A Systemic Review on Acne and Post Acne Hyperpigmentation

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Abstract— This article provides a comprehensive review of acne, a common skin condition affecting both adolescents and adults, and post-acne hyperpigmentation (PIH). Acne, characterized by various lesions such as comedones, papules, and nodules, is primarily influenced by factors like increased androgen production, excess oil secretion, bacterial activity, and inflammation. The condition has psychological impacts, and its prevalence is particularly high among teenagers. Post-acne hyperpigmentation refers to skin discoloration that develops following inflammation or injury, with acne being a leading cause. Hyperpigmentation issues, including age spots and melasma, result from excess melanin production and accumulation. The article emphasizes the aesthetic impact of hyperpigmentation on individuals of all skin types and ethnicities. The management of acne involves a range of treatments, including benzoyl peroxide, antibiotics, salicylic acid, hormonal therapies, and alternative medicines. The article highlights the effectiveness of these treatments in addressing various aspects of acne, such as inflammation, bacterial activity, and sebum production. Additionally, it emphasizes the significance of minimizing side effects and enhancing efficacy through fixed dose combinations. In addressing post-acne hyperpigmentation, the article explores the etiology, epidemiology, and pathophysiology of PIH.

Various modalities, including topical therapies, chemical peels, and laser therapy, are discussed as part of the management strategy. Herbal plants such as rose, thyme, walnut leaf, mulberry, ginseng, and aloe are also examined for their potential in treating both acne and PIH.

***Index Terms*— hyperpigmentation, Inflammation acne, Hyper proliferation of propionic bacterium acnes.**

1. Introduction

Acne vulgaris, commonly referred to as acne, is a skin disease that affects people and is characterized by scaly red skin (seborrhea), comedones, blackheads, whiteheads, pinhead-sized papules (nodules), pimples, and scarring. Acne affects skin having dense sebaceous follicles in areas including face, chest and back.

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Acne may be of inflammatory or non-inflammatory forms. In the western world,80-90% of teenagers experience acne during adolescence, in rural societies, the prevalence is reportedly lower. Usually during puberty in both males and females, an increase in androgens like testosterone is the cause of acne. As people age, acne tends to lessen and eventually go away.1 According to statistics, 85% of young adults in the world between the ages of 12 and 25, 8% of adults between the ages of 25 and 34, and 3% of adults between the ages of 35 and 44 suffer from some form of acne. In their twenties, 50.9% of women and 42.5% of men, on average, still have the illness. According to recent research, 30% of women may experience acne for the duration of their fertile period.[2]

Hyperpigmentation, or the appearance of darkened patches or spots on the skin, is one of the aesthetic issues that affect people, both male and female. This is most likely caused by an excess of melanin pigments accumulating or by a greater number of melanocytes expressing melanin synthesis in the skin layers. Hyperpigmentation issues include freckles, age spots, solar lentigo, post-inflammatory hyperpigmentation, and melasma. Skin pigment known as melanin is responsible for the color of the skin, hair, and eyes.[3] The term "post-inflammatory hyperpigmentation" (PIH) refers to a reactive, acquired cutaneous hypermelanosis that develops following prior inflammation or injury. One of the most prevalent inflammatory skin conditions, acne causes hyperpigmentation in the dermis, epidermis, or both, which can lead to PIH.[4]

2. ACNE

The most common Pilosebaceous unit skin condition, acne vulgaris, affects the face, back, and trunk, which are the regions with the biggest oil glands, Seborrhea, comedones, inflammatory lesions, Propionibacterium acnes, Staphylococcus epidermidis, and Malassezia furfur bacteria in the follicular canal, as well as sebum production, are the common characteristics5. Acne is a skin condition that only happens when certain conditions are met by the sebaceous glands (SGs). There is no gender preference for this disease; however, the course of the illness is more severe in men[6]

The term acne is obtained from Greek language “acme” which means prime of life. Acne is not a serious type of disease but it impacts the life quality of the patient. This is benign condition can cause severe psychological problems. It can show

its symptoms and come out in any stage of life but mostly it affects at age 12-24, the estimated population is around 85%. There are number of drugs available for the treatment of lesions, and its scar, but having some side effects. To reduce the side effects & to enhance the efficacy some fixed dose combinations are use[7].

