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SERUM IRISIN, LIPID ACCUMULATION PRODUCT AND FRAMINGHAM RISK SCORE AS CVD RISK PREDICTORS IN YOUNG ADULTS

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Background

Irisin, is an adipomyokine, acts as a potential link between obesity, insulin resistance and cardiovascular disease. Notable marker is needed to predict disturbed metabolic environment and early cardiovascular danger in young adults. The objective is to evaluate irisin, lipid accumulation product and Framingham risk score as predictors of cardiovascular risk in young individuals.

Methods

This research work included the young adults (n = 80) between 18 to 35 years attending the Master Health Checkup. Basic anthropometric measurements taken, blood samples were drawn to analyze serum Irisin (Bio-Rad ELISA using standardized Abbkine kit), lipid profile parameters (TC, HDLc,

LDLc, triglycerides) were estimated, lipid accumulation product (LAP) and cardiac risk ratios were calculated. With ANOVA statistical analysis the analytes were compared between low, moderate and high Framingham risk score category. Diagnostic performance was assessed with Receiver's operating characteristic curve (ROC).

Result

Mean irisin levels (0.44 ± 0.18 ng/ml) were decreased in the category with high Framingham risk score (FRS) category compared to moderate and low FRS category. Waist circumference was elevated with significant increased triglycerides in high FRS category. TGL/HDLc (4.17 ± 0.86) and non-HDLc (201 ± 19.9 mg/dl) levels were elevated in high FRS category. Pearson correlation analysis of LAP revealed significant inverse correlation with irisin (r = - 0.41) and FRS (r = -0.35). Diagnostic sensitivity through ROC revealed significant AUC for irisin and lipid accumulation product (0.85) and (0.905) respectively.

Conclusion

Decreased irisin levels highlight the risk of cardiovascular disease in young individuals with elevated lipid accumulation products. Irisin and LAP enables highlights the diagnostic importance to identify the young adults with metabolic dyslipidemic status.

identification of individuals with metabolic and atherogenic risk.

Keywords: Serum irisin, Lipid accumulation products, Framingham risk score category

1.0 Introduction

Young adults experience a variety of difficulties in their demanding lives and exhibit an aggressive phenotype that causes premature development of complications. Irisin is considered as an exercise induced adipomyokine. Irisin is a novel myokine that is thought to be a good metabolic factor and to have an adverse relationship with non-communicable diseases. It's been notified the beneficial effects of irisin pertaining to formation of brown adipose tissue, increased insulin sensitivity, and antioxidant and anti-inflammatory properties [1]. Physical activity had increased the PPAR-coactivator and subsequently Fibronectin type III Domain-Containing expression is also favored. A membrane protein called FNDC5 is present in both the brain and skeletal muscle. The benefit of irisin is projected by the proteolytic cleavage of FNDC5 which is known to function as transmembrane protein [2]. The mitochondrial uncoupling protein expression is carried out by irisin indirectly by boosting the PPAR coactivator. This is way towards thermogenesis and energy expenditure which happens in the skeletal muscle and brown adiposity tissue also. Irisin leads as a metabolic marker and therapeutic target to improvise metabolic dyslipidemic situation [3,4].

Lipid accumulation products are said to assist as predictors of atherogenic potential among Indian guys from Southern India who were neither obese nor hypoglycemic, the LAP index demonstrated higher prediction accuracy for the likelihood of insulin resistance [2]. Particularly in the early adult stage, it is crucial to identify the dyslipidemic metabolic unhealthy people using basic measures. In this context, serum irisin and, Lipid accumulation products and FRS were evaluated to assess cardiovascular risk in young adults.

2.0 Method

2.1 Study design

The Master Health Checkup at our institution served as the context for this analytical cross-sectional study. Following the institutional ethics committee granted its approval (IEC/2867/2021), the study officially began by enrolling participants in accordance with the inclusion and exclusion criteria. After understanding the research protocol and comprehending it, the participants signed a consent form. The size of the sample was calculated using the 2.5% prevalence of diabetes among young adults in India. [5]. Sample size of n = 80 were calculated and recruited with convenient sampling process.

