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#### **Review Article**

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## A comprehensive Review on Buthūr Labaniyya (Acne vulgaris) with special references of Unani System of Medicine

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#### ABSTRACT

Buthūr Labaniyya (Acne vulgaris) is one of the oldest and commonest dermatological problem, which are known since antiquity and it has been called by different names in different parts of the world. It is a disorder of pilosebaceous unit which mainly affects the peripubertal population and clinically manifests as comedones (open/closed), papules, pustules, nodules, and cysts and heals with scars. As per Unani classics, Buthūr Labaniyya (Acne vulgaris) is termed as Muhāsā or Kīl characterised by small, white eruptions on the nose and cheeks, which resemble a condensed milk drop. Renowned Unani physicians Zakariyya Rāzī, Ibn Hubal, Ibn sīnā, Dā'ūd Antāki and Hakīm Akbar Arzānī have stated that, it is a dermatological disorder of adolescents that present as whitish eruptions over the face caused by  $M'\bar{a}dda$ Sadīdiya (Suppurative material) or preponderance of Ghalīz (filthy) M'ādda Balghamiyya. Acne vulgaris affected 681.2 million people worldwide in 2016. This was a 10% rise from 612 million in 2006. Acne ranks eighth on the list of the world's most common diseases (9.4%) in 2010, with a worldwide prevalence of 645 million. In Unani Medicine, Buthūr Labanivva (Acne vulgaris) is a well recognize disease entity and has been treated successfully since antiquity with various single and compound drugs having Jāli (Detergent), Muhalil (Resolvent) and Mujaffif (Desiccative), Musaffi-i Khūn advia properties. In this review, we tried to compile all the available information till date from both unani and other published scientific papers and textbooks which will fruitful for further research.

Keywords: Buthūr Labaniyya, Acne vulgaris, Unani, Management.

## **INTRODUCTION**

Skin is the largest organ enveloping the whole body and performing multiple functions, including temperature regulation, fluid balance, sensory perception, immune responses and protection ultra violet damage etc. Skin disease is one of the most common human illnesses. It pervades all cultures, occurs at all age and affecting 30-70% of individuals <sup>[1]</sup>. Acne is one of them which consistently represent the top eighth on the list of the world's most common diseases. 70% of the population has clinically significant acne at some stage between adolescence and early adulthood <sup>[2]</sup>. It is the most frequent disorder treated by dermatologists <sup>[3]</sup>. It is a pleomorphic skin disorder and can be noticed at any time during life. But most frequently, it presents among ages of 12-24 years which estimates 85% of population affected <sup>[4]</sup>. According to World health organisation, Acne is a skin condition that affects pilosebaceous units in face, chest, neck, and upper back. As per unani literature, Buthūr Labaniyya is derived from an Arabic word which is composed of two components, Buthūr that means Boil and Labaniyya means Milk<sup>[5, 6]</sup>. According to a great Unani physician Qarshī, it is a Mutā'ddi (infectious) disorder characterised by small white eruptions on the face, nose, and cheeks. When pressed, a cheesy stuff comes out <sup>[7]</sup>. Ibn Sīnā mentioned in Al-Qānūn that Buthūr Labaniyya (Acne vulgaris) is characterised by small white eruptions on the nose and cheeks that resemble condensed milk drops <sup>[8]</sup>. According to Masīhul Mulk, Hakīm Ajmal Khān, sometimes small, pointed, firm and bright red colour eruptions appear on face, neck, cheeks and nose. After maturity, they discharge  $k\overline{l}$  as well as some pus [8]

#### Synonyms

Arabic	Buthūr Labaniyya [9, 10, 11, 12]
Persian	Buthūr Dohniyya <sup>[13]</sup>
Urdu	Muhāse, Dāne Funsi <sup>[10, 13, 14]</sup>
Hindi	Kīl, Muhāse <sup>[13, 15]</sup>
English	Acne [16, 17, 18], Pimples [19]
Ayurveda	Yuvana Pidaka <sup>[20]</sup>

## HISTORICAL REVIEW

*Buthūr Labaniyya* (Acne vulgaris) is one of the oldest and commonest skin diseases which are known since antiquity and it has been called by different names in different parts of the world. The history of *Buthūr Labaniyya* is very old. Since ancient times, *Buthūr Labaniyya* has been also known as a serious skin disorder. It frequently affects young people, when they are most susceptible to any disfigurement. Acne has been known back to certain well-known ancient civilizations, including as the Greeks, Romans, and Egyptians.

#### Acne in Egypt History

In ancient Egypt, it is observed that pharaohs used to suffer with and had also made efforts to resolve it. It is recorded that several pharaohs were acne sufferers. The description of its treatment is present in *Ebers papyrus* with some animal origin preparations and honey <sup>[21]</sup>.

#### Acne in Greece History

From ancient Greece comes the word "acne" meaning 'point' or 'peak'. The Greek antiquity writings, the first Acne description had seemed in the Greek history writings of the physician *Aetius Amidenus*. From the historical background, The Great Greek scholars, *Aristotle* and *Hippocrates* were familiar with this disease and *Aristotle* explained it in detail <sup>[22]</sup>.

