

## RESEARCH ARTICLE

# Factors Involved in the Pathogenesis of Acne and Its Psycho-Social Impact

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With acne as one of the most common and frequent conditions of young adult patients, we looked for significant associations, associated conditions with influence on the skin condition with the idea of outlining a different approach of the acne patient. With a multifactorial, multi-disciplinary etiopathogeny, the purpose of this study was to highlight the factors involved in the pathogenesis of this condition and to identify those that should be taken into account when prescribing the treatment.

**Keywords:** acne, associated conditions

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## Introduction

Acne is a common condition of the pilosebaceous unit. It is considered a chronic condition, with an increased relapse rate that requires long-term care and treatment. It has a major psycho-social impact, an element that should not be forgotten considering that 80% of acne cases occur in adolescents [1]. The etiopathogeny of acne is multifactorial, not completely elucidated, but there are several elements that contribute to maintaining a chronic inflammation around the pilosebaceous unit: the excretion of sebum is increased (the involvement of androgen hormones), the appearance of hyperkeratinization which leads to the obstruction of the follicular ducts (as cause the local application of comedogenic preparations cannot be excluded), the presence of *Cutibacterium acnes*, the increase of FGFR2 (increased fibroblast growth receptor-2), and, last but not least the genes of the patients (family history). All these factors are interdependent and under immune, as well as hormonal control [2-4]. Higher sebum production has been observed in patients with acne than in the rest of the population. Triglycerides, lipoperoxides make up the composition of sebum and take part in the pathogenesis of the disease. The latter produce pro-inflammatory cytokines, whereas triglycerides are degraded by *Cutibacterium acnes*, favoring the comedogenic process and bacterial proliferation. The result of follicular hyperproliferation is the microcomedone. The infundibulum becomes hyperkeratotic with increased agglutination of keratinocytes. The follicular ostium, due to the excess of newly formed cells, will be blocked by a plug. It forces keratin, sebum, and bacteria to gather in the hair follicle. This small collection represents the microcomedone. The causes of keratinocyte hyperproliferation are varied including: low linoleic acid, androgen stimulation, dihydrotestosterone, increased interleukin-1

alpha (IL-1) activity, and the consequences of *Cutibacterium acnes*.

With a multifactorial, multidisciplinary etiopathogeny, the purpose of this study was to highlight the factors involved in the pathogenesis of this condition and to identify those that should be taken into account when prescribing the treatment.

## Material and methods

As research instrument we used an anonymous questionnaire that tracked socio-demographic aspects, hereditary-collateral history, relevant pathological personal history, the type of acne lesions, the treatment of the patient, the presence of the antibiotic treatment and its effectiveness. We investigated the use of comedogenic products or the excess use of degreasing substances. Finally, we tried to evaluate the psychological comfort of these patients. The questionnaire was distributed to a target audience, namely the patients diagnosed with the condition. The distribution of the questionnaire took place both in the online environment and in a private dermatovenerology practice. The study group included 121 patients (87 women and 34 men) with a mean age of 15 years. The most frequent age of onset of the condition was in descending order 22.3% at 14 years, 17.4% at 13 years, 16.5% at 15 years, and 11.6% at 16 years. All patients consented to the fact that their data should be published anonymously, and a signed informed consent was obtained.

Nominal variables were described as absolutes and relative frequencies (%) and the association between them was analyzed by Pearson's Chi-square test or Fisher's Exact Test. The level of statistical significance for all two-sided tests was set at  $\alpha < 0.05$ . Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 22, Chicago, IL, USA).

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## Results

The study group included 121 patients (34 men and 87 women), with a mean age of 15 years. Patients participating in the study reported the following distribution of acne: T-zone 52.10%, cheekbones 34.4%, interscapular 22%, entire face region 19%, and presternal 9.1%. Open comedones predominated in 71.9%, closed comedones in 54.5%, cystic lesions 35.5%, and papulo-pustular lesions 55.4%. Their distribution was not uniform in the affected area, in 46.3% of cases more lesions are found and grouped unilateral compared to the contralateral side (Table I).

