ORIGINAL RESEARCH

A study on association between acne vulgaris and metabolic syndrome in a tertiary care hospital in north Karnataka

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Abstract

BackgroundAcne vulgaris is a multifactorial, chronic inflammatory disease of the pilosebaceous unit. It is caused due to follicular hyperkeratinisation, hormonal influence on increased sebum production & composition, inflammation, interaction of Propionibacterium acnes with innate immune system. Metabolic syndrome is a multisystem disorder that increases the risk of diabetes mellitus, stroke and cardiovascular disease. In the pathogenesis of metabolic syndrome and acne, inflammatory markers like TNF-α, IL-1, IL-6, IL-8, IL-17 and oxidative stress have shown a possible correlation.

Objective To study the association between acne vulgaris and metabolic syndrome.

Methods Total of 55 patients, attending dermatology out-patient department at KIMS, hubballi and clinically diagnosed with acne vulgaris were subjected to detailed history taking and their waist circumference, blood pressure, fasting lipids (mainly triglycerides and HDL) and fasting blood glucose tests were done after obtaining written informed consent. Clearance from institutional ethics committee is obtained. Patient who refused to give consent for the study and having dermatological disorder such as psoriasis, rosacea, hidradenitis suppurativa etc. were excluded from the study.

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. An increased occurrence of metabolic syndrome was observed.

Conclusion Patients with acne vulgaris have a greater chance of developing metabolic syndrome. Hence, an in-depth examination of clinical, anthropometric and biochemical parameters that may lead to the development of metabolic syndrome is necessary in order to prevent occurrence of cardiovascular accidents.

KeywordsAcne vulgaris, metabolic syndrome, dyslipidaemia, inflammatory markers

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]. It is one of the most common diseases affecting humanity and its impact on quality of life (QoL) is important [2]. It is a vital issue during dermatological consultations because of its impact on patients social lives.

The first step in the pathophysiology of acne is increased sebum production, which causes follicular hyper keratinization. Followed by infestation of Propionibacterium acnes (recently renamed Cutibacterium acnes), which causes release of inflammatory mediators. Studies have shown that an increased insulin level can aggravate acne [3].

Insulin-like growth factor-1 (IGF-1) has shown to cause excess sebum production and cause acne independently [4]. Elevated IGF-1 levels in cases of acne, indicating a possible influence of insulin and growth hormone levels [5,6].

The metabolic syndrome (MetS) described 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]. Parameters include elevated triglyceride levels, reduced high-density lipoproteins, elevated blood pressure, and increased fasting blood sugar and increased waist circumference. The presence of any three out of the five parameters in an individual is labeled as MetS[9].

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]. Systemic metabolic derangements can result in cutaneous manifestations [11]. The deposition of excess adipose tissue and insulin resistance in MetS initiates a spectrum of hormonal disturbance [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 study the association between acne vulgaris and metabolic syndrome and analyze the changes in markers of MetS observed in patients with acne vulgaris. Identifying such a positive association between acne vulgaris and MetS at an earlier stage will enable us to take necessary preventive measures to minimize the burden of the disease.

Materials and Methods

The study was conducted in tertiary care hospital in Karnataka Institute of Medical Sciences Hubballi, Karnataka for one year. Clearance from Institutional ethical committee was taken. This study is a cross sectional study and the sample size was calculated using the formula $n = [Z\alpha/2]^2 * P(1-P)/ d^2$, considering 95% confidence interval (n = sample size, $Z\alpha/2$ = level of significance,P = prevalence and d=desired error of margin). A total of 55 clinically diagnosed acne vulgaris subjects were included. Patient clinically diagnosed as acne vulgaris of all ages and genders and who gave informed written consent for the study were included in the study.Patient who refused to give consent for the study and having dermatological disorders such as psoriasis, rosacea, hidradenitis suppurativa, alopecia, systemic lupus erythematosus, atopic dermatitis, etc were excluded from the study.

