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Serum Circulating Irisin is a Promising Prognostic Biomarker of Diabetes-Mediated Atherosclerotic Cardiovascular Disease

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Abstract

Diabetes mellitus stands out as a primary independent risk factor, significantly advancing fatal cardiovascular pathophysiology through the acceleration of atherosclerosis, a key factor in the development of numerous cardiovascular diseases (CVDs). Notably, the comparative risk is stated to be higher in Pakistan than in other Asian countries. There is a critical need for effective measures to identify novel and dependable prognostic biomarkers to mitigate the chronic consequences faced by the diabetic population in Pakistan.

Irisin, a muscle-derived factor secreted during endurance exercise, has gained attention due to its potential crosstalk with CVDs. This study aims to evaluate the serum stages of irisin in Pakistani individuals with type 2 diabetes (T2DM), both male and female, with atherosclerosis, and to explore potential associations between the biomarker and other relevant parameters. In this case-control study, 435 volunteers participated, including 145 with type 2 diabetes, 145 with type 2 diabetes and atherosclerosis (T2DM-ASCVD), and 145 healthy controls, meeting specific inclusion criteria. Serum levels of irisin and insulin were measured by means of sandwich ELISA.

The results revealed a significant decrease in irisin levels in both type 2 diabetic and T2DM-ASCVD groups compared to healthy subjects. Notably, statistically significant Spearman correlations were observed between irisin levels and fasting blood glucose in both T2DM and T2DM-ASCVD groups. In conclusion, this study, to the best of

our knowledge, is the first to shed light on the positive correlation between irisin levels and atherosclerotic diabetes patients. This suggests the potential utility of irisin as an effective prognostic biomarker for monitoring and preventing the progression of CVDs in diabetes-mediated cardiovascular impairment.

Introduction

The diagnosis of diabetes mellitus (DM) has become quadrupled over the last three decades, globally (Laurindo et al., 2025) Saeedi et al., 2019). As per the estimate of international diabetes federation (IDF), around 9.3% (463 million) population was affected by type 2 diabetes mellitus (T2DM)(Aminov, Folan, & Pisconti, 2025). Among them, 10.8% belonged to urban areas (Saeedi et al., 2019). In keeping with a recent investigation, above 30% of the Pakistani population has high susceptibility to develop atherosclerosis cardiovascular disease (ASCVD) (Hassan et al., 2019). DM is accountable to progress multiple impairments including vascular dysfunction; micro- and macro-vascular. In this, the formation and adhesion of atheroma plaque are one of the crucial elements that triggers macro-vascular aliments (Wang, Wu, Yin, & Dou, 2025) Papatheodorou et al., 2018; Papatheodorou et al., 2016). Norhammar et. al were highlighted that DM is the susceptible factor in the development of cardiovascular diseases in males (around 2-3 times) and females (around 3-4 times) (Norhammar & Schenck-Gustafsson, 2013). Therefore, estimation of promising metabolic biomarkers is essential to regulate and impede the development of T2DM-mediated atherosclerosis.

DM-induced atherosclerosis improperly regulates the propagation of vascular smooth muscle cells (VSMCs) which subsequently leads to the production of atheroma plaque and causing arterial and vascular tissues stiffness (Khan & Jandeleit-Dahm, 2025)Madonna & De Caterina, 2011). Several organs and their physiological regulations are affected by ASCVDs in diabetes (Abejew et al., 2015; Ma, 2018; Papatheodorou et al., 2015). In heart arteries, it increases the risk of angina, coronary heart disease, carotid artery disease and peripheral artery disease (Einarson et al., 2018; Takahara et al., 2019; Wilcox et al., 2018). Whereas atherosclerosis in the cerebral region leads to ischemic stroke and haemorrhagic stroke (Fu et al., 2018) Furthermore, its development in kidneys leads to hypertension, renal artery stenosis or renal failure (Charles et al., 2017; Kwon & Lerman, 2015).

The identification of factors that prevent the development of diabetes mellitus is under the focus of attention (Li et al., 2017; Tsuda, 2015). In which, irisin, a hormone-like polypeptide, is identified in blood circulation that has shown its preventive role for diabetes (Khalil et al., 2025). It produces in blood muscular activity via the activation of PGC-1α (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha); irisin induces beige fat formation (Jeremic et al., 2017). According to the study of Crujeiras et al and Xiong et al, irisin produces metabolic effect by lessening body weight and elevated total body energy expenditure and insulin sensitivity (Crujeiras et al., 2014; Xiong et al., 2015). Prominently, the assessment in murine model reported the protected effect of irisin against atherosclerosis. The defined underlying mechanism involves the thwarting of tarnished low-density lipoprotein-mediated vascular inflammation and dysfunction of endothelial cells. Accordingly, irisin is anticipated to be a capable element to treat multiple metabolic disturbances and cardiovascular diseases (Spiegelman, 2013; Y. Zhang et al., 2016).