Inclusion criteria:

Participants of both sexes in the age group between 18 to 35 years with Triglyceride glucose index cut-off greater than 4.5 were included [6].

Exclusion criteria

Young adults with dysglycemia, known diabetes, high blood pressure, renal diseases, liver diseases and cardiovascular diseases were excluded.

2.2 Data collection

After an overnight fast of 8 to 10 hours, blood samples were taken. Hexokinase was used to measure fasting blood glucose, total cholesterol and triglycerides were measured enzymatically, likewise estimation of HDLc and LDLc levels via direct immune inhibition approach. samples were stored in a - 20° C deep freezer until analysis of serum irisin in BioRad ELISA assay approach using the standardized Abbkine kit. Furthermore, Lipid accumulation products were calculated with the formula:

"LAP: Men: [WC (cm) – 65] × [TG (mmol/l)]

Women: [WC (cm) – 58] × [TG (mmol/l)] [7]"

2.3 The individual's ten year cardiovascular risk is calculated using the Framingham risk score, which incorporates risk factors on a gender-specific score sheet. Framingham Heart Study evaluated the risk score

The Framingham Risk Score was initially created to calculate the 10-year likelihood of developing coronary heart disease using results from the Framingham Heart Study. The FRS score analyses the likelihood of suffering a heart attack or heat illness within the next ten years. [8]

2.4 Statistical analysis was performed with SPSS version 16.0. ANOVA was used to compare the biochemical parameters between the groups. Results are expressed as mean ± standard deviation.

Receiver's operating characteristic curve (ROC) was utilized to evaluate the diagnostic performance of the analyte of interest.

Risk score	**Severity of 10 year cardiovascular risk**
Less than 10%	Low risk
10 – 20%	Moderate risk
More than 20%	Severe risk

3.0 RESULT

The study was conducted in young adults attending the master health checkup had the mean age of male 32 years and females 30 years. Visceral adiposity as revealed by the waist circumference in the young adults were found to be significantly increased in high FRS category. Table 1: represent the comparison of irisin and lipid accumulation products (LAP) in categories of low, intermediate and high Framingham risk score. LAP was found to be significantly elevated in the participants with high FRS (Figure 1).

Table 1: Comparison of Irisin and LAP in young adults based on Framingham risk scoring system

PARAMETERS	**LOW FRS n =66**	**INTERMEDIATE FRS n = 12**	**HIGH FRS n = 2**	**F value**	**P value**
WC (cm)	95.03 ± 3.53	102 ± 2.47	111 ± 1.76	50.46	0.000***
BMI	24.71 ± 1.64	25.82 ± 1.78	27.72 ± 1.21	5.148	0.008**
TC (mg/dl)	161.12 ± 32.7	216 ± 36.2	244 ± 37.3	23.24	0.000***
TGL(mg/dl)	85.66 ± 16.5	137.05 ± 15.5	171 ± 15.85	38.18	0.000***
HDL-cholesterol (mg/dl)	47 ± 8.2	44.6 ± 9.1	41.1 ± 84	3.51	0.03*
LDL-cholesterol (mg/dl)	115 ± 17.5	128 ± 17.9	168 ± 21.4	11.67	0.001**
TC/HDL- cholesterol ratio	3.42 ± 0.74	4.8 ± 0.82	5.9 ± 1.1	4.78	0.004**
LDL / HDL-cholesterol ratio	2.44 ± 0.69	2.87 ± 0.73	4.09 ± 0.84	5.22	0.007**
TGL/HDL-cholesterol ratio	1.82 ± 0.21	3.07 ± 0.84	4.17 ± 0.86	14.34	0.000***
Non-HDL- cholesterol	131.4 ± 25.17	172 ± 22.4	201 ± 19.9	25.5	0.001**

