Review Article

Acne Vulgaris Burden, Risk Factors, Lifestyle Modification Influence and Treatment Options – A Review

ABSTRACT

Acne vulgaris is a widespread health issue affecting teenagers, young adults, and adults. The prevalence of this unpleasant condition varies between populations. A thorough literature review was carried out to discuss this underestimated issue through multiple perspectives. The search found that acne vulgaris has a substantial negative psychological impact on individuals leading to low quality of life and less productivity, yet it is usually neglected. Various factors, modifiable and non-modifiable) were associated with the progression of acne, such as family history, genetics, and diet, yet others were controversial. Lifestyle modifications are of high importance since they may contribute to the development of acne. Numerous anti-acne drugs are available in the form of topical and systemic, however, topical treatment options in general are preferred thanks to their effectiveness and less severe side effects.

Keywords: Acne, acne vulgaris, burden, lifestyle modification, risk factors, treatment, Saudi Arabia

1. INTRODUCTION (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

Acne, medically known as acne vulgaris, is a common chronic dermatological disorder that is caused by abnormal desquamation of follicular epithelium tissue, which leads to abstraction of the pilosebaceous canal [1,2]. *Cutibacterium* triggers acne with the impact of normal circulating dehydroepiandrosterone (DHEA). Acne vulgaris, primarily, affects young adults' faces mostly, as well as upper arms, trunk, and back. It appears as inflammatory lesions, non inflammatory lesions, or a combination of both [3–5]. Acne is clinically characterized by a variety of skin lesions, classified as mild, moderate, or severe. Mild acne is defined as non-inflammatory lesions, also called comedones, or few inflammatory lesions (papulopustular lesions), or both. Moderate acne, on the other hand, is more of an inflammatory lesion with nodules and scarring that is mild. Severe acne is often described as inflammatory extensive lesions, nodules or cysts , scarring, or acne that does not improve after six months of treatment. In addition, acne of any class associated with severe psychological impact is considered sever acne [6]. Acne vulgaris prevalence varies greatly among ethnic groups and countries. It is the 8th most common disease worldwide; and is estimated to affect 633 million people globally [2]. It affects almost everyone between the ages of 15 and 17, with 15-20% of adolescents suffering from moderate to severe acne. In the US, a study was conducted and reported the prevalence of acne in 85% of teenagers [7]. Another study was carried out in Turkey, and it showed adolescents aged 13 to 19 years had a prevalence of 60.7% [8]. In Saudi Arabia, there is a lack of prevalence statistics regarding acne vulgaris. A review of previously published studies resulted in a wide range of prevalence estimates

which may indicate a variation in the prevalence of acne among different regions in Saudi Arabia. for example, one of the studies that was conducted in Saudi Arabia's capital, found that the overall prevalence of acne vulgaris among teenagers and young girls was 68.2 percent [9]. Another study was conducted in the central region of Saudi, and found a 56.2 percent prevalence of acne among Qassim University students, however no statistically significant difference between males and females was observed [10]. Whereas, in the south of Saudi Arabia, specifically Jizan, the overall prevalence of self-reported acne was 65.1%, with females more affected than males (71% and 60%, respectively) and this difference achieved statistical significance [11]. In the west of Saudi Arabia, a study was carried out in Makkah and found that 56.6 percent of female patients attending dermatology outpatient clinics at three hospitals suffered from acne vulgaris [12].

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

A comprehensive search was carried out by five co-authors independently on PubMed and Google scholar using the following terms: “acne vulgaris”, “burden”, “pharmacological treatment”, “lifestyle interventions”. Then, search results were filtered based on title, abstract, study included humans only, and availability in English language as well as availability of full texts. A total of 67 articles were found and based on the previously mentioned criteria and whether they provide benefit towards achieving the aim of the study, 43 were selected.

3. RESULTS AND DISCUSSION

3.1 Burden

There is an increased awareness of the psychological impact of dermatological diseases around the world, since it affects different aspects of the patient’s life including, psychological, social, and cultural perspectives. In acne vulgaris, patients carry the same consequences because acne cannot only cause physical discomfort and disfigurement, indeed, it can be a source of dysphoria, depression, low academic performance, social isolation and avoidance of daily activity [13–15]. In addition, acne vulgaris can reach ages from 11 to 30, making it vital to understand the burden and psychological impact of it on quality of life [13–16].

