Study on Gender Differences in Acne Vulgaris Associated with Insulin Resistance:A Cross-Sectional Study

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Abstract

Objective The present study investigated the clinical characteristics and gender differences of acne vulgaris associated with insulin resistance (IR).

Methods The present study was conducted in 100 patients, comprising 52 males and 48 females, having acne vulgaris. Of the total, 18 male patients and 9 female patients exhibited IR, whereas 34 male patients and 39 female patients exhibited non-IR (NIR). The height, weight, acne grade, sex hormone, lipid metabolism, plasma glucose, and insulin levels of all the patients were measured and statistically analyzed.

Results In the male group, the body mass index of the group with IR was significantly higher than that of the group with NIR ($P < 0.05$). No significant difference was observed in the sex hormones and insulin-like growth factor-1 (IGF-1) between female patients having acne associated with IR and those having acne associated with NIR. Levels of testosterone and sex hormone-binding globulin in male patients having acne associated with IR were lower than those in patients having acne associated with NIR, whereas the estrogen and IGF-1 levels in male patients with acne in the IR group were higher than those in the NIR group. Significant differences were observed in the fasting plasma glucose and fasting and 2-h postprandial plasma insulin levels between male and female groups ($P < 0.05$).

Conclusion Disorders of sex hormone in male patients with acne vulgaris are related to IR; however, this correlation is not significant in women. Levels of sex hormones and metabolism in male patients having acne associated with IR must be actively monitored, and appropriate intervention must be administered.

Introduction

Acne is a chronic inflammatory skin disease that often occurs during adolescence. Its clinical manifestations include acne, papules, nodules, cysts, and even scars. More than 95% of people exhibit varying degrees of acne. The prevalence rate in people aged 20–30 years is approximately 64%, with 3%–7% of people having a disfiguring scar, which affects the physical and mental health of patients [1]. Acne vulgaris is regarded as a common and frequently-occurring disease. It seriously affects the facial appearance of most young people that deserves continuous attention and research by dermatologists.

Although the pathogenesis of acne is poorly understood, it is known to be related to excessive sebaceous gland secretion, abnormal keratinization of the sebaceous ducts of the hair follicle, proliferation of hair follicle microorganisms, such as *Propionibacterium acne*, inflammation, and immune response [2]. Studies have demonstrated acne is one of the metabolic skin diseases highly associated with insulin resistance (IR). High insulin and abnormal IGF-1 levels may also be related to acne [2].Hyperinsulinemia induces acne by increasing IGF-1 and reducing insulin-like growth factor binding protein-3 levels. That can increase the average facial sebum excretion rate, serum dihydrotestosterone and dehydroepiandrosterone sulfate levels, and stimulate the proliferation of sebocytes. Hyperinsulinemia will also increase the levels of epidermal growth factor and transforming growth factor beta to increase the level of non-esterified fatty acids in the plasma, leading to inflammation and acne. Women with polycystic ovary syndrome (PCOS) often have hyperandrogenemia and IR, which may be associated with facial acne. Although numerous studies on acne have been conducted, only a few studies have focused on investigating the prevalence of acne in men with IR.

Thus, in the present study, we excluded patients with PCOS and studied changes in the hormone and metabolic levels in male and female patients to explore the acne etiology across male and female genders and to propose a targeted monitoring and treatment strategy.

Materials And Methods

1. Source of data

The present cross-sectional study was conducted in 100 patients with acne vulgaris who visited the dermatology clinic of the Affiliated Hospital of Southwest Medical University from May 2019 to November 2019. This study was approved by the institutional ethics committee (ethics batch number: KY2019040), and all the patients signed informed consent forms.

2. Inclusion and exclusion criteria

Patients in the age group of 15–35 years who willingly participated in the study, fulfilled the diagnostic criteria of acne vulgaris according to the “Chinese Clinical Dermatology” [3], and understood the content of the informed consent were included in the study.

Patients with other skin diseases; smokers; pregnant and lactating patients; and those having other types of acne such as occupational and aggregative acne were excluded from the study. Additionally, patients with liver and kidney relating disease, or malignant tumors; those with endocrine diseases such as diabetes and thyroid diseases; patients with PCOS, acanthosis nigricans, menstrual disorders, adrenal hyperplasia, and mental diseases; and those on drugs such as hormones, oral contraceptive, diuretics, and isotretinoin, which affect insulin metabolism and sex hormone levels, within the preceding 3 months were excluded from the study.

