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Etiopathogenesis of Acne Vulgaris

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Abstract

Objectives: Describe examine the function of sebaceous glands in the development and progression of acne vulgaris and talk about its causes and prevalence. Acne, which often affects the face, upper chest, and back, is a condition that typically manifests in children and teenagers and is associated with an overproduction of the male hormone androgen by the sebaceous glands and the adrenal glands. Where the Data Came from: Finding research that explain the pathophysiology, etiology, and prevalence of acne vulgaris as well as the function of sebaceous glands up to the year 2024 was the goal of this search and study of Medline databases (Pub Med and Medscape). Research Question Selection: For inclusion, each study underwent an independent evaluation. They were considered for inclusion if they met the following requirements: 1. The text was written and published in English. 2. Bound in scholarly publications that undergo a rigorous peer review process.3. Discuss the function of sebaceous glands in the prevalence of acne vulgaris and describe its causes and pathophysiology. When extracting data, studies were discarded if they did not meet the inclusion criteria. Ethical permission, established eligibility criteria, sufficient information, and well-defined evaluation metrics were all variables in determining the study's quality. For our concerned research outcomes, data were independently extracted from all qualifying studies utilizing a data collecting form. In conclusion, stress, oxidative stress, hormones, obesity, and other variables are all contributors to the pathophysiology of acne and, by extension, the incidence of AV. There are four main elements that contribute to the pathogenesis process: inflammation, follicular hyperkeratosis (changes in follicular development and differentiation), seborrhea (increased sebum production), and the colonization of pilosebaceous units by C. acnes.

Key words: Acne vulgaris.

1.Introduction

Acne vulgaris (The face, upper chest, and back are typical sites of AV, a common skin condition that mainly affects regions with a comparatively high concentration of sebaceous glands [1]. Nutrition, medicine, occupational variables, pollution, climate, psychological issues, and lifestyle choices are all contributors to AV's high incidence [2]. It develops when inflammation and the bacteria Cutibacterium acnes exacerbate the sebaceous glands' sensitivity to the body's natural androgen levels [3].

It is believed that the release of reactive oxygen species (ROS) and sebum from the inflamed follicular walls is a key step in the development of acne [4]. Sebaceous glands are responsible for producing sebum.

2.Materials and methods

Data Sources: The A literature review was conducted using the Medline databases (Pub Med and Medscape) to gather information on the causes of acne vulgaris and the function of androgens in the decrease of its prevalence till the year 2024.

Research Question Selection: Research was selected via an open, honest, and thorough evaluation procedure. They were considered for inclusion if they met the following requirements:

One, written and published in English [2]. Having an appearance in journals that have a rigorous peer-review procedure [3]. Explain how sebaceous glands contribute to the development of acne vulgaris and talk about how common it is.

Research papers that failed to fulfill the inclusion criteria were not included in the data extraction process. Considerations for the study's quality included ethical approval, information, eligibility requirements, and well specified assessment tools. To ensure that our research results were accurately represented, data were independently extracted from all eligible and qualifying studies utilizing a data collecting form.

Literature review:

Plain Old Acne

Open and closed comedones, papules, pustules, nodules, and cysts are the hallmarks of acne vulgaris, a prevalent chronic inflammatory disease of the pilosebaceous unit [5]. A self-limiting inflammatory condition of the pilosebaceous unit, acne vulgaris has a chronic history. During puberty, when levels of normal circulating dehydroepiandrosterone (DHEA) are at their highest, the acne-causing bacteria Propionibacterium acnes (P. acne) sets it off. Inflammatory and non-inflammatory lesions may be seen on the face, upper arms, torso, and back of affected individuals; nonetheless, this skin condition is rather frequent [6].

It often first manifests in teens and continues well into one's 30s. Severe acne, which leaves scars in almost 20% of those who have it [7].