Methodology

Patients clinically diagnosed with acne vulgaris attending OPD of Department of Dermatology venerology and leprosy, KIMS, Hubballi. After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria are enrolled for the study after obtaining informed written consent. Blood pressure, fasting blood glucose levels, fasting lipids (triglycerides & high density lipoprotein) and waist circumference are measured which are necessary to calculate and make diagnosis of metabolic syndrome. All the cases of acne were graded according to the system provided by the Indian authors [14]. 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]. NCEP ATP III criteria is used (table 1). Here, five parameters were considered, with the presence of any three confirming the diagnosis of MetS

Table 1: NCEP ATP III criteria

Diagnostic Criteria (any 3 below)	Defining Points
Elevated waist circumference	Men >102cm (>40in)Women >88cm (>35in)
Elevated triglycerides (TG)	≥150mg/dlORDrug treatment for elevated TG
Reduced HDL-C	Men <40mg/dlWomen <50mg/dlORDrug treatment for reduced HDL-C
Elevated blood pressure	≥130/85 mmHgORDrug treatment for hypertension
Elevated fasting glucose	≥100mg/dlORDrug treatment for elevated glucose

Waist Circumference

It 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 8 hours

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 55 cases of acne vulgaris. The mean age of the case group is 24 years. Out of which female sex being more in number i.e. 38 (69%) & 17 (31%) were male. 20-30 year age group is highest in number (53%). After clinical examination & grading of acne lesions, we observed that out of 55 patients: 22 (40%) had grade 2 acne – making it highest grade of acne, followed by 12 (22%) with grade 1, 11 (20%) with grade 3, and 10 (18%) with grade 4.

We observed that 29% of patients (n:16) with acne had metabolic syndrome. i.e. three of the following of abnormal waist circumference/ triglyceride/ HDL/ fasting blood glucose/ blood pressure

