The Egyptian Journal of Hospital Medicine (April 2024) Vol. 95, Page 2310- 2318

Assessment of Serum Adiponectin Level and Insulin Resistance in Premenopausal Females with Hirsutism

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ABSTRACT

Background: The existence of profuse terminal hair in androgen-dependent areas of a women constitutes hirsutism. The association between insulin resistance & hirsutism, especially when accompanied by ovarian or adrenal hyperandrogenism, has been extensively documented. Nevertheless, the adiponectin role, as an indicator of metabolic consequences, in cases with hirsutism has not been conclusive.

Aim: This study aimed to assess serum adiponectin level & insulin resistance in females with idiopathic hirsutism, as well as hirsutism with polycystic ovary syndrome (PCOS), compared to controls.

Patients and methods: This case control investigation included twenty-five cases with hirsutism, & 25 age matched non-hirsute control females. Height, body weight, BMI, modified ferrimangallawy (mFG) scale, serum fasting glucose, & insulin were measured. Homeostasis model assessment of insulin resistance (HOMA-IR) & serum adiponectin were evaluated by enzyme-linked immune-sorbent assay. Serum total testosterone has been measured for females with menstrual irregularities.

Results: Females with hirsutism either with or without PCOS had significantly lower serum adiponectin level compared to controls ($p<0.001$). Serum fasting glucose, HOMA-IR & serum fasting insulin, were significantly greater in cases with hirsutism, especially with polycystic ovary syndrome, than controls ($p<0.001$in all comparisons). HOMA-IR was significantly greater in females with lateral hirsutism, progressive course, high testosterone, acne, menstrual irregularities, with a significant positive association with body mass index and mFG scale ($p<0.001$in all comparisons).

Conclusion: Hirsutism, whether idiopathic or associated with PCOS, is correlated to insulin resistance & low adiponectin level, implying that this metabolic abnormality potentially contributes to the pathogenesis of the illness.

Keyword: Hirsutism, PCOS, Adiponectin, Insulin resistance.

INTRODUCTION

Hirsutism is characterized by the excessive development of terminal hair within females, specifically in areas known to be androgenic dependent on this hormone (e.g., the anterior side of the beard, thighs, chest, mustache, lower abdomen, & lower back) [(1)]. The incidence of hirsutism differs across races & depending on the specific definition of the condition being discussed. The occurrence of hirsutism amongst females of reproductive age ranges from five percent to fifteen percent [(2)]. Fifty percent of females with modest hirsutism & eighty percent of women with moderate hirsutism are afflicted with hyperandrogenism [(3)].

Hyperandrogenism is most frequently attributed to polycystic ovarian syndrome in premenopausal women who also have hirsutism. An uncommon occurrence, other factors contribute to hyperandrogenism in just 0.2 percent of cases [(4)]. When idiopathic, levels of androgen in serum are normal, hirsutism is caused by greater local transformation of testosterone to more powerful forms & heightened skin sensitivity to alpha reductase activity [(5)]. Congenital adrenal hyperplasia, androgen-secreting tumors (adrenal or ovarian), acromegaly, Cushing's syndrome, medication (including danazole, anabolic steroids, metoclopramide, methyldopa, & sodium valproate), are additional factors that can contribute to hirsutism. Ovarian suppression of estrogen production in postmenopausal females leads to a relatively elevated concentration of testosterone, which may contribute to a rise in hair growth [(6)].

Insulin resistance is a pathological state described by a decrease in the body's measurable response to insulin below the expected threshold. Considered the most prevalent cause is obesity. Increased fasting insulin levels serve as an effective insulin resistance screening indicator. An additional advantageous method for evaluating insulin resistance is the computation of the homeostasis model evaluation of insulin resistance [(7)].

The insulin resistance involvement in instances of hirsutism correlated with ovarian or adrenal hyperandrogenism has been extensively documented [(8)]. Insulin resistance accompanied by hyperinsulinemia significantly contributes to the initiation of hyperandrogenism by promoting a rise in the biosynthesis of ovarian androgen hormones [(9)].

Adiponectin is a highly prevalent adipokine that is exclusively found in adipose tissue and is both secreted & expressed within this tissue. Enhanced insulin sensitivity, prevention of vascular inflammation, & anti-atherogenic properties are among its protective effects [(10)]. It has been hypothesized that adiponectin and other hormones secreted by adipose tissue contribute to the PCOS development. PCOS cases have

Received: 21/01/2024
Accepted: 20/03/2024

a decreased level of serum adiponectin as a result of concurrent insulin resistance [11].

