Multifactorial Hyperpigmentation Disorder Melasma

Nilangekar Sakshi D[1], Sirgire Kavita S[2], Pathan Atika L[3], Mujawar Ayesha R[4], Kalegore Sumit M[5]
[1,3,4,5]*Student, Shivlingeshwar College of pharmacy, Almala*
[2]*Assistent Professor, Shivlingeshwar College of pharmacy, Almala*
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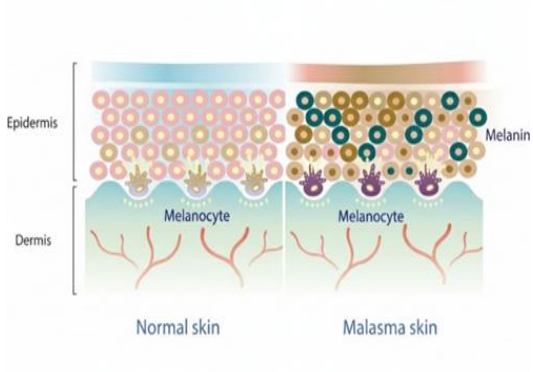
***Abstract*—Melasma is a common acquired skin disorder characterized by symmetrical brown or gray-brown patches, primarily appearing on sun-exposed areas of the face. It most frequently affects women of reproductive age and individuals with darker skin tones. The exact cause of melasma remains multifactorial, involving a complex interaction between genetic, hormonal, and environmental factors. Excessive ultraviolet (UV) radiation exposure, hormonal fluctuations during pregnancy or from oral contraceptives, thyroid dysfunction, and genetic predisposition are among the main contributors. Recent studies also highlight the roles of oxidative stress, inflammation, and vascular factors in its development. Understanding these causative mechanisms is essential for effective prevention and treatment strategies. Early identification of triggering factors and patient education remain key in managing melasma and reducing recurrence.**

***Index Terms*—Melasma, Hyperpigmentation, Symptoms, Causes, Hormonal factors, Ultraviolet radiation, Genetics, Pathogenesis**

I. INTRODUCTION

Melasma is a skin condition that many people notice as brown or dark patches on the face, especially on the cheeks, forehead, upper lip, and sometimes even the neck and forearms. While anyone can get it, melasma is more common in women and people with darker skin types, making it not just a cosmetic concern but also something that can affect confidence and quality of life. The word "melasma" actually comes from the Greek word for "black," which describes its distinctive, patchy appearance. In day-to-day practice and through patient experiences, it's clear that melasma can be stubborn and difficult to manage, with many people frustrated by how it returns or worsens with sun exposure or hormonal changes. Even though the patches themselves aren't harmful, the emotional impact should not be underestimated. Understanding why melasma happens its symptoms and underlying causes is crucial for both better management and patient counseling. In this review, an effort has been made to summarize what is currently known about the symptoms of melasma and the key factors thought to cause it, with the aim of offering a clearer, updated picture of this challenging skin disorder.



II. TYPES OF MELASMA

Melasma can be classified into three major histological subtypes based on the depth of pigmentation deposition in the skin.

Epidermal Melasma

Epidermal melasma is characterized by well-defined dark brown macules and patches. The pigment is primarily located in the epidermis, which makes this subtype more prominent under Wood's lamp examination. Due to its superficial pigment distribution, epidermal melasma generally exhibits a favorable response to therapeutic interventions.