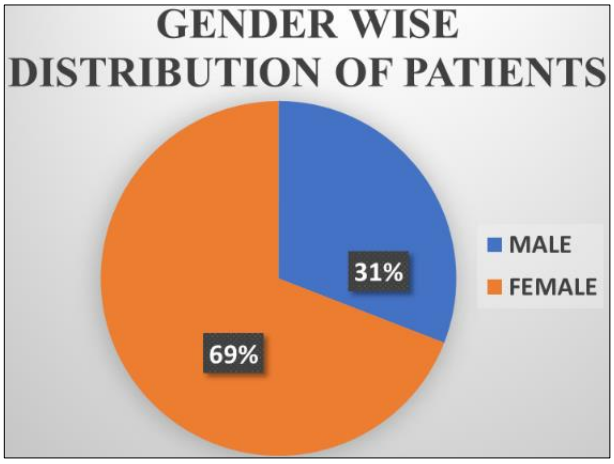

Fig. 1: Gender wise distribution of patients

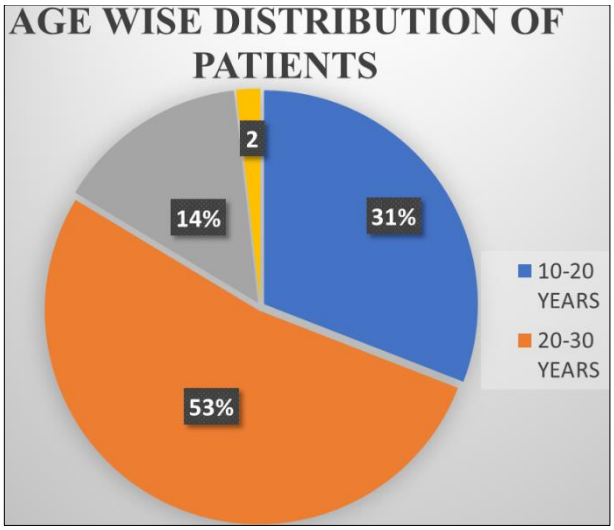

Fig. 2: Age wise distribution of patients

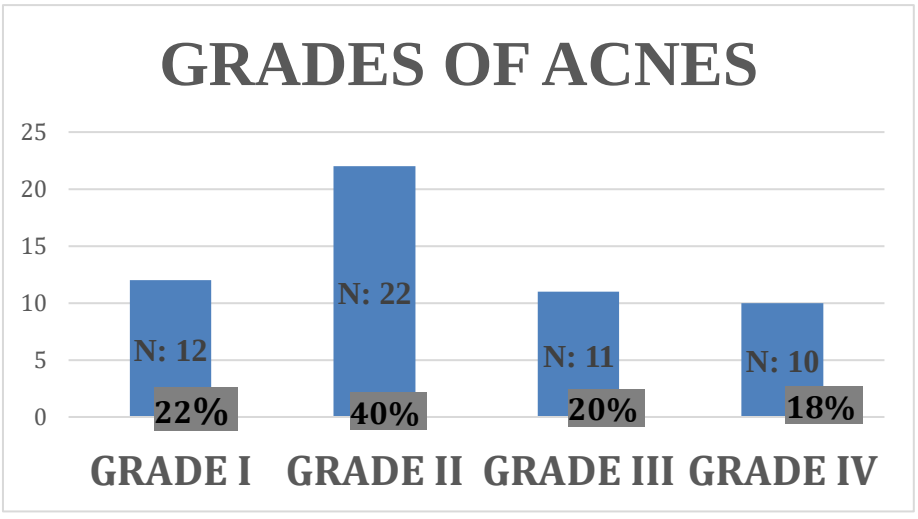

Fig. 3: Distribution of grades of acne

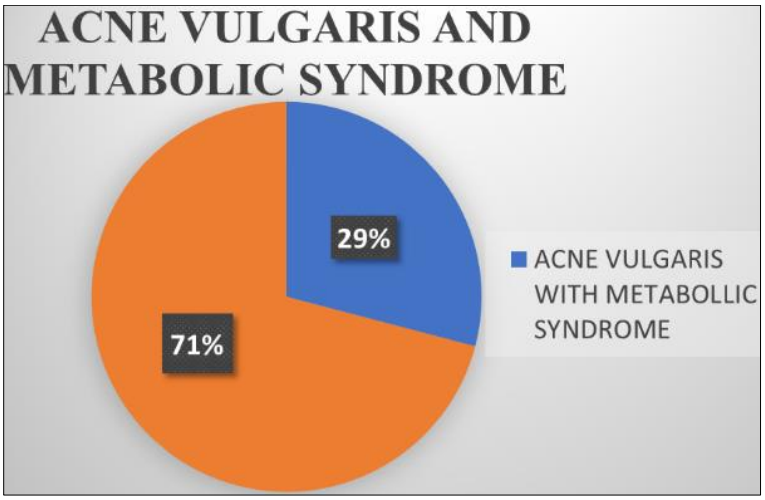

Fig. 4: Distribution of patients having acne vulgaris with metabolic syndrome

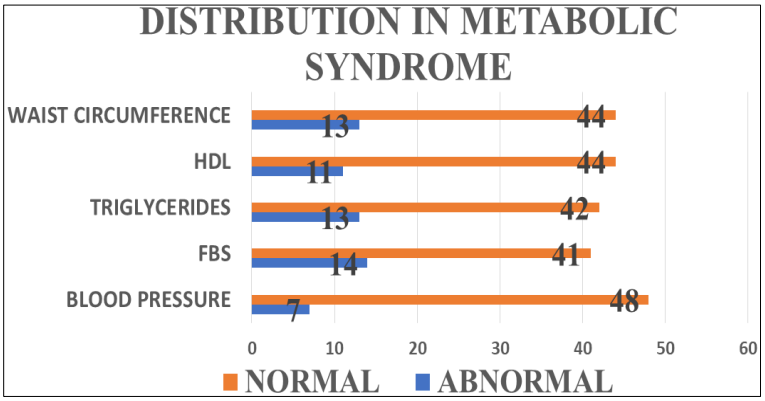

Fig. 5: Distribution in metabolic syndrome

Discussion

Our cross-sectional study included a total of 55 subjects. 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 24 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[15,16,17].

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 (69% females and 31% males). Balta *et al*. and Podder *et al*. have also observed similar genetic predispositions in their studies [17,20]. In our study, the maximum cases were of grade 2 (40%), while the least were of grade 4 (18%). 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]. Study performed by Biaga *et al*. showed no significant difference in value of triglycerides, LDL, HDL [22].

