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IRISIN IN TYPE 2 DIABETES MELLITUS: A CASE CONTROL STUDY

Biochemistry

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ABSTRACT

Introduction: Globally, an estimated 463 million adults are living with diabetes mellitus and 4.2 million deaths are caused by diabetes according to the IDF Diabetes Atlas 2019. Its prevention is through lifestyle modification. However, no cure is available despite new insights and drugs. Irisin is a newly discovered adipo-myokine, that reduces obesity and improves insulin resistance via the browning of white adipose tissues. Several studies reported low irisin level in diabetic patients as compared to controls. The aim our study was to estimate serum irisin in cases with type 2 diabetes mellitus and healthy controls and to compare serum irisin with fasting blood glucose levels.

Materials and methods: A case control study was conducted in the Department of Biochemistry in collaboration with Department of Medicine, Regional Institute of Medical Sciences, Imphal, for a period of 24 months. Altogether 80 people were involved, consisting of 40 diagnosed cases of type 2 diabetes mellitus and 40 normal healthy individuals.

Results: The level of serum irisin was significantly decreased in cases of diabetes mellitus (mean=14.54±8.59 ng/ml) as compared to healthy controls (mean=28.45±3.92 ng/ml) and the difference was statistically significant (p-value = 0.00). We found a negative correlation between serum irisin level and fasting blood glucose and it was statistically significant (r = -0.32, p = 0.04).

Conclusion: This study shows that serum irisin may be a novel biomarker for diagnosis and an adjunct in the treatment of patients with type 2 diabetes mellitus and may serve as a potential new target for improving insulin resistance.

KEYWORDS

Adipo-myokine, Diabetes, Fasting blood glucose, Irisin

INTRODUCTION

Globally, an estimated 463 million adults are living with diabetes mellitus and 4.2 million deaths are caused by diabetes according to the IDF Diabetes Atlas 2019. The global prevalence of diabetes is 9.3%.[1] Among the people living with diabetes, three in four of them (352 million people) are of working age (i. e. between 20 and 64 years old).[2]

Diabetes Mellitus (DM) is a condition characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism caused by defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. The characteristic symptoms include thirst, polyuria, blurring of vision, and weight loss.[3]

Type 1 Diabetes Mellitus (insulin-dependent diabetes) accounts for only 5-10% of those with diabetes. Type 2 Diabetes Mellitus (non-insulin-dependent diabetes) accounts for around 90- 95% of those with diabetes. Other specific types of diabetes include: genetic defects of the β-cell, genetic defects in insulin action, diseases of the exocrine pancreas, endocrinopathies, drug- or chemical-induced diabetes, infections, uncommon forms of immune-mediated diabetes and other genetic syndromes sometimes associated with diabetes. Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[4]

The prevalence of Type 2 Diabetes Mellitus has been increasing steadily all over the world. Country wise India ranks second to China (116.4 million) in the number of people with diabetes.[2] Its prevention is through lifestyle modification. However, no cure is available despite new insights and drugs.[5]

Irisin is a newly discovered adipomyokine, discovered in 2012 by Boström and colleagues, that reduces obesity and improves insulin resistance via the browning of white adipose tissues. It is expressed and secreted in response to exercise, providing a hormonal link between exercise and improved insulin sensitivity. Several studies reported low irisin level in diabetic patients as compared to controls. Therefore, it has been assumed that irisin may be used as an injectable remedy for diseases relating to metabolism and various other health disorders in which physical exercise leads to improvements such as Type 2 Diabetes Mellitus (T2DM).[6] Irisin is a fragment of a cell membrane protein called fibronectin type III domain-containing protein 5 (FNDC5).[7] It is composed of 209 amino acids (aa) residues. It contains an N-terminal signal sequence consisting of 29 aa, a fibronectin type III domain with 94 aa, an unidentified region consisting of 28 aa, a transmembrane domain having 19 aa, and a C-terminal part with 39 aa. The C- terminal fragment of FNDC5 is located in the cytoplasm, while the extracellular N- terminal portion is proteolytically cleaved to produce irisin which is ultimately released into the circulation.[8,9]

AIMS AND OBJECTS

1. To estimate serum irisin in cases with type 2 diabetes mellitus and controls
2. To compare and correlate serum irisin with fasting glucose levels

MATERIALS AND METHODS

This was a case control study done in the Department of Biochemistry in collaboration with Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur for a period of 24 months. Altogether 80 people were involved in the study, consisting of 40 diagnosed cases of type 2 diabetes mellitus and 40 normal healthy individuals.

INCLUSION CRITERIA:
Adult diagnosed cases of type 2 diabetes mellitus and normal healthy individuals matched with age and sex, free from any systemic diseases.

EXCLUSION CRITERIA:
Type 1 diabetes mellitus, metabolic syndrome, chronic kidney disease, anorexia nervosa, pregnancy, coronary artery diseases and past history of vascular diseases.

Biochemical parameters:
Overnight fasting venous blood of about 5 ml were collected from the anterior cubital vein. Estimation of serum irisin was done by ELISA method[10] and fasting blood glucose was done using using GOD/PAP (glucose oxidase-phenol 4 amino phenazone) method as described by Barham D et al.[11]

STATISTICALANALYSIS:
The data were analyzed using IBM : SPSS version 21 for Windows. Descriptive statistics like mean, percentage and proportion were used. Independent samples t-test Chi-square test were used to compare means and Pearson's correlation was used to find out the correlation between the variables. P value <0.05 was taken as significant.