3. The scale used in the study

A general data sheet of sex, age (in years), height (in meters), weight (in kg), body mass index (BMI) (kg/m^2), and course of disease (in years) was maintained.

Global acne grading system score table

The common acne sites were divided into six regions, namely forehead, right cheek, left cheek, nose, chin region, chest, and upper back. A score of 0 indicated no skin lesions, 1 indicated ≥ 1 acne, 2 indicated ≥ 2 acne, 3 indicated ≥ 3 acne, and 4 indicated the most severe score with multiple skin lesions. The total score of a region was calculated by multiplying the factor score (see Table 1) with the lesion score. Acne was graded as mild (1–18), moderate (19–30), severe (31–38), and extra severe (≥39) according to the total score of different regions.

Table 1 Global acne grading system score scale for patients with acne vulgaris

Region	Factor score	Lesion score	Region score
Forehead	2		
Right cheek	2		
Left cheek	2		
Nose	1		
Chin region	2		
Chest and upper back	3		
Total score of GAGS			

4. Methods

4.1 Grouping

The patients were divided on the basis of sex into male and female groups. The patients in these groups were further divided into IR and non-IR (NIR) groups based on the presence of IR.

4.2 Observation indicators

Fasting venous blood was collected at 8:00 a.m., and serum dihydrotestosterone (DHT), sex hormone-binding globulin (SHBG), and IGF-1 were detected using enzyme-linked immunosorbent assay. Fasting insulin (FINS), 2-h postprandial plasma insulin, testosterone (T), estradiol (E2), progesterone (P), luteinizing hormone (LH), follicle stimulating hormone (FSH), pituitary prolactin (PRL), and cortisol were measured using radioimmunoassay. Fasting plasma glucose(FPG), 2-h postprandial plasma glucose, and blood lipids (cholesterol, triglyceride, low density lipoprotein [LDL], high density lipoprotein [HDL]) were detected using an automatic blood biochemical analyzer. The homeostatic model assessment for IR (HOMA-IR) was applied for the quantitative estimation of IR: FPG level (FPG, mmol/L) × FINS level (FINS, μU/mL)/22.5. A HOMA-IR value of ≥ 2.5 was regarded as IR [4].

4.3 Statistical analysis

The clinical characteristics and laboratory index data of patients having acne associated with IR or NIR were collected using a cross-sectional study, and differences between the two groups of patients were compared using SPSS 20.0 statistical software. The quantitative data in accordance with the normality distribution were described by ± s, and independent sample t-tests were used for the comparison between the two groups. Similarly, the data that did not accord with the normality distribution were described as median. The Mann–Whitney rank sum test (Mann–Whitney U test) was used for comparison between the two groups. The categorical variables were described as percentage, and the comparison of these variable between the two groups was performed using chi-square test. A *P* value of <0.05 was considered statistically significant in all the tests.

Results

1. Comparison of baseline data between male and female patients having acne associated with IR or NIR

In the male group, the BMI of the IR group was found to be higher than that of the NIR group, and the difference was found to be statistically significant (*P* < 0.05); however, no significant difference was observed in the age, course of disease, and global acne grading system (GAGS) score. In the female group, no significant difference was observed in the age, course of disease, BMI, and GAGS score between the two groups (Table 2).

Table 2 Comparison of baseline data of patients having acne associated with IR or NIR as a function of gender

	Male				Female			
	IR group	NIR group	t or Z	*P*	IR group	NIR group	t or Z	*P*
Number	18	34			9	39		
Age（y）	19.00	18.00	-0.058	0.958	22.00	24.00	-1.378	0.173
Disease course（y）	3.00	4.00	-0.107	0.919	3.00	3.00	-0.466	0.659
BMI（kg/m^2）	23.09	19.35	-3.106	0.001	20.03	18.50	-1.308	0.199
GAGS	28.67±8.35	26.56± 8.51	-0.855	0.396	22.00	23.00	-0.622	0.550

Abbreviations: BMI, body mass index; GAGS, Global acne grading system.