Our study reports an increased incidence of MetS in patients with acne (29%). This indicates a positive association between acne in the occurrence of MetS. Del Prete *et al*. reported a similar significant association [16]. A higher prevalence of MetS in acne patients of 32% was also reported by Podder *et al*.[17]. Nagpal*et al*. also observed a higher proportion of acne cases having MetS. In their study, 17% of subjects fulfilled MetS criteria [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. In agreement with our study, similar values of SBP and DBP 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 [15, 17]. Raised blood glucose values are associated with acne patients because an increase in blood glucose levels triggers insulin secretion, which decreases the binding protein for IGF-1, promoting cell proliferation by IGF-1. Higher fasting and postprandial insulin values can cause acne flare-ups by increasing basal keratinocyte proliferation. Insulin also causes stimulation of androgen secretion, leading to increased sebum production [20]. Insulin sensitivity decreases during puberty and adolescence, along with an increase in IGF1 and insulin serum levels. Sex hormone-binding globulin (SHBG) and insulin-like growth factor-

binding protein-1 (IGFBP-1) serum levels show a reduction. Insulin and IGF-1 levels, peak in late adolescence and steadily fall in third decade. Acne appears at about the same time as the preadolescent increase in plasma insulin, IGF-1, and BMI and usually clears up by the end of puberty, even though circulating androgens stay unchanged [23].

Patients revealed an increased mean value of waist circumference in the acne patients. This finding was reciprocated in the study performed by Del Prete *et al*. [16]. However, no significant difference in waist circumference was observed in previous studies [15,17,20].A peculiar finding of the analysis performed by Snast *et al*. revealed that obesity had a protective effect against acne [24]. Increased aromatase activity is seen in obese individuals, escalating the peripheral conversion of androgens to estrogens in the adipose tissue. Estrogen, having an action opposite to androgens, decreases sebum production. Obesity also suppresses the 5- alpha-reductase 2 activity that converts testosterone to dihydrotestosterone (DHT). DHT is an essential component in the pathogenesis of acne.

In lipid parameters, no statistical difference was reported in the mean value of triglycerides. Significantly increased mean values of HDL-C were recorded from patient. Previous studies have also reported similar triglyceride levels in subjects [15, 17,20,22]. Studies by Nagpal *et al*. and Balta *et al*. did not reveal any significant difference in HDL levels [15,20]. Elevated HDL-C levels are reported in normal subjects without acne was reported [15,25,26].

A study performed by Utami*et al*. in 2019 conferred that there are three main types of blood lipids in our body: triglycerides, phospholipids, and cholesterol [27]. De novo synthesis of blood lipids or sebaceous glands results in the formation of sebum lipids. The levels of blood lipids in the body may play a dynamic role in determining the sebum lipid composition. Follicular infundibulum epithelial hyperplasia and hyperkeratosis lead to comedone formation when lipid peroxide increases. They also cause sebaceous gland proliferation. Peroxisome proliferator-activated receptors (PPARs) play a role in lipid control, lipoprotein metabolism, inflammatory response, epidermal cell proliferation, differentiation, and sebaceous gland cell apoptosis triggered by lipid peroxides [27].

Our study reveals a positive association with MetS in patients with acne vulgaris, due to biochemical and hormonal alterations expected in acne pathophysiology. The study's primary limitations are limited sample size and a non-uniform distribution of subjects across different grades. Hence, this study could not ascertain the correlation of MetS with the increasing severity of acne. The analysis of serum insulin levels to confirm insulin resistance was beyond the scope of the study. Therefore, a large sample size longitudinal study with a significant number of cases of each severity and an in-depth laboratory workup is recommended.

Result

Acne vulgaris is considered one of the most common skin disorders in the adolescent and young adults. A higher incidence of altered waist circumference, triglyceride levels, HDL levels, and fasting blood glucose levels is observed. Consequently, a significant association between metabolic syndrome with acne is observed. Screening by the dermatologist for metabolic syndrome in patients with acne vulgaris could be advantageous for the detection of at-risk individuals and the initiation of preventive therapy before cardiovascular disease or diabetes mellitus sets in.

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