Previous research has only examined the association between insulin resistance & adiponectin levels in females with hirsutism who have been diagnosed with PCOS Compared to the healthy control women. The purpose of the investigation was to compare the serum adiponectin & insulin resistance levels of cases with idiopathic hirsutism & hirsutism correlated with PCOS.

PATIENTS & METHODS

This case-control research was performed at Suez Canal University Hospitals' Dermatology Outpatient Clinics in Ismailia, Egypt, between March 2021 and November 2023.

Inclusion criteria: Twenty-five premenopausal female cases aged among 25 to 45 years with idiopathic hirsutism or hirsutism associated with PCOS were enrolled in the study. 25 age-matched control females with regular menstrual cycles, & without hirsutism, nor clinical or laboratory signs of PCOS were also included.

Exclusion criteria: Patients receiving medications causing hirsutism (steroids, oral contraceptive pills, minoxidil, cyclosporine, L-thyroxin, diazoxide, phenytoin, or carbamazepine) or medical treatment for hirsutism for at least 3 months before the investigation, lactating & pregnant women, cases with malignancy, active infections, autoimmune disorders, cardiovascular, renal, hepatic, and endocrinal disorders, patients on dietary regimen for as a minimum 3 months before the study were excepted.

Patients with hirsutism were diagnosed by a trained dermatologist and were subjected to history taking & physical examination including their age, age at disease onset, onset, course, and duration of hirsutism, rate of hair removal, body hair distribution, other signs of hyperandrogenism (acne, seborrhea, female pattern hair loss), virilization symptoms (e.g., increased mass of the muscle, deepening of voice & oligomenorrhea), menstrual history (including menstrual irregularity, menarche, previous oligomenorrhea, dysmenorrhea, & marital status), family history of PCOS or hirsutism. Anthropometric measurements, such as height (centimeters) & weight (kilogram), were performed. To determine an individual's body mass index (BMI), split their weight in kg by the square of their height. The established range for BMI was 18–24.9 kg/m^2. A BMI between twenty-five and 29.9 kg/m^2 was indicative of overweight status for females, whereas a body mass index of more than thirty kilograms per square meter was indicative of obesity.

In order to diagnose Polycystic ovary syndrome , cases were assessed using the Rotterdam criteria [12], which included the following clinical manifestations: Oligomenorrhea (menstruation occurring at least every thirty-five days) or amenorrhea (absence of menstruation for six months or longer), hyperandrogenism (with a total testosterone level exceeding seventy nanograms per deciliter), and polycystic ovaries (with a minimum of twelve follicles measuring between two and nine millimeters in diameter & an ovarian volume exceeding ten milliliters in one ovary).

The pattern of hirsutism was classified clinically as lateral hirsutism (mainly localized on the breast (areolas) & the lateral surface of the neck & face. It indicates that androgens usually have an ovarian origin). Central hirsutism (localized on the chin, neck, parasternal region, upper abdominal region and pubic triangle), which indicates that the androgens have an adrenal origin. Localized hirsutism (localized on the lateral aspect of the face & on the back), which indicates iatrogenic cause. Idiopathic hirsutism was denoted as hirsutism with regular menstrual cycles, and normal total testosterone.

Hirsutism severity was evaluated via modified Ferriman Gallawy (mFG) Score [13]. Nine of eleven body areas (chin, upper lip, lower lip & chest, upper back, upper & lower abdomen, forearm, arm, lower leg, & thigh) were scored. (0) score indicates no terminal hair growth in the examined area, (1) score indicates minimal terminal hair growth, (2) score indicates greater than minimal terminal hair growth but not equivalent to that of an adult man, (3) score indicates terminal hair growth like to a minimally hairy man, and (4) score indicates terminal hair growth like a well well-virilized adult males. Hirsutism was identified by the presence of mFG score ≥ 8. An mFG score of 9 to14 indicates functional hirsutism, and of 15 indicates organic hirsutism. Furthermore, Abraham's classification [14] was used to assess the degree of mFG severity of hirsutism as follows: < 8: Normal, 8 to16: Mild hirsutism, 17 to 25: Moderate hirsutism and ≥ 25: Significant hirsutism.

