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Review Article

Global Epidemiology: Melasma

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ABSTRACT

Melasma is a hyperpigmentary condition that primarily affects areas of the face that are exposed to sunlight, particularly in women and people with darker skin tones. Globally, its prevalence varies from roughly 1% in the general population to 9–50% in specific ethnic groups or those who are exposed to a lot of sunlight. According to regional data: Southeast Asia: 0.5%, Saudi Arabia: 2.9%. Arab-Americans: 13.4% to 15.5%, Latinos: 8.2–8.8%, Hispanics: 2.5 %, Iran: 16–39.5%, Morocco: up to 37 %, Paddy field workers in India and Pakistan: as much as 41–46%. These rates highlight both genetic and environmental factors and are based on population-based surveys and dermatological clinic studies. Most commonly affecting women of reproductive age and people with darker skin types who are exposed to sunlight, melasma is a common hyperpigmentation disorder with a varied global prevalence. The 8.8% of Latino women in the southwestern United States participated in a prospective telephone-based survey, and 8.2% of Latino patients participated in a follow-up dermatology practice study in New York City. Compared to clinic-based surveys, which may systematically overestimate prevalence by preferentially recruiting patients seeking treatment, these population-based studies offer more accurate estimates.

INTRODUCTION

Definition and Overview :-

Melasma is a common acquired pigmentary disorder that usually affects sun-exposed areas like the forehead, upper lip, and cheeks. It is characterized by symmetrical, brownish facial hyperpigmentation. It is more common in populations with darker skin phototypes and

among women, particularly those who are of reproductive age.

Geographic, genetic, and environmental factors are important in determining its expression, as evidenced by the wide range of prevalence rates worldwide: approximately 1% in the general population of Western countries, but up to 15–35% in Brazilian women, 39.5% in Iranian women, and 41% in Indian paddy field workers. According to

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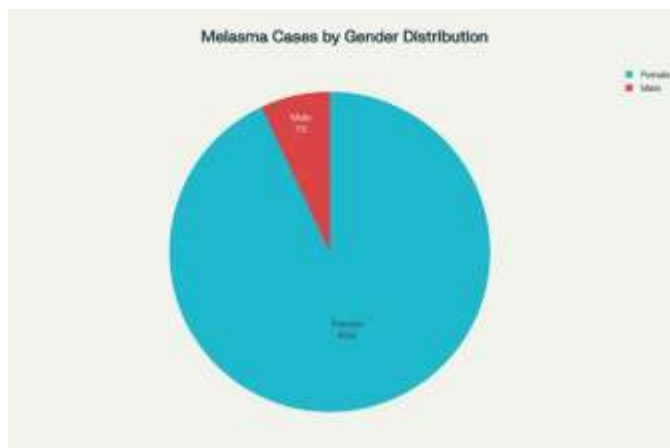
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reports, the prevalence of melasma in the US is 2.5% among Hispanics, 13.5% to 15.5% among Arab-Americans, and 8.8% among Latinos in Texas.



- **Clinical Significance :-**

Apart from skin discoloration, melasma has significant psychosocial effects. Social inhibition and a lower quality of life are frequently reported outcomes, and affected people frequently experience emotional distress, frustration, embarrassment, and depression.

With documented cases of deteriorating social relationships and mental health, including prevalence rates of anxiety and depression ranging from 8.7% to over 16% among sufferers, melasma can lead to stigmatization because of facial appearance.

- **Objectives of the Review :-**

To compile epidemiological data from significant studies and surveys in order to systematically evaluate melasma prevalence rates in various populations and geographical areas across the world.

To describe the psychological effects and clinical significance of melasma, citing current research on the emotional well-being and quality of life of those who are impacted.

To offer a current overview of research trends, knowledge gaps, and suggestions for upcoming clinical and epidemiological studies in melasma.

1) Epidemiology and Global Prevalence :-

- **Global Overview :-**

One of the most common pigmentary disorders in the world, melasma rates are significantly impacted by a number of factors, including skin type, gender, hormonal status, climate, and ethnicity. According to population-based studies, prevalence rates worldwide are generally reported to be between 1 and 10% for the general population, but they can significantly increase in high-risk groups.