### Acne in Rome History

In ancient Rome, acne is treated with a simple mixture of Sulphur in the mineral baths as mentioned by *Aulus Cornelius Celsus* (25 BC-50 AD) in his extant medical work *De Medicina*. In the fourth century AD, Theodosius' court physician advised acne patients to clean their "pimples" with a cloth while seeing a falling star then Acne would 'fall from the body'. The term Acne *was coined by Aetius, a physician to Emperor Justinian. Galen was the first to propose that 'ionthoi'* might refer to more than one illness, and he proposed distinct preparations for the two categories of ionthoi based on the consistency of lesions <sup>[22]</sup>.

### Acne in Unani Medicine

Renowned Unani scholars have detailed a dermatological disorder called *Buthūr Labaniyya* in their illustrative literature, which is clinically similar to Acne vulgaris today.

In 770-850 AD Abu al-Hasan Ali ibn Sahl Rabba-al Țabarī described in his famous book 'Firdous al-Hikmah' (paradise of wisdom) a full explanation of sebaceous glands [23]. In 836-901 AD Al-Ṣābi' Thābit ibn Qurrah al-Harrānī has described various unani compound formulations for the treatment of funsī (small eruptions) over the face <sup>[24]</sup>. Abū Bakr Muhammad ibn Zakariyyā' al-Rāzi explained the treatment of Buthūr Labaniyya (Acne vulgaris) in his famous book Al-Hāwī (The Virtuous Life) [15]. In 980-1037 AD Abū 'Alī al-Husayn ibn 'Abdullāh Ibn-Sīnā (Avicenna) in his renowned book Al-Qānūn fi'l Tib (The Canon of Medicine) had explained the clinical presentation and etiopathogenesis of Buthūr Labaniyya (Acne vulgaris) [25]. Ibn Hubal (1122-1213 AD) explained in his famous book 'Kitāb al-Mukhtārāt fi'l tib' about the cause and clinical presentation of Buthūr Labaniyya [26]. Abu Al-Hassan 'Ali ibn 'Abd al-Aziza al-Jurjāni (12th century AD) in his renowned book Zakhīra Khawārizm Shāhī (Thesaurus of the Shāh of Khawārizm) has explained the etiology of skin eruptions [24]. In 1542-1599 Dau'd ibn *Umar al-Antāki* explained in his famous book '*Tadhkirah ūli al-Albāb*' about the humoral cause of *Buthūr Labaniyya*<sup>[27]</sup>. In 1772 AD, *Muhammad Akbar Arzāni* and in 1813-1902AD, *Mohammad Ā'zam Khān* had explained the clinical presentation of *Buthūr Labaniyya* in their famous book '*Tib-i Akbar'*, '*Mīzān al-Tib*' and *Aksīr-i Ā'zam*<sup>[22]</sup>.

#### Acne in the Elizabethan Era

The appearance of a woman was givn great attention during the Elizabethan era (1558-1603 AD). Women became accustomed with the use of layers of Venetian Ceruse, a thick white lead-based paint that created a great breeding ground for acne, because an excessively pale complexion was a symbol of the elite. A different form of mercury make-up was used for the treatment of *Buthūr Labaniyya* (Acne vulgaris)<sup>[22]</sup>.

*Riolanus and Johnston*, in 1638 and 1648, respectively, linked acne to menstrual problems. In a manner quite similar to modern psychosomatic beliefs on the subject, Johnston also related acne with heterosexual behaviour patterns. He also quoted that acne are different in size, little hard tumours on the skin of the face curdled up of a hard-thick fluid. They affect youngsters and are about the size of a hemp seed <sup>[28-31]</sup>.

According to the type of lesions, *William and Bateman* categorised acne into three types based on *'ionthoi or 'vari'* that are *simplex*, punctata, and indurate. These also clarified the key distinctions between acne rosacea and the other three kinds of acne. The first three categories were supposed to be local lesions that could be treated with topical medications, whereas acne rosacea was supposed to be an indication of liver or stomach disorders.

*Fuchs* coined the term "Acne vulgaris" in 1840 AD and classified acne into three types: Acne vulgaris, Acne mentagra, and Acne rosacea. *Erasmus Wilson* distinguished acne simplex (Acne vulgaris) from acne rosacea in 1842 <sup>[22]</sup>.