Taken all together, identification of biomarker is the crucial step to develop preventive approaches. Few researchers have focused the risk of ASCVD Pakistani population but failed to address the reliable diagnostic marker, therefore the present study is aimed to identify the possibility of using serum irisin as a predictive metabolic marker for the development of the cardiovascular impairment that is related with diabetes mellitus. The current study defines its correlation with atherosclerosis in T2DM patients, evaluates the possible association among metabolic markers (irisin and lipid profile), and between other parameters of study such as fasting blood glucose (FBG), fasting insulin and Homeostasis Model Assessment (HOMA) in the selected Pakistani population.

Sample Collection:

435 participants of the identical age and socioeconomic rank were recruited for Present case-control study. Following the guidelines of the National Diabetic Data Group (WHO criteria), 290 participants remained designated as cases, while 145 were identified as healthy controls. The diabetic participants were further categorized into two groups:145 those with Type 2 Diabetes Mellitus (T2DM) and 145 Atherosclerotic Cardiovascular Diseases (ASCVDs), and those with T2DM alone. The classification was grounded on the criteria outlined by the American Heart Association.

Prior to commencing the study on human samples, ethical sanction was obtained from the University of Karachi, Karachi, Pakistan's ethical review board, and written informed agreement was obtained from all subjects. The enrolled diabetic patients were under treatment at Jinnah Hospital and Civil Hospital, Karachi, Pakistan, while healthy subjects were recruited from the general community.

Participants aged between 50 to 60 years, without comorbidities such as renal impairment, neoplastic disease, hepatic dysregulation, acute or chronic illness, or cancer, were comprised in the study. All patients were undergoing antidiabetic treatment (either oral agents or insulin). Those with secondary diseases, individuals actively or passively smoking, or consuming alcoholic products were excluded from the study. Inclusion criteria for normoglycemic volunteers were based on a normal health status, not receiving medical treatment (e.g., anti-thyroids, glucocorticosteroids), and being non-smokers.

Initially, diagnoses of T2DM were done at the beginning of the study in both diseased groups. The mean age (T2D with ASCVD: 56.1 ± 3.3 years, T2M: 55.4 ± 4.3 years), BMI (T2M: 26.8 ± 2.7 $kg/m^{2;}$ T2D with ASCVD: 28.9 ± 3.1 kg/m^2) and socioeconomic status were similar in both of these groups. The age and BMI of healthy members were 55 ± 4.5 years and 26.3 ± 2.66 kg/m^2, respectively.

The clinical evaluation of all participants was done by taking the record on duration of diabetes (years), antiquity of diabetes/ diabetic coma and co-morbidities. The data of smoking, physical motion and medication were identified and analysed. The detailed study on anthropometric profile was identified by using weight and height. The quantification of body mass index (kg/m2), percent body fat, and waist to hip ratio (WHR), waist to height ratio (WHtR), A body shape index (ABSI) and conicity index (CI) were done as previously reported studies with slight modifications.

Material and methods:

The overnight fasting (12 hours) blood specimen of 6 mL was withdrawn from vein by keeping the syringe motionless to prevent the vein from collapsing. The blood sample was collected into vacuum tube and gently inverted 6 to 8 times to mix the contents. For the analysis of serum, sample was centrifuged at 3000 rpm for 15 minutes and the supernatant was castoff. Serum was stored at -80˚C till quantification of irisin and insulin by using commercially available human serum irisin sandwich ELISA kit (Cell Biolabs, Inc.7758 Arjons Drive, San Diego, CA 92126 USA) and human serum sandwich insulin ELISA kit (Sigma-Aldrich St. Louis, Missouri, United States), respectively.

For the spectrophotometrically colorimetric quantification of serum irisin and insulin, wavelength of 450 nm was used. The concentrations of both in the samples were then evaluated by comparing the optical density (O.D) of sample with standard curve. The detection range of 5-19 μIU/mL and 0.2-2 μI/ml were reported for insulin and irisin, respectively.

Biochemical Estimation:
Other parameters of the study, such as fasting blood glucose (FBG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triacylglycerol (TAG) were assessed by using standard automated laboratory method. For the quantification of insulin resistance (IR), Homeostasis Model Assessment (HOMA-IR) index and QUICKI were used (Antunes et al., 2016; Gutch et al., 2015).