According to a large global health network study, 93% of 41,283 melasma patients were female, demonstrating the condition's pronounced female predominance, with women typically making up over 90% of cases diagnosed in clinical settings.

- **Regional and Country-Specific Prevalence**

Significant differences in melasma rates by geography, ethnicity, and environmental exposure are highlighted by global epidemiological studies:

Region/ Country	Prevalence (%)	Note
General Western Population	1-2	Lowest prevalence among lighter-skinned individuals
United State (Latino Women)	8.2-8.8	Particularly in New York city and Texas cohorts
United State (Hispanics)	2.5	Increased risk among population with darker skin
United State (Arab-Americans)	13.4-15.5	Based on recent clinic data
Saudi Arabia	2.9	Highest measured rates in adult women; linked to intense UV
Brazil (Women)	15-35	Community -based study
Iran (Women)	39.5	Occupational sun exposure dramatically increases risk
India (Paddy Workers)	41	Among the lowest rates reported
Ethiopia	1.5	Variable, but can be high in certain city-based population
Southeast Asia	0.025-4	High prevalence in equatorial urban population

Melasma is most common in tropical and subtropical regions and among individuals with intermediate-to-dark skin, as the table shows.

2) Regional and Country-Specific Prevalence:-

• Asia -

Southeast Asia: The prevalence varies between 0.025% and 4% in the general population, but it can be significantly higher in certain groups, such as some female populations in India, where it can reach 40%. India: According to population studies, the prevalence can reach 41.1%. Research indicates that rates in China and Nepal are 13.6% and 6.8%, respectively.

• Middle East –

According to population studies, the prevalence in Saudi Arabia is approximately 2.9%. According to one population survey, 39.5% of women are Iranian (Ardebil). According to US studies, the prevalence is higher among Arab-Americans, ranging from 13.4% to 15.5%.

• Americas –

Population studies quote the prevalence to be around 2.9% in Saudi Arabia. In one population survey, Iranian women accounted for 39.5%. US

studies report a higher prevalence amongst Arab-Americans of 13.4% to 15.5%.

• Africa –

Ethiopia: Studies show prevalence at around 1.5%. South Africa (Durban): Melasma is among the top three most common pigmentary disorders, with prevalence around 4% in some black populations.

• Europe –

Data from Europe is less specific, but rates among hospital or clinical dermatology patients are generally lower, usually under 4% in most reported series, especially compared to populations with greater sun exposure or darker skin types.

3) Demographic patterns :-

• Gender Distribution -

Melasma shows a significant gender difference among skin conditions, with more women affected than men. This condition mainly impacts women, especially during their reproductive years, commonly known as menacme. Women make up 80-96% of all reported cases.



A global analysis using a large health research network database (TriNetx) that included 41,283 melasma patients found that 93% of them were female, with an average age of 48.8 years. Analysis of large-scale clinical trials shows a consistent female representation of 96.58% among trial participants

- **Age Distribution:-**

Melasma shows a specific age pattern. It mainly starts during the reproductive years and decreases significantly after menopause. The condition is uncommon before puberty and most often appears in women in their late 20s to early 40s.

The average age when melasma starts is between 20 and 30 years worldwide, though there are differences based on location and demographics. Some studies report an average onset age of 25.9 years in a large series, 29.4 years in a study from Pune, and 29.99 years in a study of 312 patients in India.

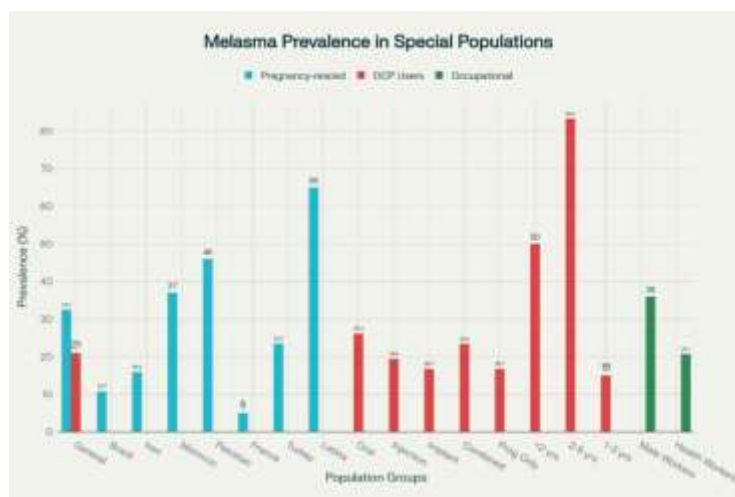
Ethnic and Racial Predisposition:-

Melasma shows clear differences among ethnic and racial groups. It is much more common in people with darker skin tones and in populations with genetic roots from areas with a lot of sunlight. Although melasma can happen in all races and ethnicities, studies consistently show significant variations in its prevalence among different ethnic groups.