The following factors may contribute to the development of acne: the use of certain drugs (such

as lithium, steroids, or anticonvulsants), prolonged exposure to sunlight, occlusive clothing (such as backpacks, headbands, or shoulder pads), hormonal imbalances (such as polycystic ovarian syndrome), and, of course, pregnancy. There are hereditary variables that influence the proportion of branched fatty acids in sebum [8].

Why Does Acne Vulgaris Occur?

The importance of stress in the development of acne is becoming more and more recognized. The hormonal, neuropeptide, and inflammatory cytokine responses to emotional stress impact the pilosebaceous unit's activity, which in turn affects the chronic course and worsening of acne. A number of neuropeptides and hormones, including melanocortins and corticotrophin-releasing hormone (CRH), are involved in these processes via the neuro-immunocutaneous system and the hypothalamus pituitary adrenal (HPA) axis [9]. Cortisol levels rise in response to stress because it triggers the secretion of CRH and pro-inflammatory cytokines. The hypothalamic-pituitary adrenal axis, the release of stress hormones, and the likelihood of acne flare-ups are all negatively impacted by the lack of sleep that many contemporary women experience [10].

One possible role of oxidative stress is to prime acne patients to be more susceptible to co-occurring mental health issues like anxiety and depression [11]. Low blood antioxidant enzymes and elevated malondialdehyde (MDA) levels are hallmarks of acne, as contrasted with healthy persons [12]. Acne sufferers had decreased total antioxidant capacity and higher blood MDA levels compared to controls, according to Awad et al. [13].

Hormones Play a Role: While acne isn't normally thought of as an endocrine illness, researchers have linked androgens including testosterone, dihydrotestosterone, growth hormone, and insulin-like growth factor (IGF) to the development of acne [10]. The sebaceous gland's heightened sensitivity to androgenic hormones: Similar to adult vulgaris (AV), adult female acne (AFA) is characterized by an increase in the number and sensitivity of androgenic hormone receptors found in sebocytes and keratinocytes [14]. The enzyme needed to convert testosterone to the stronger DHT, 5α-reductase, is inhibited by progesterone. Basal epidermal keratinocytes are the only cells in the skin that express progesterone receptors, which is responsible for both menstrual flare and sebum exacerbations [15]. Sebum production and acne lesions may be reduced with adequate dosages of oral contraceptive tablets containing estrogen, which increases sex hormone binding globulin and decreases circulating free testosterone [16].

The role of genetic factors: a person's vulnerability to comedogenesis and the severity of the illness may be influenced by their genes. Chromosomal aberrations and human leukocyte antigen (HLA) phenotypes are also implicated in the pathophysiology of acne, while investigations into the relationship between acne and other genes have also been conducted. The HSD3B gene family and the cytochrome P450 (CYP) gene family are two examples of gene families that have been investigated extensively and may have a role [17].

Impact of Being Obese: Increased sebum production and the onset of severe acne may be associated with obesity-related peripheral hyperandrogenism and insulin resistance (IR). The prevalence of overweight and obesity may be quantified statistically using the body mass index (BMI) [18]. An increase in androgen production, which stimulates sebaceous glands, and an increase in endogenous androgen production, which causes acne to develop or worsen, are both possible outcomes of hyperinsulinaemia. Dietary restrictions for those with AV may be necessary [10].

What Smoking Does: Micro and macro comedones, with minimal inflammatory lesions, describe the comedonal form, which is more common in smokers [10]. When exposed to nicotine, the sebaceous gland releases the sensitivity hormone acetylcholine. The effects of acetylcholine on cells include hyper-keratinization, changes in sebum production and composition, and cellular regulation and differentiation [17].