5 ml of blood samples were obtained from the antecubital vein after overnight fasting period of eight hours, under aseptic precautions. Serum was coagulated at room temperature for ten-twenty min. Samples were centrifuged at the speed of 2000-3000 Revolutions per minute for twenty minutes. Following this, the serum was extracted, promptly analyzed, or frozen at minus twenty degrees Celsius until use. Homeostasis model evaluation of insulin resistance (HOMAIR) [15]. Serum insulin (μIU/ml) multiplied by fasting blood glucose (milligrams per deciliter)/405 was utilized to quantify insulin resistance. A threshold reference value of 2.5 was established, and a value greater than 2.5 was indicative of insulin resistance [16].

Human insulin enzyme-linked immunosorbent assay reagent (Ray Bio, catalog number ELH-Insulin-1, USA) was utilized to quantify serum insulin. Furthermore, the concentration of adiponectin in the serum was determined via a human adiponectin

enzyme-linked immunosorbent assay reagent (Ray Biotech, catalogue no. ELH-Adiponectin-1, USA) in accordance with the protocol provided by the manufacturer.

Ethical considerations: All subjects provided their written informed consents. The Ethics Committee of the faculty of Medicine, Suez Canal University approved the research (approval number 4415). The purpose of this study was to perform research on humans in compliance with the Declaration of Helsinki, the code of ethics of the World Medical Association.

Statistical analysis

The information was analyzed utilizing version 20.0 of the IBM SPSS software program (Armonk, NY: IBM Corp). Qualitative data were described in terms of percentages and numbers. Utilizing the Shapiro-Wilk test, the distribution's normality was confirmed. Utilizing mean, range, median, standard deviation, & interquartile range, quantitative information was described.

To compare two groups based on quantitative variables that followed a normal distribution, the student t-test was utilized. For one-way ANOVA & pairwise comparisons among 2 groups, the Post Hoc Test (Tukey) was employed. The Mann–Whitney test was utilized to analyze non-normally distributed quantitative variables after the Kruskall–Wallis test. For qualitative variables, the chi-square test was applied. The Pearson correlation coefficients were utilized to assess the association among levels of serum adiponectin & insulin resistance. At the five percent significance level, the derived results were deemed significant.

RESULTS

Demographics and clinical data of participating females:

Table (1) illustrated the clinical data of females with hirsutism. 13 (52%) females had lateral hirsutism pattern, while 4 (16%) had a localized pattern and 8 (32%) had a central pattern. Mean of mFG score was 13.48 ± 2.99. 17 (68%) females had mild hirsutism, while 8 (32%) had moderate hirsutism. High total testosterone was detected in 13 (52%) hirsute females, while 12 (48%) had menstrual irregularities, and 13 (52%) were diagnosed with PCOS. Acne was prevalent among 14 (56%) hirsute females, while 4 (16%) had androgenetic alopecia. None of the hirsute females had deepening of voice.

Table (1): Clinical characteristics of cases with hirsutism (n=25)

	No.	**%**
Age of onset (years) Mean ± SD.	18.12 ± 3.38	
Course		
Stationary	13	52.0
Slowly progressive	12	48.0
Duration (years) Mean ± SD.	14.40 ± 5.08	
Pattern of hirsutism		
Localized	4	16.0
Central	8	32.0
Lateral	13	52.0
High total testosterone		
Yes	13	52.0
No	12	48.0
Acne	14	56.0
Androgenic alopecia	4	16.0
Deepening of voice	0	0.0
Menstrual irregularities	12	48.0
PCOS		
Yes	13	52.0
No	12	48.0
Family history of hirsutism		
Positive	15	60.0
Negative	10	40.0
Severity of hirsutism		
Mild	17	68.0
Moderate	8	32.0
Modified Ferriman Gallawy score (mFG score) Mean ± SD.	13.48 ± 2.99	

PCOS: Polycystic ovary syndrome; SD: Standard deviation

The mean age of hirsute females was 32.72 ± 5.21 years, while the mean age of control females was 33.24 ± 5.55 years. Regarding BMI, in hirsute females with a mean of 32.74 ± 4.87 kg/m^2. Two (8%) hirsute females had normal body mass index, 7 (28%) were overweight, & 16 (64%) were obese. In healthy controls, mean of BMI was 31.20 ± 2.56 kg/m^2. 3 (12%) control females had normal body mass index, 10 (40%) were overweight, & 12 (48%) were obese. There was insignificant difference between females with hirsutism and controls as regards age and BMI (Supplementary table 1).

