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Association of Acne with Metabolic Syndrome and Insulin Resistance in Young Men

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Abstract
Objective: To study the association of acne with metabolic syndrome and insulin resistance in young men. **Study Design:** A Cross-sectional study. **Place and Duration of Study:** Department of Dermatology Services Hospital, Lahore. From January 5, 2016 to January 5, 2018. **Methodology:** A total of 158 patients were selected for study. Age, weight, height, waist, systolic and diastolic blood pressures, serum HDL-C levels, serum triglycerides, fasting blood glucose, fasting plasma insulin, and HOMA-IR score were documented in each patient. Student t-test was applied to compare these variables between cases and controls; and ANOVA test was applied to compare among the acne severity groups. Patients having metabolic syndrome and insulin resistance were compared by applying chi-square test. The data was analyzed by using SPSS v.23 software, considering $p \leq 0.05$ statistically significant. **Results:** Mean systolic and diastolic blood pressures, fasting blood glucose and HOMA-IR score of the cases were significantly high when compared with controls (p-value .015, .002, .022 and .040, respectively). The frequency of metabolic syndrome was 26.58% in the cases and 8.86% of the controls ($p=0.004$); and of Insulin resistance was 27.85% in cases, while 11.39% in controls ($p=0.008$). The differences were statistically significant. The difference of systolic and diastolic blood pressures was statistically different in four acne severity groups (p-value .024 and .015, respectively), with systolic blood pressure being the lowest and diastolic blood pressure being the highest in mild acne group. **Conclusion:** The observations of our study concluded that post-pubertal males with acne are at higher risk of developing metabolic syndrome and insulin resistance when compared with the normal population.
Keywords: Acne, Metabolic syndrome, Insulin Resistance, Blood pressure

Introduction

Acne is an illness of pilosebaceous units [1]. Adolescents are the part of population that are most affected by this disorder [2]. Size of sebaceous gland, increased production of sebum and keratinocyte proliferation are stimulated by the androgens [3], this in turn leads to increased incidence of acne after puberty. Hyperinsulinemia occurs due to development of physiologic resistance to insulin, during puberty [4], in turn increasing the synthesis of androgens. Acne formation is augmented by both these events. Hyperinsulinemia results in raised levels of insulin like growth factor1 (IGF-1); and thus decreasing the levels of insulin-like growth factor-binding protein level in the serum. The consequences of increased insulin like growth factor1 (IGF-1) levels are raised serum dihydrotestosterone and dehydroepiandrosterone sulfate, deceased production of sex hormone-binding proteins by the liver, increased sebocyte proliferation and increased rate of facial sebum excretion. Levels of transforming growth factor and epidermal growth factor are also increased in hyperinsulinemia, in turn elevation of non-esterified fatty acids component of plasma, thereby triggering inflammation and acne. A critical role is played by insulin resistance in many metabolic aberrations that are constituents of the metabolic syndrome.

Acne is associated with polycystic ovarian syndrome (PCOS) [5, 6, 7], in women, is a disorder linked with hyperinsulinemia, insulin resistance and hyperandrogenism [6]; and this supports the concept of role of insulin in the progression of acne. The treatment options which decrease the insulin secretion and/or improve the sensitivity of insulin, for example metformin or acarbose [8], have also shown to decrease serum androgens level, gonadotropins and to improve hirsutism, acne, fertility, menstrual cycle and ovulation. Women, who don't have explicit polycystic ovarian syndrome but have post-pubertal acne, often sustain raised serum concentration of insulin like growth factor1 (IGF-1); and are somewhat insulin resistant as well. In adult women, the acne lesion numbers have been analogous to the insulin like growth factor1 (IGF-1) levels [9] and significantly higher levels insulin like growth factor1 (IGF-1) were demonstrated in such women as compared to the controls.