Dark Spots

One of the main causes of acne is an overproduction of sebum. Sebum production essentially creates a lipid-rich, anaerobic follicle where Propionibacterium acnes may flourish [18]. Changes in sebum content and secretion rate are thought to be the root cause of comedogenesis [19]. During puberty, the synthesis of androgens, particularly testosterone, increases, which in turn stimulates the growth of the sebaceous glands and the generation of more sebum. The enzyme type I 5α-reductase converts testosterone to the more active DHT. The body responds by producing more sebum in response to this androgen's enhanced activity. Therefore, elevated sebaceous gland sensitivity to androgen [20] is the primary cause of increased sebum production seen in acne patients.

Hyperkeratosis in follicles

Hyperkeratosis results from altered follicular keratinization. Loosely layered keratinocytes are seen in healthy hair follicles. Sebum transports them to the skin's surface once they're periodically desquamated. Desquamated cells and freshly generated cells are in a steady state of equilibrium. In contrast, the rate of keratinocyte growth is elevated in acne-affected follicles. Due to inefficient desquamation, sebum is unable to carry the closely packed horney lamellae to the skin's surface. Eventually, a comedo forms from a retention-proliferation hyperkeratosis, which first manifests as a microcomedo [21]. Hyperproliferation of

keratinocytes lining the follicle wall and decreased desquamation owing to greater cohesiveness between keratinocytes are two alterations to the usual pattern of keratinization that occur during comedogenesis. A buildup of cornified keratinocyte within the follicle is the result of these alterations [19].

Proliferation of the acne-causing microbe

Changes in sebaceous gland activity, comedone development, and host inflammation are some of the suggested processes of acne pathogenesis involving C. acnes [22]. 1-Sebum secretion enhancement: Cytocystis acnes uses sebum as a metabolic substrate to fuel its development [22]. 2-Releasing free fatty acids from sebaceous gland produced triglycerides, C. acnes promotes comedone production. One of the primary components of sebum is squalene, and the porphyrins released by C. acnes serve as catalysts for this process. Comedogenesis may be facilitated by oxidized squalene and free fatty acids [23]. When C. acnes binds to toll-like receptors (TLR)-2 and -4 on keratinocytes, it triggers inflammatory responses by inducing monocytes and other cells to produce IL-1α, IL1-β, IL-6, IL-8, IL-12, tumor necrosis factor (TNF)-α, interferon (IFN), chemotactic factors, β-defensin, and other cytokines and polypeptides, thus triggering or intensifying inflammatory responses [24].

The state of inflammation

Finally, many pathogenic processes feed the inflammatory response, the fourth component in the acne etiology. Comedones burst and release their contents into the dermis, causing inflammation and the development of nodules, pustules, and papules [25]. Interactions between C. acnes and TLR-2 are definitely necessary for the generation of IL-6, IL-8, and IL-12, which are inflammatory cytokines. C. acnes activates Toll-like Receptor-2, which in turn recruits neutrophils to the pilosebaceous unit and induces the secretion of proinflammatory cytokines by monocytes, IL-8 in particular. As a result of C. acnes activating TLR-2, a cascade of proinflammatory chemicals may be released into the skin, which in turn may drive the invasion of inflammatory cells and cause inflammation [26].

Clinical Signs of Uncommon Acne

Acne usually shows up on the face and neck, but it may also appear on the back, shoulders, and chest. Additionally, keratosis pilaris and other lesions may appear on the upper arms in the form of acne. Comedones, inflamed papules, pustules, and nodules are the acne lesions. Nodulocystic is a term used to characterize severe instances of inflammatory acne; the word "cyst" was previously used to describe some of the big nodules [27].

Open and closed comedones are two types of non-inflammatory acne lesions. Whiteheads are closed comedones, which are papules that seem white to flesh-colored and have an apparently closed surface. Flat or slightly elevated plugs ranging in color from brown to black, known as open comedones, enlarge the follicular openings. As a result of melanin pigment oxidation, the color is dark [28].

How Bad is Acne Vulgaris?