Statistical analysis:
The facts were statistically examined by using Statistical Package (version 22). The normality of all quantitative parameters was identified by via the Kolmogorov and Smirnov normality test. One-way ANOVA followed by posthoc Tukey test was performed to associate three groups (healthy subjects, T2DM and T2DM-ASCVD) with each other. To explore the possible relationships between irisin and lipid profile and with other parameters of study, Pearson rank correlation was calculated. Whereas binary logistic model was applied to explore the increasing odds ratio between patient and control set for Irisin. Multiple linear regression investigation was performed to predict the risk for increasing fasting plasma glucose, fasting plasma insulin, insulin resistance and Insulin Sensitivity in association with several quantitative parameters, with 95% confidence interval. P-value ≤ 0.05 was measured as statistically significant.

Results:
Baseline features of the study population:
As expected according to the diagnosis of patients, the significantly increased level of FBG level was found in T2DM (P<0.01) and T2DM with ASCVD patients (P<0.001) as associated to healthy subjects (Figure 1). By comparing the fasting insulin level in both groups with control, there was significantly increased level found in only in T2DM-ASCVD group by showing p-value <0.05 (Figure 2). Consistently, identification of IR and % sensitivity of beta cells was reflecting the significantly worsened fasting IR (HOMA-IR: P<0.01 and QUICKI: P<0.001) and decrease % sensitivity of beta cells in T2DM with ASCVD group (P<0.001). Whereas, relatively no clinical significance was observed to IR and % sensitivity of beta cells in T2DM group than control group, as shown in figure 3 and 4, respectively But, percent of beta cells were significantly low in both groups of diabetes (P<0.001), as depicted in figure 5. The quantification of insulin resistance by using is shown in supplementary figure 1. Besides, the age of all the patients and control were insignificant (P>0.05). The noteworthy upsurge in the BMI of T2DM with ASCVD group was found as linked to control group (P<0.001). The anthropometric profile of other parameters (% body fat, WHR ratio, WHtR, ABSI and CI) was found in different ranges, as shown in supplementary figure 2-6. Whereas, the systolic blood pressure (SBP), diastolic blood pressure (DBP) of patients were statistically insignificant compared with control (P>0.05), as depicted in figure 6.
As for the lipid profile, the levels of serum triacylglycerol (TG) in T2DM with ASCVD and T2DM were found to be significantly higher as compared to control group (P<0.01 and P<0.001, respectively), but in T2DM patients the TG value lies in normal range. The increase differences of TG levels were found between patients' group (P<0.001). There were significant differences regarding total cholesterol,

VLDL-c among T2DM with ASCVD group and control. Only VLDL-c were found significant in T2DM ($P<0.01$), as shown in figure 7.

The study observed expected outcomes in patients diagnosed with Type 2 Diabetes Mellitus (T2DM) and T2DM with Atherosclerotic Cardiovascular Diseases (ASCVD). Fasting blood glucose (FBG) levels were significantly higher in both groups compared to healthy subjects. Elevated fasting insulin levels were specifically noted in the T2DM-ASCVD group. Insulin resistance and decreased beta cell sensitivity were more pronounced in T2DM with ASCVD, while the T2DM group showed relatively minimal changes. Notably, the age of patients and controls did not differ significantly.

T2DM with ASCVD patients exhibited a substantial surge in body mass index (BMI). Various anthropometric parameters and blood pressure levels were generally comparable between patients and controls. In terms of lipid profiles, serum triacylglycerol (TG) levels were knowingly advanced in both patient groups compared to controls, with T2DM patients maintaining values within the normal range. Differences in TG levels were more pronounced between patient groups. Significant variations were observed in total cholesterol and very-low-density lipoprotein cholesterol (VLDL-c) levels between T2DM with ASCVD patients and controls, while in T2DM, only VLDL-c showed significance.

Serum irisin in T2DM and T2DM with ASCVD patients:

Serum irisin levels in T2DM- ASCVD group were significantly decrease in comparison to T2DM (0.70 ± 0.17 µI/ml, 0.84 ± 0.54 µI/ml; $P<0.05$) and control (1.3 ± 0.54 µI/ml; $P<0.001$). It is worth mentioning that further reduction in the mean of serum irisin level was observed in T2DM with ASCVD relative to T2DM figure 8.

Importantly, the current study originate a moderate negative association between serum level of irisin with FPG, fasting plasma insulin, % Beta Cell, insulin resistance, HDL-c, triglyceride, cholesterol, LDL-c, VLDL-c and BMI in T2DM-ASCVD patients and T2DM (95% Confidence Interval, $p<0.001$). The other anthropometric indices include % body fat, WHR ratio and WHtR were shown weak negative correlation in both groups, as shown in supplementary table 1. Moreover, we observed a momentous positive correlation between irisin and % sensitivity of beta cells. No other significant correlations were found ($P>0.05$), as shown in Table 1).