Although acne is not a life threatening condition, it can be still compared to other chronic disabling diseases, such as back pain, epilepsy and asthma in regards to their significant negative impact on quality of life [14,15]. This impact can be detected through the utilization of a specific questionnaire for acne, such as Cardiff Acne Disability Index (CADI) questionnaire which includes several questions assessing factors like feeling of shame, frustration, aggression and self-perception problems [14,15]. A study conducted in Jakarta including subjects with an age range of 19 – 22 years old, found that different levels of psychological impact is associated with patients’ treatment-seeking behavior [15]. In UK, a study investigated the psychological sequelae of acne and assessed the participants help-seeking behaviors found a significant correlation between the severity of acne and CADI, moreover, the feeling of embarrassment and unsuitable schedules were observed as obstacles to help seeking among young adults [17]. In a systematic review carried out by Athena et al, found that myths and misconceptions regarding causes of acne do exist, and poor experience between the patient and health care provider with the latter not recognizing the magnitude of psychological impact of acne may lead to misperception and self-blame [18]. Furthermore, including the family members in the management and encouraging their support have shown a positive impact and did improve the experience and make it less uncomfortable [18].

3.2 Risk factors

It is a noteworthy fact that acne vulgaris is a multi-factorial skin disease. Many studies identified a few associated risk factors of acne, such as genetics, hormonal, and lifestyle factors including diet [19]. Various genes have been reported to be associated with the occurrence of acne signifying the contribution of genetic factors [20]. Moreover, in a review of the emerging evidence by Hazarika N, six gene loci, namely 11q13.1, 5q11.2, 11p11.2, 1q41, and 1q24.2 were found to be associated with severe acne cases [21]. Several genetic related factors including chromosomal abnormalities, human leukocyte antigen (HLA) phenotypes, polymorphism of human cytochrome P-450 1A1 and MUC1 were found to play a significant role in the pathogenesis of acne [[20]]. According to a study that compared acne history in first-degree relatives between patients affected with acne and non-acne controls, 36.1% of affected group had a positive history while 12.2% of control group had a positive family history [[20]]. Dietary glycemic index and glycemic load were observed to be inversely associated with adiponectin concentrations, which plays a role in proinflammatory cytokines inhibition and induction of anti-inflammatory cytokines [[21]]. Furthermore, hypoadiponectinemia associated with a high glycemic index diet may enhance the inflammatory response during acne vulgaris course [21]. Diet-induced hyperinsulinemia has been reported in recent studies to trigger the hormonal cascade, enhance tissue growth, and stimulate androgen synthesis [22]. As an example, cow milk contains anabolic androgen precursors of dihydrotestosterone [21]. Moreover, cow milk contains insulin-like growth factor 1 (IGF-1) and carbohydrates, which causes hyperglycemia and hyperinsulinemia [23]. Furthermore, hyperinsulinemia may promote acne by its well-established androgenic effect, consequently stimulates IGF-1 which induces acne via hyperkeratinization [22]. Therefore, insulin and IGF-1 stimulate the synthesis of androgens in ovarian and testicular tissues which contribute to the pathogenesis of acne vulgaris since androgens are essential in sebum production which is vital for the development of acne [22]. A recent published research found that positive familial history strongly correlates with acne presentation, severity, and scarring [24]. The aforementioned research reported that demographics i.e. gender and age, and lifestyle factors (increased computer/TV usage) may affect acne presentation, while diet (milk and butter consumption) could contribute to the severity and scarring level of acne [(24)].

3.3 Lifestyle modification impact on acne

Acne is a global skin condition concerning many people from different ages and gender [25,26]. Various factors have been suggested to have an impact on the development of acne including environmental factors, chemicals like skin products, hormonal factors, stress, and most recently diet and lifestyle modifications [19,26,27].

Overweight and obesity have been reported in some studies to demonstrate positive correlation with increasing risk of acne [28]. Another study showed a significant correlation between body mass index and the severity of acne in adolescents population [29]. Thus, it has been suggested that reduction of body wight should be taken into consideration when managing acne cases [29].