In the same year, Gustav Simon hypothesised that the disease predominantly affects hair follicles and was one of the first to identify the 'acarus' or 'Demodex folliculorum,' which he suggested could be an underlying cause. Gustav Simon proposed in the same year that the disease primarily affects hair follicles and was one of the first to find the 'acarus' or 'Demodex folliculorum,' which he considered might be an underlying cause. Around 1930, laxatives were widely used to cure pimples. Tetracyclines were initially recommended in 1950 after it had been discovered that acne was caused by bacteria. Tretinoin (Retin -A), a topical therapy for acne, began in the 1960. In 1975 Kligman and Plewig disagreed with the FDA's sulphur product recommendation. Isotretinoin, an innovative acne treatment that was first launched on America in 1980. It was discovered to be incredibly effective, but it also had serious adverse effects, including stroke, seizure, heart attack, and hair loss. Laser therapy was first used to treat acne in 1990, and it is now a widely used treatment because it removes both new and old scars caused by acne, as well as active lesions. Blue/red light therapies, as well as laser acne treatment, were introduced in the year 2000. Micro-needling with dermaroller emerged as a Nobel treatment modality for the treatment of acne scar. In 1995, Orentreich introduced subcision dermal needling for scars, and Fernandes created per-cutaneous collagen induction therapy with a dermaroller around 2006  $^{\left[ 22\right] }.$ 

A vaccination against inflammatory acne was successfully tested in mice in 2007. However, human testing is still required <sup>[22]</sup>.

#### **EPIDEMIOLOGY**

In 2016, 681.2 million people worldwide affected from *Buthūr Labaniyya* (Acne vulgaris). From 612 million in 2006, this was an increase of 10%. In 2010, acne ranked 8<sup>th</sup>in the list of most prevalent disease in the world, with a global prevalence of 645 million <sup>[32]</sup>. According to epidemiological data, acne is a common condition affecting 80% of young people (12-18years age group) and 5% of females and 1% of males in adulthood.

In a cross-sectional study, *Halvorson et al.* reported that suicidal thoughts and serious acne were three times more common in males than mild acne <sup>[33]</sup>. Acne was shown to be more frequent in high socioeconomic groups in a cross-sectional study from Saudi Arabia <sup>[34]</sup>. In the United States, about three billion dollars is wasted each year in direct and indirect treatment costs, as well as lost productivity <sup>[35]</sup>.

#### Etiopathogenesis

The main cause of *Buthūr Labaniyya* (Acne vulgaris), according to Unani physicians, is hyperactivity of the *Ghudud-i Dohniyya* (sebaceous glands), which leads to increased production of oily substance (sebum). The apertures of these glands become blocked with greasy substances. These glands become inflamed and packed with *Mādda-i Sadīdiyya* as a result of this (Pus). Due to increased *Ifrāt-ī Harārat* (abnormal heat), the *Mādda-i Sadīdiyya* (pus) penetrates the skin and is difficult to remove. *Mādda-i Sadīdiyya*, in other words, is caused by *Bukhārāt-i Badan* and then moves towards the skin. The yellow acne liquid is made up of body vapours (*Bukhārāt-i Badan*) that have accumulated in the skin, and its light ingredients (*Raqīq M'ādda*) are transformed into a dense fluid owing to the effect of air, and these thick materials are difficult to resolve, resulting in clogged pores <sup>[32, 33, 37, 38]</sup>.

#### Asbāb-i-Mard (Causes of Disease)

- Blockage of the sebaceous gland which produces fat <sup>[36, 40]</sup>
- Young age <sup>[36]</sup>
- Increased secretion of male sex hormone after puberty (Testosterone)<sup>[41]</sup>
- Propioni bacterium acnes<sup>[9]</sup>
- Indigestion <sup>[42]</sup>
- *Qillat-i Dam* (anaemia)<sup>[41]</sup>
- Fasād-i Dam (Impurities of blood) <sup>[35, 42]</sup>
- Hārr food items like Kabāb etc <sup>[42]</sup>
- *Qābḍ* (Constipation) <sup>[9]</sup>
- *Shiddat-i Harārat* (extreme hotness) <sup>[41]</sup>
- Stoppage of *Khūn-i Bawāsīr* (hemorrhoidal blood) <sup>[9, 36]</sup>
- Irregular menses <sup>[9, 42]</sup>
- Pregnancy <sup>[42]</sup>
- Ehtebās-i Tams (amenorrhea) <sup>[43]</sup>
- Thaqīl-wa raddī food items <sup>[36]</sup>
- Sharāb (alcohol)<sup>[42]</sup>
- More exposure to sunlight <sup>[36]</sup>
- Zardāb-i Mādda (yellow watery matter)
- Emotional stress <sup>[43]</sup>
- Imtilā-i khūn (accumulation of excess blood) Wa-ḥiddāt-i-Dam (hotness of blood) <sup>[43]</sup>
- Hereditary <sup>[41]</sup>
- Air pollution <sup>[41]</sup>
- Use of oil-based soap and cream<sup>[41]</sup>
- Excessive humidity in environment <sup>[43]</sup>

 Maghziyāt like peanut (Arachis hypogaea), Pista (Pistacia vera), Chilghoza (Pinus gerardiana), oily and sweet food items <sup>[44]</sup>

Exogenous and endogenous variables play a role in developing acne vulgaris. Acne is caused by four basic pathogenic factors that interact in a complicated way to form lesions <sup>[45]</sup>.