Supplementary Table (1): General characteristics of cases have hirsutism (n=25) & healthy controls (n=25)

	cases with hirsutism (n = 25)	Controls (n = 25)	T	P
Age (years) Mean ± SD.	32.72 ±5.21	33.24 ±5.55	0.341	0.734
Body mass index (BMI) (kg/m^2) Mean ± SD.	32.74 ±4.87	31.20 ± 2.56	1.400	0.170

SD: Standard deviation, t: student t test, p: p value < 0.05 is significant.

Evaluation of insulin resistance: mean of Serum fasting glucose, in cases with hirsutism was 128.80 ± 12.16 mg/dl, while in female controls mean was 81.68 ± 9.03 mg/dl. 13 (52%) hirsute females had impaired fasting glucose (110 – 125 mg/dl) and were considered prediabetic, while 12 (48%) had fasting blood glucose level more than 126 mg/dl and they might have diabetes (the diagnosis of diabetes requires 2 separate serum fasting blood glucose readings ≥126 mg/dl). On the other hand, all control females had serum fasting blood glucose within the normal range. Regarding serum fasting insulin, in hirsute female mean was 8.80 ± 1.87 µIU/ml, while in control females mean was 3.36 ± 1.04 µIU/ml. Serum fasting glucose, and serum fasting insulin were significantly better in hirsute women than in controls (p <0.001 in all comparisons) **(**Table 2).

Table (2): Serum fasting insulin & serum fasting glucose in females with hirsutism (n=25) compared to healthy controls (n=25)

	cases with hirsutism (n = 25)	Controls (n = 25)	T	P
Serum fasting glucose(mg/dl) Mean ± SD.	128.80 ± 12.16	81.68 ± 9.03	15.558*	<0.001*
Serum fasting insulin (µIU/ML) Mean ± SD.	8.08 ± 1.87	3.36 ± 1.04	11.044*	<0.001*

t: Student t test *: Statistically significant at p < 0.05

As for HOMA-IR, in females with hirsutism mean was 2.57 ± 0.65. In hirsute females with PCOS, mean was 3.05 ± 0.39, while in those without PCOS mean was 2.05 ± 0.42. In female controls, mean was 0.68 ± 0.22. Homeostasis model assessment of insulin was significantly higher in hirsute females, both with PCOS & without PCOS, than in healthy controls. Also, it was significantly greater in hirsute females with PCOS than in hirsute females without PCOS (p<0.001 in all comparisons) (Table 3).

Table (3): Comparison among hirsute females with PCOS (n=13) & hirsute females without PCOS (n=12) & healthy controls (n=25) according to HOMA-IR.

HOMA-IR	Hirsute females with PCOS (n= 13)	Hirsute females without PCOS (n= 12)	Controls (n = 25)	F	P
Mean ± SD.	3.05 ± 0.39	2.05 ± 0.42	0.68 ± 0.22	238.201*	<0.001*
Significance	p_1<0.001*, p_2<0.001*, p_3<0.001*				

F: One-way ANOVA test, pairwise comparison between each 2 groups were done using Post Hoc Test (Tukey)
p1: p value for comparing among hirsute females with PCOS and without PCOS p2: p value for comparing among hirsute females with PCOS and controls p3: p value for comparing among hirsute females without PCOS and controls, *: Statistically significant at p < 0.05; SD: Standard deviation; PCOS: Polycystic ovary syndrome.

HOMA-IR was significantly the highest in females with lateral hirsutism, lower in those with central hirsutism and the least in females with localized hirsutism. Additionally, HOMA-IR was significantly higher in females with progressive course of hirsutism, high total testosterone, acne, and menstrual irregularities. Moreover, there was a significant positive association among HOMA-IR of hirsute females and both their BMI, and severity of hirsutism (p<0.001 in all comparisons) (Supplementary tables 2 and 3).

Supplementary table (2): Relation among HOMA-IR & various parameters in females with hirsutism (n = 25).