In order to establish a standard for the severity of acne, the American Academy of Dermatology held a Consensus Conference. Over time, many dermatologists throughout the globe began to accept a new system of categorization that was both successful and acceptable. The following AV grading system is proposed by this consensus: mild acne, moderate acne with comedones and few to several papules-pustules; severe acne with many nodules and either numerous or extensive papules-pustules; and very severe acne, including the most destructive forms of the disease like acne conglobata, acne fulminans, and the follicular occlusion triad [25].

Acne Grading System in the World (GAGS)

For each of the six sections of the GAGS—the face/forehead, the left and right cheeks, the nose, the chin, and the chest and upper back—the number of pilosebaceous units is rated from 0 (no lesions), 1 (one comedone), 2 (one papule), 3 (one pustule), and 4 (one nodule), with each section's rating multiplied by a location-specific factor. After adding together all the local scores, you get the global score. On a scale from 0 to 39, acne is classified as mild, moderate, severe, or extremely severe.

3.Conclusion

Acne has several root causes, some of which are associated with AV prevalence, including as hormonal changes, stress, oxidative stress, and obesity. There are four main elements that contribute to the pathogenesis process: inflammation, follicular hyperkeratosis (changes in follicular development and differentiation), seborrhea (increased sebum production), and the colonization of pilosebaceous units by C. acnes.

References

[1] T, El-Tonsy M, Y,MohammedHamed et al.: Bacteriological study of Acne Vulgaris in Cairo Egypt. Egy J Hospital Med; vol:72(9): pp.5203-5209. **(2018)**

[2] M, Aghasi M, Golzarand S, Shab-Bida et al.: Dairy intake and acne development: a meta-analysis of observational studies. Clin Nutr; vol:38(3): pp.1067- 107. **(2018)**

[3] C, Motosko G, Zakhem M, Pomeranz et al.: Acne: a side-effect of masculinizing hormonal therapy in transgender patients. Br J Dermatol;vol:180(1):pp.26-30. **(2019)**

[4] C, Folle N, Díaz-Garrido E, Sánchez-López et al.: Surface-Modified Multifunctional Thymol-Loaded Biodegradable Nanoparticles for Topical Acne Treatment. Pharmaceutics; vol:13(9):pp. 1500-1501. **(2021)**

[5] H, Abd Elwahab M, Ragaie and A, Ali.: Evaluating the Effect of Adapalene in Treatment of Acne Vulgaris. MJMR;vol: 33(3):pp. 62-64. **(2022)**

[6] H, Yan H, Zhao D, Guo et al.: Gut microbiota alterations in moderate to severe acne vulgaris patients. J Dermatol;vol:45(10):pp.1166-1171. **(2018)**

[7] S, Ozçelik İ, Kulaç M, Yazıcı et al.: Distribution of childhood skin diseases according to age and gender, a single institution experience. Turk Pediatri Ars;vol:53(2):pp.105-112. **(2018)**

[8] P, Nair and F, Salazar.: Acneiform Eruptions. Book from StatPearls Publishing, Treasure Island (FL); vol:29083685. **(2017)**

[9] A, Jović B, Marinović K, Kostović et al.: The Impact of Pyschological Stress on Acne. Acta Dermatovenerol Croat; vol:25(2):pp.133–141. **(2017)**

[10] E, Bagatin T, Proença M, Rivitti-Machado et al.: Adult female acne: a guide to clinical practice. Ann Bras Dermatol; vol:94(1):pp. 62-75. **(2019)**

[11] V, Papa F, Pomi F, Borgia et al.: "Mens Sana in Cute Sana"—A State of the Art of Mutual Etiopathogenetic Influence and Relevant Pathophysiological Pathways between Skin and Mental Disorders: An Integrated Approach to Contemporary Psychopathological Scenarios. Cells; vol:12(14):pp.1828. **(2023)**

[12] F, Puspita ,Jusuf K, Nelva and A, Yosi.: "Plasma malondialdehyde levels related to acne vulgaris severity. Journal of General - Procedural Dermatology & Venereology Indonesia: vol: 5: Iss. Pp.3, Article 3. **(2021**)