The relationship between diet and acne have been the question of literature in the last decades as many dermatology manuals have often recommended diet as a supplementary method for the treatment of various skin diseases [25]. It has been reported that high glycemic diet, dairy products, and greasy fatty foods are risk factors for acne [28].

Smoking on the other hand have been a controversial topic. Some studies reported significant correlation between acne and active smokers than non-active smokers. However, other studies showed that smoking was inversely associated with acne [28]. Therefore, further studies regarding the association between acne and smoking need to be conducted.

Other factors, such as inadequate and poor quality of sleep, psychological factors like stress, higher altitudes and lower temperature and humidity, sun exposure, and air pollution have been reported to aggravate acne [28].

Therefore, it can be concluded that lifestyle modifications, such as reducing body mass index, diet changes, increasing quality of sleep, and other factors may play a role in reducing the risk of acne and its severity.

3.4 Treatment

Pharmacological agents for acne can be classified according to their effects on the pathogenic factors: oral and topical retinoids, zelaic acid, salicylic acid, and hormonal therapies target the follicular hyperproliferation and abnormal desquamation. Oral isotretinoin and hormonal therapies decrease the sebum production. Benzoyl peroxide, topical and oral antibiotics, and azelaic acid affect the cutibacterium (formerly Propionibacterium) acnes proliferation. Oral isotretinoin, oral tetracyclines, topical retinoids, and azelaic acid work as anti-inflammatory Medications [30,31].

One of the most commonly used topical treatment in acne vulgaris is topical retinoids, Retinoids can be used solo or in combination with other topical/systemic drugs in order to treat more severe acne manifestations [32]. Moreover, it is usually combined with topical antibiotics to manage inflammatory form of acne. This class of anti-acne treatment has an effect on AV through prevention and control of comedones, and controlling the abnormal desquamation of follicular epithelium tissue [33]. A noteworthy side effect to mention is exacerbation of acne during the very first few weeks of using topical retinoids, thus it is vital to educate the patient about this probable adverse effect to enhance patient adherence [34]. This class is thought to be the first line of treatment for most acne types as indicated in a review conducted in 2003 [31]. Indeed, in a guidelines, developed by a team of experts in acne, retinoids class was listed among the first line treatment in all levels of severity of acne vulgaris with various combination according to the case presentation [30]. Numerous topical retinoids exist, for example, tretinoin, adapalene, and tazarotene. Tretinoin is being used in the treatment of acne vulgaris for a very long time, and adapalene is usually the first choice, among topical retinoids, a clinician would prescribe for their patients [30–32]. However, a newer option among topical retinoids class has been recently used that is tazarotene. It acts on the keratinocyte in the epithelium and may act as anti-inflammatory agent. Tazarotene is often used in case the first two options (tretinoin and adapalene) have failed to be effective

[32,35,36]. It is worth mentioning that certain adverse effects are reported and shown to be much severe in patients using tazarotene, such as irritation, scaling, dryness, erythema and burning [32,37].

Another available option that cannot be neglected is benzoyl peroxide. Benzoyl peroxide has an effect on comedones and acts as an antibacterial agent, too [37]. It can be used as a monotherapy, however combining it with topical antibiotics such as clindamycin makes it more potent against *P.acnes* species. It is very popular among patients suffering from acne vulgaris since it is affordable and an over the counter medication [30,32]. Benzoyl peroxide can be used in combination with other retinoids, but it may reduce the efficacy of some retinoids such as tretinoin [30,32]. Several side effects are associated with the use of benzoyl peroxide, for example dryness, erythema and burning [32,37].

Topical antibiotics are available for the treatment of mild to moderate acne. Multiple drugs have been used in the past, however, due to weakened effectiveness and the emerging of *P.acnes* resistance, only few antibiotics are still used. The currently prescribed antibiotics are clindamycin and erythromycin [31,32]. Nevertheless, recent studies found that erythromycin has a high resistance to *P.acnes* which makes it less effective in treating inflammatory acne as concluded in Fox L et al. review article [32]. Clindamycin is the most commonly used topical antibiotic in treating acne vulgaris nowadays. In general, it is recommended to be combined with retinoids or benzoyl peroxide to enhance effectiveness and prevent resistance, moreover, topical antibiotics should not be used for a long time period (12 weeks maximum) [30,38].

