Indian Journal of Clinical Biochemistry (2024) 39:136–141
https://doi.org/10.1007/s12291-022-01083-3

ORIGINAL RESEARCH ARTICLE

Irisin and Triglyceride Glucose Index as Markers of Dyslipidemia in Young Adults

M. K. Nilofer Sagana[1] · K. A. Arul Senghor[2] · V. M. Vinodhini[2] · Renuka P[2]

Received: 9 May 2022 / Accepted: 2 August 2022 / Published online: 6 September 2022

Abstract

Irisin, is a new myokine, considered a favorable metabolic factor and inversely associated with non-communicable diseases. The biological activities of irisin are currently unknown; however, they include browning white adipose tissue, insulin sensitivity, and anti-inflammatory and antioxidant effects. Triglyceride glucose index is a notable insulin resistance marker that predicts the risk of metabolic dyslipidemia and cardiovascular risk. The study aimed to evaluate the relation of irisin and Triglyceride glucose index (TyG) in young adults to assess the cardiovascular risk. This observational cross-sectional study included 80 participants aged 18 to 35 years (male and females) with cut-off TyG > 4.5 as the prime criteria. With consent, anthropometric measurements were documented. Fasting lipid profile parameters were analyzed, and atherogenic lipid ratios and TyG index were calculated. Serum irisin was analyzed in Bio-Rad ELISA using a standardized Abbkine kit. Decreased irisin levels (0.32 ± 0.04ng/ml) and increased TyG index (4.95 ± 0.012) were observed in the participants with elevated triglyceride levels. The lipid profile parameters and atherogenic lipid ratios were observed to be elevated in males as compared to females. Correlation of irisin with lipid parameters revealed statistically significant positive correlation with HDLc (r = + 0.305) and negative correlation with non-HDLc (r = − 0.393), TC/HDLc (r = -0.508), LDLc/HDLc (r= -0.475) and TyG (r = -0.28). The study concludes that decreased irisin and increased TyG index in young adults reflect the state of metabolic dyslipidemia which enables the identification of individuals with metabolic and atherogenic risk.

Keywords Irisin · Triglyceride glucose index · non-HDLc

Introduction

Young adulthood is a critical phase that faces multiple challenges in their stressful life. Most young adults experience transitions during this unstable developmental period. Because of the unhealthy diet pattern, young adults are more prone to develop metabolic abnormality and premature development of cardiovascular complications. Obesity is frequently linked to metabolic abnormalities, which may or may not be present in all obese people. However, some non-obese people can have aberrant metabolic findings that go unreported. It is important to identify metabolically unhealthy individuals using simple parameters, especially in the young adulthood stage.

The hormone Irisin was originally recognized as an exercise induced adipomyokine, as described by Bostrom et al. [1]. In response to physical activity, peroxisome proliferator, PGC-1α causes which leads to the release of the fibronectin type III domain from proteolytic cleavage of the mature (FNDC5) domain [2]. Evidence supports the beneficial role of long-term exercise training that up-regulates PGC-1α which is essential for irisin release [3].

Meta-analysis recognized the biologically direct association of irisin with insulin resistance in non-diabetic individuals [4]. Irisin is a protein that plays a role in the intricate relationships between exercise and metabolic health. Irisin has an inverse relationship with obesity, diabetes, and

✉ K. A. Arul Senghor
arulsenk@srmist.edu.in

M. K. Nilofer Sagana
knilofer58@gmail.com

V. M. Vinodhini
hod.biochem.ktr@srmist.edu.in

Renuka P
renukap@srmist.edu.in

[1] MSc. Medical biochemistry, Final year SRM Medical college Hospital and Research centre, SRM IST, Chengalpattu District, Kattankulathur, India

[2] Department of Biochemistry, SRM Medical college Hospital and Research centre, Kattankulathur, India

insulin resistance, according to a few clinical trials [5]. Interventional studies on exercises of different intensities identified irisin as a beneficial hormone that is released on contraction of skeletal muscle [6].