- Increased production of sebum [seborrhea] and hyperplasia of the sebaceous glands.
- ✤ Alteration in the keratinization of skin
- Follicular colonization
- Release of inflammatory mediators into the skin

Other contributing factors include hormonal influences from androgens and estrogens, such as DHEAS [de-hydroepiandrosterone sulfate], which increases sebum production in pre-teenagers, leading to acne <sup>[46-48]</sup>.

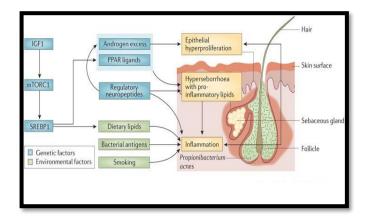


Figure 1: Etiopathogenesis of Acne

#### **Risk factors**

Age: People of any age group can get acne but common in teenagers.

**Hormonal changes**: Hormonal changes play an essential role in pathogenesis. The main influence of androgen on acne is the proliferation of sebocytes and infra infundibular keratinocytes <sup>[49]</sup>.

#### **Genetic factors**

Acne prevalence is influenced by a number of factors, one of which is genetic. A substantial family predisposition for acne has been shown in several researches from France, China, and the United Kingdom. A positive family history of acne increases the likelihood of acne by about 2.3 percent to 4.69 percent <sup>[50-51]</sup>.

**Diet:** Food products which contain 5 alpha-reduced steroid hormones and other steroid precursors of DHT drive sebaceous gland function. Milk direct increases the IGF-1 level and these levels during the teenagers closely parallel to acne activity <sup>[49]</sup>. High glycemic load diet worsening the acne.30% dietary fiber per day and a low-fat diet are reported to decrease the acne instances <sup>[50]</sup>.

**Socioeconomic factors:** A cross-sectional study of healthy adolescents of Arequipa and Peru, reported the low prevalence of acne. In another study on 9955 school children age 6-16years in a rural region in Brazil, only 2.7% were found to suffer Acne vulgaris <sup>[50, 52]</sup>.

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**Smoking:** It is reported that smoking is one of the modifiable risk factors that alter the risk of acne. Schafer et.al observed a significant dose-dependent relationship between acne and cigarette consumption [53].

#### **Sweating and Exercise**

Short term effect of exercise-induced acne is noticed [54].

#### **Other factors**

External factors occasionally contribute to acne, like stress, mechanical trauma, cosmetics, some tropical and oral medications (corticosteroid, iodine, anti-epileptics) <sup>[53, 54]</sup>.

#### **Clinical Presentation**

Renowned Unani physicians quoted that this disorder is common in adolescents, predominantly in males <sup>[6, 55]</sup>. This skin condition is evident with the presence of eruptions resembling to milk drops over the face, forehead, nose, and arms. It may also associated with *Ihtibās-i Tams*(amenorrhea) <sup>[15, 25, 26]</sup>.

The lesions of acne are polymorphic consisting of comedones, papules, pustules, nodules, cysts, and scars. Post-inflammatory pigmentation and pyogenic granulomas may also occur <sup>[56-8]</sup>.

- 1. Non-inflammatory lesion or Obstructive lesion: Whitehead [Closed comedones] and Blackhead (Open comedones)
- 2. Inflammatory lesion: Papules, Pustule, Cysts, Scars

**Microcomedone:** Microcomedones is the primary lesion of acne. The exact trigger is unknown, but a certain fraction of the sebum, like squalene and linoleic acid, playsa very important role <sup>[59-61]</sup>.

**I. Obstructive or Non-inflammatory lesions (Comedones):** Acne comes in the form of comedones that appear 1 to 2 years before puberty.

## a. Closed comedones

The Whitehead (closed comedones) characterized a pilosebaceous duct distended with thickened ductal material and it is generally 0.1-3.0 mm in diameter <sup>[62]</sup>. It does not covered by the epidermis and takes approximately five months to reach this degree of maturity <sup>[63]</sup>. Twenty-five percent resolve within 3-4 days and 75 % develop into inflamed lesions <sup>[62]</sup>.

#### b. Open comedones

Blackheads (Open comedones) is one that protrudes from the follicle and not covered by the epidermis <sup>[64]</sup>. The start of the blackhead is

marked by the enlargement of the orifice by a projecting mass of darkly coloured horny substance with a diameter of 5 mm, occasionally even more <sup>[63]</sup>. The epithelial sac has an enlarged aperture and is filled with keratin and lipids. There are a large number of enzymatically active melanocytes. Whiteheads and blackheads have various colors because of this <sup>[65]</sup>.

#### **II. Inflammatory lesions**

**a. Pustule:** These are lesions having a visible purulent center <sup>[66]</sup>. Pustules usually begin as solid lesions (papules) which soon liquefy and represent a partial break down of the comedones. The pustule's roof usually breaks, enabling pus to escape. The comedo's beaten fragments are then expelled, and healing takes place in a manner that is extremely similar to the typical wound healing <sup>[63]</sup>.