The aforementioned drugs are some of the most common topical treatment used for acne vulgaris. And these topical drugs are effective and preferred because they can be applied directly at the affected area of the patient's skin, which allows for high exposure of the pilosebaceous units of hair follicles to the treatment agents. However, multiple side effects are expressed by patients when using topical anti-acne drugs, some of which are skin irritation, erythema and dryness [32].

Systemic treatment options are available too. These options include oral antibiotics, hormonal therapy, and systemic retinoids. Tetracyclines are commonly used because of their effectiveness and affordability. However, the use of oral antibiotics in treating acne is unfavorable because they are used for a long time which precipitate into resistance and ineffectiveness of these antibiotics. Thus, when in need to use systemic antibiotics, it is recommended to use antibiotics in combination with retinoids or benzoyl peroxide [30,32,37]. Hormonal therapy can be used to treat acne in female patients. As shown previously in this article, sebaceous glands play a major role in the pathogenesis of acne vulgaris. In addition, they are androgen dependent, therefore hormonal therapy can be utilized in treating acne, usually in the form of contraceptive pills [39].

Systemic retinoids, oral isotretinoin in particular, are very effective and widely used drugs in acne. Isotretinoin, a synthetic vitamin A agent, is widely used as the treatment of choice for sever and recalcitrant nodular acne vulgaris [40,41]. Isotretinoin acts on the pathological factors and leads to reduction of the sebaceous gland size and ultimately inhibit the sebum production, which consequently results in changing the composition of skin surface lipid [41]. In the biggening isotretinoin were limited to patients with severe acne [42]. However, currently prescribing isotretinoin is recommended not only for severe acne cases but also for patients with acne that is associated with scarring, or for treatment-resistant cases which showed no improvement with the use of topical antimicrobial or oral antibiotics for a long period [43]. In fact, the literature shows that in patients with severe or refractory acne there was 60% to 95% improvement in the treatment of inflammatory lesions and prolonged

remission and healing after completing the course of isotretinoin for 3 to 4 months with a dose of 1 to 2 mg/kg/day [42]. On the other hand, there is a wide spectrum of mucocutaneous and systemic side effects that might limit the usage of isotretinoin. According to a review conducted by Ward A et al. regarding the pharmacological properties and therapeutic efficacy of isotretinoin, cheilitis was reported in 90% of patients and it was not dependent to the dose [42]. However, the aforementioned article found that most other side effects are dose dependent including dry mouth, pruritus, epistaxis, facial desquamation, and gastrointestinal disturbances. All these sides effects were reported in 20% to 30% of patients who were on a dose of 1 mg/kg/day [42]. Also, approximately 50% of the patients experienced conjunctivitis or eye dryness and itchiness that were associated with a higher dose. Nevertheless, these sides effect were not associated with treatment discontinuation [42]. One uncommon side effect that is usually necessitate the treatment discontinuation is hair loss 42]. With the use of isotretinoin for a long term, there were some reported sides effects associated with development and related to spinal and bone structure. In addition, some labs abnormalities occur usually with the use of isotretinoin such as elevation of serum triglyceride or abnormal liver function tests [42]. Numerous treatment options are available for patients suffering from acne vulgaris; however, the decision is based on the disease severity and patients' preferences.

4. CONCLUSION

Acne vulgaris is a prevalent health condition, which affects a wide range of age groups. The disease is usually neglected, though it has a huge psychological impact on patients resulting in low quality of life and less productivity. Various factors were associated with the progression of acne, such as family history, genetics, and diet. Thus, an individual should adhere to lifestyle modifications that may prevent acne. Of all available anti-acne drugs, topical treatment in general is preferred because of their effectiveness and less severe side effects.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

Abbreviations:

- AV: Acne vulgaris
- DHEA: Dehydroepiandrosterone
- CADI: Cardiff Acne Disability Index
- HLA: Human leukocyte antigen
- IGF-1: Insulin-like growth factor 1