The logistic regression was shown that the level of irisin is a promising biomarker for not only T2DM but also for T2DM-ASCVD (Table 2). It produces association with FPG, fasting plasma insulin, insulin resistance, percent sensitivity, as shown in supplementary table 2-5.

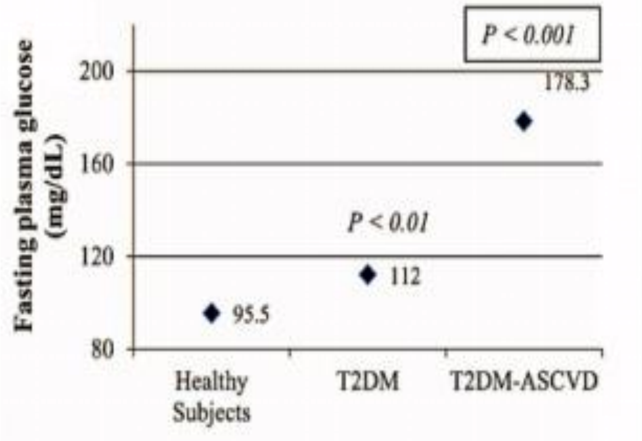

Fig 1: Fasting plasma glucose in Healthy subjects, T2DM and T2DM-ASCVD patients. The statistically significant increase FPG level was observed in both groups of patients as related with healthy subjects followed by overnight fasting.

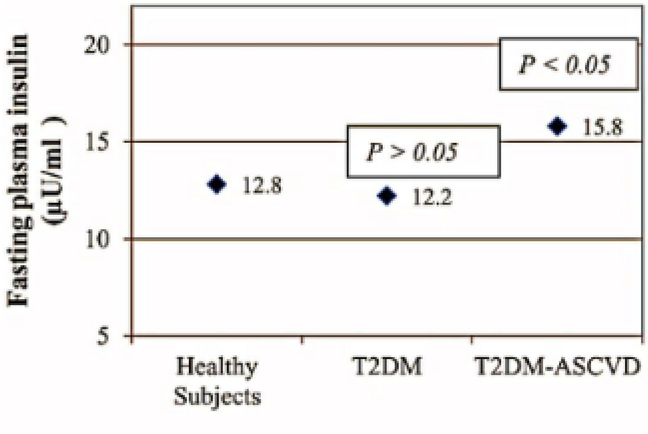

Fig 2: Fasting plasma insulin in Healthy subjects, T2DM and T2DM-ASCVD patients. The statistical scrutiny by performing one-way Anova analysis for the detection of insulin level was showed significantly elevated fasting plasma insulin in only T2DM-ASCVD patient as compared with healthy subjects.

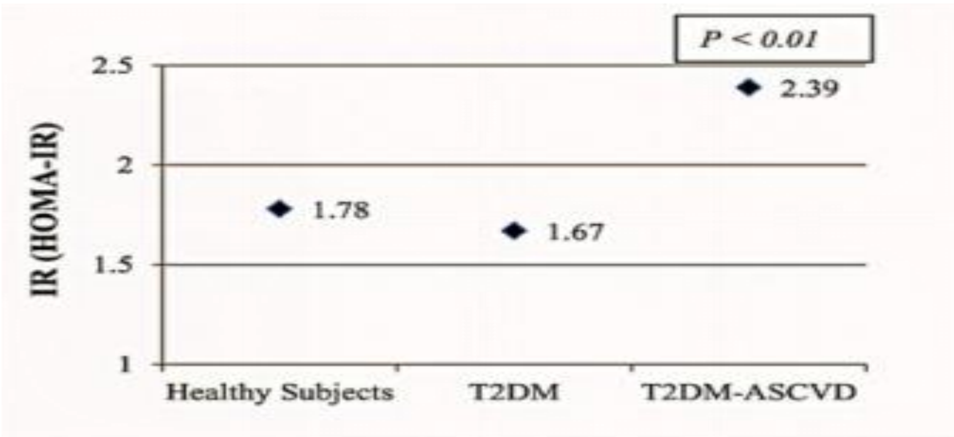

Fig 3: Insulin resistance in Healthy subjects with T2DM and T2DM-ASCVD patients. The statistical analysis by executing one-way Anova analysis for the identification of resistance of insulin was showed significantly increase IR in only T2DM-ASCVD patient as compared with healthy subjects.