[13] S,Awad H, Morsy A, Sayed et al.: Oxidative stress and psychiatric morbidity in patients with facial acne. JCD; vol:17(2):pp. 203-208. **(2018)**

[14] T, Cong D, Hao X, Wen et al.: From pathogenesis of acne vulgaris to anti-acne agents. Arch Dermatol Res; vol:311(5):pp.337-349. **(2019)**

[15] S, Azarchi A, Bienenfeld K, Lo Sicco et al.: Androgens in women: Hormone-modulating therapies for skin disease. J Am Acad Dermatol; vol:80(6): pp.1509-1521. **(2019)**

[16] L, Ragmanauskaite B, Kahn B, Ly et al.: Acne and the lesbian, gay, bisexual, or transgender teenager. Dermatol Clin; vol:38(2): pp.219-226. **(2020)**

[17] A, Heng and F, Chew: Systematic review of the epidemiology of acne vulgaris. Sci Rep;vol:10:pp.5754. **(2020)**

[18] M, Listiawan C, Prakoeswa D, Handamari et al.: Effects of Blue Light Emitting Diode (Led) and Doxycycline to Sebaceous Gland in Acne Vulgaris. Folia Medica Indonesiana;vol:53(4):pp.272-275. **(2017)**

[19] F, Fontao M, Engelbrechten C, Seilaz et al.: Microcomedones in non- lesional acne prone skin. New orientations on comedogenesis and its prevention. J Eur Acad Dermatol Venereol; vol 357- pp.364. **(2020)**

[20] D, Marks S, Prasad B, De Souza et al.: Topical Antiandrogen Therapies for Androgenetic Alopecia and Acne Vulgaris. Am J Clin Dermatol; vol:21(2):pp.245-254. **(2020)**

[21] K, Diegel L, Mecklenburg L, Andrews-Jones et al.: Pathology of the Integumentary System. In: Steinbach T., Patrick D., Cosenza M. (eds) Toxicologic Pathology for Non-Pathologists. Humana, New York, NY. **(2019)**

[22] T,Do.: Interactions of Human Immune Responses with Lipid Metabolism and the Skin Microbiome in Acne Vulgaris. Diss. UCLA; pp.1-97. **(2020)**

[23] H, Xu and H, Li.: Acne, the skin microbiome, and antibiotic treatment. Am J Clin Dermatol; vol:20(3): pp.335-344. **(2019)**

[24] T, Zhu W, Wu S, Yang et al. : Polyphyllin I inhibits Propionibacterium acnes-induced inflammation in vitro. Inflammation; vol:42(1): pp.35-44. **(2019)**

[25] G, Plewig B, Melnik and W,Chen.: Acne Clinic: Morphogenesis. Plewig and Kligman´ s Acne and Rosacea. Springer, Cham; vol:63-pp.189. **(2019)**

[26] K,Chen C, Yang T, Li et al.: Suppression of Propionibacterium acnes-stimulated proinflammatory cytokines by Chinese bayberry extracts and its active constituent myricetin in human sebocytes in vitro. Phyto Ther Res; vol:33(4): pp.1104-1113. **(2019)**

[27] L, Shakiba A, Minaii J, Aliasl et al.: Herbal Remedies for Acne Vulgaris from the Viewpoint of Per-sian Medicine. Iran J Public Health; vol:49(5): pp.1014-1015. **(2020)**

[28] G, Latter J, Grice Y, Mohammed et al.: Targeted topical delivery of retinoids in the management of acne vulgaris: current formulations and novel delivery systems. Pharmaceutics; vol:11(10): pp.1-490. **(2019)**

[29] E, Bernardis H, Shou J, Barbieri et al.: Development and Initial Validation of a multidimensional Acne Global Grading System Integrating Primary Lesions and Secondary Changes. JAMA Dermatol; vol:156(3): pp.296-302. **(2020).**