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Serum Irisin Level in Association with Serum Levels of Lipid Profile and Insulin as a Marker of Metabolic Syndrome in Vitiligo Patients

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Abstract:

Introduction: Vitiligo is a disfiguring condition that is asymptomatic. It is the most prevalent skin depigmentation condition brought on by a selective loss of epidermal melanocytes. Irisin hormone can trigger vital alterations in adipose tissue, enhancing muscular function. Insulin resistance and metabolic syndrome improved with moderate elevations in irisin. Patients diagnosed with vitiligo have an increased chance of developing metabolic syndrome.

Aim of the study: Investigate the serum irisin level in vitiligo patients and investigate its association with serum levels of both lipid profile and insulin as a marker of metabolic syndrome.

Subjects and Methods: A case-control study was conducted on 60 participants; 30 were vitiligo patients and 30 were control. Complete history taking and dermatological examination were performed. Serum irisin, lipid profile and insulin levels were investigated. Cases assessed by VASI, and VIDA scores.

Results: Cholesterol and LDL levels were statically higher among vitiligo cases. A statistically positive correlation was found between Irisin level with both cholesterol and LDL levels. In addition, a statistically significant positive correlation between insulin level (absorbance) and triglyceride level was observed. According to the risk factors of vitiligo (age, sex, Irisin, insulin and lipid profile levels), there is no statistical significance.

Conclusion: Vitiligo cases show higher levels of cholesterol and LDL which are positively associated with an increase in irisin levels, which indicates the risk of metabolic syndrome development among vitiligo cases.

Keywords: Irisin; Cholesterol; LDL; Insulin; Metabolic syndrome.

1. Introduction

Vitiligo is a widespread autoimmune condition in which the skin's melanocytes are destroyed, leaving areas of skin devoid of pigment. This deformity, which often affects the face and other visible bodily parts, is extremely debilitating psychologically. Vitiligo usually starts in younger people and worsens over time, leaving a hefty medical burden and a reduced quality of life [1]. Because melanocytes have anti-inflammatory properties and a diminished quantity, vitiligo can cause immunological and inflammatory processes. Since vitiligo is a systemic condition, it is possible to notice metabolic abnormalities such as lipid profile abnormalities and insulin resistance in vitiligo that involve the skin. Vitiligo patients have an increased chance of acquiring metabolic syndrome [2]. At least three of the following five criteria meet the diagnostic criteria for metabolic syndrome: Decrease in level of high-density lipoprotein, abnormally high fasting plasma glucose, abnormally high blood pressure, raised serum triglycerides, and abdominal obesity. Obesity, overweight, and sedentary lifestyles are typically linked to the syndrome [3]. The myokine and adipokine irisin help white adipose tissue (WAT) transform into beige adipose tissue. There are irisins in several tissues throughout the body. It's been proposed that it affects inflammation, neurogenesis, ageing, and metabolic diseases. Numerous factors, including nutrition, exercise, obesity, pharmaceutical drugs, and other clinical situations, affect the levels of irisin in the blood [4]. The β cells of the pancreatic Langerhans islets generate insulin, a peptide hormone that regulates blood glucose levels by improving cellular glucose uptake, controlling the metabolism of proteins, fats, and carbohydrates, and stimulating cell division and growth through its mitogenic activities [5]. Insulin resistance is a pathogenic state characterized by insufficient cell response to insulin, which results in impaired absorption and utilization of glucose [6]. A type of disease related to lipoprotein metabolism known as dyslipidemia includes both excess and insufficiency of lipoproteins. The symptoms included elevated levels of blood total cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol as well as decreased levels of high-density lipoprotein (HDL) cholesterol [7]. The current study aimed to assess the level of serum irisin level in vitiligo patients and to investigate its

association with serum levels of both lipid profile and insulin as a marker of metabolic syndrome.

2. Subjects & Methods

2.1. Subjects

To conduct a case-control study design; sixty patients were selected from the outpatient clinic, Department of Dermatology and Andrology in the Faculty of Medicine- Fayoum University, from 10/1/2022 to 20/11/2022. They were split into two groups:

- Group 1 consisted of 30 vitiligo cases.
- Group 2 consisted of 30 age- and sex-matched control participants.

