at 3000 (rpm).

3 Biochemical parameters analysis

3.1 Evaluation of fasting blood sugar (F.B.S) and HbA1C test

Value of F.B.S., was calculated according to the technique of copper kit (Randox, England). The glycohemoglobin (HbA1C) measured by Icroma instrument ichroma. "Body mass index (BMI)" is a determine of someone´s weight in linked to their height, and then we put these measurements in the equation:

\[\text{BMI} = \text{Weight (kg)} / \text{Height (m)}^2\]

The irisin, insulin and C-peptide hormone, concentration was calculated match up with to the ELIZA, based on the sandwich principle. Serum cholesterol and triglyceride enzymetic method described by [1] but Evaluation of"(HDL)" was calculated by the chemical substance is only for healing of specimen previous to calculate of HDL-C add to reagent for sum cholesterol. Low density lipoproteins (LDL) very low density (vLDL) and ‘chylomicrons’ from specimen are precipitate by phosphotungstic acid (PTA) and magnesium chloride”. HDL,Cobtained floating following of centrifuged, so then calculated add to sum cholesterol. Evaluation of”Low density lipid protein” (L D L)

by the following function:

\[\text{LDL} = \text{Cholesterol con.} - \text{(Tg5)} + \text{HDL con.} = \text{mmol/L}\]

3.2. Inflammatory parameters

3.2.1. IL-6 and C-Reactive protein (CRP)

The diaclone IL_6 ELISA kit is a solid phase sandwich ELISA for the in-vivo qualitative and quantitative determination of IL-6.

4 Calculate of "Hemostatic Model Assessment-Insulin Resistance (HOMO-RI)"

HOMO-RI= Glucose (mmol/L) × Insulin (µIU/mL) / 22.5.

5 Statistical Analysis

Statistical analysed was done by using the software (SPSS v.20); the results were expressed as mean ± stander deviation ( mean ± SD ). due to sample T-test,P-value(p≤0.05) were considered statistically significant.
6 Results

6.1 Biochemical parameters

The FBS, HbA1C and irisin level in blood of patients type 1 (GI) significantly amplified at (P ≤ 0.05) contrast with of manage group. On the other hand, the results explained significantly decreased (p≤ 0.05) of BMI, C-peptide, insulin and HOMO-IR. So, the present study explained there was non-significant decreased (p≤ 0.05) of Cholesterol and Tg, but the mean level of HDL in GI patients showed a significant decrease (p≤ 0.05) compared with control group. While the results explained a significant increase (p≤ 0.05) of LDL value in GI compared with control group. as summarized in (Table 1).

6.2. Inflammatory Parameters

Table 1 explained a significant increased (p≤ 0.05) of IL-6and CRP levels in GI patients compared with control groups (Table 1).

Table 1: Level of hormonal and physiological and inflammatory parameters in Type I DM.

| Parameters        | Patient group(GI) | Control group |
|-------------------|-------------------|---------------|
|                   | Type I DM N= 60   | N=40          |
|                   | mean ± SD         | mean ± SD     |
| FBG ( mmol/L)     | 7.95±2.02         | 4.94±0.47     |
| HbA1C ( mmol/L)   | 6.91±1.09         | 4.28 ±0.56    |
| BMI               | 19.04±0.71        | 22.62±1.19    |
| Irisin Ng/dl      | 0.19±0.04         | 24.99±0.73    |
| Insulin Ng/dl     | 0.21±0.02         | 6.11±0.50     |
| C-peptide         | 33.38±7.35        | 27.24±4.50    |
| Homo-IR           | 1.55±0.21         | 3.96±0.46     |
| T-Ch (mmol/L)     | 1.02±0.15         | 1.62±0.37     |
| TG (mmmol/L)      | 2.45±0.58         | 1.52±0.37     |
| LDL (mmol/L)      | 2.11±0.45         | 2.17±0.93     |
| IL-6              | 1.109             | 1.001         |

7 Correlation analysis

The results indicated was a negative relationship among irisin with glucose, HbA1c, cholesterol, Tg, LDL and HOMO-IR in type I group, on the other hand the correlation study explained a positive association among irisin value with each of BMI, C-peptide, insulin, HDL, IL-6 and CRP (Table 2).

8 Discussion

8.1 Biochemical parameters

8.1.1 Glycohemoglobin (HbA1c)

The results explain an important elevated in levels of HbA1c in GI contrast with control grope, that is might be most exactly reflects the preceding 2-3 months of glycemic control, thus the patient with 2-3 months period of DM., and bad organize to the disease so this situation lead to a high level of HbA1c in blood[12]. The high level of HbA1C in this study was coordinated with other study by [15] who reported the bad control. This study showed a negative association among irisin with hemoglobin A1C (HbA1c). Thus, level’s irisin might reveal the metabolic condition of patients suffer as of metabolic disorders. In adding to glycemic or HbA1c, ‘irisinemia’ can also grow to be a new gifted idea to observe disorders of metabolism like obesity or T.2D.M., in future might be appear for a useful means in organization of metabolic diseases [23].