Irisin (ng/ml) **LAP (cm.mol/L)**	1.71 ± 0.18 41.37 ± 15.29	0.87 ± 0.175 79.59 ± 15.4	0.44 ± 0.18 93.17 ± 14.2	93.12 53.05	0.000*** 0.000***
WC waist circumference (cm), TC -Total Cholesterol (mg/dl), TGL -Triglycerides (mg/dl), TC/HDL - Total Cholesterol /HDL ratio, LDL/HDL - LDL/HDL cholesterol ratio, TGL/HDL - Triglycerides/HDLc ratio, LAP – Lipid accumulation product					
ANOVA	*p value less than 0.05 is statistically significant NS stands for "not significant." ** Significant ***Extremely Significant				

Likewise participants with high FRS were found to have collectively increased triglycerides, LDLc and non-HDLc. Likewise LAP was found to be elevated in male compared females (Figure 2).

Table 2: Correlation analysis of LAP with Lipid parameters in young adults

PARAMETERS	**r value**	**P value**
BMI	**+ 0. 47**	**0.002** [b]
Triglycerides (mg/dl)	**- 0.303**	**0.008** [b]
HDL-cholesterol (mg/dl)	**+ 0.305**	**0.006** [b]
LDL-cholesterol (mg/dl)	**- 0.332**	**0.003** [b]
Non-HDLc (mg/dl)	**- 0.393**	**0.000** [c]
Irisin(ng/ml)	**- 0.41**	**0.000** [c]
Pearson correlation analysis	*p value less than 0.05 is statistically significant a Correlation Small (0.3 to 0.1) b Shows strongest correlations (0.5 to 0.3) c Indicates highly significant (1.0 to 0.5) NS – Not significant	

Furthermore, (Table 2) the analyte LAP revealed statistically significant negative correlation with triglycerides, LDLc and non-HDLc that justified the cardiovascular risk in the participants. Whereas Table 3 represent the diagnostic performance of the target analytes with cut-off irisin (0.24 ng/ml) and LAP (61cm.mol/L) which revealed better diagnostic sensitivity with area under the curve 0.85 and 0.905 respectively (Figure 3).

Table 3: Diagnostic performance with ROC analysis

MARKERS	**Cut-off value**	**Diagnostic Sensitivity (%)**	**Diagnostic Specificity (%)**	**Area under curve**	**Significance p value**
Irisin ng/ mL	0.24	85.3 %	53 %	0.85**	0.000
LAP (cm.mol/L)	61	95 %	58%	0.905**	0.000

Receiver's operating characteristics	LAP –Lipid accumulation product	
	Area under curve: * 0.5 - no discrimination; ** 0.7 -0.8: considered acceptable, at 95% confidence interval *** 0.8 -0.9: considered excellent; > 0.9: outstanding	

4.0 Discussion

Beyond the apparent cost to one's physical health, CVD has enormous economic effects on both individuals and society. Given this burden and rising incidence, professional groups emphasize the value of prevention by identifying and managing risk factors before a significant cardiovascular event occurs in order to improve cardiovascular and other health outcomes.

Young adults are at very high cardiovascular and metabolic risk due to the existing lifestyle with less physical activity. As revealed from the study, 82.5% had low FRS score with low cardiovascular risk. Whereas the habit of smoking had elevated the FRS risk scoring in the participants thus 15% of young adults had intermediate risk too. and for the majority of ethnic groups in the country According to CDC 2020, cardiovascular disease is considered as the common cause of death in male and female and for the majority of ethnic groups in the country. In this study young adults reported to possess android obesity with elevated waist circumference and BMI with increased circulatory triglyceride concentration and

The young adults with intermediate and high FRS score had waist circumference and high triglyceride levels. Visceral fat buildup is closely associated with an increased risk of cardiovascular disease. These young adults can be rightly identified as hypertriglyceridemic waist phenotype linked to the proatherogenic modifications in lipoproteins [10].