		N	HOMA-IR		Test of Sig.	P
			Mean	± SD.		
Pattern of hirsutism	Localized	**4**	1.92	0.51	F=	
	Central	**8**	2.12	0.39	18.683*	<0.001*
	Lateral	**13**	3.05	0.39		
High Total testosterone	Yes	**13**	3.05	0.39	t=6.112*	<0.001*
	No	**12**	2.05	0.42		
Acne	Yes	**14**	2.92	0.62	t=3.780*	0.001*
	No	**11**	2.13	0.34		
Androgenetic alopecia	Yes	**4**	2.82	0.54	t=0.841	0.409
	No	**21**	2.53	0.67		
Menstrual irregularities	Yes	**13**	3.07	0.41	t=5.437*	<0.001*
	No	**12**	2.12	0.46		
Family history	Positive	**15**	2.6	0.64	t=0.231	0.819
	Negative	**10**	2.54	0.69		
Course of hirsutism	Stationary	**13**	2.11	0.45	t=5.652*	<0.001*
	Slowly progressive	**12**	3.08	0.4		

t: Student t-test **F**: F for One-way ANOVA test *: Statistically significant at p < 0.05

Supplementary table (3): Correlations among HOMA-IR and different parameters in females with hirsutism (n = 25).

	HOMA-IR	
	R	P
Age	0.148	0.480
Body mass index (BMI)	0.765*	<0.001*
modified Ferriman Gallawy score (mFG score)	0.761*	<0.001*
Age of disease onset	-0.499	0.011

R: Pearson coefficient ***:** Statistically significant at p < 0.05

Serum adiponectin level: mean of Serum adiponectin level, in females with hirsutism was 17.08 ± 3.75 µg/ml. In hirsute females with PCOS, mean was 16.25 ± 4.0 µg/ml, while in hirsute females without PCOS, mean was 17.85 ± 3.48 µg/ml. In female controls, mean was 69.16 ±13.83 µg/ml. Serum adiponectin level was significantly reduced in females with hirsutism, both with PCOS and without PCOS, compared to controls (p<0.001 in all comparisons) (Figure 1).

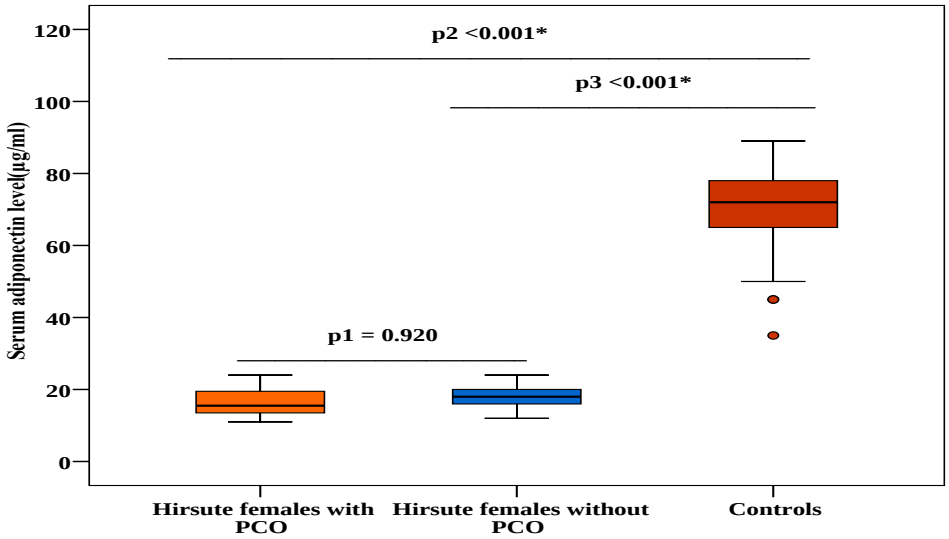

Figure (1): Comparison among hirsute females with PCOS (n=13) & hirsute females without PCOS (n=12) & healthy controls (n=25) regarding serum adiponectin (µg/ml).

There was insignificant difference in serum level of adiponectin between hirsute females having PCOS and those without PCOS **(**Table 4).

Table (4): Comparison between hirsute females with PCO (n=13) and hirsute females without PCO (n=12) & healthy controls (n=25) according to serum adiponectin (µg/ml).

Serum adiponectin (µg/ml)	Hirsute females with PCOS (n= 13)	Hirsute females without PCOS (n= 12)	Controls (n = 25)	F	P
Mean ± SD.	16.25 ± 4.0	17.85 ± 3.48	69.16 ±13.83	162.171*	<0.001*
Significance	p_1=0.920, p_2<0.001*, p_3<0.001*				

Serum level of adiponectin, in females with hirsutism, didn't vary significantly in relation to their ages, serum fasting insulin, BMI, HOMA-IR, serum fasting glucose, age at disease onset, pattern, course, severity of hirsutism, presence of high total testosterone, acne, female pattern hair loss and menstrual irregularities, or positive family history (Tables 5 and 6).