Inclusion and exclusion criteria

Patients between the ages of 10 years and 65 years were included in the current study; however, those with hematological disorders, other skin conditions, or those who had recently had treatment were excluded.

2.2. Methods

Complete history taking and dermatological examination were performed. History taking included personal history, present history for duration, onset, and course of the disease, history for systemic and dermatological disease, and family history for autoimmune diseases. Dermatological examination included Vitiligo Area Scoring Index (VASI), and Vitiligo Disease Activity Score (VIDA). The VASI score was determined using the following method, which incorporates contributions from everybody region (score range between zero and 100). VASI = sum of All sites in the body (hand unites) × (depigmentation residual). A hand unit is about 1% of the total body surface area. It consists of the volar surfaces of all the digits and the palm areas. VIDA score It incorporates a six-point rating system for vitiligo activity, which is determined by the patient's assessment of the disease's activity (growth of current lesions or emergence of new lesions) over time. The grading scheme is as follows:

- + 4 (six weeks of activity).
- +3 denotes activity between six weeks and three months.
- +2 between three months and six months.
- +1 between six months and twelve months.

- 0 denotes stability for a year or more. For Specimens

Collection, each research participant had 4 mL of venous blood drawn from the antecubital vein using a sterile 5 mL syringe. Simple vacutainer tubes were used to collect blood samples to separate the serum. Using 800 D centrifuges, they were incubated for 10 to 15 minutes at 37°C before being centrifuged at 3000 rpm to separate the serum. Insulin, the lipid profile, and irisin were measured on serum samples that were frozen at -20°C. Irisin and insulin are measured using an ELISA kit. To separate the sera, fasting venous samples were obtained. The sera will be separated using low-speed centrifugation for 15 minutes. Using spectrophotometric assay kits, enzymatic methods were utilized to measure serum total cholesterol, HDL, and triglycerides.

2.3. Statistical Analysis

Statistical Package of Social Science (SPSS) software was used in data analysis, with version number 22 (SPSS Inc., Chicago, IL, USA). Arithmetic means are used to measure central tendency in simple descriptive analysis, and standard deviations are used to measure the quantitative data dispersion. The qualitative data are expressed as numbers and percentages. The quantitative measures to compare between two independent groups independent t-test was used. For qualitative data, the Chi-square test was used. To determine whether two variables are related, use the Pearson correlation test. A sensitivity and specificity test using the ROC curve to evaluate a new test. - The relationship between categorical dependent and independent variables and the identification of predictors is examined using the logistic regression test. P-values were considered statistically significant if they were less than 0.05.

3. Results

Cases and control groups show no difference (p >0.05) as regards demographic data (age and sex) with the predominance of females in this study. The mean age among cases was (35.6 ±17.6) years versus (35.8 ±15.5) years in controls. Females in cases represent 23 (76.7%) versus 24 (80%) in controls. Family history of vitiligo patients represents 5 (16.7%) in cases and 3 (10%) in control. History of fast food intake represents 25 (83.3%) in cases and 23

(76.7%) in control with no significant difference.

All vitiligo cases show a gradual onset of disease 26 (86.7%) had a progressive course and the mean duration was (7.5 ±8.1) years ranging between (0.5-40) years. Regarding the VIDA score; the mean score was (2.8 ±1.3). VIDA score grading is as follows; lesions were active (≤ 6 weeks) in 12 (20%) of cases, Active (6W-3M) in 8 (13.3%) of cases, Active (3-6 M) in 5 (8.3%) of cases, Active (6-12 M) in 1 (1.7%) of cases and Stable (≥ 1 year) in 4 (6.7%) of cases. For the VASI score, the mean score was (3.5 ±3.4) ranging between 0.5 and 14.25.

Irisin and insulin levels (in both absorbance and concentration forms) show no significant difference between control and vitiligo cases (p >0.05). On the other hand, cholesterol and LDL levels show statistically significant higher levels in vitiligo cases (p <0.001), whereas HDL and triglyceride levels show no difference between vitiligo cases and controls (**Table 1**).

Table 1: Comparisons of Irisin, insulin, and lipid profile levels between vitiligo cases and controls.