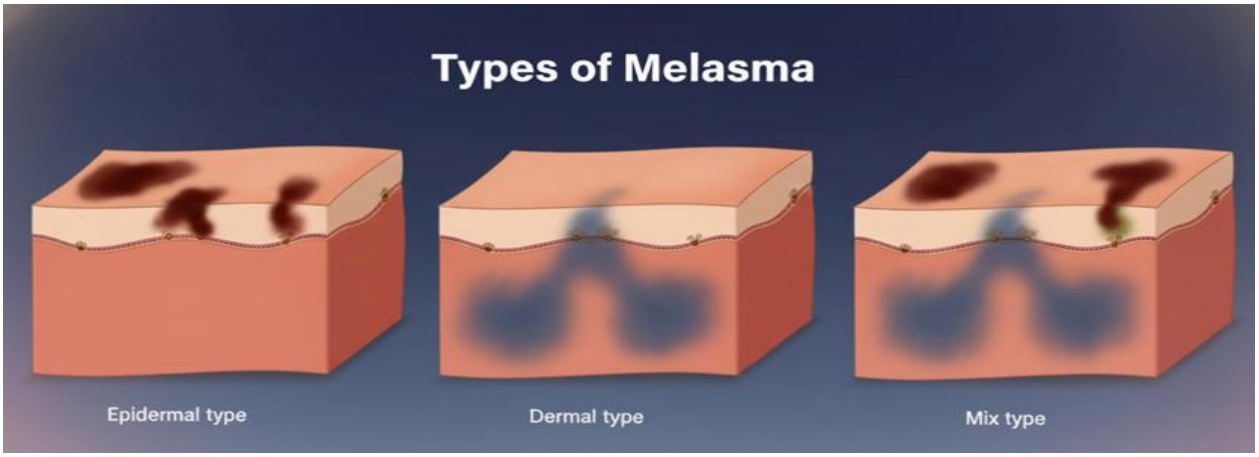
Dermal Melasma

Dermal melasma presents as light brown to bluish-gray patches with poorly defined margins. In this subtype, melanophages are located deeper within the dermis, leading to reduced visibility under Wood's lamp evaluation. Because of the deeper pigment

placement, treatment outcomes are often less satisfactory compared to the epidermal form.

Mixed Melasma

Mixed melasma is the most prevalent variant and displays features of both epidermal and dermal pigmentation. Clinically, patients show both brown and bluish discoloration. Response to therapy tends to be variable, though improvement is generally better than dermal melasma.



III. COMMON ANATOMIC PATTERNS OF MELASMA

Melasma distribution varies among individuals and is typically categorized based on the anatomical regions involved.

Centrofacial Pattern

This is the most frequently observed pattern, involving the central face, including the forehead, cheeks, nose, and upper lip.

Malar Pattern

This pattern primarily affects the cheeks and nasal bridge, giving a characteristic butterfly-shaped appearance.

Mandibular Pattern

In this variant, pigmentation is localized along the jawline and mandibular region.

Lateral Cheek Pattern

Pigmentation predominantly appears symmetrically over the lateral cheeks.

Brachial Patter

Although less common, some individuals may develop melasma over the upper arms and shoulders, particularly after chronic sun exposure.

Neck Pattern

Certain cases feature hyperpigmented patches on the neck, indicating a rarer extrafacial presentation.

IV. EPIDEMIOLOGY

Parameter	Findings
Global Prevalence	Approximately 1% in general populations; 9–50% in high-risk groups (darker skin types, high UV exposure regions)
Gender Distribution	Strong female predominance; commonly 9:1 (female: male); some studies report up to 39:1
Age of Onset	Most commonly 20–40 years; some reports suggest later onset in mandibular melasma (~40s)

Ethnic Groups at Higher Risk	Individuals of East Asian, South Asian, Middle Eastern, Mediterranean-African, and Hispanic descent
Geographic Influence	Higher prevalence in intertropical regions and areas with intense UV radiation (e.g., Brazil, India, Iran, Latin America)
Prevalence in Pregnancy	Varies by population: ~5% in European cohorts; 15–40% in Middle Eastern and South Asian groups; up to ~50% reported in Indian women
Association with Contraception and Hormonal Therapies	8–34% incidence among combined oral contraceptive users; also observed with hormone replacement therapy
Role of Sun Exposure	Higher rates among individuals with chronic outdoor exposure, agricultural workers, and those living in sunny climates
Notable Community Studies	Brazil: 15–35% of adult women; Iran: ~40% of women; India (field workers): ~41%; Latino populations in US: ~8–9%
Persistence and Natural Course	May decrease after 50 years; rare spontaneous remission (~6%); high recurrence, especially in subsequent pregnancies

V. ETIOPATHOGENESIS OF MELASMA

Melasma is a complex, acquired hyperpigmentary disorder of multifactorial origin. It is characterized by an increase in melanin synthesis and deposition within the epidermis and dermis, triggered by genetic, hormonal, environmental, and cellular mechanisms. Although the main etiology remains incompletely understood, substantial evidence indicates that the interaction among melanocytes, keratinocytes, fibroblasts, and vascular cells plays a vital role in its development.

1. Genetic and Familial Susceptibility

Genetic predisposition is one of the strongest risk factors for melasma. Epidemiological data suggest that nearly 55–64% of patients have a positive family history of the disorder. It predominantly affects individuals with darker phototypes (Fitzpatrick III–V) and is more prevalent among Asian, Hispanic, and Middle Eastern populations.