4) Special Populations:-

- **Pregnancy-Related Melasma (Chloasma Gravidarum) :-**

Pregnancy is one of the leading hormonal precipitants for melasma, and its prevalence continues to vary dramatically among populations and geographic regions. Among pregnant women worldwide, melasma has been reported to occur from 15% to 50%, the condition also historically called chloasma gravidarum or the "mask of pregnancy."



- **Occupational Groups:-**

Outdoor Workers and UV Exposure: Outdoor workers are exposed to much higher UV radiation compared to indoor workers. Estimates from studies have varied from 3 to 10 times higher

annual UV exposure among outdoor workers as compared to indoor workers; some workers receive about 10% of available ambient UV radiation. This occupational exposure is cumulative over years or decades and thus

contributes to both the development and difficulty in treatment response of melasma.

- **Oral Contraceptive Users:-**

Other major triggering factors include hormonal contraceptive use, which can induce melasma in 8-34% of women using combined oral contraceptives. One comprehensive study investigated hormonal contraceptive acceptors and noted that 20.5% developed melasma overall, though the prevalence varied with the type of contraceptive used. Contraceptive Type and Melasma Risk: Oral contraceptives had the highest association among users of different formulations of hormonal contraceptives, with 26.1% of users developing melasma.

5) Pathophysiology:

- **Melanogenesis and Cellular Mechanisms:**

MITF, tyrosinase, TYRP1/TYRP2, MC1R activation, Wnt/ β -catenin signaling, melanocyte morphology changes

- **UV and Visible Light Effects:**

UV radiation mechanisms, ROS generation, MC1R upregulation, stem cell factor pathways, blue light mechanisms via OPN3 activation

- **Cellular Interactions:**

Dermal-epidermal cellular network, fibroblast-derived melanogenic factors, senescent fibroblasts, melanosome transfer to keratinocytes

- **Vascular Component:**

Increased vascularity, VEGF upregulation, 68.75% increase in vessel density, endothelial factors, vasodilation mechanisms

- **Basement Membrane and Barrier Dysfunction:**

95.8% of lesions show basement membrane damage, type IV collagen reduction, MMP-2 and MMP-9 activation, melanocyte migration into dermis

6) Clinical Presentation and Classification

- **Clinical Patterns by Distribution:-**

Clinically, melasma presents as symmetric, hyperpigmented macules and patches with irregular contours and well-demarcated limits, appearing predominantly on sun-exposed areas, with particular predilection for the face and cervical region. Brownish macules develop gradually over weeks to months or years, forming patches that vary in size from 0.5 cm to greater than 10 cm in diameter, depending on disease duration and severity.

- **Histological Classification:-**

Epidermal melasma is characterized histologically by increased melanin pigmentation throughout the layers of the epidermis, with particular concentration in basal and suprabasal layers, occasionally extending through the stratum corneum. Importantly, melanocytes in the epidermal type are enlarged, display prominent dendrites, and contain increased melanosomes, yet no quantitative increase in melanocyte number is typically observed, indicating that increased melanin production by existing melanocytes drives epidermal melasma rather than melanocyte proliferation

- **Clinical Characteristics and Features:-**

Epidermal type Light brown coloration which can easily be camouflaged by cosmetics and visible lighting. Dermal type Brown to bluish-grey



pigmentation due to the Tyndall effect; darker and more distinct clinically. Fitzpatrick skin types IV - VI Predominantly bluish-grey pigmentation, which needs iron oxide-containing sunscreens that protect against visible light and infrared radiation. Mixed type Dark brown colour, variable colouration reflecting both epidermal and dermal components

7) Diagnostic Approaches:-

• Clinical Diagnosis-

The diagnosis is often made by the dermatologist on examination, noting the classic patterns of brown to grayish-brown patches on sun-exposed areas, most notably the face. Key clinical clues included specific location pattern findings (cheeks, forehead, nose, upper lip, and chin), with absence of scaling and sparing of the eyelids.