Insulin resistance is considered a major risk factor that results in reduced sensitivity of the peripheral tissues. Triglyceride Glucose index (TyG) can be considered a simple reliable indicator of peripheral insulin resistance. Lifestyle changes in the current generations had increased the risk of a metabolically unhealthy environment. As a cost-effective screening tool, the Triglyceride glucose index can be used as a predictive tool to identify metabolic lipid abnormality and in apparently healthy individuals. The log of the product of fasting plasma glucose and triglyceride levels is used to calculate this index, which is used as a surrogate measure of insulin resistance.

Serum irisin levels were found to be lower in people with Type 2 Diabetes Mellitus [7]. Increased irisin levels through regular physical activity [8] would reduce insulin resistance, suggesting it may be a real breakthrough in treating metabolic dyslipidemic status. The known concept is that dyslipidemic profile represents well-established ground for cardiovascular diseases. According to National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines, HDLc has been a key determinant in Framingham and Systematic Coronary Risk Evaluation risk equation for coronary heart disease. Cardiac risk ratios such as TC/HDLc, LDLc/HDLc and non-HDLc are strong predictors of cardiovascular disease than LDLc among the general population.

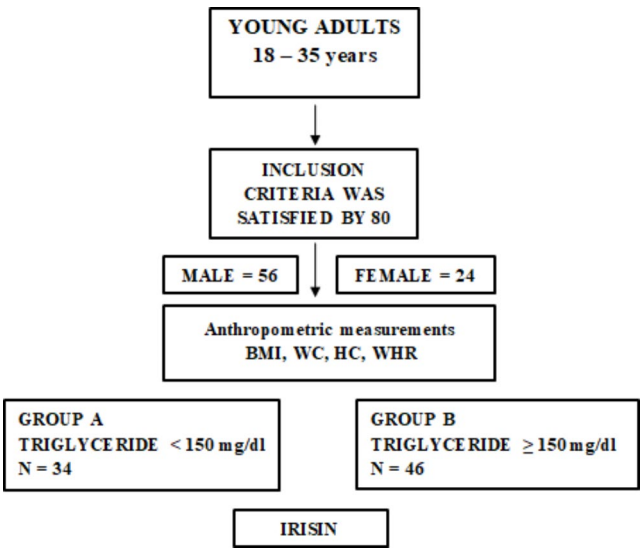
In this context, we evaluated irisin level and TyG index as dyslipidemic markers in young adults. We determined the clinical usefulness of serum irisin levels, cardiac risk lipid ratios, and Triglyceride glucose index in young adults with triglycerides levels below and above 150 mg/dl.

Materials and Methods

Our hospital's Master Health Checkup was the setting for this observational cross-sectional study conducted between July 2021 to February 2022. The study began with the recruitment of subjects based on the inclusion and exclusion criteria after receiving approval from the institutional ethical committee (IEC/2867/ 2021). The research protocol was described to the participants, and consent to participate in the study was obtained. The sample size was calculated based on the prevalence of diabetes in young adults in India as 2.5% [9]. $n = Z^2 [p (1 - p)] / d^2$ [Z – Statistic level at 95% confidence interval (Z = 1.96); p –Prevalence; d – Precision (If the precision is 5% then d = 0.05). By convenient sampling technique 80 participants were recruited with the following **inclusion criteria**:

i. The age group of 18–35 years undergoing the master health check-up.
ii. Both sex: male and female.
iii. Triglyceride glucose index of more than 4.5 [10].

The participants were divided as group (A) n = 34 with triglyceride < 150 mg/dl and group (B) n = 46 triglyceride ≥ 150 mg/dl to further analyze dyslipidemic parameters [11]. Individuals with impaired fasting glycemia, known history of Diabetes mellitus, hypertension, kidney, liver diseases, and cardiovascular diseases were excluded.