**b. Papule:** The comedo collapses, resulting in a deep-seated, long-lasting papule that can be considered as tiny nodules (diameter < 5 mm). Papules present superficially may resolve in 5-10 days, leaving a small scar and causing post-inflammatory hyperpigmentation. Deep papules usually have more intense, takes more time to resolve and my form scar<sup>[63]</sup>.

**c. Nodule:** The nodule represents the total disintegration of a comedo with far-flung consequence. Two or more adjacent comedones often break down and fuse to create these dreadful lesions <sup>[63, 67]</sup>.

**d. Cyst:** Acne cysts, also known as big secondary comedones, are the result of repeated punctures and re-encapsulation. Cysts can be found all over acne's region, but they're most prevalent on the trunk. They are soft and fluctuant, slowly enlarge over time. The epithelial wall becomes quite thin and can easily rupture by trauma. Ruptured cysts leave abscesses in their walls which never disappear spontaneously and heaving two results that are, rupture with abscess formation, a bad scar formation, or surgical removal of the cyst wall <sup>[63, 68]</sup>.

**III. Scars:** Acne scars are the second most common symptom after comedones. The most severe effect is permanent scarring <sup>[69, 70]</sup>.



Figure 2: Different types of Acne vulgaris lesions

#### Table 1: Acne Grading severity [71]

Grade	Severity	Clinical findings
1	Mild	Comedones (blackheads or whiteheads) that are open and closed, with a few inflammatory papules and pustules. The blockage of the pilosebaceous orifice by sebum on the skin surface causes open comedones. Keratin and sebum block the pilosebaceous orifice beneath the skin surface, resulting in closed comedones. The more oil that accumulates and more probable bacteria will grow, leading in inflammatory acne. If an individual only has a few or little pimples, they are considered to have "mild acne."
2	Moderate	Small papules with erythema indicate inflammatory lesions. Inflamed pimples are known as "papules" (little bumps) or "pustules" (filled with yellow pus).
	Moderately	On the chest and back, there are numerous papules and pustules, as well as a few inflammatory
	Severe	nodules.
4	Severe	People with severe acne have quite a lot of papules and pustules on their skin, as well as nodules. These nodules are often reddish in colour, painful and scarring may be occur.

#### **Psychological Impact of Acne**

In addition to acne, Acne scarring is linked to low selfesteem, unhappiness, nervousness,

impaired interpersonal interactions, changes in physical view, embarra ssment, irritability, poor

academic achievement, and unemployed, among other things [72] Acne's psychological impacts significantly affect more females than males, according to research [73]. The facial look plays an important role in how we perceive ourselves, during interaction with someone and also affect on a woman's quality of life <sup>[74]</sup>. The psychological effects of acne are commonly important and are mostly underestimated. Anxiety, stress, especially sleep quality in professional and personal life, correlates with susceptibility and severity of disease [75]. In 6-7 percent of acne patients, suicidal thoughts were reported. Social instability, such as reduction of social interactions with colleagues and the opposite gender, has also been documented as a psychiatric problem. Acne may negatively affect intention to play sports [76]. Psychiatric symptoms like somnolence, obsessions, sensitivities, hostility, paranoid thoughts, and psychosis have also been related with acne [77].

#### Diagnosis

Diagnosis of Acne vulgaris (*Buthūr Labaniyya*) is based on history and physical examination. Lesions commonly found in the areas with the greatest concentration of sebaceous glands that include the face, neck, upper arms, and back.

#### Method for assessment of acne severity

The assessment of acne is a challenge for the dermatologist. Grading of acne is useful for recording severity, prognosis and for treatment decisions <sup>[78]</sup>.

The grading system of acne came into being in the 1950s when there was an increase in therapies for its management. A systemic review on Acne vulgaris revealed 25 different methods of assessing the severity and more than 19 methods of counting lesions <sup>[79]</sup>.

#### Grading Systems: Several grading scales are

**1**. A classification scheme for primary Acne vulgaris in 1990 was developed by The American Academy of Dermatology. This grading scale described three levels of acne, mild, moderate and severe <sup>[80]</sup>.

#### 2. Cook system

Assessing the overall severity of the acne on a 0 to 8 scale fixed to photographic standards <sup>[81]</sup>.

## 3. Leeds system

This system comprises counting and categorizing lesions into inflammatory and Non-inflammatory. The scale extends from 0 (no acne) to 10 (the most severe acne) <sup>[82]</sup>.

#### 4. Cunliffe pictorial method

This grading scale assesses facial acne along with other areas affected on the trunk. The severity of acne is graded into mild, moderate, moderately severe and severe acne <sup>[83]</sup>.

#### 5. Marquis et al grading

This system grades acne into four groups- I, II, III and IV grades [84].

#### 6. The global acne severity scale (GAGS)

Local score is given to each location. This is finally added to given a global score. The merits of this system are accuracy, reproducibility, and elimination of lesion counting <sup>[85]</sup>.

#### Investigations

- In most cases of acne, No investigation required.
- Some women may be advised to have blood tests to measure hormone levels.
- The possibility of pregnancy, which would influence treatment, as appropriate.