• Wood's Lamp Examination-

A Wood's lamp uses UV light to highlight contrast and fluorescence, to distinguish epidermal from dermal and mixed melasma. Epidermal melasma is accentuated by the lamp while dermal type is not. Mixed melasma is partially accentuated.

• Dermoscopy-

Dermoscopy is a noninvasive technique that enables the examination of pigment distribution and its color within skin layers in closer detail. It distinguishes epidermal (brown network), dermal (blue-gray homogeneous), and mixed patterns. These studies also showed moderate to substantial concordance between Wood's lamp and demographic findings, but dermoscopy may offer even greater precision and additional information on vascular and follicular features.

• Other Diagnostic Tools-

Although rarely needed, a skin biopsy may be performed when the diagnosis is uncertain or to rule out other conditions. Advanced techniques, such as reflectance confocal microscopy or digital photography, may contribute to research and monitoring but are not generally used in standard diagnostic work.

8) Treatment and Management-

Melasma, which can affect 0.025-50% of the population, depending on geographical region and ethnicity, requires a multifaceted approach to treatment that may include topical agents, systemic therapies, procedural interventions, and combination strategies. Selection of the modality of treatment is based on the severity of the disease, skin phototype, tolerance, and availability of advanced procedures. This section discusses the current status of management options in melasma, from first-line topical therapies to advanced combination approaches.

• Topical Treatments-

Hydroquinone is considered the gold standard of topical therapy for melasma. It acts as a competitive tyrosinase inhibitor and thus decreases melanin production by competitively interfering with copper at the active site of the enzyme. Common concentrations for treating melasma range from 2 to 4%; clinical lightening typically starts after 2-3 weeks of use.

However, hydroquinone has several notable disadvantages: rapid oxidation in formulations reduces the effective concentration, and long-term use beyond recommended periods may have a risk of developing exogenous ochronosis, which is a permanent blue-black discoloration. This usually requires treatment courses of 8-12 weeks or longer; maintenance therapy thereafter is needed.



Tretinoin is a form of vitamin A, also called a retinoid; it has several modes of action that help to improve the management of melasma. It suppresses the transcription of tyrosinase and related proteins that interrupt melanin synthesis after UV exposure; it decreases melanosome transfer and enhances penetration of other active ingredients. However, optimal clinical improvement with tretinoin occurs after 24 weeks or longer. Continuous therapy is often associated with adverse effects of burning, erythema, itching, and scaling in most patients. A retinoid alternative, adapalene, has similar efficacy but is better tolerated.

• Systemic Therapies-

TXA has emerged as a well-supported systemic therapy for melasma. Oral TXA, at dosages of 500-750 mg daily in multiple doses for up to 6 months, has shown mild-to-moderate improvement in melasma. The agent, through its mode of action, results in the inhibition of melanin synthesis and reduction of vascularity. A favorable adverse event profile supports its use as an adjunctive therapy in the treatment of melasma.

Polypodium leucotomos extract is a botanical extract with antioxidant and photoprotective activity, which has shown favorable effects in melasma improvement. Several randomized controlled trials demonstrated efficacy with few adverse events, although evidence in monotherapy is still scarce.

Procyanidin and Pycnogenol are plant-derived antioxidants that have shown good-to-moderate efficacy in the treatment of melasma in available randomized controlled trials. However, evidence so far is still insufficient to recommend these agents as monotherapy; instead, their use is reserved for combination approaches.

• Procedural Interventions-

The Q-switched Nd: YAG laser 1064 nm is the most investigated laser modality for treating melasma. With this technology, low fluence of 1.6-2.0 J/cm² is used to target melanin without causing thermal injury to the surrounding tissue. A number of studies showed the efficacy level of this laser alone, from high to very high.

Treatment usually entails 2-6 sessions at 4-week intervals with very few adverse effects consisting of mild post-treatment erythema. Notably, 81% achieved >75% clearance, with 40% with >95% clearing; remission lasted at least 6 months with proper maintenance care.