Anthropometric Measurements

With the consent of the participants, a physical examination was done by the Medical Officer. Anthropometric measurements such as weight were measured in participants in light clothing without shoes on a calibrated weighing scale in kilogram. Height was measured with a standardized meter scale. The waist circumference (WC) was measured using inelastic tape midway around the waist. Similarly, the circumference of the hip was measured in centimeters. Weight (kg) / height (m^2) and WC / HC were used to determine BMI and waist-hip ratio (WHR). BMI (Normal: 18.5–22.9, overweight: 23–24.9, obese: >25) and WHR (male < 0.95, female < 0.85) cutoff was defined according to criteria for the Asian population [12].

After overnight fasting of 10 to 12 h, the fasting venous sample was collected in grey and red BD vacutainer tubes. Beckman Coulter AU480 auto analyzer, fasting glucose was measured by hexokinase, total cholesterol and triglycerides

Table 1 Anthropometric details between young males and females

PARAMETERS	MALES n = 56	FEMALES n = 24	t value	P value
Age (yrs)	31.4 ± 0.65	28.7 ± 0.7	0.547	0.05 *
Weight (Kg)	78.27 ± 1.43	66.45 ± 1.7	− 8.088	0.000***
Height (mts)	1.69 ± 0.01	1.57 ± 0.01	− 4.804	0.000***
BMI	27.29 ± 0.48	26.79 ± 0.704	− 0.58	0.56 (NS)
WC (cm)	99.17 ± 0.623	93.83 ± 1.03	− 4.574	0.000***
HC (cm)	104.27 ± 0.74	100 ± 1.05	− 3.207	0.002**
WHR	0.95 ± 0.002	0.93 ± 0.004	− 2.537	0.013*
Independent students t test	*p value 0.05 is considered significant. Values are expressed in Mean with Standard Error of Mean. NS stands for "not significant." ** Significant ***Extremely Significant			

by enzymatic method, HDL and LDL were estimated by direct immunoassay method. Samples were kept in a – 20° C deep freezer for analysis of serum irisin levels in Bio-Rad ELISA reader and washer using a standardized Abbkine kit. The normal reference range of irisin is 3.6 to 4.6 ng/ml.[13] Triglyceride Glucose index (TyG) was calculated in excel with the logarithmical formula (Ln fasting triglycerides (mg/dl) X fasting glucose (mg/dl)) multiplied by 2 [14].

Table 2 Lipid profile, cardiac risk ratios, TyG index and irisin levels between young males and females

PARAMETERS	MALES n = 56	FEMALES n = 24	t value	P value
FPG (mg/dl)	105.64 ± 1.21	101.91 ± 1.54	− 1.103	0.273 (NS)
Total Cholesterol (mg/dl)	208.16 ± 5.36	203.29 ± 5.92	− 0.55	0.58 (NS)
Triglycerides (mg/dl)	176.32 ± 5.36	158 ± 5.89	− 2.804	0.01*
HDL-cholesterol (mg/dl)	44.98 ± 1.07	49.87 ± 1.0	− 2.81	0.007**
LDL-cholesterol (mg/dl)	148.78 ± 5.06	141.708 ± 5.56	− 2.48	0.015*
Total Cholesterol /HDLratio	4.57 ± 0.13	4.13 ± 0.12	− 2.05	0.04*
LDL / HDL cholesterol ratio	3.52 ± 0.09	3.04 ± 0.16	− 3.08	0.0028**
Triglycerides/HDLc ratio	4.05 ± 0.16	3.36 ± 0.17	− 2.56	0.012*
Non-HDLc	166.17 ± 4.17	151.41 ± 3.25	− 2.19	0.03*
Triglyceride Glucose index Irisin (ng/ml	4.9 ± 0.018	4.8 ± 0.03	1.48	0.14 (NS)
	0.52 ± 0.074	0.35 ± 0.09	− 2.48	0.015*
Independent students t test	*p value 0.05 is considered significant. Values are expressed in Mean with Standard Error of Mean. NS stands for "not significant." ** Significant ***Extremely Significant			

