Acne Vulgaris and Metabolic Syndrome: A Possible Association

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Abstract

Introduction

Acne vulgaris is an androgen-dependent disorder with excessive sebum production and proliferation of Propionibacterium acnes. Metabolic syndrome (MetS) is a multisystem disorder that increases the risk of diabetes mellitus, stroke, and cardiovascular diseases. This study aims to analyze the association of MetS with acne vulgaris.

Methods

A cross-sectional study was conducted with 65 cases of acne vulgaris and 65 age and sex-matched controls. We used the system provided by the Indian authors for grading acne according to the clinical severity. In addition, the criteria updated according to the joint consensus of 2009 were employed for the diagnosis of MetS.

Results

On clinical examination, grade 2 was the most prevalent grade of acne. We observed an increased incidence of abnormal waist circumference, triglyceride, HDL, and fasting blood glucose among the cases (p<0.05). Consequently, an increased occurrence of MetS was observed in the case group (p=0.011). While comparing the mean values of the parameters, we noted a significant difference in terms of waist circumference and HDL values. An increased mean value of waist circumference was noted in the case group while an increased mean value of HDL was reported from the control group (p<0.05).

Conclusion

Patients with acne vulgaris have a greater chance of developing MetS. Hence, an in-depth examination of clinical, anthropometric, and biochemical parameters that may lead to the development of MetS is necessary.

Introduction

Acne vulgaris is considered one of the most common skin disorders worldwide, involving chronic inflammatory infection of the pilosebaceous unit of the skin [1]. Acne affects more than 85% of adolescents and young adults [2]. Therefore, it is a vital issue during dermatological consultations because of its prevalence and impact on patients' social lives.

The first step in the pathophysiology of acne is increased sebum production, which causes follicular hyperkeratinization. This is followed by an infestation of Propionibacterium acnes (recently renamed Cutibacterium acnes), which causes the eventual release of inflammatory mediators. The usual inflammatory acne prevalent in the pubertal age group commonly occurs due to increased circulating androgen levels. Studies have also shown that an increased insulin level can aggravate acne [3].

The role of lipid metabolism and hormonal action in the differentiation of sebocytes are causative factors for acne. Insulin-like growth factor-1 (IGF-1) has also been shown to cause excess sebum production and cause acne independently [4]. A previous study reported elevated IGF-1 levels in cases of acne, potentially indicating a possible influence of insulin and growth hormone levels [5,6].

The metabolic syndrome (MetS), first described as Syndrome X by Reaven [7], comprises a set of laboratory and physical parameters predisposing the cases to the causation of cardiovascular diseases and diabetes mellitus (Type 2) [8]. Central obesity is considered one of the major constituents of MetS. The International...
Diabetes Federation (IDF) guideline regards it as a defining criterion. Subsequent consensus by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) in 2009 recommended considering central obesity as just one of the criteria. Also, it recommended incorporating ethnicity-specific waist circumference (separately for males and females) [9].

The other parameters include elevated triglyceride levels, reduced high-density lipoproteins, elevated blood pressure, and increased fasting blood sugar. The presence of any three out of the five parameters in an individual is labeled as MetS. The pathophysiology of MetS is intricately associated with insulin resistance. The tissues like muscles, fat, and other cells, become insensitive to insulin levels in the bloodstream and fail to absorb blood glucose [10]. Central obesity and adipose tissue accumulation play a significant role in developing insulin resistance.

**MetS and the skin**

Systemic metabolic derangements can often result in cutaneous manifestations and vice versa [11]. The deposition of excess adipose tissue and insulin resistance in MetS initiates a spectrum of hormonal disturbances [12]. In the pathogenesis of MetS and acne, inflammatory markers like TNF-α, IL-17, IL-23, and oxidative stress have shown a possible correlation [13]. With this study, we aim to analyze the changes in markers of MetS observed in patients with acne vulgaris in contrast to those with no such skin manifestations. Identifying such a positive association between acne vulgaris and MetS at an earlier stage would enable us to take necessary preventive measures to minimize the brunt of the disease.

**Materials And Methods**

The study was carried out in a tertiary care hospital in Central India over two years. Institutional Ethics Committee (IEC), Datta Meghe Institute of Medical Sciences, and Jawaharlal Nehru Medical College, clearance was obtained before starting the study. The research approval number is DMIMS(DU)/IEC/Aug-2019/8229. This study was a prospective, cross-sectional, case-control study. The sample size was calculated using the formula $n = \frac{Z_{\alpha/2}^2 \times P(1-P)}{d^2}$ considering 95% confidence interval ($n$ = sample size, $Z_{\alpha/2}$ = level of significance, $P$ = prevalence and $d$=desired error of margin). A total of 65 clinically diagnosed cases of acne vulgaris and 65 age and sex-matched controls were included.