• Combination Approaches-

Triple Combination Therapy (Hydroquinone + Tretinoin + Corticosteroid) represents the most extensively studied combination approach. The classic Kligman formula, which combines 4% hydroquinone, 0.05% tretinoin, and 0.1% mometasone furoate, is very highly effective through synergistic mechanisms: hydroquinone provides melanin bleaching, tretinoin enhances cell turnover and penetration of other agents, and corticosteroids reduce inflammation. Treatment duration involves 8-12 weeks of daily application followed by maintenance therapy, with a reduction in Modified Melasma Area and Severity Index (mMASI) scores averaging 8.88 by the fourth visit compared to baseline.

However, long-term use of triple combination is associated with high steroid-related side effects. A retrospective study among 60 Indian patients found that the majority (51.7%) were on triple combination for much beyond the recommended duration, with steroid-related complications like atrophy -19/60 patients, telangiectasia-26/60, hypertrichosis-17/60, and acneiform eruption-

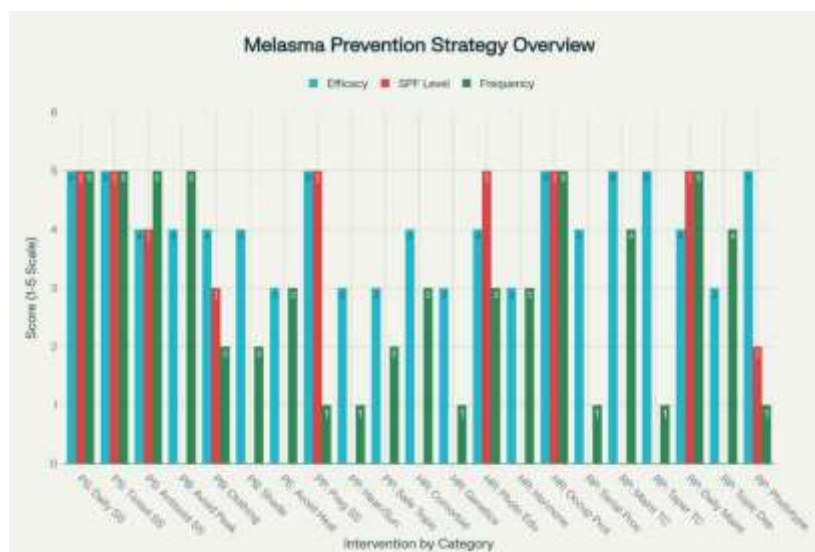


11/60. One-third of the patients showed aggravation of pigmentation, and all the side effects significantly increased beyond 6 months of use.

9) Prevention Strategies-

Melasma remains among the most resistant pigmentary disorders to treat, and prevention has become as important as treatment itself. Melasma

has a wide variation in its global prevalence, ranging between 0.025 and 50%, depending on ethnicity and geographic region. Adequate prevention has been shown to greatly reduce its incidence and recurrence rates. This broad-based review covers evidence-based prevention strategies, including photoprotection, pregnancy-specific measures, strategies for high-risk populations, and mechanisms for preventing recurrence.



- **Photoprotection: The Critical Foundation**

Photoprotection is the cornerstone of melasma prevention and management, with UV radiation considered the most important modifiable risk factor. The role of photoprotection in melasma is much broader than traditionally thought, with recent studies showing that HEVL (400-450 nm) and UVA1 (370-400 nm) radiation play equally important roles in the pathophysiology of melasma. These ranges promote the generation of free radicals and ROS, which in turn stimulate pro-inflammatory cytokines and melanogenesis, especially in darker skin phototypes (FST V-VI).

Sunscreen Formulation and Application Standards:

The gold standard for patients with melasma is a broad-spectrum sunscreen with SPF ≥ 50 , since most patients apply only 50% of the recommended layer, and thus higher values are required for adequate protection. SPF mainly covers against UVB radiation; for UVA protection, it is necessary to check the Persistent Pigment Darkening (PPD) factor. Dermatologists recommend a PPD in a range of 20-30 in pigmentary disorders, which balances protective efficacy against the cosmetic nature of formulations.