Most patients reported hypersecretion of sebum in the face area, encountered in the category of oily/ oily skin types - 42%, or mixed (seborrhic areas alternating with normal or dry areas) - 44%. As a result, patients frequently use face cleansing gels, 56% of them using such products on a daily basis.

Following the application of the inferential statistics tests, we found a statistically significant correlation, with  $p < 0.05$  between these patients and the presence of open comedones. Another statistically significant association, with a  $p$  under 0.05 was found between the presence of closed comedones and the skin types present in the study (a majority comprising oily and mixed types). Over a quarter (26.4%) of the patients consider that they have an increased activity of exocrine sweat glands compared to the rest of the population. Regarding the family history, 58.7% have at least one relative of the first degree who suffered from this condition, and with  $p = 0.004$  these patients are associated with the presence of open comedones.

To target the group of female subjects, we included a few specific questions regarding polycystic ovary syndrome, the regularity of the menstrual cycle, or the influence of menstruation on the appearance of the lesions. The results show that 29% of patients do not have menstrual cycles at regular intervals. The period before menstruation is known due to the increased number of comedones, the statistics confirming this in 50.4% of cases. In hyperandrogenism syndrome, the presence of polycystic ovaries was 16.09%, whereas 28.7% had never been under investigation for this condition. Another sign would be excess hair – hirsutism – present in 18.39% in the female group (Table II).

Subjects diagnosed with endocrine disorders were 10.7% and among the most common conditions were those involving the thyroid gland (thyroiditis, goitre, thyroid nodules, hypothyroid), breast node, adrenal disorders or previously diagnosed cases of hyperandrogenism.

After applying the inferential statistical tests and more specifically, applying the Pearson Chi-Square test, a statistically significant association was found between the presence of open comedones and disorders associated with gastric conditions (gastritis, ulcers, constipation, dyspepsia, intestinal transit disorders) with a  $p < 0.05$ .

At the time of completing the questionnaire, 65.3% had already used a drug treatment against acne. In these cases we found a  $p = 0.008$  following the application of the Chi-

Square test for the initiation of drug treatment in closed comedone type lesions. This treatment was recommended by the dermatologist (52.9%), the general practitioner (8.3%), or by friends, relatives or self-medication (17.4%). The treatment of this group varies greatly from local, topical treatments with tretinoids, or antibiotics, dermatocosmetic products, pharmacy preparations, contraceptives, oral isotretinoin, oral antibiotics, sulfur preparations.

However, a therapeutic formula stands out: the use of ointments intended exclusively for veterinary use. They contain a combination of 3 types of antibiotics, and usually 2 types of corticosteroids. Obviously, their use is not recommended by the doctor.

A percentage of 39.7 used antibiotic treatment either topically or orally. We observed a statistically significant association between the commencement of antibiotic treatment and the patients with papulo-pustular lesions. Overall, after treatment by the attending physician, either specialist or general practitioner, 57.9% of patients observed improvement in symptoms and a curative effect.

Compliance with the dermatological treatment was difficult for most patients, only 57.9% of them strictly followed the doctor's recommendations, 14% omitted administering treatment one day a week, and 5% two days a week.

Acne being a condition with a localization on an exposed area, frequently encountered in young patients, we have to take into account the psycho-social impact, 45% of the subjects considered that their daily life was affected by this condition.

## Discussions

Acne has long been treated as a condition with purely dermatological and cosmetic implications. However, some studies have focused on the association with other systemic diseases [5]. The role of androgen hormones in the pathogenesis of acne has often been studied and mentioned in the literature [6], especially in female patients, who, in 37%, had one or more signs of hyperandrogenism [7]. In

Table I. Lesion distribution

Type of lesion	Percentage (%)
Closed comedones	71.9
Open comedones	54.5
Papulo-pustular lesions	55.4
Cystic lesions	35.5
Unilaterality*	46.3