Acne occurrence matches more with the fluctuations in the insulin and insulin like growth factor1 (IGF-1) levels than it matches with the change of plasma androgen levels. This is for the reason that the insulin-like growth factor-1 (IGF-1) and insulin levels become highest during adolescence [10] and gradually fall during the third decade of life. Insulin resistance might continue, in post-pubertal patients with acne. Hence, insulin resistance might have part in the progress of post-pubertal acne.

The relationship of acne with metabolic syndrome and insulin resistance has been studied poorly, in the past. Current study is intended to study the frequency of metabolic syndromes and insulin resistance in the young male individuals who present with acne. We aim to study the effects of these events over the metabolic profile of the patients.

Material n methodology

This is a cross-sectional study and the relevant data was collected in Department of Dermatology Services Hospital, Lahore, over a time period from January 5, 2016 to January 5, 2018. The consent was taken from the hospital ethical committee. Sample size was calculated using the study by Nagpal M. et al. [11] as reference. Non-probability consecutive sampling technique was used to select seventy nine cases i.e. male patients diagnosed of acne and an equal number of age-matched controls.

Informed consent was taken from all the subjects enrolled in the study on written forms. Clinical examination was performed after taking comprehensive history. Weight, height, waist circumference, blood pressure were measured and defining the severity of acne according to the Global Acne Grading System was completed. The measuring tape was placed tightly round the belly at the level of iliac crests and waist circumference was noted. Mercury sphygmomanometer was used to measure blood pressure level, in sitting position. Modified National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII) was applied to diagnose metabolic syndrome; which includes minimum three of the subsequent criteria: central obesity (waist circumference ≥ 102cm; modified for Asian men > 90cm) ; dyslipidemia (serum triglyceride level ≥ 150mg/dl) or medical treatment for elevated levels; dyslipidemia (serum HDL-C levels < 40mg/dl) or medical treatment for altered levels; blood pressure of 135/85 mmHg or medical treatment for hypertension; and fasting blood glucose levels of ≥ 100mg/dl or medical treatment for diabetes mellitus. An electrochemiluminescence immunoassay was used to assess the fasting plasma insulin levels. Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) score was calculated by the application of subsequent principle: Fasting Plasma Insulin (µIU/ml) × Fasting Blood Glucose (µg/dl)/405. Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) score of more than 2.5 was considered as insulin resistance. All the subjects who had history of hepatic disorders, malignancies, thyroid dysfunctions, acromegaly, Cushing syndrome and smoking; and those who were recently treated with isotretinoin, were excluded from our study, owing to the ability of these factors to alter insulin and insulin like growth factor levels and status of insulin resistance.

Age, weight, height, waist, systolic and diastolic blood pressures, serum high density lipoprotein-cholesterol, serum triglycerides level, fasting blood glucose, fasting plasma insulin, and Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) score were documented in each patient. Student t-test was applied to compare these variables between cases and controls; and ANOVA test was applied to compare these parameters among the cases according to the severity of the acne. Patients having Insulin resistance as per HOMA-IR score >2.5 and metabolic syndrome as per National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) were counted in both groups and the data was analyzed by applying chi-square test. All the data was collected by the researcher himself, on a preformed Performa. SPSS v.23 software was used to analyze the data. P ≤0.05 was taken as statistically significant.