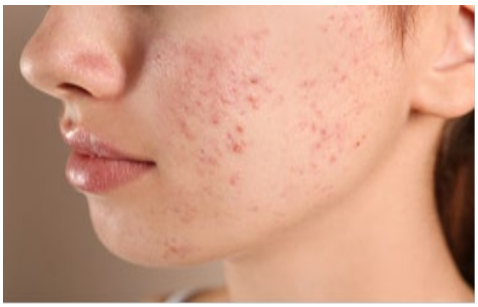

Fig.1. Acne

A. Classification

One of the most common diseases in India is acne vulgaris. According to Indian custom, acne vulgaris is rated using a straightforward system that divides the condition into the four categories shown in the table[8].

Mild (Grade 1)	The mildest type of acne, which can be treated with over-the-counter products, manifests as blackheads or whiteheads, medius, and small pimples without inflammation.
Moderate (Grade 2)	There are more blackheads and whiteheads on this. Papules and pustules are common skin lesions. OTC medications are another option for treating Grade II.
Severe (Grade 3)	Widespread papules and pustules characterize this moderate to severe case of acne. Redness and inflammation are characteristics of grade III acne.
Very severe (Grade 4)	Another name for this is cystic acne. This is the acne category that is the worst. Numerous pustules, nodules, cysts, blackheads, and whiteheads will all be visible on the skin. In addition to the face, other body parts are also affected by the inflammation and breakouts.

B. Sign and Symptoms of Acne

There are different-different sign and symptoms of acne, such as:

- Formation of whiteheads (closed plugged pores)
- Formation of blackheads (open plugged pores)
- Pimples(papules)
- Pustules (pimples with pus at their tips)
- Nodules (solid painful lumps beneath the surface of the skin)
- Cysts (painful pus-filled lumps beneath the surface of the skin)9.

C. Etiology

Follicle blockage, hyperkeratinization, keratin plug formation, and sebum (microcomedo) all contribute to the development of acne. Increased androgen production causes the sebaceous glands to enlarge and produces more sebum. The microcomedo may enlarge to form an open comedo (blackhead) or closed comedo. Comedones are caused by sebum, naturally occurring oil, and dead skin cells clogging sebaceous glands. Inflammation and inflammatory lesions, such as infected pustules, nodules, and papules in the dermis surrounding the microcomedo or comedone, can be brought on by the naturally occurring commensal bacteria Propionibacterium acnes, which can cause redness, scarring, or hyperpigmentation.[10]

D. Pathophysiology of acne

There are a number of causal factors that are thought to be important in the traditional aetiology of acne vulgaris. As was previously mentioned, increased rates of sebum excretion, endocrinological factors like androgens, abnormal keratinization of the follicular infundibulum, the growth of bacterial infections, and the inflammation that results are the causes of chronic acne skin diseases.

Increase in sebum production: One of the main reasons acne forms is an increase in sebum production in the hair follicles. Gollnick and colleagues have reported that the production and secretion of sebum are enhanced by androgen hormones, particularly testosterone and Insulin Growth Hormone (IGH-1). Increased sebum production is clearly correlated with the frequency and severity of acne lesions; therefore, it is an important factor to take into consideration in patients with acne vulgaris[11].

Hyperkeratinization abnormalities of the pilosebaceous folicles: Single-cell keratinocytes are typically shed by healthy follicles into the lumen, where they are eventually removed. However, hyperproliferating keratinocytes that are not shed into the lumen cause acne patients' pilosebaceous follicles to accumulate irregularly desquamated corneocytes along with lipids and monofilaments[12].

Hyper proliferation of propionibacterium acnes: Another agent that causes acne is Propionibacterium, which is involved in the pathophysiology of inflammatory acne13. Cutibacterium acnes, originally identified as Propionibacterium acnes, is a gram-positive, lipophilic, anaerobic pathogen that thrives in sebaceous follicles due to their high sebum production and ability to serve as an ideal anaerobic growth medium. P. acnes secretes a lipase enzyme that breaks down sebum triglycerides into fatty acids and glycerol, which can cause skin inflammation and comedones to form[14].

Inflammation acne: In keeping with the previous P. acne process, the inflammatory process starts as soon as the immune system recognizes P. acnes. Strong inflammatory responses to P. acnes can result in the production of chemostatic agents such as neutrophils, macrophages, and lymphocytes. Furthermore, these disorders result in follicular damage, rupture, and the dermal layer's release of bacteria, fatty acids, and lipids. The inflammatory lesions caused by these mechanistic processes

include ulcers (pustules, nodules, cysts, and papules)[15].