\*: uneven distribution of the lesions

Table II. Distribution of endocrine symptoms

Symptoms	Percentage (%)
Hirsutism	18.39
POS*	16.09
Other conditions**	10.7

\*: polycystic ovary syndrome; \*\*: other endocrinological disorders

our study we found that 29% did not have menstrual cycles at regular intervals, 16% were diagnosed with polycystic ovary syndrome, and 18.39% had hirsutism (which indicates a hyperandrogenism syndrome), factors considered aggravating by Ewa Chlebus et al. [8]. Among the syndromes associated with this condition, we mention: POS (polycystic ovary syndrome) - where insulin resistance and hyperandrogenism are responsible for skin involvement, SAHA syndrome (seborrhea, acne, hyperandrogenism, and androgenetic alopecia) [9]. One study concludes that, in most cases, acne is not just a purely cosmetic condition and further investigation on the side of endocrine pathology is recommended [10]. Adjuvant treatment of acne using ultraviolet radiation is known, and more recently, light emitting diodes have been applied [11]. In our study, 55.4% of the patients considered sun exposure useful, which is also found in other studies [12,13]. Of or patients, 41.3% suffered from gastrointestinal disorders, and previous studies confirm a significant association with the condition in question. A study conducted on approximately 13,000 subjects of Chinese nationality found correlations between sebaceous gland condition (including acne) and constipation, gastric reflux, or bloating. A clinical success in the treatment of sebaceous gland dysfunction is the use of H2 histamine receptor blockers, which have an inhibitory effect on gastric secretion, hence the connection between the two conditions [14,15]. A controversial topic, the influence of diet as an aggravating factor, has often been debated in specialized articles, with different opinions and results. The risk factors include sweets, carbonated beverages, white bread, family history, however, the intake of milk, yogurt, cheese are considered irrelevant [16]. Our results are biased towards dairy consumption.

Regarding the use of veterinary ointments, we believe that a further study with a question specifically aimed at this would bring more data, because patients seem reluctant to admitting such usage, nevertheless this practice seems not that uncommon.

Taking into consideration that most patients reported hypersecretion of sebum in the affected areas, patients resort to frequent use of face cleansing gels. Often, an adverse effect of sebum overproduction can occur due to excessively drying of the skin by aggressive degreasing methods (alcoholic solutions, abrasive cleaning gels).

Several sources cite that this condition is genetically inherited [17], and is considered a genetic disease of the follicles prone to acne [18]. Based on our statistics we found that 58.7% have at least a first-degree relative who suffered from this condition. Although the psychological impact of acne in our country is not present in specialised publications, other countries often approach this topic. Increased risk for depressive states and anxiety in this condition has been described several times, being compared, in terms of impact, with epileptic disease. Moreover, the location of the lesions, their shape and the patient's psyche should also be taken into consideration [15,19]. Our results reflect

these assertions, however, future studies should view age, shape (mild or severe), and social environment.

## Conclusion

Many patients do not seek medical attention for confirming the right diagnosis and therapeutic conduit, we underline the importance of doing so, in order to avoid the danger of self-medication. Long term use of topic corticotherapy may produce local skin atrophy, induce eczema and other well-known side effects. Being a skin pathology that seems to be easily recognized by civilians, self-medication is often the first line treatment (ranging from dermato-cosmetics to ointments intended for veterinary use), medical advice being sought only if empiric, over the counter medication does not work.

In the case of female patients, it is recommended to investigate the endocrine condition for hyperandrogenism and polycystic ovary syndrome. It is recommended to investigate all patients for digestive disorders.

Psychological guidance and counseling of these patients should be implemented when appropriate.

As the frequency of open comedones take up to 72% comedogenic products should be avoided, and, if necessary, usage of only gentle cleansing gels with moisturizing properties, underlining the importance of moisturizing agents, we would encourage that the doctor consultation will provide further support and education towards adequate skin care routine, in addition to writing a prescription, also taking phototherapy into consideration as an adjuvant treatment.

It is also recommended to inform patients about the long duration of therapy and the importance of observing the course and evolution of treatment.

## Conflict of interest

None to declare.

## Authors' contributions

SV (Conceptualization; Methodology; Supervision; Writing – review & editing)

RT (Conceptualization; Methodology; Supervision; Writing – review & editing)

TV (Conceptualization; Methodology; Supervision; Writing – review & editing)

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