RESULTS
In this study, the two groups (cases and controls) were matched in terms of age and sex. The fasting blood glucose was significantly higher (p<0.05) in cases than controls (163.65±64.04 vs 86.65±9.16 mg%).

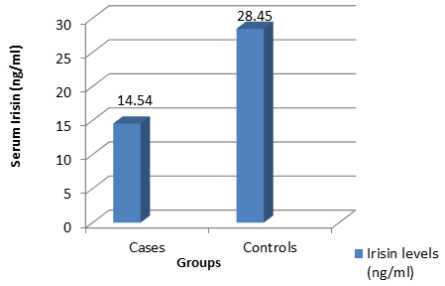

Fig. I: Serum Irisin level in cases and controls

Serum irisin level (figure I) was significantly decreased (p-value = 0.00) in diabetes mellitus cases (mean=14.54±8.59 ng/ml) as compared to healthy controls (mean=28.45±3.92 ng/ml).

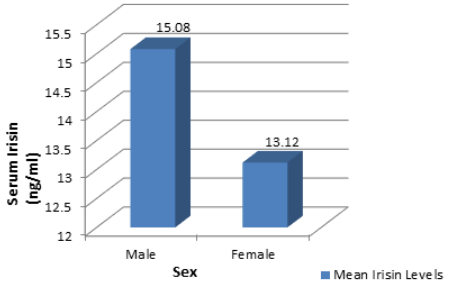

Fig. II: Distribution of the cases by serum Irisin level stratified by sex

Serum irisin in cases (figure II) was higher among males (15.08±8.83 ng/ml) as compared to females (13.12±8.17 ng/ml) however the difference was not statistically significant (p-value = 0.53).

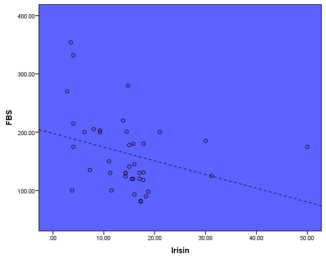

Fig. III: Scattered diagram showing correlation between FBS and irisin

Scattered diagram shows good amount of clumping in (fig. III) and the pattern of dots slopes from upper left to lower right indicating a negative correlation between serum irisin level and fasting blood glucose which was statistically significant (r = -0.32, p = 0.04).

DISCUSSION
This study is conducted to estimate serum irisin in patients with type 2 diabetes mellitus and normal individuals and to compare the findings between normal individuals and patients with type 2 diabetes mellitus.

In the present study, (Figure I) the mean irisin level of diabetic cases are significantly lower than the controls (14.54±8.59 vs 28.45±3.92 ng/ml). Similar findings of lower irisin level in diabetic cases as compared to controls were observed in the studies done by Xuan et al[12], Balaban YA et al[13] , Zhang C et al[14], Elizondo-Montemayor L et al[15], Shanaki M et al[16] and Wang L et al[17]. Although the mechanism of reduced irisin levels in patients with T2DM is not fully understood, some scholars believe that reduced PGC-1α (peroxisome proliferator-activated receptor gamma coactivator-1α) activity in the muscle tissue of patients with T2DM can explain the decreased irisin level in patients with T2DM leading to reduced FNDC5 synthesis and reduced irisin production.[18,19] In addition, insulin resistance led to hyperglycemia and an increase in circulating free fatty acids, which also led to a decrease in PGC-1α activity.[19]

In this study, (Figure II) irisin in study group shows a higher level in males compared to females (15.08ng/ml vs 13.12ng/ml). This is in accordance with the study conducted by Jameel F et al.[20] This may be due to the higher value of skeletal muscle mass in males as compared to females found in their study. The gender differences might be explained by the differences in the distribution of fat (white and brown) in males and females.[21,22] Another plausible explanation may be the hormonal differences in males and females. Estradiol, a primary female sex hormone, has been shown to be positively correlated with circulating irisin levels, while there was no significant relationship with free testosterone levels.[23]

In the study group, (Figure III) a negative correlation is obtained between the fasting blood glucose and serum irisin (r= -0.32, p = 0.04). This correlation is in accordance with the studies conducted by Kurdiova T et al[24], Choi YK et al[25], He WY et al[26] and Xiang L et al[27] who found that serum irisin and fasting blood glucose have an inverse relationship. These data suggest that decreased blood irisin levels may be associated with the development of insulin resistance and Type 2 Diabetes Mellitus.

CONCLUSION
This study shows that serum irisin level is significantly decreased in type 2 diabetes mellitus patients as compared to controls and it also shows negative correlation with fasting blood glucose. Studies have also suggested that irisin may be a novel risk factor of patients with diabetes and may serve as a potential new target for improving insulin resistance. Thus, it can be concluded that serum irisin estimation may be a useful biomarker for diagnosis of type 2 diabetes mellitus and it may be a useful adjunct in the treatment of type 2 diabetes mellitus.

The limitations of this study are the small sample size and the short duration of the study. Further prospective and population based large-scale studies are recommended to confirm the utility of serum irisin as a convenient sensitive biomarker and possible therapeutic uses for type 2 diabetes mellitus.

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