2. The constituent ratio of severity of acne in male and female patients

No significant difference was observed in the constituent ratio of severity between male and female patients with IR or NIR (*P* > 0.05) (Table 3).

Table 3 Constituent ratio of severity of acne in male and female patients

		n	Mild	Moderate	Severe	Extra severe	c²	*P*
Male	IR group,%	18	5.6	55.6	22.2	16.7	2.105	0.543
	NIR group,%	34	17.6	47.1	26.5	8.8		
Female	IR group,%	9	33.3	55.6	11.1	0	0.875	1.000
	NIR group,%	39	25.6	56.4	15.4	2.6		

3. Comparison of glucose metabolism, lipid metabolism, and hormone levels between male and female groups with IR or NIR

No significant difference was observed in the hormone and IGF-1 levels between female patients with acne in the IR and NIR groups. The testosterone and SHBG levels in male patients with acne in the IR group were lower than those in the NIR group. Similarly, the E2 and IGF-1 levels in male patients with acne in the IR group were higher than those in the NIR group. Significant differences were observed in FPG and fasting and 2-h postprandial plasma insulin levels between the male and female groups (*P* < 0.05) (Table 4).

Table 4 Comparison of glucose metabolism, lipid metabolism and hormone levels in male and female groups with IR or NIR

		Male				Female			
		IR	NIR	t or Z	*P*	IR	NIR	t or Z	*P*
Glucose (mmol/L)	FPG	5.29±0.25	4.94±0.27	-4.574	0.000	5.24±0.35	4.89±0.25	-3.491	0.001
	2-h postprandial	5.41	5.05	-1.539	0.124	5.47±0.39	5.05±0.80	-1.522	0.135
Insulin (μU/mL)	FINS	13.06	6.13	-5.886	0.000	14.44±2.71	7.72±1.90	-8.809	0.000
	2-h postprandial	33.92	23.94	-2.212	0.027	29.96	19.51	-2.523	0.010
IGF-1 (pg/mL)		107.89	59.88	-3.136	0.002	144.89	60.25	-1.824	0.068
Lipid metabolism (mmol/L)	Cholesterol	3.89	3.62	-1.318	0.188	3.91±0.60	4.00±0.57	0.402	0.690
	Triglyceride	1.28	0.87	-3.338	0.001	0.73	0.81	-0.238	0.815
	LDL	2.43±0.92	2.14±0.51	-1.259	0.221	1.82	2.17	-0.964	0.348
	HDL	1.21	1.25	-1.078	0.281	1.50	1.55	-0.912	0.375
Hormone levels	SHBG (nmol/L)	10.12±6.34	16.42±10.54	2.317	0.025	12.05	11.54	-0.740	0.466
	DHT (nmol/L)	51.78	44.63	-1.577	0.115	55.80	47.05	-0.700	0.499
	T (ng/dL)	553.45±131.61	640.17±152.26	2.044	0.046	36.14	44.82	-1.149	0.261
	E_2 (pg/mL)	41.99±9.50	35.65±10.47	-2.142	0.037	38.11	41.57	-0.436	0.678
	P (ng/mL)	0.60	0.66	-0.231	0.817	0.38	0.64	-1.163	0.250
	LH (mIU/mL)	3.33	3.35	-0.154	0.878	3.89	4.69	-0.859	0.404
	FSH (mIU/mL)	4.23	4.14	-0.433	0.665	7.87±1.75	8.15±2.11	0.367	0.715
	PRL (ng/mL)	10.73	10.50	-0.029	0.977	12.63	15.49	-1.043	0.309
	Cortisol (μg/dL)	16.06	14.83	-0.750	0.453	13.44±4.40	14.08±4.42	0.391	0.697

Abbreviations: FPG, Fasting plasma glucose; FINS, fasting insulin level; IGF-1, insulin-like growth factor-1; LDL, density lipoprotein; HDL, high density lipoprotein; SHBG, sex hormone-binding globulin; DHT, dihydrotestosterone; T, testosterone; E2, estradiol; P, progesterone; LH, luteinizing hormone; FSH, follicle stimulating hormone; PRL, pituitary prolactin.