Variables	Vitiligo Cases (N=30)		Control (N=30)		*P*-value
	Mean	SD	Mean	SD	
Irisin level					
Absorbance	1.29	0.63	1.23	0.49	0.7
Concentration	11.9	12.8	10.8	12.1	0.7
Insulin level					
Absorbance	0.58	0.36	0.49	0.45	0.4
Concentration	26.4	21.3	24.1	35.9	0.7
Lipid profile					
Cholesterol	279.2	85.9	181.7	36.7	<0.001
LDL	213.4	83.4	112.2	34.9	<0.001
Triglyceride	93.4	49.7	108.4	57.9	0.3
HDL	46.7	5.3	49.03	6.02	0.1

A statistically significant increase in serum level of Irisin was associated with an increase in cholesterol and LDL level but there was no statistically significant correlation with age, VASI and VIDA score, insulin level, triglyceride, and HDL. An increase in serum insulin level (absorbance) was associated with an increase in

triglycerides level, but there was no statistically significant association with any of age, VASI and VIDA score, cholesterol, LDL and HDL **(Table 2).**

Table 2: Correlation between serum Irisin and insulin levels and study variables.

Variables	Irisin level				Insulin level			
	Absorbance		Concentration		Absorbance		Concentration	
	r	*P*-value	r	*P*-value	r	*P*-value	r	*P*-value
Age (years)	0.13	0.3	0.11	0.4	-0.04	0.8	-0.06	0.7
VASI score	-0.20	0.3	-0.19	0.3	0.03	0.9	-0.02	0.9
VIDA score	-0.04	0.8	-0.03	0.9	0.06	0.8	0.08	0.7
Lipid profile								
Cholesterol	0.27	0.03*	0.26	0.04*	0.05	0.7	-0.008	0.9
Triglyceride	-0.05	0.7	-0.07	0.6	0.27	0.04*	0.22	0.09
HDL	-0.09	0.4	-0.19	0.2	0.05	0.7	0.09	0.5
LDL	0.28	0.02*	0.28	0.03*	0.009	0.9	-0.04	0.8
Insulin level								
Absorbance	-0.04	0.7	-0.08	0.5				
Concentration	-0.02	0.8	-0.08	0.5				

A statistically positive correlation was illustrated between age and cholesterol level (r =0.38, p =0.04) with no association between age and other lipid profile tests (triglyceride, HDL, and LDL) (r =0.29, -0.01, and 0.19, $p > 0.05$). On the contrary, there was no significant association between each of the VASI and VIDA scores among vitiligo cases with lipid profiles (r = -0.007, -0.03, 0.03, 0.04, $p > 0.05$), and (r= -0.21, 0.03, 0.14, and -0.21, $p > 0.05$) **(Figure 1).** For Irisin absorbance and concentration shown that the sensitivity of irisin to detect vitiligo cases was 70%, and 60% while specificity was 40%, and 56.7% respectively. On the other hand, insulin absorbance & concentration show that the sensitivity of insulin in the determination of vitiligo cases was 73.3% while specificity was 50 % **(Figure 2).**