Molecular studies have shown that melasma-affected skin exhibits significant gene expression alterations. Down regulation of H19 and Wnt inhibitory factor-1 (WIF-1) results in increased Wnt/β-catenin signaling, promoting melanocyte proliferation and melanin synthesis. Simultaneously, up regulation of microphthalmia-associated transcription factor (MITF) and its target genes—tyrosinase (TYR), TRP-1, and TRP-2—enhances melanin production. These genetic changes predispose individuals to excessive pigment response following exposure to sunlight or hormonal fluctuations.

2. Role of Ultraviolet and Visible Light

Ultraviolet (UV) and visible light exposure are well-established triggers in melasma pathogenesis. Chronic sun exposure not only initiates but also perpetuates pigmentation.

a. Ultraviolet Radiation (UVA/UVB)

UV radiation stimulates reactive oxygen species (ROS) formation, which activates tyrosinase, the rate-limiting enzyme of melanogenesis. Keratinocytes exposed to UV light secrete multiple melanogenic mediators, such as α-melanocyte-stimulating hormone (α-MSH), endothelin-1, and stem cell factor (SCF), which promote melanocyte proliferation and dendricity [5]. UV-induced fibroblasts also release neuregulin-1 (NRG1) and basic fibroblast growth factor (bFGF), further augmenting melanogenic activity.

b. Visible Light

Visible light (400–700 nm), particularly blue light (415 nm), contributes to sustained hyperpigmentation through opsin-3 activation in melanocytes, leading to prolonged up regulation of MITF and tyrosinase expression. In darker skin types, visible light–induced pigmentation can persist for several weeks. Hence, the use of broad-spectrum sunscreens containing physical filters such as zinc oxide, titanium dioxide, and iron oxide is strongly recommended for photoprotection.

3. Hormonal and Endocrine Influences

Hormonal factors are another critical determinant in melasma development. The condition predominantly affects women of reproductive age and often correlates with pregnancy, oral contraceptive use, and hormone replacement therapy.

Estrogen and progesterone receptors are overexpressed in lesional skin, indicating their role in pigment regulation. Estrogen enhances melanin synthesis via activation of the cAMP/PKA/CREB/MITF pathway, increasing tyrosinase and melanosome formation. Progesterone, although not directly melanogenic, modifies the effects of estrogen and promotes dermal vascular changes. In pregnancy, elevated levels of ACTH and MSH further stimulate melanocortin-1 receptors (MC1R), leading to excessive pigmentation.

Thyroid dysfunction has also been associated with melasma. Studies have reported higher frequencies of thyroid autoantibodies and hypothyroidism among patients. Altered thyroid hormone levels can disturb oxidative balance, cytokine activity, and melanin metabolism.

4. Vascular and Inflammatory Components

Emerging research describes melasma as a vascular-inflammogenic disorder rather than a purely pigmentary one. Increased dermal vascularity and overexpression of vascular endothelial growth factor (VEGF) are consistent histological findings. These vascular changes maintain melanocyte activation and may explain the erythematous hue seen in dermoscopic evaluations.

Inflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), and IL-6 disrupt the basement membrane, allowing melanin to leak into the dermis (a process known as melanin incontinence) . Additionally, mast cells release histamine and prostaglandins, which upregulate melanogenesis via H_2-receptor-mediated signaling.

5. Dermal and Structural Alterations

Histopathological studies show multiple photoaging-related changes in melasma lesions, including solar elastosis, collagen degeneration, and matrix metalloproteinase (MMP) overactivity. Damage to the dermoepidermal junction allows melanin granules to drop into the dermis, resulting in persistent pigmentation that is often resistant to topical therapy. Dermal fibroblasts in these regions secrete neuregulin-1 (NRG1), SCF, and hepatocyte growth factor (HGF), maintaining melanocyte stimulation even after the cessation of UV exposure.

6. Barrier Dysfunction and Lipid Abnormalities

Recent transcriptomic analyses have highlighted the role of epidermal barrier impairment in melasma. Lesional skin exhibits reduced expression of genes regulating lipid metabolism, such as PPARα and PGC-1α, leading to a thinner stratum corneum and delayed barrier recovery. This weakened barrier predisposes to chronic low-grade inflammation and oxidative stress, further perpetuating melanogenesis. Therefore, barrier-repair formulations with ceramides or niacinamide can serve as valuable adjuncts to therapy.