Discussion

In the present study, significant differences were observed in the BMI, blood lipid, insulin, and IGF-1 between male patients with acne vulgaris in the IR and NIR groups. Studies have suggested obesity and abnormal lipid metabolism as high risk factors for IR [5]. IR results in increase in insulin and IGF-1 levels and is a crucial factor in the development of acne that promotes the synthesis of androgen in the adrenal gland and gonads. It induces acne formation by stimulating the proliferation of epidermis, dermis, and sebaceous glands [6].

The effect of hormone levels on IR between male and female patients with acne vulgaris was found to vary in the present study. In male patients, the testosterone and SHBG levels in the IR group were lower than those in the NIR group, whereas the E2 level was higher in the IR group than in the NIR group. This finding is concurrent with that of a study by Vikan et.al. conducted in men with type 2 diabetes (T2D) [7], which reported that the risk of T2D is high in men with high levels of estrogen and low levels of total testosterone and SHBG.

Several cross-sectional and longitudinal studies have reported that the total T level in men is negatively correlated with the incidence of T2D [8,9], suggesting that T may play a protective role in the pathogenesis of T2D. Although the current epidemiological evidence is insufficient, some studies have reported a negative correlation between SHBG and T2D risk in men [10,11]. On the other hand, some

studies have demonstrated no association between these parameters [12,13]. The molecular mechanism of T involved in IR is still unclear. However, some studies have exhibited that T can control the expression of key regulatory enzymes involved in glucose and lipid metabolism in major insulin responsive target tissues such as liver, adipose tissue, and skeletal muscle, thereby regulating IR [14,15]. Low T levels may promote IR by impairing the mitochondrial function [16], and IR leads to an increase in insulin and IGF-1 levels, which promotes the occurrence of acne. Thus, factors such as the imbalance between E2 and androgen, sex hormone disorders, and IR can induce or aggravate acne.

The situation is completely different in female patients. Studies on patients with PCOS have found that the T levels in these patients with IR are significantly higher than in those with NIR [17], and hyperandrogenemia is a vital factor for the pathogenesis of PCOS [18]. The free and total T levels in elderly women were positively correlated with the incidence of IR and T2D. E2 seems to play a protective role in female patients with IR because it can improve insulin sensitivity at the muscle level [21], promote fatty acid metabolism, and stimulate the pancreatic β-cell function [22]. The insulin level is correlated to androgen secretion by the ovary, which is highly sensitive to insulin. The chronic stimulation of ovary by insulin determines the amount of androgen secretion [24]. In the female patients in our study, the E2 level in the IR group was found to be lower than that in the NIR group; however, the difference was not statistically significant. This may be due to the small sample size of the female patients having acne associated with IR. The consistency in the relationship between hormone levels and IR in female patients without PCOS and that in male patients or in patients with PCOS must be verified through further studies with a larger sample size. Based on our findings, we infer that the pathogenesis of acne varies across the male and female gender.

Conclusion

The present study observed differences in the effect of hormone levels on IR in male and female patients with acne. This is the first clinical gender analysis of patients having acne associated with IR. The relationship between male sex hormones and IR is consistent with that of male T2D patients. An increase in androgen can not only cause acne but also cause IR by decreasing the T levels. Therefore, only the increase or decrease in a hormone index should not be evaluated for male patients having acne associated with IR. Further monitoring of sex hormone levels and metabolism in addition to appropriate intervention is essential.

Declarations

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Conflicts of interest:Wen-Yao Mi, Xia Feng, Zheng-Qun Wang, Xin Ye, Hui-Ling Shu, Bei Yu, Chang-Qiang Li have no conflicts of interest to declare.

Ethics approval:This study was approval by the Ethics committee of Affiliated Hospital of Southwest Medical University, and all participates provided written informed consent.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Not applicable

Availability of data and material The datasets generated during and/or analyzed during the current

study is available from the corresponding author or reasonable request.

Code availability SPSS 20.0

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Hui-Ling Shu, Xia Feng, Bei Yu, Zheng-Qun Wang, Wen-Yao Mi,Ye Xin, and Chang-Qiang Li. The first draft of the manuscript was written by Wen-Yao Mi and Xia Feng, Wen-Yao Mi and Xia Feng contributed equally to the paper, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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