Ages <18 years and >40 years, presence of any systemic comorbidities like diabetes mellitus, hypertension, dyslipidemia, etc., patients having a history of topical application of or ingestion of oral-systemic drugs (steroids, isotretinoin, etc.) for the last six weeks and dermatological disorders having any association with MetS will not be included (psoriasis, rosacea, hidradenitis suppurativa, alopecia, systemic lupus erythematosus, atopic dermatitis, etc.). Written informed consent was taken from all cases and controls of the study in their vernacular language for voluntary participation.

The same dermatologist made the diagnosis of acne vulgaris in all cases. Along with routine history, detailed history of all the participants (cases and controls) regarding the duration of acne and family history of acne was taken. In addition, the demographic data, general examination, cutaneous examination, and subsequent anthropometric and biochemical analysis were done for all cases and control group subjects. For clinical grading of acne, this study considered the Indian grading system provided by the Indian authors [14].

**Height, weight, and BMI**

Height measurements were recorded in centimeters using a wall-mounted scale. The individuals were made to stand erect against the wall and face forward. They were also asked to be barefoot with their feet lying flat on the floor. Weight was recorded in kilograms on a weighing scale. BMI was calculated as weight in kilograms divided by height in meters squared ($\text{kg/m}^2$). The individuals were categorized as normal (18.5-24.9 $\text{kg/m}^2$), overweight (25-29.9 $\text{kg/m}^2$), and obese (>30 $\text{kg/m}^2$).

**Waist circumference**

The waist circumference was measured using a measuring tape in a standing position, halfway between the level of the lower margin of the last palpable rib superiorly and the tip of the iliac crest inferiorly.

**Blood pressure**

Blood pressure (mmHg) was measured at the right brachial artery using a standard sphygmomanometer cuff in a sitting position, twice in each subject, to obtain the mean value.

**Laboratory investigations**

The blood samples for fasting lipid profile and fasting blood sugar were taken from the anterior cubital vein, in the morning hours, after overnight fasting of 10-12 hours. The lipid profile, which includes total cholesterol, high-density lipoprotein (HDL), and triglycerides (TG), was measured.
The diagnosis of MetS was based on the Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity [9]. Here, five parameters were considered, with the presence of any three confirming the diagnosis of MetS (Table 1).

| Parameters                                    | Cut-off Values                  |
|----------------------------------------------|---------------------------------|
| Elevated Waist Circumference (Asian population) | Men: ≥90cm                       |
|                                              | Women: ≥80cm                     |
| Elevated Blood Pressure                       | Systolic Blood Pressure: ≥130 mmHg and/or |
|                                              | Diastolic Blood Pressure: ≥85mmHg |
| Elevated Triglycerides                        | ≥150 mg/dL (1.7 mmol/dL)         |
| Reduced High-Density Lipoprotein              | Men: <40 mg/dL (1.0 mmol/L)      |
|                                              | Women: <50 mg/dL (1.3 mmol/L)    |
| Elevated Fasting Glucose                      | ≥100mg/dL                        |

**TABLE 1: Revised NCEP: ATP III Criteria for Metabolic Syndrome.**

In accordance with the consensus statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity in 2009 [9].

**Statistical analysis**

Data were entered in a Microsoft Excel spreadsheet. All entries were double entered, checking consistency. All the analyses were performed using SPSS ver. 26.0 (IBM Corp, USA), and the statistical significance was evaluated at a 5% level. Pearson’s chi-square test was used for nonparametric data, whereas ANOVA and t-tests were applied for parametric data.

**Results**

We included 65 cases of acne vulgaris and 65 age- and gender-matched controls in this study. The mean age of the case group was 23.43 ± 3.99 years, and a comparable mean age of 23.63 ± 4.03 years was observed in the control group. After clinical examination of acne lesions, we observed that out of 65 patients, 26 (40%) had grade 2 acne, followed by 24 (36.9%) with grade 1, 11 (16.9%) with grade 3, and four (6.2%) with grade 4. There was no significant difference in both the groups concerning BMI. However, we did find a statistically significant difference in waist circumference between the two groups (p=0.003). In the control group, there were 61 (95.8%) subjects with systolic BP <130 mmHg, while four (6.2%) had ≥130 mmHg. In the case group, there were 59 (90.8%) with systolic BP <130 mmHg, while six (9.2%) had ≥130 mmHg. The difference in the distribution was not significant (p=0.510). The distribution of subjects for diastolic BP was the same in both the groups, with 59 (90.8%) subjects having <85 mmHg and six (9.2%) having ≥85 mmHg (p=0.999).