Signs suggesting high levels of male sex hormone, Excessive prolactin, Cushing's syndrome.

These hormone tests are best taken between 8:00 to 10:00 Am during the first half of the menstrual cycle. They include: Testosterone, Sex hormone-binding globulin (SHBG), Free androgen index (FAI), Dehydro epiandro steronesulfate (DHEAS), 17-hydroxy progesterone, Synacthen test of adrenal stimulation by an adreno-corticotrophic hormone (ACTH), Luteinizing hormone (LH) and follicular stimulating hormone (FSH), Prolactin, Cortisol, Dexamethasone suppression test. A pelvic ultrasound scan is usually very good at excluding ovarian cysts and tumours on the ovary and adrenal gland.

Table 2: Laboratory investigations in patients with suspected hormonal acne<sup>[72]</sup>

Testosterone	Minimal to moderate rises of <200 ng/dL are indicative of adrenal or benign ovarian aetiology, whereas values beyond this level should be suspicious of adrenal or ovarian malignancy.
Androstenedione	Early morning samples are the ideal to test since it is secreted equally by the ovaries and adrenals and follows a circadian pattern.
Dehydroepiandrosterone (DHEA)	DHEA levels >8,000 ng/dL and DHEAS levels >4,000–8,000 ng/dL suggest benign adrenal hyperplasia, whereas DHEAS values 4,000–8,000 ng/dL suggest adrenal tumours.
Sex hormone bining globulin (SHBG)	Reduced SHBG levels result in an increase of free unbound testosterone, resulting in more visible signs.
Prolactin	High Prolactin levels may indicate hypothalamic or pituitary reasons for further assessment and analysis.
Luteinizing hormone (LH)	LH: FSH ratio >2 is may suggested to PCOS.
17-Hydroxy progesterone	Due to a deficit or lack of 21-hydroxylase, level of 17-Hydroxy progesterone are elevated that is >200 ng/dl in congenital adrenal / non-classic congenital adrenal hyperplasia.
Serum cortisol	High levels are an indication of adrenal tumour
Fasting and Post prandial (PP) Insulin	Insulin levels should be tested in obese and overweight patients.

#### Management of Buthūr Labaniyya in Unani medicine

#### Usūl-ī Ilāj

- Treatment of the main cause of disease <sup>[36]</sup>.
- Tanqiya-i Badan wa Dimāgh (evacuation of body and brain) followed by Itfā'-ī Dam (To modulate the heat of sanguine) <sup>[55, 86–88]</sup>
- *Tanqiya* of *Balgham* from body <sup>[40]</sup>
- Systemic therapy by *Musaffi-i Khūn* advia<sup>[55]</sup>
- Tajliya [topical cleansing] by jāli advia (Detergent drug) <sup>[55]</sup>
- TahlīlwaTajfīf (Resolution and Desiccation) <sup>[55, 86]</sup> stand treatment
- Correct menstrual abnormalities <sup>[89]</sup>
- Işlāḥ-i Hadm (Correction of digestion) <sup>[40]</sup>

## 'Ilaj [Treatment]

It comprises of '*Ilaj bi'l Tadbir* (Regimenal Therapy), '*Ilaj bi'l Ghidha*' (Dieto-therapy), '*Ilaj bi'l Dawa*' (Pharmacotherapy)

## 'Ilaj bi'l Ghidha' (Dieto-therapy)

- Use of easily digestible foods like soups and chapatti.
- Use of vegetables which heaving cold properties.
- Use only *Ghidha'-i Sāda* (simple food items) like *Turai* (ridge gourd), *Kaddu* (pumkin), *Palak* (spinach), *Shalgham* (urnip), *Mū* ng (green gram), *Arhar* (split red gram), mutton, etc. <sup>[8]</sup>
- Regular intake of fruits i.e. oranges, pomegranates, apples and pears.
- Avoid *Raddi* (waste), *Fasid* (Putrified) and *badi* (flatulent) *agdhiya* like *mash* dāl (black gram), *matar* (pea), gobhi (cauliflower)
- Avoid to *sharāb* (Alcohal) intake <sup>[36]</sup>.

## 'Ilaj bi'l Tadbir (Regimenal Therapy)

## Tanqiya-ī Badan wa Dimāgh

Unani scholar recommended *tanqiya* of the whole body by *Fas'd* and *Ishāl. Fas'd* <sup>[36]</sup> of *Sarar'o* (*Qīfāl*) and vessels of the nose. *Ishāl* (purgation) by oral intake of *Aftimūn*, *Habb-ī Quqāyā* or *Habb-ī Sibr*, or *Habb-i Ayārij* <sup>[55, 86, 88]</sup>.

### 'Ilaj bi'l Dawa' (Pharmacotherapy)

#### Mussaffī-i Dam Advia:

#### Some single drugs are:

- Shahtra (*Fumaria parviflora*) <sup>[89]</sup>
- Mundi (Sphaeranthus indicus) <sup>[89]</sup>
- Siras (*Albizia lebbeck* L. benth) <sup>[89-92]</sup>.
- Neem (Azadirachta Indica) <sup>[93]</sup>.