Results

A total of 158 male patients were involved in the study. Seventy nine patients with acne were selected and equal number of age matched controls were selected. The mean age, weight, height and waist circumference of the cases were 22.91±2.93years, 65.34±8.17Kg, 160.87±4.28cm and 87.44±6.46cm; and of controls were 22.54±3.05years, 62.00±6.91Kg, 160.87±4.71cm, and 85.39±5.76cm, respectively (p-value 0.442, 0.006, 0.778 and 0.037, respectively). The mean systolic and diastolic blood pressures of the cases were 129.65±9.13mmHg and 78.01±7.27mmHg, and were significantly high when compared with controls i.e. 119.57±8.29mmHg and 71.49±6.39mmHg, respectively (p<0.001 for both). The mean fasting blood glucose level and HOMA-IR score of the cases were 90.33±5.44mg/dl and 2.32±1.14, and were significantly higher than they were of controls i.e. 80.34±7.03mg/dl and 1.74±0.93, respectively (p <0.001 and 0.001, respectively). The mean serum triglyceride level of the cases (94.00±40.39mg/dl) was significantly lower (p=0.019) than that of controls (108.14±34.08mg/dl). Both the groups were comparable in terms of serum HDL cholesterol levels and fasting plasma insulin concentrations (47.07±8.52mg/dl and 9.56±4.83 µIU/ml in the cases; and 44.86±8.17mg/dl and 8.33±3.07 µIU/ml in controls, p-value 0.097 and 0.059, respectively. The percentage of metabolic syndrome was 26.58% in the cases and 8.86% of the controls and the difference was statistically significant (p=0.004). Insulin resistance, defined as HOMA-IR score of more than 2.5, was noticed in 27.85% of the cases and 11.39% of the controls and the difference was also statistically significant (p=0.008). (Table-I)

The differences of mean age and weight were significantly different in four different groups of acne severity, in mild acne being the lowest and in very severe acne being the highest (p-value .017 and <.001, respectively). The mean height and waist circumference was not statistically different (p-value .308 and .893, respectively). The difference of systolic and diastolic blood pressure was statistically different in four acne severity groups (p-value .024 and .015, respectively), with systolic blood pressure being the lowest and diastolic blood pressure being the highest in mild acne group. There was no statistically significant difference in serum HDL-Cholesterol level, serum triglycerides level, fasting blood glucose levels, fasting plasma insulin levels and HOMA-IR score among these four groups (p-value .952, .970, .571, .718 and .594, respectively). The percentage

of metabolic syndrome and insulin resistance was 20% and 25% in mild acne; 25% and 30% in moderate acne; 30% and 20% in severe acne; and 31.58% and 36.84% in very severe acne groups, respectively. The differences were not statistically significant (p-value .842 and .681 for metabolic syndrome and Insulin resistance, respectively). (Table-II)

Table-I
Study Factors in Two Study Groups

Factor	Cases	Controls	p-value
Age (years)	22.91±2.93	22.54±3.05	0.442
Weight (Kg)	65.34±8.17	62.00±6.91	0.006
Height (cm)	160.87±4.28	160.87±4.71	0.778
Waist Circumference (cm)	87.44±6.46	85.39±5.76	0.037
SBP (mmHg)	129.65±9.13	119.57±8.29	<0.001
DBP (mmHg)	78.01±7.27	71.49±6.39	<0.001
Serum HDL-C (mg/dl)	47.07±8.52	44.86±8.17	0.097
Serum Triglycerides (mg/dl)	94.00±40.39	108.14±34.08	0.019
Fasting Blood Glucose (mg/dl)	90.33±5.44	80.34±7.03	<0.001
Fasting Plasma Insulin (µIU/ml)	9.56±4.83	8.33±3.07	0.059
HOMA-IR	2.32±1.14	1.74±0.93	0.001
Metabolic Syndrome (%) *	26.58	8.86	0.004
Insulin Resistance (%) **	27.85	11.39	0.008

Data are mentioned as Mean ± S.D lest specified otherwise; SBP=systolic blood pressure; DBP=diastolic blood pressure; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; HDL-C=high density lipoprotein cholesterol; *Metabolic syndromes assessed by National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII); **Insulin resistance was outlined as HOMA-IR score >2.5.