7. Environmental Pollutants

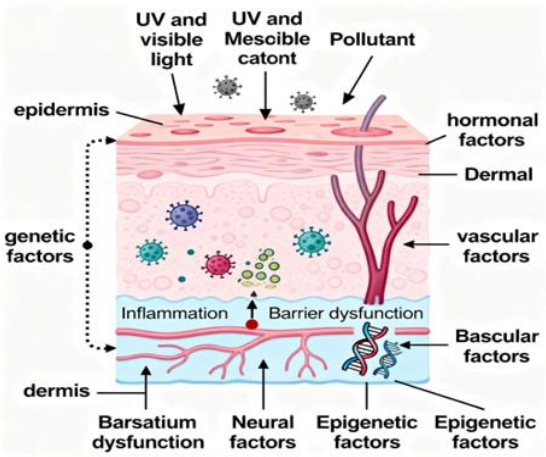
Exposure to airborne particulate matter (PM2.5) and polycyclic aromatic hydrocarbons (PAHs) can induce oxidative stress and inflammatory responses via activation of the aryl hydrocarbon receptor (AhR) pathway. This mechanism enhances tyrosinase activity and melanogenesis, explaining the higher incidence of melasma in individuals residing in urban, high-pollution regions.

8. Neural and Psychogenic Mechanisms

The facial distribution of melasma along trigeminal nerve branches implies a potential neurogenic contribution. Neuropeptides such as substance P and nerve growth factor (NGF) promote melanocyte proliferation and melanin transfer. Additionally, psychological stress elevates CRH and ACTH levels, stimulating MC1R signaling and increasing pigmentation.

9. Epigenetic and MicroRNA Regulation

Recent studies have identified altered expression of several microRNAs (miRNAs) involved in melanin synthesis. Down regulation of miR-125b, miR-137, and miR-675 leads to up regulation of tyrosinase and TRP expression. Likewise, increased miR-21 and miR-155 correlate with inflammation and oxidative imbalance in lesional skin. These findings highlight the emerging role of epigenetic modulation in melasma and open possibilities for future gene-targeted therapies.



VI. IMPACT ON LIFE

Melasma greatly affects the daily life and emotional well-being of patients. Because the patches usually appear on the face, they are easily noticed, which often leads to embarrassment and reduced self-confidence. Many individuals feel stressed and unhappy with their appearance, and they may spend considerable money on treatments that do not always give the expected results. This situation can cause disappointment and emotional strain.

Patients commonly report feeling ashamed of their skin, losing self-esteem, avoiding social situations, and lacking interest in going outside or meeting people. In some cases, severe emotional reactions such as sadness and negative thoughts have been reported, showing that melasma can have a serious psychological effect on some individuals.

To measure this impact, Balkrishnan and colleagues developed the Melasma Quality of Life Scale (MelasQoL) in 2003. It contains ten questions and evaluates how melasma affects a person's emotions, social life, and everyday routine. This scale has strong reliability and is more specific for melasma than other tools like the DLQI or Skindex-16. It has been tested and used in many countries.

Research from Brazil shows similar findings. In a study with 300 patients from different regions, a large number reported feeling uncomfortable about their melasma most of the time. Around 65 percent felt bothered by the patches, 55 percent felt frustrated, and 57 percent felt embarrassed about their facial appearance. Another study in Campinas with 56 patients showed low confidence, social withdrawal, and lower productivity at work or school. A study in pregnant women with melasma also showed a negative effect on emotional well-being, self-image, and confidence.

Interestingly, the emotional impact measured by MelasQoL does not always match the clinical severity measured by the Melasma Area and Severity Index (MASI). This means that even mild melasma can cause significant emotional distress. Therefore, treatment plans must consider both the physical appearance and the emotional needs of patients.

Individuals with lower education levels or those who already have mild anxiety or depression tend to experience a greater emotional burden. Many people think melasma is just a cosmetic problem, but this limited view can prevent proper support and treatment. Healthcare providers should address emotional concerns and be sensitive when using the MelasQoL tool in patients with limited literacy to ensure accurate understanding and reliable results.

VII. CLINICAL ASSESSMENT AND PSYCHOLOGICAL IMPORTANCE OF MELASMA

Evaluating melasma can be challenging because the condition appears differently in each patient. To manage it effectively, clinicians use standardized tools that help measure how severe the pigmentation is, track progress during treatment, and understand the emotional effect it has on individuals.

The Melasma Area and Severity Index (MASI) is one of the most commonly used scoring systems. It assesses both the extent of pigmentation and its distribution across four major facial regions—the forehead, malar areas, and chin. A simplified version, the Modified MASI (mMASI), was later introduced to improve consistency between examiners. This version removes the homogeneity parameter and focuses only on the darkness and surface area involved, creating a clear scoring range from 0 to 24 for clinical and research use.