#### Some compound:

- Joshanda for Mussafi-i <u>Khūn</u> advia as: Shahitra 4 g, Chraita 4 g, Sarfhooka 4 g, Gul-i Mundi 4 g, Unnab 5 adad.
- Majūn Ushba 12 g at bed time <sup>[36]</sup>
- Qurs-i Mavīzi 2 tab in morning and Mugarabi 2 tab in evening with water <sup>[36]</sup>
- Qurș-i Mușaffi (500 mg) 2 tab thrice a day
- 'Itrīfal shāhtara 7 g twice a day <sup>[94–96]</sup>.
- Majūn Mundi 5 g twice a day <sup>[95, 97]</sup>.
- Majūn chobchīnī 5 g twice a day <sup>[95, 97]</sup>.

#### **Topical therapy**

Many preparations are suggested for relieving lesions of *Busūr* Labaniyya some of them are:

### Ubtan

Local application of paste prepared with *Magz-i Ghongchī* (kernel of *Abrus precatorius* Linn) mixed with *Roghan-i kunjad* on affected part overnight and wash in next morning <sup>[55]</sup>.

- Local application of paste prepared with Salīkha (Cinnamomum cassia Blume) mixed with Honey <sup>[86]</sup>.
- Local application of paste prepared with Kaf-ī Dariya and Zarnabad mixed with water <sup>[86]</sup>.
- Local application of paste prepared with Sīrkhām (garlic cloves) mixed with Honey and Vinegar<sup>[55]</sup>.
- Local application of paste prepared by *Murdār Sang* (litharge) mixed with Vinegar <sup>[86]</sup>.
- Local application of paste prepared with the powder of khūbkalān (Sisymbrio irio Zinn), Sandal Safaid (Santalum album Linn.) and Sandal Surkh (Pterocarpus santalinus Linn.) mixed with rose water <sup>[86]</sup>.
- Local application of paste prepared with powder of *Post-i* Darakht-i Saras (bark of Albizia lebbeck L. Benth) and Kunjad Siyah (seed of Sesamu mindicum L.), mixed with Vinegar <sup>[98]</sup>.

#### **Dimād**

- Irsa, Gungchi safaid, Barg-ī Neem, Post-ī Saras and Namak-ī Sāmbhar in equal proportion [99].
- ✤ Salīkha along with Shahed (Honey)<sup>[55]</sup>.
- ✤ Karsanah admixed Shahed (Honey)<sup>[55]</sup>.
- Shunīz, Bū'raq, Naushādar along with Sirka<sup>[55]</sup>.

## Tila

- Tila-i Muhasa
- Tila-i Akbar
- Fine powder of Zubdat al-Bah'r (kafe-i Dariya) 1part, Badam talkh 2 part <sup>[100]</sup>.
- ✤ Barg-ī Neem, Beikh-ī Sosan, and Post-ī Saras<sup>[55]</sup>.

#### **Other formulations**

- Bura'h Armani 7 g, Gīl-i Makhtūm 3.5 g, Kafūr 250 mg, Zāfrān 2.7 g along with Rose water (Ārq Gulāb) and vinegar (sirka)<sup>[55]</sup>.
- Paste formed from 1 part Arad Turmus, 1 part Arad Bāqla, and 1 part Arad 'Adas 1/2 of the paste is applied to the face for the entire night and cleaned off the next morning <sup>[55]</sup>.

#### Aqrās/ Tablets

Kaf-ī Dariya 36 g, Tukm-i Turb 36g, Zarawand mudharaj 36 g, Afsanteen 6g, Beikh-ī Sosan 6 g are powdered and made it into tablets. The tablets, mixed with a small amount of water, are placed to the lesions<sup>[55]</sup>.

#### Lat'ūkh

- ✤ Anjīr and Shunīz along with Sirka <sup>[25]</sup>.
- ★ *Khurbak* 1part, *Irsa* 1/2 part with *roghan-i Gul* <sup>[26, 101]</sup>.

Tiryaq muhasa <sup>[102]</sup>, Dawae bassor labani <sup>[103]</sup>, Dimad majali, Dawa-i Muhasa, Dawa-i chuhara, Ubtan ajeeb <sup>[104]</sup>.

## Management of Acne vulgaris (*Buthūr Labaniyya*) in Conventional Medicine

- Non-drug measures or General measures
- Drugs-Topical therapy, Systemic therapy and Combination of both
- Physical measures

#### General/Non-drug measures: [47]

- Reassurance is a great way to relieve stress.
- Patient counselling about the nature of the disease, therapeutic approaches, and expected results
- Suggestions to stop irritating lesions.
- Examine the endocrine system and look for signs of premenstrual syndrome.
- Advise the patient that Acne-causing medicines, oils, emollients, and excessive makeup should be avoided.
- Advise balanced diet and avoid hyperglycaemic diet.
- Face cleaning with soap and water on a routine basis.