E. Management of acne

Benzol peroxide, antibiotics, antiseborrheic drugs, sulfur and sodium sulphacetamide, anti-androgen drugs, salicylic acid, hormonal therapies, alpha-hydroxy acid, retinoids, azelaic acid, keratolytic soaps, and nicotinamide are a few of the medications used to treat acne. There is also minor subcision surgery and the use of lasers and light devices. Because of its effectiveness and less severe side effects, such as dermatitis that can cause irritation, skin dryness, redness, and peeling, benzoyl peroxide is the first choice for treating mild to moderate acne. It has anti-inflammatory qualities and aids in preventing the development of comedones brought on by the P. acnes bacteria. Sunscreen is combined with topical application to prevent sunburn, as the latter increases sensitivity to the sun[16].

Antibiotics and benzoyl peroxide are frequently mixed together. At all concentrations, benzoyl peroxide is found to be just as effective as antibiotics, despite the fact that it does not cause bacterial resistance[17].

F. Antibiotics

Because of their antimicrobial activity against P. acnes and anti-inflammatory qualities, antibiotics are used in more severe cases. With P. acnes becoming more resistant all over the world, they are losing their effectiveness. Acne is treated topically or orally with antibiotics such as clindamycin, erythromycin, and tetracyclines like minocycline, oxytetracycline, lymecycline, and doxycycline[18].

G. Salicylic Acid

Because of its keratolytic and bactericidal qualities, salicylic acid reduces acne. Although salicylic acid encourages the shedding of epithelial skin cells and opens blocked pores in the skin, it hyperpigmentates the skin in people with darker skin types[19].

H. Anti-androgen Treatment

Combining oral contraceptives is one way to treat acne in females. It may be more advantageous to use third or fourth generation progestins, such as norgestimate, desogestrel, Or drospirenone combination product. Oestrogenic oral contraceptive is an effective for acne. Norethisterone is contradicted in acne because of the androgenic qualities of oral contraceptives[20].

I. Antiseborrheic Drugs

Sulfur acts as a mild keratolytic and antiseborrheic at concentrations ranging from 1 to 10%, but it also leaves a bad smell and stains clothing. Zinc sulfate and alcohol-ether in equal proportions also function as sebum-reducing agents[21].

J. Topical retinoids

Topical retinoids have anti-inflammatory qualities. They function by restoring the normalcy of the follicle cell life cycle and preventing the hyperkeratinization of these cells, which may lead to an obstruction. It contains tazarotene, adapalene, and tretinoin. They have far less severe side effects, such as flushing and skin irritation, and are related to vitamin A and isotretinoin.

A mild-effecting form of vitamin A, retinol is found in many over-the-counter moisturizers and other topical treatments[22].

K. Alternative medicines

Numerous natural products have been researched as acne treatments. It has been demonstrated that applying topical azelaic acid (20%) twice day for six months is beneficial in treating mild to moderate acne. It works similarly well to topical benzoyl peroxide at 5%, isotretinoin at 0.05%, and erythromycin at 2%. Sometimes azelaic acid may cause skin irritation. A topical application of tea tree oil is also effective for acne treatment[23].

3. Herbal plant used in the treatment of acne

A. Rose

For everyday skin care, an aqueous extract of the petals of the Rosa species (Family: Rosaceae) is utilized. Black heads and acne can also be effectively treated with rose water. The principal components are tannins, andrugosal, phenylethyl alcohol, eugeniin, pentagalloyl, and pyrogallol; monoterpenoids, eugenol, and geraniol[24].

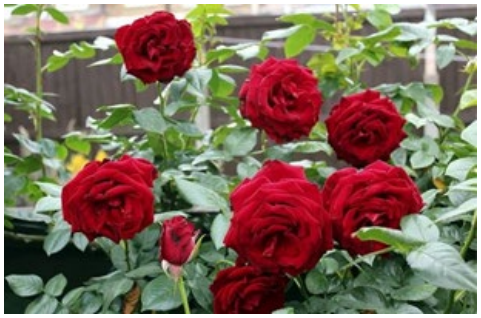

Fig 2. Rose

B. Thyme

One of the first herbs used for its potent medicinal qualities throughout history was thyme. Strongly antimicrobial volatile oils are found in thyme. The antiseptic, antibiotic, disinfectant, and germicidal qualities of the herb help to cleanse and stop acne breakouts. With a minimum inhibitory concentration (MIC) of 0.016%, thyme essential oil was found to have the best antibacterial properties[25].