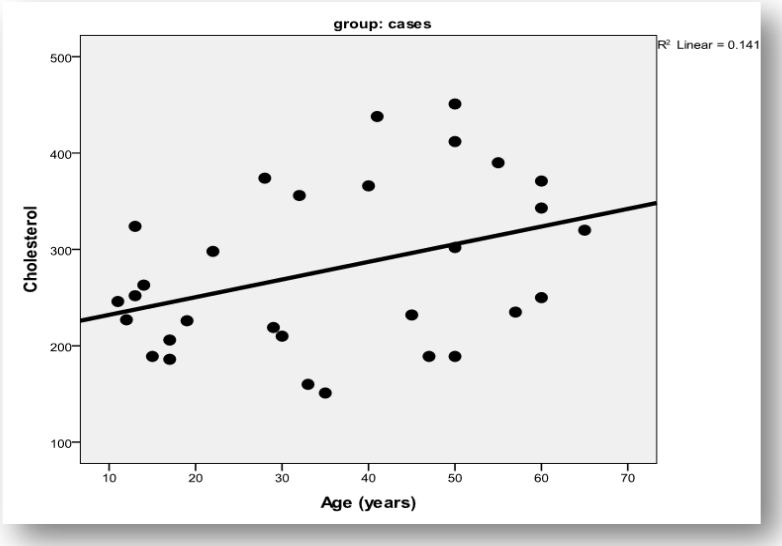

Figure 1: correlation between cholesterol level and age among vitiligo cases

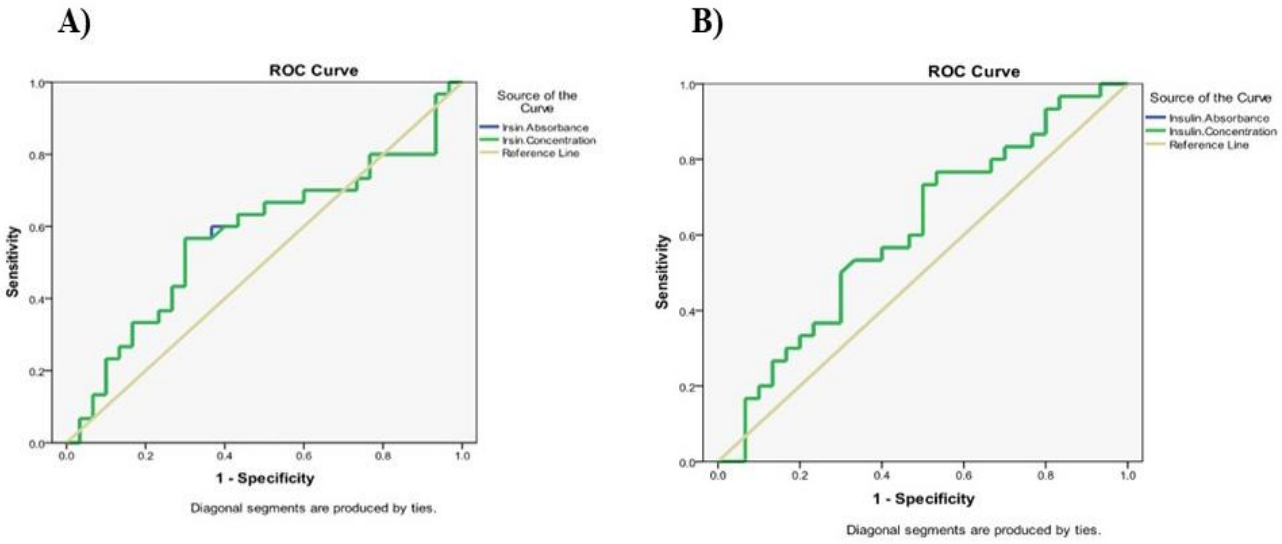

Figure 2: ROC curve for (A) Irisin and (B) Insulin absorbances and concentrations in diagnosis of vitiligo.

According to the logistic regression model in the prediction of vitiligo cases, there was no statistically significant prediction effect to any of (age, sex, Irisin, insulin or lipid profile levels), (p > 0.05) (**Table 3).**

Table 3: Logistic regression analysis to determine the predictors for vitiligo disease.

Variables	B	SE	Sig.	Exp (B)
Constant	3.9	4.6	0.4	53.1
Age	-0.002	0.03	0.9	0.99
Sex	0.27	1	0.8	1.3
Irisin level				
Absorbance	0.41	3	0.9	1.5
Concentration	0.03	0.14	0.8	1.5
Insulin level				
Absorbance	-5.1	4.9	0.3	0.006
Concentration	0.05	0.08	0.5	1.1
Lipid profile				
Cholesterol	-0.003	0.08	0.9	0.99
Triglyceride	0.01	0.02	0.4	1.01
HDL	0.03	0.11	0.8	1.03
LDL	-0.04	0.08	0.6	0.9

4. Discussion

Vitiligo is a common autoimmune disease usually associated with the development of metabolic syndrome, irisin has a role in Insulin resistance and metabolic syndrome improvement [1, 4].

The mean patient's age was (35.6 ±17.6) years and the control group's age was (35.8 ±15.5). The age range in our study was between 11 and 40 years. Women predominate because they are more concerned with their appearance and cosmetic outcomes. Italian research, which supported our findings, revealed that the majority of patients under 40 years of age were female [8].