## Specific measures [105]

The main concepts of treating acne sufferers using four different tactics can be coupled depending on the clinical situation.

- Reducing sebum gland secretion.
- Fixing duct hyper-cornification.
- Lowering the number of P. acne and its accompanying microorganisms.
- Having an anti-inflammatory effect. Remember that "one treatment does not fit all."

#### **Topical therapy**

A wide range of topical treatments are being used for the anticomedogenic and anti-antibacterial effects.

Topical Retinoids: <sup>[106]</sup> There are numerous topical retinoid formulations available <sup>[107]</sup>

- Tretinoin: 0.025 percent gel/cream, 0.05 percent gel/cream, 0.1 percent gel/cream
- Isotretinoin gel, 0.05 percent
- Adapalene: 0.03 percent gel and 0.1 percent gel
- Tazarotene: 0.1 and 0.05 percent gel <sup>[107, 108]</sup>.

Reconstruction of damaged keratinization, increased cell cycle, and control of prostaglandin synthesis are among the mechanisms of action. Topical retinoids diminish the amount of precursor lesions and their production, as well as mature comedones and inflammatory lesions. The predominant side effect of these medications is primary irritant dermatitis, which can manifest as erythema, scaling, and burning sensations and varies depending on skin type, sensitivity, and composition <sup>[109]</sup>.

#### • Benzoyl Peroxide

It is as effective as topical retinoids and comes in a range of strengths from 2.5 to 10% in gel, cream, or lotion form. It is an antibacterial

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agent with a broad spectrum of activity that works by oxidising bacteria. Anti-inflammatory, keratolytic, and comedolytic properties are all present in it. It is meant for acne that is mild to moderate. Severe drying, irritability, allergic skin reactions, and whitening are the most common adverse effect <sup>[110]</sup>.

#### • Topical antibiotics

Inflammatory acne is managed with these. The most frequent external used antibiotics are erythromycin and clindamycin <sup>[110]</sup>, that are taken in a single formulation either alone or in combination with benzoyl peroxide or adapalene. Adverse reactions include erythema, peeling, itching, dryness, burning, and resistance development.

Other local applicants are given below

- Azelaic acid is a lotion that contains 10-20% azelaic acid and is used to treat inflammatory and comedonal acne <sup>[111-2]</sup>.
- Salicylic acid is a comedolytic medication, although it isn't as efficacious as topical retinoids <sup>[113]</sup>.
- Lactic acid has been reported to be effective in decreasing acne lesions <sup>[114]</sup>.
- Oil of tea tree
- 10 percent gel of Picolinic acid<sup>[115]</sup>
- 5 percent gel of Dapsone gel <sup>[116]</sup>

#### Systemic therapy

Tetracycline <sup>[117]</sup>, Doxycycline, Minocycline, Lymecycline, Sulpha drugs, Cotrimoxazole (80 trimethoprim + 400 sulphamethoxazole), Dapsone day, Macrolides <sup>[118]</sup>, Erythromycin <sup>[119]</sup>, Hormonal therapy <sup>[120]</sup>, Oestrogen 30µg along with progesterone, Anti-androgenic therapy: like Acetate Spirono-lactones daily, Corticosteroids like Prednisolone daily <sup>[121]</sup>, Oral zinc 200 milligram daily, Oral retinoids like isotretinoin 0.1/ kg daily <sup>[122]</sup>.

#### Phototherapy

The presence of porphyrins in p-acne contributes to UV radiation's efficacy in acne <sup>[123]</sup>. Comedones, papules, and pustules are drastically decreased after chemical exfoliation with 10-50 percent glycolic acid or 10-30 percent salicylic acid. Acne scars and cystic lesions require frequent glycolic acid exfoliation <sup>[124]</sup>.

## CONCLUSION

Skin diseases also have a substantial, financial and psychological burden for the patients and their families. Acne is a common condition affecting 80% of young people (12-18years age group). The global burden of acne is estimated to be 9.4% and it has been ranked as 8th most prevalent disease all over the world. Approximately 85% of young adults between the ages of 12 and 25 years, 8% of adults between the ages of 25 and 34 years, and 3% of people between the ages of 35 and 44 years have acne to some extent. Acne is a common inflammatory dermatosis that is frequently linked to significant psychological morbidity. Renowed Unani physicians have explained a skin disease Buthūr Labaniyya in their famous texts which is clinical resemblance to present-day Acne vulgaris and this skin condition is evident with the presence of eruptions resembling to milk drops over the face, forehead, nose, and arms. Despite of numerous successful therapies are available currently in modern system of medicine but several patient struggles to respond adequately and experience adverse effects that result raises the demand and uses of alternative medicine like Unani, Ayurveda, Yoga, Siddha and Homeopathic system of medicine with their popularity and wide acceptability. Unani system of medicine contains successful and safe treatment of Acne vulgaris. So, there is need to explore and clinical studies should be conducted on the line of mentioned Unani treatment to substantiate their efficacy in prevention and control of *Buthūr Labaniyya* (Acne vulgaris).

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