Fig 3. Thyme

C. *Walnut Leaf*

Numerous bacteria have been shown to be susceptible to the antibacterial properties of various parts of walnut leaves (Juglans regia). Its leaves exhibit antibacterial and antioxidant properties when applied to Propionibacterium acnes. It has been established that walnut leaves have antibacterial properties against Propionibacterium acnes in vitro[26].

Fig.4. Walnut Leaf

4. Hyperpigmentation

Hyperpigmentation is a common, generally benign condition in which certain skin patches darken more than the surrounding normal skin tone. The brown pigment known as melanin, which creates normal skin tone, accumulates in excess and causes skin deposits that result in this darkening. People of any race can have skin color changes due to hyperpigmentation[27].

The pigment known as melanin is responsible for the color of skin. The complex process of melanogenesis is how melanocytes create melanin, which protects the tissues and organs from external factors like UV radiation and infections. However, hyperpigmentation is only a result of excessive melanin production. Thus, controlling the production of melanin is essential for the treatment of disorders related to pigmentation. Post inflammatory hyperpigmentation, age spot, melasma is a common type of hyperpigmentation[28].

5. Post Inflammatory Hyperpigmenttion

The medical term for skin discoloration that occurs after an inflammatory wound is postinflammatory hyperpigmentation, or PIH. It is an innate reaction of the skin to inflammation. Depending on the type of skin and extent of the discoloration, PIH manifests as a flat area of discoloration on the skin (macule) that can range in color from pink to red, purple, brown, or black. An acquired increase in cutaneous pigmentation brought on by an inflammatory process is the hallmark of peripheral immune hemolysis (PIH)29. The epidermis or both the epidermis and the dermis may exhibit excessive pigment deposition30. PIH is highly prevalent in people with acne. While it can happen to any skin type, darker skin types tend to experience it more frequently31. It has an equal impact on men and women. PIH is highly prevalent in people with acne. While it can happen to any skin type, darker skin types tend to experience it more frequently. It has an equal impact on men and women. PIH isn't really a scar. Acne, allergic reactions, drug eruptions, papulosquamous disorders, eczematoid disorders, vesiculobullous disorders, and other conditions can all lead to postinflammatory hyperpigmentation[32].

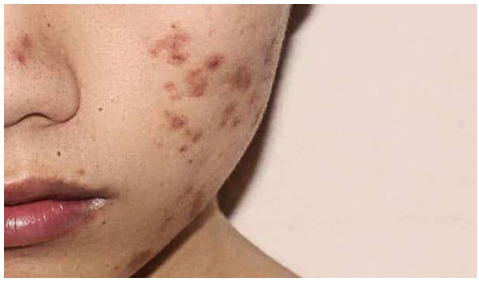

Fig.5. Post Inflammatory Hyperpigmentation

Infections that start as papules, pustules, or acne can spread to the dermis, the deepest layer of skin. An abnormal amount of darkness is caused by the infected area producing more melanin than usual[33]. Thus, the true causes of hyperpigmentation are infections of the sebaceous glands and hair follicles. If acne is not severe, it usually does not result in hyperpigmentation. Additionally, popping and squeezing pimples causes hyperpigmentation. One of the main causes of acne and hyperpigmentation is sun exposure. Sunlight (ultra violet rays) activates melanocytes, causing them to produce an excess of melanin[34].

A. *Etiology*

While any inflammatory skin condition can result in hyperpigmentation, the most common causes of PIH in patients with darker skin color are acne vulgaris, atopic dermatitis, and impetigo[35].

B. *Epidemiology*

While PIH can affect any skin type at any age, Fitzpatrick skin types III–VI are more likely to experience it. Hypermelanosis tends to be more severe and long-lasting in people with darker skin tones. Gender differences do not exist. In patients with darker skin tones who suffer from acne, the prevalence of PIH can reach 65%[36].

C. *Pathophysiology*

Postinflammatory hyperpigmentation, or hypermelanosis, results from overproduction of melanin or abnormal melanin deposition in the epidermis or dermis following inflammation. Inflammatory mediators trigger melanocyte hypertrophy and activity, which increases melanin production in the epidermis. In deeper processes extending to the dermis, basal keratinocytes are damaged and release large amounts of melanin. The melanin is phagocytosed and deposited, causing a blue-gray discoloration of the skin, which may be permanent. Hyperpigmentation limited to the epidermis has a higher likelihood of resolution than dermal hyperpigmentation[37].