The present study focuses on the relationship of the lipid levels and cardiovascular risk in young adults. Cardiac risk ratios such as TC/HDL-C ratio, LDL / HDL-C ratio and TGL/HDL-C ratio calculated considering the worth of HDLc in an individual the ratios were found to be elevated.
Likewise Lipid accumulation products were also found to be elevated in support to hypertriglyceridemic phenotype [11].

Waist circumference (WC) and fasting triglyceride concentration are the two variables that interact to form the current indication of visceral obesity, known as lipid accumulation product (LAP). The concomitant use of biochemical and anthropometric data to compute LAP enables the depiction of both morphological and biochemical abnormalities related to lipid over accumulation in individuals. LAP is frequently utilized as a predictor of cardiovascular problems and a marker of metabolic abnormalities [12]. Though some individuals have conditionally normal healthy metabolic activity, in the current scenario various modern diagnostics has revealed that young adults do develop cardiovascular issues. Thus, simple markers such as LAP leads towards early identification.

Irisin levels were decreased in individuals with abnormal lipid status and high Framingham score. Irisin levels were comparatively more in men than women. Indeed, it is surmised that production of irisin was from increased adipose deposits too. The concept revealed by Blizzard et al viewed that

30% reduction of irisin levels in anorexic patient would be because of muscle or adipose tissue atrophy [13]. The data clearly reveals that young adults have overweight BMI which had a positive correlation with LAP. Also beneficial irisin levels are decreased in obese individuals with high FRS. This is in concordance with the concept of peripheral tissue irisin resistance in young individuals.

Whereas obese individuals may have irisin resistance as studies revealed positive correlation between BMI and irisin that directs the link of irisin which is secreted by the adipose tissue. Thus circulating lrisin is evidenced to possess protective role through endothelium dependent or independent mechanism involving Nitric oxide – c GMP. Irisin is so effective that even slightly elevated amounts in the bloodstream can significantly enhance energy expenditure, cause weight loss, and ameliorate diet-induced insulin resistance [14]. Irisin is considered as a promising biomarker that regulates normal lipoprotein metabolism. Fuku N et al had studied the interaction of candidate genes FOXOA3 and APOE thus justifies the findings in this study the positive correlation of irisin and HDLc [15]. A step ahead by the research study conducted in irisin gene have shown single nucleotide polymorphism rs3480 and rs726344 which was found to be associated with increased cardiovascular risk [16].

Study has reported the inverse association of LAP with TC, Triglycerides and LDLc that signifies the potential role of irisin as treatment of metabolic disease. Moreover the diagnostic performance sensitivity of LAP and irisin justified the role as cardiovascular risk marker. Epidemiological studies had demonstrated that individuals with Diabetes mellitus seem to have lowered irisin levels and emphasized its potential as diagnostic tracking marker to monitor the progression of cardiovascular disease in diabetic patient [17, 18].

5.0 Conclusion

The classic risk variables are computed to detect the individuals with cardiovascular atherogenic risk. When modifiable risk factors are identified early on, prevention is the key to combating CVD. Framingham risk scores of low, intermediate and high risk assists the Physician towards primary and secondary prevention. This study is an awareness to look upon general health of each and every individual especially younger age group which drives towards lifestyle modifications and non-pharmaceutical therapy.

Currently future studies have focused on the vaso-relaxant effect on vascular beds. It is quite interesting to gain experimental knowledge on irisin and lipid accumulation product. This study had opened the window for the research scholars to conduct epidemiological studies on the beneficial effect of irisin on micro vascular beds.

Limitations: This study has the limitation of small sample size of young adults. Also advanced cardiac biomarkers were not utilized that facilitates the benefit of simple calculated tools at the Physician's office to identify the metabolically unhealthy young adults.

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Declaration of interest: - Nil

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Conflict of interest declared none.

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