When fasting blood sugar was considered, a larger number of subjects had values above the reference in the case group compared to the control group (p=0.007). Similarly, among lipid profile parameters, the difference in the distribution of subjects in the two groups regarding HDL-C (p=0.0003) and triglyceride levels (p=0.024) was significant, with increased occurrence of abnormal levels noted in the case group (Table 2).
| Parameters                   | Cases (n) | Controls (n) | P value |
|------------------------------|-----------|--------------|---------|
| **BMI (kg/m²)**              |           |              |         |
| Normal                       | 41 (63.1%)| 48 (73.8%)   | 0.326   |
| Overweight                   | 18 (27.7%)| 11 (27.7%)   |         |
| Obese                        | 6 (9.2%)  | 6 (9.2%)     |         |
| Normal                       | 40 (61.5%)| 55 (84.6%)   |         |
| Waist circumference (cm)     |           |              | 0.03 (S)|
| Normal                       | 40 (61.5%)| 55 (84.6%)   |         |
| Abnormal                     | 25 (38.5%)| 10 (15.4%)   |         |
| SBP (mmHg)                   |           |              | 0.51    |
| Normal                       | 59 (90.8%)| 61 (93.8%)   |         |
| Abnormal                     | 6 (9.2%)  | 4 (6.2%)     |         |
| DBP (mmHg)                   |           |              | 0.999   |
| Normal                       | 59 (90.8%)| 59 (90.8%)   |         |
| Abnormal                     | 6 (9.2%)  | 6 (9.2%)     |         |
| FBS (mg/dl)                  |           |              |         |
| Normal                       | 47 (72.3%)| 59 (90.8%)   | 0.007 (S)|
| Abnormal                     | 18 (27.7%)| 6 (9.2%)     |         |
| HDL-C (mg/dl)                |           |              |         |
| Normal                       | 29 (44.6%)| 49 (75.4%)   | 0.0003 (S)|
| Abnormal                     | 36 (55.4%)| 16 (24.6%)   |         |
| Triglycerides (mg/dl)        |           |              |         |
| Normal                       | 48 (73.8%)| 58 (89.2%)   | 0.024 (S)|
| Abnormal                     | 17 (26.2%)| 7 (10.8%)    |         |
| Metabolic Syndrome (%)       |           |              | 0.011 (S)|
| Yes                          | 17 (26.2%)| 6 (9.2%)     |         |

**TABLE 2: Distribution of subjects in the case and control groups according to different parameters relating to metabolic syndrome.**

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-C: High-density lipoprotein-cholesterol (S): Significant

For the assessment of MetS, we used the NCEP: ATP III criteria modified in 2009. In the control group, there were six (9.2%) subjects with MetS, while in the case group, there were 17 (26.2%) subjects with the syndrome revealing a significant difference between the two groups (p=0.011) (Table 2).

The mean values for FBS and TG parameters were comparable between the two groups (p>0.05). The mean HDL level in the case group observed was 44.11 ± 7.42 mg/dL, which was significantly smaller than the control group, 48.25 ± 7.81 mg/dL (p=0.002). Whereas an elevated mean value of waist circumference was noted in the case group (p=0.0037). The mean systolic and diastolic BP were fairly similar in the two groups (Table 3).
TABLE 3: Comparison of parameters for metabolic syndrome between the two groups.

HDL-C: High-density lipoprotein-cholesterol, BP: Blood Pressure, (S): Significant

| Parameter                  | Group     | N  | Mean     | Standard Deviation | P-value* |
|----------------------------|-----------|----|----------|--------------------|----------|
| Fasting Blood Sugar (mg/dL)| Control   | 65 | 93.91    | 10.70              | 0.895    |
|                            | Case      | 65 | 94.18    | 12.52              |          |
| Triglycerides (mg/dL)      | Control   | 65 | 112.29   | 32.37              | 0.157    |
|                            | Case      | 65 | 121.60   | 41.52              |          |
| HDL-C (mg/dL)              | Control   | 65 | 48.25    | 7.81               | 0.002 (S) |
|                            | Case      | 65 | 44.11    | 7.42               |          |
| Waist Circumference (cm)   | Control   | 65 | 78.14    | 8.97               | 0.037 (S) |
|                            | Case      | 65 | 81.57    | 9.54               |          |
| Systolic BP (mmHg)         | Control   | 65 | 117.38   | 8.67               | 0.528    |
|                            | Case      | 65 | 118.45   | 10.37              |          |
| Diastolic BP (mmHg)        | Control   | 65 | 78.29    | 5.58               | 0.61     |