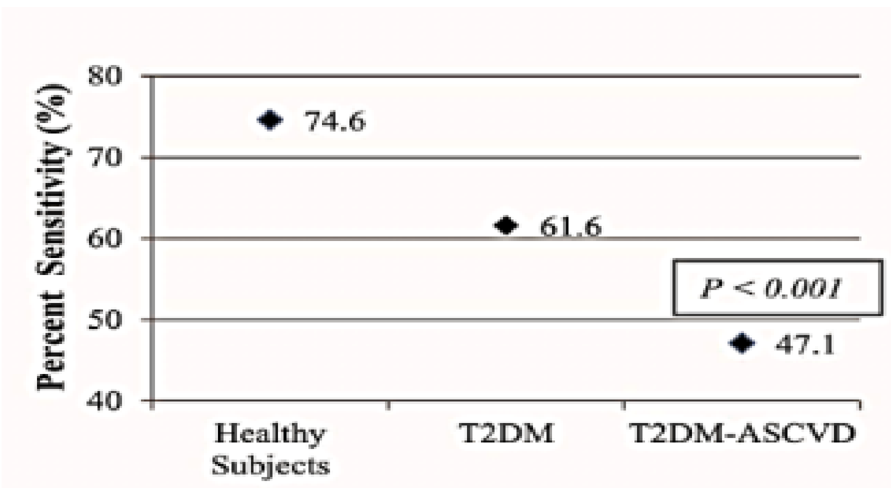

Fig 4: Percent sensitivity in Healthy subjects, T2DM and T2DM-ASCVD patients. Relatively, the percent sensitivity of pancreatic beta cells was found to be decline in T2DM-ASCVD patient than control, whereas T2DM patients was shown insignificantly decrease sensitivity of beta cells.

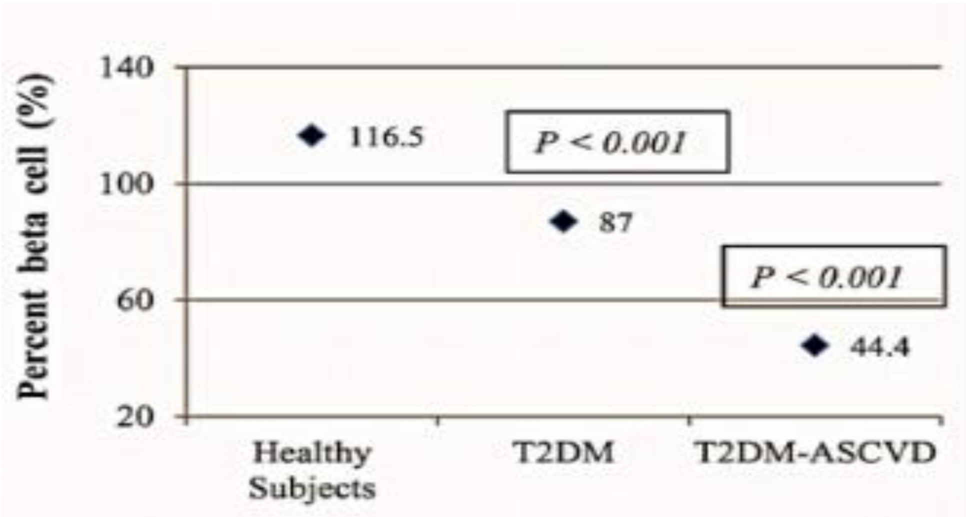

Fig 5: Percent beta cells in Healthy subjects with T2DM and T2DM-ASCVD patients. The statistical decrease percent of pancreatic beta cells were found in both groups of patients as compared with healthy subjects.

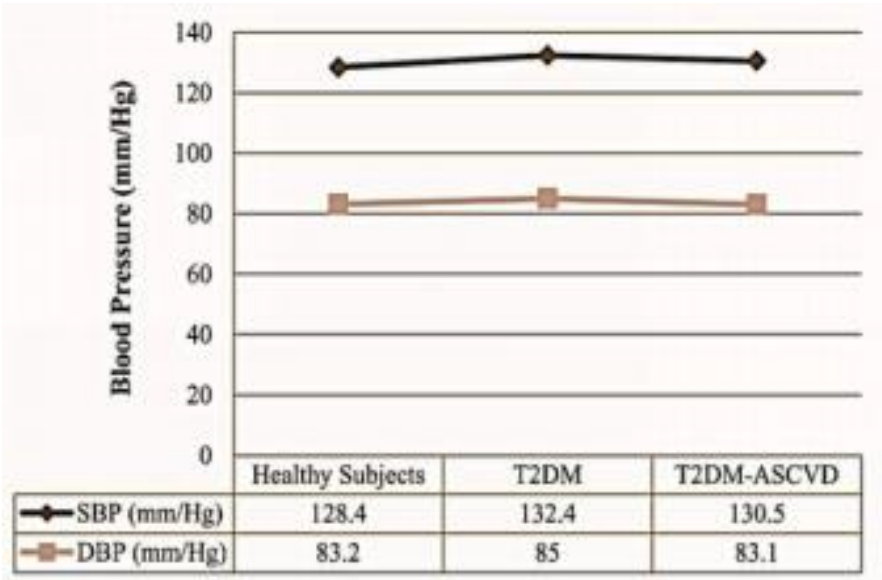

Fig 6: Blood pressure in Healthy subjects, T2DM and T2DM-ASCVD patients. The systolic and diastolic pressure were found similar in all groups.