Table (5): Relation among serum adiponectin level (µg/ml) & clinical parameters in females with hirsutism (n=25)

	N	Serum adiponectin (µg/ml)		Test of Sig.	P
		Mean	± SD.		
Pattern of hirsutism					
Localized	**4**	15.75	3.86		
Central	**8**	16.50	4.31	F=0.597	0.559
Lateral	**13**	17.85	3.48		
High total testosterone					
Yes	**13**	17.85	3.48	t=1.066	0.298
No	**12**	16.25	4.0		
Acne					
Yes	**14**	17.57	3.50	t=0.732	0.472
No	**11**	16.45	4.13		
Androgenetic alopecia					
Yes	**4**	18.0	3.56	t=0.527	0.603
No	**21**	16.90	3.85		
Menstrual irregularities					
Yes	**13**	17.67	3.58	t=0.744	0.464
No	**12**	16.54	3.97		
Family history					
Positive	**15**	17.33	3.52	t=0.406	0.688
Negative	**10**	16.70	4.24		
Course of hirsutism			4.27		
Stationary	**13**	16.77	3.26	t=0.424	0.676
Slowly progressive	**12**	17.42			

t: Student t-test **F**: F for One-way ANOVA test ***:** Statistically significant at $p < 0.05$

Table (6): Correlations between serum adiponectin level (µg/ml) and different parameters in females with hirsutism (n = 25)

	Serum adiponectin (µg/ml)	
	R	P
Age	–0.212	0.309
Body mass index	0.171	0.415
Serum fasting glucose	0.394	0.051
Serum fasting insulin	0.154	0.464
HOMA-IR	0.301	0.144
Modified Ferriman Gallawy score	0.231	0.267
Age of disease onset	-0.421	0.036

R: Pearson coefficient *****: Statistically significant at $p < 0.05$

DISCUSSION

Numerous researches have focused on the probable inclusion of insulin resistance in the pathogenesis of hirsutism either due to PCOS or idiopathic hirsutism [17]. Adiponectin is an adipocyte-derived collagen-like protein. It plays a variety of roles such as insulin-sensitization, anti-inflammatory, anti-atherosclerosis, lipid metabolism regulation, and cardiovascular protection [18]. This is the first study, to our knowledge, to compare serum adiponectin level in females with hirsutism either due to PCOS or idiopathic hirsutism to healthy controls.

The study revealed that serum fasting glucose and serum fasting insulin were significantly greater in females with hirsutism compared to controls. HOMA-IR was significantly higher among females with hirsutism, both with PCOS and without PCOS, compared to healthy controls. In addition, it was significantly greater in hirsute females with PCOS than in hirsute females without PCOS. It is well-established that abnormalities in carbohydrate metabolism are associated with excessive androgen diseases, specifically PCOS. Hyperinsulinism & insulin resistance are correlated with PCOS, which can lead to increased ovarian androgen production due to dysregulation of cytochrome P450c17α enzyme activity. Furthermore, although insulin does not exhibit a direct impact on hair follicle growth stimulation, it may potentially influence hair follicles by increasing the expression of IGF-1, which in turn promotes the proliferation of hair follicle cells [19].

This fact can explain the high HOMA-IR in patients with idiopathic hirsutism. In accord with our findings, **Bakry *et al.*** [20] stated that both female groups with idiopathic hirsutism and hirsutism with PCOS showed significantly higher fasting serum insulin compared with healthy controls. However, there wasn't significant distinction among patients & controls regarding fasting blood sugar. HOMA-IR was significantly greater in both hirsute female groups compared to controls & was significantly better in hirsute cases with PCOS compared to cases with idiopathic hirsutism.

Likewise, **Sheikholeslami *et al.*** [21] demonstrated that serum level of insulin & HOMA-IR were significantly greater in hirsute PCOS female patients compared to females with idiopathic hirsutism.

Tehrani *et al.* [22] discovered that there was statistically significant variation in fasting glucose level of females with idiopathic hirsutism compared with controls. Furthermore, **Ucak *et al.*** [23] and **Talaei *et al.*** [24] revealed that serum fasting insulin level & HOMA-IR were significantly greater in females with idiopathic hirsutism compared to healthy controls.