D. *Management of Post Inflammatory Hyperpigmentation (PIH)*

A variety of modalities are used in a stepwise manner to treat

photoiosenia tarda (PIH), in addition to daily UV radiation protection. If the inflammatory disorder that is causing the problem is still active, treating it is the first step. The next step is topical lightening therapy, which is frequently combined with chemical peels and/or laser therapy for more severe or resistant cases. Patients should be informed that hypermelanosis improves slowly and that recurrences are common. Treatment can take months or even years at times[38].

1) TopicalTherapy- tyrosinase inhibitors (prevent melanin production)

A topical lightening agent like hydroquinone (or mequinol if a less irritating agent is required) is the cornerstone of treatment. It is often combined with a topical retinoid with or without a topical steroid to enhance and speed effectiveness. A commonly used triple combination includes hydroquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01%. The topical steroid can lessen the irritant effects of the skin lightener and/or the retinoid but should only be used for up to 8 weeks to minimize the likelihood of steroid-induced skin changes. Topical retinoids include tretinoin, adapalene, and tazarotene. They can be used long-term and are effective in treating both PIH and underlying acne. Acne and PIH can both be treated with azelaic acid[39].

2) Photoprotection

Photoprotection is a crucial component of PIH treatment that should not be disregarded or undervalued in order to stop PIH from getting worse. Patients need to be informed about the importance of using broad-spectrum sunscreen with an SPF of 30 every day as well as other sun safety tips like avoidance and wearing protective gear[40].

3) Chemical Peels

The way chemical peel's function is by eliminating the epidermal cells that have too much melanin. Since they can irritate skin and increase hyperpigmentation, skilled clinicians must use them with caution. Peels containing trichloroacetic, salicylic, and glycolic acids are typical. Fitzpatrick skin types IV to VI can tolerate most superficial chemical peeling agents. Erythema, burning sensation, PIH, HSV reactivation, superficial desquamation, and vesiculation are typical side effects[41].

4) Laser Therapy

Fitzpatrick skin types IV to VI can tolerate most superficial chemical peeling agents. Erythema, burning sensation, PIH, HSV reactivation, superficial desquamation, and vesiculation are typical side effects[42].

E. Herbal plant used in the treatment of PIH

1) Mulberry

Dried mulberry leaves (Morus alba) are used to make mulberry extract. Mulberry leaves are used in traditional Chinese and Thai medicine to treat and prevent diabetes, and they are also fed to silkworms in a number of East Asian countries. The active ingredient in mulberries, mulberroside F, has been shown in vitro to inhibit tyrosinase activity, melanin transfer, and melanin formation in melan-cells. It may also have anti-reactive oxygen species (ROS) properties[43].

Fig.6. Mulberry

2) Ginseng

Fresh Panax ginseng leaves were used to extract P-coumaric acid, which was found to inhibit L-tyrosine oxidation more strongly than L-DOPA-induced tyrosinase inhibition. Treatment with Radix ginseng in the presence of different concentrations of Radix trichosanthis decreased melanin content and tyrosinase activity, but it slightly increased B16 melanoma cell proliferation, suggesting that this combination could be useful as a skin-lightening agent[44].

Fig.7. Ginseng

3) Aloe

Aloe vera is used to extract a substance called aloesin. It has been demonstrated to competitively inhibit tyrosinase in human, mushroom, and murine sources. Tyrosine hydroxylase and DOPA oxidase activities are inhibited by aloesin in a dose-dependent manner. It was found that aloesin and arbutin can work together to synergistically inhibit melanin production by inhibiting tyrosinase activity through the integrated mechanisms of noncompetitive and competitive inhibitions[45].

Fig.8. Aloe

6. Conclusion

Hyperpigmentation and acne vulgaris are common dermatological conditions that can have a major effect on a person's quality of life. A significant portion of the population,

especially adolescents and young adults, suffers from acne, which is typified by a variety of lesions including comedones, papules, pustules, nodules, and cysts. Its etiology includes things like inflammation, bacterial infections, aberrant keratinization, increased sebum production, and follicle blockage. Hormonal therapy, topical and oral medications, and complementary therapies like herbal remedies are examples of management techniques[46].

On the other hand, hyperpigmentation, which is frequently brought on by inflammation or other skin injuries, is the outcome of excessive melanin production and deposition. A common side effect of conditions like acne is post-inflammatory hyperpigmentation (PIH), especially in people with darker skin tones. Topical lightening medications, chemical peels, laser therapy, and photoprotection are among the PIH treatment options. Herbal remedies that have demonstrated potential in inhibiting melanin production include ginseng, aloe vera, and mulberry[47].

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