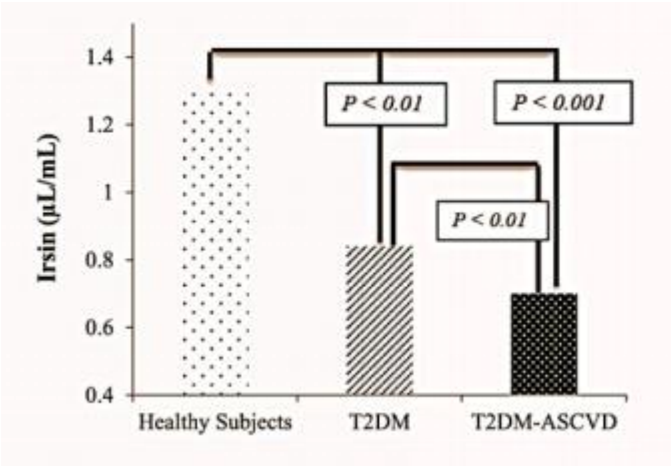

Fig 7: Serum irisin level in Healthy subjects with T2DM and T2DM-ASCVD patients. Serum irisin levels in patients were significantly decrease as compared to control. The one-way anova post hoc analysis were shown clinically significant difference among patients' group.

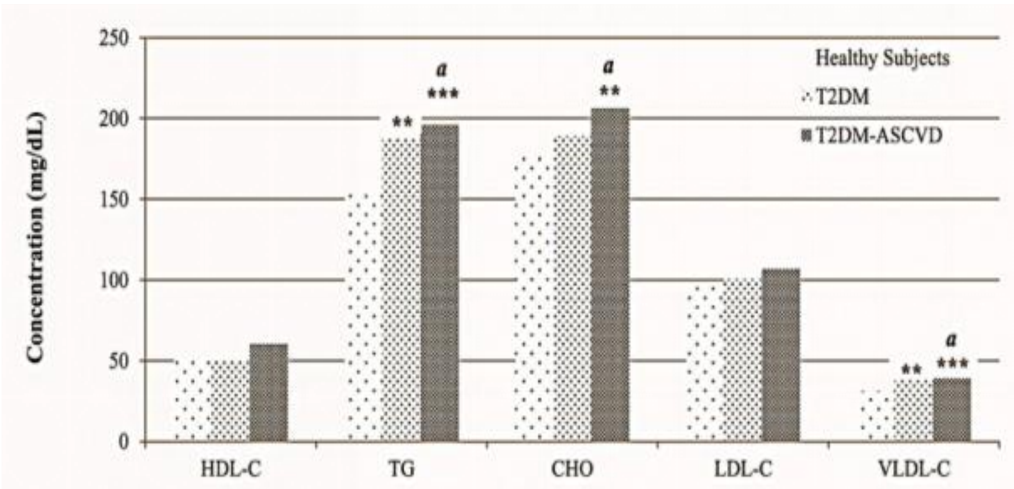

Fig 8: Lipid Profile in Healthy subjects with T2DM and T2DM-ASCVD patients. Lipid profile were identified as per standard labortary protocol. Diabetes-mediated dyslipidemia was observed in T2DM-ASCVD as compare with healthy controls and T2DM. *** P-value <0.001 vs healthy subjects, [a] P-value <0.01 vs T2DM.

Table # 1: Correlation of irisin with clinical parameters in T2DM and T2DM+ASCVD

Characteristics	T2DM (Pearson Correlation)	T2DM+ASCVD (Pearson Correlation)
Age (Years)	0.175	0.112
Fasting Plasma Glucose (mg/dl)	-0.498**	-0.491**
Fasting Plasma Insulin (µU/ml)	-0.698**	-0.873**
Percent Beta Cell	-0.444**	-0.075**
Percent Sensitivity	0.792**	0.847**
HOMA-IR	-0.770**	-0.846**

High Density Lipoprotein (mg/dl)	0.689**	0.583**
Triglyceride (mg/dl)	-0.675**	-0.779**
Cholesterol (mg/dl)	-0.559**	-0.627**
Low Density Lipoprotein (mg/dl)	-0.567**	-0.609**
Very Low-Density Lipoprotein (mg/dl)	-0.675**	-0.779**
Systolic Blood Pressure (mm/Hg)	0.054	0.029
Diastolic Blood Pressure (mm/Hg)	0.078*	0.083
Body Mass Index (kg/m^2)	-0.648**	-0.807**
P-value < 0.05 considered as significant using Pearson correlation ***** :** P-value < 0.001 , **** :** P-value < 0.01, *** :** P-value < 0.05		