In addition, the current research results showed that homeostasis model assessment of insulin resistance in females with hirsutism wasn't influenced by their ages or age of disease onset. On the other hand, there were significant positive associations among HOMA-IR of hirsute females & both their BMI & severity of hirsutism. Moreover, HOMA-IR among females with hirsutism, varied significantly in relation to pattern and course of hirsutism, presence of high total testosterone, acne and menstrual irregularities. Nevertheless, it didn't vary significantly in relation to androgenetic alopecia and family history of hirsutism. In accordance with our findings, **Bonakdaran *et al.*** [25] and **Cebeci *et al.*** [26] informed that insulin level & insulin resistance was significantly associated with BMI.

Bakry *et al.* [20] & **Ucak *et al.*** [23] reported that HOMA-IR & fasting insulin levels were significantly correlated with hirsutism. **Majid *et al.*** [27] documented a greater frequency of insulin resistance in females with PCOS suffering from menstrual irregularity and hyperandrogenism. On the other hand, **Fattah and Darwish**[28] reported that the correlation between the insulin resistance measurements of the various groups and their BMI revealed statistically non-significant associations.

Also, **Bonakdaran *et al.*** [25] found no significant association amongst both insulin level & insulin resistances with hirsutism severity.

Regarding serum adiponectin level, the present investigation revealed that it was significantly lower in cases with hirsutism both with PCOS & without PCOS than in healthy controls. In contrast, an insignificant variation was observed in serum adiponectin level among hirsute women having PCOS & those with idiopathic hirsutism. Adiponectin acts as an insulin sensitizing factor. High level of adiponectin was stated to be independently correlated with increased insulin sensitivity [29].

Low adiponectin level was discovered to be related with conditions for instance insulin resistance, obesity, type2 diabetes mellitus, metabolic syndrome, & cardiovascular disease [29].

Low levels were also correlated with PCOS and is primarily attributed to either obesity or insulin resistance within these cases. The precise function of adiponectin in these metabolic disorders remains unclear. It might function as a marker of insulin resistance or be regulated by insulin; in which case it might play a causal role. [30].

Adiponectin may also have a direct effect on hair follicles. Prior research indicates that human hair follicles have adiponectin receptors. Treatment with adiponectin promoted hair growth and shaft elongation in micro-dissected human hair follicles ex vivo, partially by upregulating insulin-like growth factor one, vascular endothelial growth factor, & hepatocyte growth factor in dermal papilla cells. Thus, the low level of adiponectin in females with idiopathic hirsutism may be one of the compensatory attempts of adipose tissue to suppress growth of hair follicles. However, this low level is not sufficient to reverse the pathogenic consequences.

In accordance with our results, **Niafar and Nader** [31] discovered that serum adiponectin level was

lower in cases with PCOS with both metabolic syndrome and insulin resistance. The authors concluded that adiponectin could be utilized as a biomarker to recognize cases with PCOS at a greater risk of diabetes, insulin resistance, & cardiovascular diseases.

Similarly, **Mirza *et al.*** [32] concluded that serum adiponectin level was independently related to PCOS & was only partly described by insulin resistance. The correlation between PCOS & low adiponectin level persisted stable & statistically significant even following accounting for a body mass index.

This study also showed that serum level of adiponectin in females with hirsutism wasn't influenced by their ages, BMI, serum fasting glucose, serum fasting insulin, homeostasis model evaluation of insulin resistance, age of disease onset and severity of hirsutism or high total testosterone. In the same manner, **Amer *et al.*** [30] reported no significant association among serum level of adiponectin and patient age or fasting insulin.

Also, **Erkan *et al.*** [19] reported that no association was detected among resisting, another adipokine, HOMA-IR, fasting insulin & BMI in cases with idiopathic hirsutism, hirsute cases with PCOS, and healthy controls. In contrast with our results, **Yildiz *et al.*** [33] observed statistically significant inverse correlations among serum adiponectin level & BMI, HOMA-IR, fasting glucose level, insulin level, & prolactin level. Moreover, **Chin *et al.*** [34] concluded that adiponectin was negatively associated with BMI, insulin resistance, & total testosterone.

CONCLUSION

Hirsutism, whether idiopathic or associated with PCOS, is linked to insulin resistance, & low adiponectin serum level. Thus, insulin resistance and impaired adiponectin secretion may have a vital role in the pathogenesis of hirsutism.

DECLARATIONS

- **Funding:** No fund
- **Availability of data and material:** Available
- **Conflicts of interest:** No conflicts of interest.
- **Competing interests:** None,

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