Table 3 Pearson correlation analysis of circulating irisin levels with anthropometric measures, lipid profile, cardiac risk ratios and TyG index

PARAMETERS	r value	p value
Weight (kg)	- 0.137	0.23
Height (mts)	0.12	0.2 (NS)
BMI	- 0.19	0.07 (NS)
WC (cm)	- 0.17	0.155 (NS)
HC (cm)	- 0.16	0.147 (NS)
WHR	0.118	0.2 (NS)
FPG (mg/dl)	- 0.164	0.15 (NS)
Total Cholesterol (mg/dl)	- 0.303	0.006 [b]
Triglycerides (mg/dl)	- 0.29	0.01 [a]
HDL-cholesterol (mg/dl)	0.305	0.006 [b]
LDL-cholesterol (mg/dl)	- 0.332	0.003 [b]
Total Cholesterol /HDLc ratio	- 0.508	0.000 [c]
LDL / HDL cholesterol ratio	- 0.475	0.000 [b]
Triglycerides/HDLc ratio	- 0.25	0.03 [a]
Non-HDLc	- 0.393	0.000 [b]
Triglyceride Glucose index	- 0.28	0.01 [a]

a weak correlation (0.3 to 0.1)

b moderate correlations (0.5 to 0.3)

c strong correlation (1.0 to 0.5)

NS – Not significant

Table 4 Comparison of lipid profile, cardiac risk ratios, TyG index and serum irisin levels in young adults with less and more than 150 mg/dl of triglycerides

PARAMETERS	Group A n = 34 (TGL < 150 mg/dl)	Group B n = 46 (TGL ≥ 150 mg/dl)	t value	P value
FPG (mg/dl)	103.3 ± 1.8	105.46 ± 1.6	0.73	0.46 (NS)
Total Cholesterol (mg/dl)	174.78 ± 4.63	219.76 ± 4.9	5.81	0.000***
Triglycerides (mg/dl)	125.73 ± 3.5	193.9 ± 3.75	11.56	0.0001***
HDL-cholesterol (mg/dl)	47.47 ± 1.16	41.42 ± 1.12	- 3.14	0.0023**
LDL-cholesterol (mg/dl)	127.43 ± 7.67	151.94 ± 4.42	3.177	0.0021**
Total Cholesterol /HDLratio	4.045 ± 0.18	4.83 ± 0.13	2.72	0.008**
LDL / HDL cholesterol ratio	2.94 ± 0.17	3.32 ± 0.09	2.316	0.023*
Triglycerides/HDLc ratio	2.92 ± 0.13	4.32 ± 0.14	6.39	0.0001***
Non-HDLc	130.3 ± 7.34	173.33 ± 4.54	3.699	0.0004***
TyG index	4.72 ± 0.018	4.95 ± 0.012	8.02	0.0001***
Irisin (ng/ml)	0.57 ± 0.06	0.32 ± 0.045	- 2.56	0.012*
Independent students t test	*p value 0.05 is considered significant. Values are expressed in Mean with Standard Error of Mean. NS stands for "not significant." ** Significant ***Extremely Significant			

Statistical Analysis

The results were documented in an excel sheet and used SPSS 25 (Statistical Package for Social Sciences, SPSS Inc) software for statistical analysis. The metric continuous variables were expressed in mean and standard error of mean. Student's t test was used for comparison of normal distributed variables between the groups. Pearson correlation was utilized to establish the association between the variables such as lipid profile parameters, cardiac risk ratios, and Triglyceride Glucose index (TyG). For all the statistical analysis, p value of 0.05 was considered statistically significant.