Table # 2: Odds Of irisin for T2DM and T2DM + ASCVD

Group	Exp (B)	95% Confidence Intermission for Exp (B)	
		Lower Bound	Upper Bound
T2DM	0.332*	0.159	0.695
T2DM + ASCVD	0.345*	0.166	0.715
The reference category is: Control *: P-value < 0.01			

Discussion

In the view of the fact that cardiovascular diseases caused by diabetes-mediated atherosclerosis are the prominent reason for increase mortality rate in T2DM patients. The focus of many of the previously reported investigations was towards the identification of biochemical factors for diabetes. The complications lead from it are still counted as negligible area. Consequently, the identification of novel, reliable and highly sensitive prognostic biomarkers was essentially required to prevent the drastically increase mortality rate. (Stanković, Nikolić, Krstić, & Diabetes, 2025) Growing piece of evidence exists for atherosclerosis only, and unfortunately, none of them is approved for clinical diagnosis. As far as our knowledge, the present study for the identification of diagnostic biomarker in diabetes-mediated atherosclerosis is first from Pakistan, or even in the South Asian region.

All the recruited subjects were from Karachi, Pakistan, the average age of participants, systolic and diastolic blood pressure in all groups were similar. Figure 1-2 and 9 represented that the mean FPG, fasting plasma insulin and BMI in T2DM-ASCVD were significantly complex than the other groups. Furthermore, the comparing of IR and percent beta cells showed the increased level of resistance and decreased % sensitivity of beta cells in T2DM-ASCVD group. These findings are as per with the study of Peesa, (2013), who mentioned that hyperglycemia induces multiple micro- and vascular impairments such as ASCVDs (Muhammad, Afzaal, Khan, Baig, &

Aasim, 2025) Moreover, diabetes mellitus increases the susceptibility of cardiac diseases and stroke and nearly maximum diabetic patients are dead due to development of CVDs.

To identify the irisin as a biomarker in the progression of atherosclerosis in diabetes mellitus, initially, the assessment of lipid profile was done. The statistical analysis was shown the elevated levels of serum triacylglycerol (TG) and cholesterol in T2DM-ASCVD ($P<0.05$). Consistent with our findings, the previously reported study has highlighted that that dyslipidemia is elevated in T2DM participants when relative to normoglycemic volunteers (Ismail et al., 2001; Jacobs et al., 2005). We had insignificant dyslipidemia in T2DM group, as may be due to decrease fasting plasma glucose and insulin resistance and normal range of insulin secretion. The dysfunction of pancreatic β-cell and insulin resistance are considered as the potential underlying biochemical mechanism that stimulates dyslipidemia in T2DM. Numerous studies have revealed the increase in plasma TG concentration is because of debilitated insulin capability to limit the formation of great TG-rich VLDL (VLDL -TGs) in T2DM patients. The decrease regulation of insulin towards fat cells is believed to be accountable for the defective suppression of the TGs catabolism in the cells and the formation of non-esterified (free) fatty acids (NEFAs) in blood. These fatty acids enter into the liver and stimulate the synthesis of TG, therefore, resulting to cause hypertriglyceridemia and post-prandial hyperlipidemia because of the weakened action of the lipoprotein lipase. The increase hypertriglyceridemia induces thrombogenic modifications which prevent the normal regulation of blood coagulation. Another study has pointed out that elevated VLDL-TGs levels in circulation lessen the cardio-protective HDL-C levels, which in turns decline antioxidant mechanism and anti-atherogenic activities (Vijayaraghavan, 2010). Furthermore, one of the investigations showed the high insulin resistance by using the HOMA-IR index in patients of impaired glucose tolerance (Qian et al., 2024). Furthermore, the insulin resistance is considered as the crucial element in the appearance and evolution of T2DM-mediated cardiovascular impairments (Accili, Deng, & Liu, 2025)