Table-II
Study Factors in Four Acne Severity Groups

Factor	Mild Acne	Moderate Acne	Severe Acne	Very Severe Acne	p-value
Age (years)	22.50±2.42	22.25±2.71	22.25±2.51	24.73±3.46	.017
Weight (Kg)	59.50±5.92	63.60±6.48	68.35±8.68	70.16±7.26	<.001
Height (cm)	159.75±4.49	161.00±3.91	162.25±4.49	160.47±4.11	.308
Waist Circumference (cm)	88.15±6.48	87.60±5.31	87.45±6.65	86.52±7.66	.893
SBP (mmHg)	125.25±9.10	128.30±8.81	132.30±6.15	132.89±10.45	.024
DBP (mmHg)	82.40±8.57	77.20±6.39	76.50±6.80	75.84±5.49	.015
Serum HDL-C (mg/dl)	47.40±7.97	46.25±9.80	47.75±8.33	46.89±8.44	.952
Serum Triglycerides (mg/dl)	95.65±42.08	92.65±41.03	91.05±38.39	96.79±42.92	.970
Fasting Blood Glucose (mg/dl)	89.55±6.00	91.80±4.68	89.90±5.39	90.05±5.72	.571
Fasting Plasma Insulin (µIU/ml)	9.18±4.07	9.29±4.66	10.65±5.71	9.09±4.97	.718
HOMA-IR	2.10±1.08	2.37±1.22	2.23±1.03	2.58±1.24	.594
Metabolic Syndrome (%) *	20	25	30	31.58	.842
Insulin Resistance (%) **	25	30	20	36.84	.681

Data are mentioned as Mean ± S.D lest specified otherwise; SBP=systolic blood pressure; DBP=diastolic blood pressure; HOMA-IR=Homeostasis Model Assessment-Insulin Resistance; HDL-C=high density lipoprotein cholesterol; *Metabolic syndromes assessed by National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII); **Insulin resistance was outlined as HOMA-IR score >2.5.

Discussion

In current study, we see that the young male patients who develop acne are more predisposed to have high systolic blood pressure along with more chances of developing pre-diabetic condition. The level of serum insulin in fasting patients was also observed to be raised as compared with the normal population. When comparing the different acne severity groups, the weight and systolic blood pressure were seen to increase as the severity of acne progressed. Over all, the number of patients to develop metabolic syndrome and insulin resistance was also significantly more in the acne group as compared with the control group.

The results of the study by Nagpal M. et al. [11] were similar to those of current study. They showed that the patients presenting with acne had higher systolic as well as diastolic blood pressures, but, in current study we observed that the diastolic blood pressure was seen to be lower in the acne patients as compares to that of controls. They concluded that the adolescent patients with acne had greater risk of developing hypertension,

diabetes mellitus and other metabolic derangements, in future. Cerman et al. [12] found out that higher glycemic index was associated with acne vulgaris. The studies by Emiroğlu N et al. [8] and Del Prete M. et al. [14] suggested that insulin resistance had some role to play in the pathological sequel of the acne. Kartal D. et al.[13] directed a study on women and observed that the use of metformin, a euglycemic drug for diabetes mellitus, by the patients presenting with acne resulted in improvement of their acne symptoms. This is clearly suggestive of an association of insulin resistance and acne.

Kumari R. et al. [15] witnessed in their study that the use of hyperglycemic diets which led to the induction of insulin and IGF-1-mediated P13 kinase / Akt activation caused the sebaceous lipogenesis and increase of sebocyte and keratinocyte which could cause acne. Ben-Amitai D. [16] suggested that the deficiency of insulin-like growth factor 1 had protective role against acne. Alan S. [17] revealed that the increased circulating levels of androgens and high body mass index (BMI) increased the occurrence as well as severity of acne in the female patients.

Sabat R. et al. [18] presented that there was high occurrence of metabolic syndromes in the patients presenting with acne. According to Saleh BO. [19], the factors which could raise levels of androgens, for example increased serum level of insulin like growth factor 1 and growth hormone, also increased the incidence of acne. Due to hyperandrogenism, these patients can develop hyperlipidemias.

Conclusion

The observations of our study concluded that post-pubertal males with acne are at higher risk of developing insulin resistance and metabolic syndromes as compared with normal population. Weight and systolic blood pressure level also tend to be higher with the increasing severity of acne.

Conflict of interest: NIL
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