Result

Table (1) describes the anthropometric characteristics of healthy young males and females presenting with a mean age of 31.4 years and 28.7 years respectively. As per the inclusion criteria of TyG index, the young male had 4.9 and females with 4.8 of Triglyceride Glucose index (TyG). A statistically significant increase was observed in weight and waist circumference in males as compared to females.

There was increased concentration of triglycerides, LDLc, TC/HDLc, LDLc/HDLc, triglycerides/HDLc and non-HDLc; and decrease in HDLc in males compared to females as in Table (2). The mean concentration of irisin was found to be low in young adults with more than 4.5 of Triglyceride Glucose index.

As in Table (3), correlation analysis of irisin with parameters of dyslipidemia revealed a statistically significant negative correlation, especially with Total Cholesterol /HDLc ratio, LDLc / HDLc cholesterol ratio, Triglycerides/HDLc ratio and non-HDLc, whereas irisin was found to have positive correlation with HDLc (r = + 0. 305) (Fig. 1).

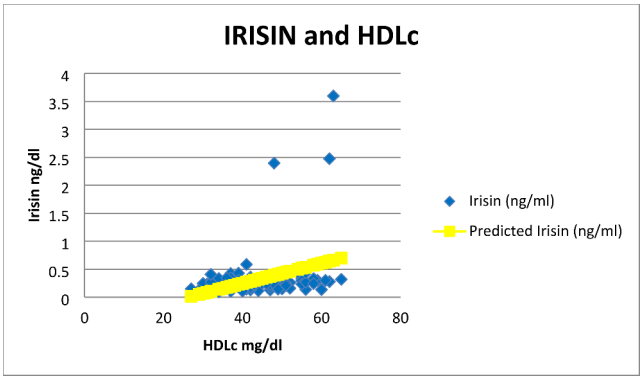


Fig. 1 Correlation analysis of serum irisin with HDL cholesterol

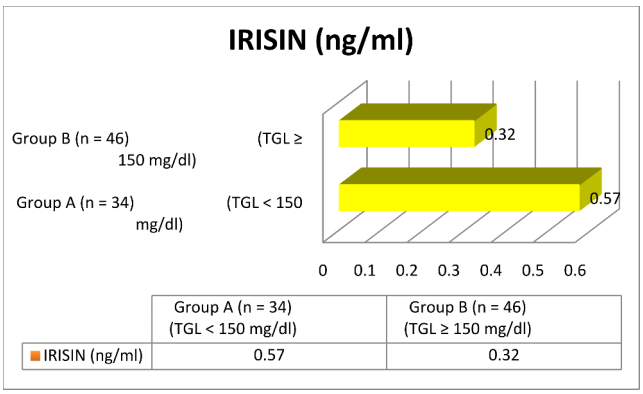


Fig. 2 Serum irisin levels in young adults Group A with Triglycerides less than and Group B with more than 150 mg/dl

Further comparison between group A and group B revealed statistically significant difference in lipid parameters and dyslipidemia ratios as seen in Table (4). Likewise, serum irisin levels (Fig. 2) were found to be significantly decreased in the participants with triglyceride levels greater than 150 mg/dl (Group B).

Discussion

In this cross-sectional study, the biochemical constellation of metabolic abnormalities associated with dyslipidemic picture is studied. Depiction of skeletal muscle as an endocrine organ modulates insulin resistance based on the release of myokines. The relation between serum irisin levels and dyslipidemic markers was studied.

The principal finding of our study was that serum irisin levels were decreased on whole in the individuals with elevated TyG index. Significant inverse association of irisin with TyG index parallels the issue of peripheral insulin resistance. This highlights the concept of an essential link contributed by irisin that promotes the expression of betatrophin and beta-cell regeneration which stages reduced insulin resistance [15]. The biological role of the myokine irisin is that it is involved in energy expenditure and augments glucose tolerance. Thus, decreased circulating irisin levels would contribute to muscle insulin resistance.