Discussion

Our cross-sectional case-control study included a total of 130 subjects consisting of 65 cases of acne and 65 age and gender-matched controls. Acne is the most common facial disorder in the adolescent age group. It affects about 85% of young adults of both genders. The mean age for the cases with acne in our study was found to be 23.45 ± 3.99 years, which was similar to the observations of Del Prete et al., Nagpal et al., and Podder et al. who reported the mean age of 18.6 ± 2.5 years, 22.7 ± 0.6 years and 21 ± 4.9 years, respectively from their studies on acne vulgaris [15-17].

Acne vulgaris has been known to affect females more than males [18,19]. The demographic details of the acne group of our study revealed a female preponderance (61.5% females and 38.5% males). Balta et al. and Podder et al. have also observed similar genetic predispositions in their studies [17,20]. All the cases of acne were graded according to the system provided by the Indian authors [14]. In our study, the maximum cases were of grade 2 (40%), while the least were of grade 3 and grade 4 (6.2%). Furthermore, a study performed by da Cunha et al. on 416 patients of acne vulgaris also reported grade 2 to be the most prevalent [21].

We observed a similar distribution of subjects concerning BMI and blood pressure indices in the two groups. However, we noted a significantly higher proportion of individuals with abnormal waist circumference, fasting blood glucose, HDL-C levels, and triglyceride levels in the case group. The study performed by Biagi et al. reported no significant difference in the number of individuals with values of triglycerides, LDL, and HDL above the reference values in subjects with and without acne [22].

Our study reports an increased incidence of MetS in the case group consisting of patients with acne (26.2%) compared with their normal counterparts (9.2%). This difference was statistically significant (p=0.011), indicating a positive association between acne in the occurrence of MetS. Del Prete et al. reported a similar significant association in their case-control study on 22 cases of acne and their age and gender-matched controls [16]. A higher prevalence of MetS in acne patients of 32% was also reported by Podder et al.; however, the difference in comparison to the control group in their study was not significant (p=0.06) [17]. Nagpal et al. also observed a higher proportion of acne cases having MetS. In their study, 17% of subjects fulfilled MetS criteria in the acne group compared to 9% from the control group (p=0.09) [15].

When comparing the mean values of different parameters associated with MetS, we observed reasonably comparable values for SBP, DBP, and fasting blood glucose levels between the two groups. In agreement with our study, similar values of SBP and DBP between cases and controls were also reported by Podder et al. [17]. However, a higher mean value of SBP and DBP was noted in patients with acne in other studies [15,16].

In contrast to our study, Podder et al., Nagpal et al., and Del Prete et al. detected significantly increased fasting blood glucose values in the case group [15-17]. Balta et al. had a similar observation of no significant difference with respect to fasting blood glucose in the case and control groups [20]. Raised blood glucose values are associated with acne patients principally because an increase in blood glucose levels triggers...
an interest in the submitted work.

financial relationships at present or within the previous three years with any organizations that might have

organization for the submitted work.

Payment/services info:

interest:

subjects:

Committee on Human Research (CECHR) issued approval DMIMS(DU)/IEC/Aug-2019/8229.

Human subjects:

Disclosures

Additional Information

Conclusions

Acne vulgaris is considered one of the most common skin disorders in the adolescent age group. A higher incidence of altered waist circumference, triglyceride levels, HDL levels, and fasting blood glucose levels is observed in the cases with acne compared to their normal counterparts. Consequently, a significant association between MetS with acne was observed. The association between acne vulgaris and MetS can be explained by different mechanisms that are not exclusive but complementary. Screening by the dermatologist for MetS in patients with acne vulgaris could prove advantageous for the detection of at-risk individuals and the initiation of preventive therapy before cardiovascular disease or diabetes mellitus sets in.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Institutional Ethics Committee on Human Research (CECHR) issued approval DMIMS(DU)/IEC/Aug-2019/8229. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
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