The current study found that all cases had a gradual onset 86.7% had a progressive course and the mean duration was (7.5 ±8.1). In agreement with our study, an Indian study found that most vitiligo patients have a progressive course [9].

The present study illustrated that family history represents 16.7% of vitiligo cases. A family history of vitiligo is associated with an earlier onset of vitiligo in children. Understanding this link enables more frequent observation, early discovery, and early treatment [10].

Among study cases, the history of fast food intake was 83.3%. Short-term or

long-term negative impacts can result from eating fast food, such as its high fat and cholesterol content. Sugar-filled, high-calorie foods can contribute to obesity. Salt and cholesterol can worsen heart disease, stroke, and blood pressure. Serum excess can exacerbate hypertension [11]. Type II diabetes in addition to cardiovascular disease is an insulin resistance risk factor [12]. Chemicals that damage melanocytes can enter the body through food, medications, contaminated water, or ready-made, preserved food. These factors may play a significant role in the development of vitiligo in a vulnerable host. These elements throw off the body's immunological equilibrium, which leads to the autoimmune breakdown of melanocytes. In childhood vitiligo, malnutrition and excessive use of junk food were highly prevalent. Before the appearance of depigmented lesions in younger age individuals, there was also a substantial correlation between the use of antibiotics and undercurrent infections [13].

In our study, vitiligo cases so no statistically significant difference in both Irisin and insulin levels from controls. It disagreed with a Turkish study that found higher insulin levels in vitiligo patients [14].

According to the current study, vitiligo cases had statistically significantly higher levels of LDL and cholesterol than controls. Furthermore, it demonstrated a positive association and correlation between Irisin and both LDL and cholesterol levels. Nevertheless, there was no association found between irisin and any of age, VASI and VIDA score, insulin level, triglyceride and HDL. There has been debate over the connection between irisin and lipid metabolism. In obese patients, subcutaneous irisin perfusion decreased blood triglycerides, cholesterol, free fatty acids, and glucose [15]. Subsequent in vitro research revealed that irisin inhibits the production of lipogenic markers and fat accumulation generated by palmitic acid (PA) by blocking the protein arginine methyltransferase-3 in mouse primary alpha mouse liver 12 (AML12) cells, and hepatocytes [16]. Additional research has indicated a positive correlation between irisin and lipids dysfunction. Independent of changes in body weight, energy restriction-induced irisin depletion was linked to a decrease in total cholesterol, and both total cholesterol HDL ratio, and LDL cholesterol ratio, in addition to apolipoprotein B [17].

The results of the current study indicate a positive association between

insulin level and triglycerides, but not with age, cholesterol, LDL and HDL, VASI and VIDA scores, or any other important variables. The development of dyslipidemia and the well-known lipid triad: (a) high triglyceride levels in plasma, (b) low levels of HDL levels, and (c) the emergence of small dense LDL may be caused by insulin resistance, which can change systemic lipid metabolism. This trio contributes to atherosclerotic plaque development together with endothelial dysfunction, which is also brought on by abnormal insulin signaling [18].

Ethical approval and consent to participate: The ethical committee in the Faculty of Medicine- Fayoum University approved this study ID: M557 date: 9/1/2022. The researcher obtained written consent from all patients before the procedure and the procedure was explained. All participants had the right not to participate in the study. All data were kept confidential. Each participant received a complete explanation of the nature, risk & objectives of the study. Any unexpected risk that appeared during the research was cleared to the participants. Enough precautions were in place to protect participant privacy and data confidentiality, including assigning a code number to each participant and limiting the research's usage to scientific purposes.

5. Conclusion

From the present study results, the conclusion was: Vitiligo cases show higher levels of cholesterol and LDL which are positively associated with an increase in irisin levels that indicate risk of metabolic syndrome development among vitiligo cases. The current study's findings urge physicians to become more aware of the relationship between vitiligo disease and the development of metabolic syndromes, as well as the disease's clinical consequences and overall burden of comorbidities in patients.

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Conflicts of Interest: All authors declare they have no conflicts of interest.

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