A negative association has been shown in this study to the irisin values with insulin and HOMA-IR, this might be of all individuals in our study were [28] with BMI. Association among irisin with insulin resistances confirming by the hypothesised participation of the p-38-PGC1a- betatrophin pathway of irisin [23].

8.1.2 Blood glucose

The results showed a significant raise of blood sugar in GI compared with the control group. The confusion of beta cells in pancreas organ lead to reduce production of insulin hormone, if beta cells don’t make sufficient insulin, glucose accumulation in the blood in its place when absorbing by cells of the body [10].
8.1.3 Irisin
Increasing of irisin level were observed in the GI compared with the control group, this might be because of the information that irisin was progressively reduced with decrease tolerance of glucose in quantity to insulin resistance or due to a highy of fat at the expenditure of muscle mass for require of activity in patients with type 2 (Yan et al., 2014, 3].
This study recommended that amplified irisin levels possibly will be due to improved release by adipose/muscle tissue in reaction to decline insulin sensitivity or a compensatory device in contact with irisin resistance [25].
8.1.4 Lipid profile
The results showed a significant increase in (cholesterol, triglyceride and high density lipoprotein) of new onset patients. Typically, the dyslipidemia is reflected largely in enlarged serum levels of triglycerides and low levels of HDL, cholesteral levels may be very high in proteinuric patients [24]. This results are corresponding with the result of [27].
The model of dyslipidemia, in diabetes is different, from that in non-diabetic people. This explain the significance of lipid and lipoprotein examination in diabetic patients and recommend a different lipid lowering agents from that used in non-diabetic population [22]. Accordingly, this study showed a negative association between irisin and cholesteral, might be that irisin possibly will inhibit the production of hepatic cholesterol through AMPK-dependent inhibition of SREBP2 and downstream of its genes target. Obstruction of irisin-induced AMPK activation by complex C., or knockdown of AMPKα1 [29].
8.1.5 C-Peptide
The necessary role of C-peptide is a helpful and broadly use method of assess pancreatic beta cell purpose [14,19] not as good as C-peptide levels have been linked with lesser glycemic organize and for this reason elevated Hba1c values [18, 17]. Decreases value of C-peptide and decrease beta cell function has been related to bigger levels of glucose change capability [16, 13].
8.1.6 Insulin and HOMO-IR
In study by [11] in obese patients create the positive correlation between irisin and insulin resistance [11]. Though others reported either no association [20] or even a negative relationship [30] among serum irisin with HOMA-IR score.
Insulin resistance might also be correlated with irisin secretion, because an increase in irisin promotes energy consumption, which contributes to weight loss, fat reduction and improved insulin resistance (3)
8.2 Inflammatory Parameters
8.2.1 Interleukin -6 (IL-6) and C-Reactive Protein (CRP)
Table 2 explained a significant augmented (p≤0.05) of IL-6 and CRP level in GI patients contrast with managed group. In this study the relationship research clarifies a positive association among irisin with both IL-6 and CRP in type I group.
A situation with chronic inflammatory might occur at the cellular level, with enlarge of the value of cytokines like IL-8, IL-15, and IL-6from a pathway (in this study an indicator of chronic inflammatory was CRP, which tested elevated in the patient group [21, 9], reply, both the immunogenicity and number of auto-antibodies that contribute in role in autoimmune incident, could raise. PGC-1α, through another pathway, raises of FNDC5 level and leads to elevate of irisin concentration [4]. Therefore, both irisin and auto-antibody values might be highy by the PGC-1α activation. So far, our clarification supports our results up to the correlation analysis branch.

| Irisin | FBS | HbA1c | C Peptide | Insulin | Chol | TGs | HDL | LDL | IL-6 | CRP hs | BMI |
|-------|-----|-------|-----------|---------|------|-----|-----|-----|------|--------|-----|
| Correlation | 1   | -0.290* | -0.353** | 0.105 | 0.055 | -0.133 | -0.071 | 0.229 | -0.163 | 0.067 | 0.171 | 0.115 |
| Sig.  | 0.024 | 0.006 | 0.426 | 0.675 | 0.313 | 0.592 | 0.078 | 0.215 | 0.613 | 0.192 | 0.381 |
| N    | 60  | 60    | 60    | 60    | 60    | 60    | 60    | 60   | 60    | 60    | 60    |

9 Conclusion
1. The level of irisin in type I patients improve of the evidence of it in low BMI.
2. From the results of correlation analysis between irisin and inflammatory factors we can concluded that irisin work as a anti agents of the inflammatory condition.
3. The negative correlation between irisin and glucose refer to the important of it on the glucose homeostasis.

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