Alongside physician-based assessments, modern melasma evaluation increasingly includes the patient's own perception. Tools like the Physician Global Assessment (PGA) help clinicians judge treatment response, while Likert-type scales capture how much improvement the patient feels they have achieved. These patient-reported measures add an important dimension by reflecting satisfaction, expectations, and real-life outcomes.

Melasma also carries a significant psychological burden because it primarily affects the face, often impacting confidence and social interactions. To assess this emotional impact, specialized tools such as the Melasma Quality of Life Scale (MELASQOL) are used. This questionnaire evaluates self-esteem, social comfort, and overall mental well-being. Broader dermatology instruments—including the Dermatology Life Quality Index (DLQI) and SKINDEX-16—further highlight that melasma is more than a cosmetic concern; it is a long-term condition that can meaningfully influence a patient's quality of life.

Together, these clinical and psychological assessment methods allow a comprehensive, patient-centered approach to melasma care. They ensure that treatment decisions acknowledge both visible improvements and the patient's emotional and social health.

REFERENCE

[1] Handel AC, Miot LD, Miot HA. Melasma: A clinical and epidemiological review. An Bras Dermatol 2014;89:771-82.

[2] 1. Sanchez NP, Pathak MA, Sato S, Fitzpatrick TB, Sanchez JL, Mihm MC Jr. Melasma: a clinical, light microscopic, ultrastructural, and immunofluorescence study. J Am Acad Dermatol. 1981;4(6):698–710 (PubMed PMID: 6787100).

[3] Abdalla, M. A. (2021). Melasma Clinical Features, Diagnosis, Epidemiology and Etiology: An Update Review. Siriraj Medical Journal, 73(12), 841-850.

[4] Miot LD, Miot HA, Silva MG, Marques ME. Physiopathology of melasma. An Bras Dermatol. 2009;84:623-35.

[5] Doolan, B. J., & Gupta, M. (2021). Melasma. Australian Journal of General Practice, 50(12), 880-885.

[6] Ho SG, Chan HH. The Asian dermatologic patient: Review of common pigmentary disorders and cutaneous diseases. Am J Clin Dermatol 2009;10:153-68.

[7] Kim NH, Lee CH, Lee AY. H19 RNA downregulation stimulated melanogenesis in melasma. Pigment Cell Melanoma Res 2010;23:84-92.

[8] Kim JY, Lee TR, Lee AY. Reduced WIF-1 expression stimulates skin hyperpigmentation in patients with melasma. J Invest Dermatol 2013;133:191-200.

[9] Kang WH, Yoon KH, Lee ES, Kim J, Lee KB, Yim H, et al.Melasma: Histopathological characteristics in 56 Korean patients. Br J Dermatol 2002;146:228-37.

[10] Carsberg CJ, Ohanian J, Friedmann PS. Ultraviolet radiation stimulates a biphasic pattern of 1,2-diacylglycerol formation in cultured human melanocytes and keratinocytes by activation of phospholipases C and D. Biochem J 1995;305:471-7.

[11] Halder RM, Grimes PE, McLaurin CI, Kress MA, Kenney JA Jr. Incidence of common dermatoses in a predominantly black dermatologic practice. Cutis.1983;32:388, 390.

[12] Souza SR, Fischer FM, Souza JM. Suntanning and risk of cutaneous melanoma: a literature review. Rev Saude Publica. 2004; 38:588-98.

[13] Taylor SC. Epidemiology of skin diseases in ethnic populations. Dermatol Clin. 2003;21:601-7.

[14] 14. Choubey V, Sarkar R, Garg V, Kaushik S, Ghunawat S, Sonthalia S, et al. Role of oxidative stress in melasma: A prospective study on serum and blood markers of oxidative stress in melasma patients. Int J Dermatol 2017;56:939-43.

[15] Mahmoud BH, Ruvolo E, Hexsel CL, Liu Y, Owen MR, Kollias N, et al. Impact of long-wavelength UVA and visible light on melanocompetent skin. J Invest Dermatol 2010;130:2092-7.

[16] Abdel-Malek Z, Suzuki I, Tada A, Im S, Akcali C. The melanocortin-1 receptor and human pigmentation. Ann N Y Acad Sci 1999;885:117e33.

[17] Cone RD, Lu D, Koppula S, et al. The melanocortin receptors: agonists, antagonists, and

the hormonal control of pigmentation. Recent Prog Horm Res 1996;51:287e318.