Furthermore, the present study determines the significantly lower level of irisin in both diabetic cohorts were significantly lower than that of the control cohort and the mean of irisin in T2DM+ATHR cohort was relatively lower than that of T2DM-ATHR cohort. Consistent with our results, one of the studies was revealed relatively lower irisin levels in macrovascular disease than normal subjects (M. Zhang et al., 2014). Therefore, the present study indicated that serum irisin level may act as a biomarker for micro- and macro-vascular complications in T2DM. Moreover, the study of Colaianni et al has shown the increased level of r-Irisin elevated the expression of betatrophin which concurrently instigated the propagation of pancreatic β cell and hence cause improvement in glucose tolerance (Colaianni et al., 2016). Another previously reported study was shown decrease circulating irisin levels in patients had new onset of T2DM deprived of angiopathy as compared to the healthy subjects of their investigation to identify the relation of irisin levels with dysfunction of endothelial cells (Xiang et al., 2014). Also, serum irisin was reduced in long-term T2DM and newly diagnosed T2DM individuals as compared with healthy controls (J. J. Liu et al., 2013; Shoukry et al., 2016). This reduction in serum irisin can be credited to its emission in retort to PGC-1α activation; this hormone persuades browning of fat cells. This type of brown fat decreases body weight through cumulative total body energy disbursement leading to an increase in the insulin sensitivity (Klangjareonchai et al., 2014). Also, Boström et al were found that overexpression of irisin in the diabetic animal model increased the energy expenditure and decline IR (Boström et al., 2012)]. Nonetheless, the influence of irisin in humans still under discussion as

Norheim et al., in their study has shown the slightly elevated level of irisin in pre-diabetics patients as compared to healthy controls, whereas the effect was not found in plasma irisin levels (Norheim et al., 2014). Thus, altogether, the consequences of the investigation on the influence of irisin on the human subjects are still contradictory (Panati et al., 2016).

The present study has certain limitations. The population size of the study is relatively small. Secondly, the potential limitation could be the study design, instead of this, the detailed cohort study will identify all the parameters at a point in time when they do not possess the outcome of interest and cohort study design associates the frequency of the outcome of interest between exposed group and unexposed group volunteers. Whereas, the present study evaluates serum irisin levels in T2DM-ASCVD and subjects for the first time in Pakistani subjects who are at higher susceptible of CVDs and the assessment of an association between the biomarker and diabetes-induced atherosclerosis by logistic regression analysis as it is the crucial step of analysis to estimate their effectiveness as innovative dependable diagnostic and/or projecting biomarker for the progression of disease. Furthermore, consistent with previously reported findings of irisin association with glycemic profile, the present study adds the detailed database of glycemic profile with respect irisin in Pakistani population. This study specifically comprises of diabetes-mediated atherosclerosis patients of Pakistani and defines conducive to incremental findings to irisin in them.

Followed by the deep analysis of irisin with diabetes-mediated atherosclerosis, it is strongly suggested to identify the association or irisin with constitutive androstane receptor; xenobiotic sensor that regulates lipid glucose metabolism. This step will be promising to provide the detail information to control the specific point to inhibit hypertriglyceridemia in diabetes. Moreover, this will highly important to answer that how much irisin produces effect on metabolic liver disease to contribute to progression of CVDs. As this metabolism serves as the principle connecting pathway that leads to cardiac impairments

In conclusion, the serum levels of irisin have potential relation with irisin in T2DM with atherosclerosis of Pakistani population. Besides, the increase in irisin is directly correlated with glycemic profile and reduced irisin intensity might collaborate to trigger T2DM and aggravate atherosclerosis. Moreover, it is novel reliable diagnostic and/or predictive biomarker of cardiovascular hazard in diabetes. However, further studies are required to investigate the potential cross-regulatory networks between lipid metabolism and irisin in T2DM and their connotation to regulate glycemia in this population.

The increased mortality rate in Type 2 Diabetes Mellitus (T2DM) patients is largely attributed to cardiovascular diseases resulting from diabetes-mediated atherosclerosis. Previous studies predominantly focused on identifying diabetes-related biochemical factors, overlooking associated complications. This pioneering study, the first of its kind in Pakistan and South Asia, aims to pinpoint diagnostic biomarkers for diabetes-mediated atherosclerosis.

Subjects from Karachi, Pakistan, exhibited elevated levels of fasting plasma glucose, insulin, and BMI in those with T2DM and atherosclerotic cardiovascular disease (T2DM-ASCVD) compared to other groups. T2DM-ASCVD also showed increased insulin resistance and decreased beta cell sensitivity. Dyslipidemia was evident in T2DM-ASCVD, indicating a potential connection between lipid profile and atherosclerosis progression in diabetes.

The study identified significantly lower levels of irisin in together diabetic allies likened to controls, displaying lower levels in T2DM-ATHR. Irisin may serve as a biomarker for micro- and macro-vascular complications in T2DM. Dysregulated irisin secretion could contribute to cardiovascular complications in diabetes.

Conclusion:

Serum irisin levels exhibit potential relevance to T2DM with atherosclerosis in the Pakistani population. Irisin levels correlate with glycemic profiles, and its decrease may contribute to diabetes progression and exacerbate atherosclerosis. Irisin is proposed as a novel diagnostic and prognostic biomarker for cardiovascular risk in diabetes, necessitating further investigation into its regulatory networks in T2DM lipid metabolism.

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