Circulating irisin levels are more in males compared to females which revealed the role of hormones and muscle mass. We speculate that anabolic effects of testosterone lead to an increase in irisin concentration via an increase in fat-free mass. As a result, irisin concentration may represent baseline muscle mass [16].

This study stratified the participants with high metabolic dyslipidemia with elevated TyG index especially in young men as compared to young women. This is in support of the Zhu D et al. researcher findings due to the impact of the female sex hormone estrogen that associates with cardio protective HDLc. Serum irisin levels represent the cardioprotective myokine which was found to have a positive correlation with HDLc [17]. Following physical exercise, irisin is released that stimulates the expression of uncoupling protein 1 and promotes induction of brown adipose tissue. Thus improves glucose tolerance and insulin sensitivity which is related to TyG index.

Waist circumference, triglycerides, and non-HDLc were high in the participants with high TyG index. However, a negative correlation was revealed between irisin with BMI, WC, and HC but not significant. A noteworthy finding is waist circumference high in young individuals which are still considered a standalone anthropometric indicator of metabolic dyslipidemia [18]. Sedentary behavior is the real culprit that leads young to obesity-related traits [19]. Previous studies in the cardiovascular field had evaluated high cardiovascular risk in individuals with elevated TC, and LDLc [20]. Inverse correlation of serum irisin with parameters such as TC, TGL, LDLc, and non-HDLc indicated metabolic risk. In the current study, individuals with low circulating irisin levels are identified to have an abnormal lipidemic pictures that demonstrates the possible concordance to develop cardiovascular risk. Moreover, men with low irisin levels are paralleled by elevated cardiac risk ratios, thus having an increased chance to develop CVD [21, 22].

Zhang et al. derived an inverse association of irisin with Intrahepatic TGL content in obese individuals [23]. The possible explanations for the relation between irisin and TGL, is that irisin (i) regulates peroxisome proliferator activator receptor-gamma that causes fatty acid oxidation resulting in thermogenesis (ii) modulates hepatic TGL accumulation (iii) up-regulates the release of myokine Fibroblast growth factor 21, which is related to insulin sensitivity and mediates the beneficial effects of exercise on metabolism [24, 25].

To identify exactly the individuals with metabolic dyslipidemia, cardiovascular risk ratios were evaluated in the participants with high and normal TGL. The study participants with TGL $\geq$ 150 mg/dl had revealed a statistically significant increase in Total Cholesterol /HDL ratio, LDL / HDL cholesterol ratio, Triglycerides/HDLc ratio, and non-HDLc; but lowered serum irisin levels as compared to the participants with TGL < 150 mg/dl. Previously Pangiotou et al. had reported the potential role of irisin concerning lipid metabolism and lipid sub-particle regulation [26]. The substantial relationship between irisin and triglyceride was highlighted in a study involving Caucasian and African American individuals, high irisin levels were linked to a higher likelihood of high TGL levels but a lower likelihood of high HDLc levels [27].

To summarize the findings of our study, the young adults with Triglyceride Glucose index (TyG) > 4.5 had decreased irisin levels which negatively correlated with cardiac risk ratios, non-HDLc, and TGL/HDLc positive correlation with HDLc. The limitation of our study is that the study should be conducted as a prospective cohort in a larger population. Insulin levels were not estimated rather TyG index a marker of insulin resistance was utilized to relate the peripheral insulin-resistant state.

Conclusion

The focus of the study on young adults with increased Triglyceride glucose index concluded that irisin levels were decreased which represents the metabolic dyslipidemic picture and cardiovascular risk. Irisin is a notable myokine, that combats muscle insulin-resistant state and comprehensive work needs to be carried out to identify more potential targets in the future.

Acknowledgements The authors thank the participants of the research study.

Funding Support The research work utilized the facility in the institution.

Declarations

Conflict of Interest The authors have no relevant financial or non-financial interests to disclose.

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