- **Prevention During Pregnancy-**

Melasma is a major clinical problem, with a prevalence that ranges from 36.4% to 75%, and disturbingly, as many as 30% of cases may persist even a decade after delivery. The majority of cases

appear during the second and third trimesters when hormonal levels are peaking, although the onset at any time during pregnancy or in the postpartum period cannot be excluded. Pregnancy-related melasma occurs in all skin types during pregnancy; however, individuals with darker skin are still at the highest risk because of the baseline increases in melanogenic capacity.

Safe Treatment Options in Pregnancy:

Treatment options during pregnancy are still limited due to teratogenic and fetotoxic effects. Topical vitamin C and azelaic acid are the safest depigmenting agents during pregnancy and have been shown to be effective in lightening patches. Mild cases may also be safely treated with glycolic acid peels. Hydroquinone, salicylic acid peels, tretinoin, and laser treatment should not be used at all during pregnancy and should be reserved for the postpartum period. This limitation again highlights the critical role of stringent prevention measures since treatment options are severely limited.

- **High-Risk Population Strategies-**

The global burden of melasma disproportionately affects certain ethnic and geographic populations. Epidemiological studies have shown that 30-50% of South Americans and Asians have melasma, while prevalence in specific contexts may be even higher: 41% among paddy field workers in India, 39.5% among Iranian women, and 15-35% of Brazilian adult women. Accordingly, Asian and Other/Unknown races have 2.0× odds ratio for developing melasma, whereas Hispanic ethnicity results in 1.3× odds compared to White populations.

Ethnic and Occupational Vulnerabilities:

These epidemiological differences are accentuated by a complicated interaction of genetic predisposition, baseline skin phototype, the intensity of UV exposure, and socioeconomic influences on access to treatment. A critical observation emerges in that dark-skinned patients consistently take fewer photoprotective measures compared with lighter-skinned counterparts. This disparity likely reflects multiple factors including historical medical racism, reduced visibility of photoaging signs in darker skin, and inadequate marketing of photoprotective products for diverse skin tones.

- **Relapse Prevention Following Treatment-**

The notoriously relapsing nature of melasma requires a systematic approach to prevent relapses. After acute treatment has been successful in achieving no or mild melasma status, maintenance therapy becomes necessary to control the disease. Clinical studies have established that without maintenance intervention, the median time to relapse averages about 190 days.

Melasma is one of the most therapeutically challenging dermatological disorders, with prevalence ranging from 0.025 to 50% depending on ethnicity and geography. Despite several decades of research and numerous therapeutic options, melasma continues to confound clinicians and frustrate patients because of its chronic nature, high relapse rates, and resistance to sustained treatment, particularly in darker skin phototypes. This comprehensive review examines current management challenges, critical research gaps, promising emerging therapies, and strategic directions for prevention in the quest to improve outcomes for this globally prevalent pigmentary disorder

10) Challenges and Future Directions-



- **Current Challenges in Treatment-**

The Relapse Paradox-

Perhaps the most significant clinical challenge in the management of melasma is the propensity for relapse of disease activity despite successful acute treatment. Once no or mild melasma status is achieved through 8 weeks of daily triple combination therapy, as attained in 78.8% of treated patients, maintenance therapy is required to avoid relapse.

Without structured maintenance protocols, approximately 47% of subjects relapse within 6 months, with a median time to relapse of approximately 190 days. Even with optimized twice-weekly or tapering maintenance regimens, only 53% of patients remain relapse-free at the 6-month mark. This persistent relapse tendency underscores the fundamental limitation that melasma represents a chronic disease requiring indefinite management rather than a condition amenable to cure.

The relapse tendency varies greatly based on the initial severity of the disease and skin phototype. Patients with initially severe melasma present higher rates of relapse, which necessitates more intensive maintenance protocols, such as twice-weekly dosing rather than tapering regimens. Individuals with Fitzpatrick skin phototypes IV-VI also revealed only 44.7% relapse-free rates compared with 63.4% in skin phototype III patients, underlining the substantially greater challenges faced by darker-skinned individuals.

Hydroquinone Limitations and Alternative Searches: Hydroquinone, the gold standard for depigmentation, has inherent limitations in long-term utility. Exogenous ochronosis, which is the permanent blue-black discoloration arising from prolonged exposure to hydroquinone, though rare,

is still a concern. Besides, the rapid oxidation of hydroquinone in formulations compromises shelf stability and thus clinical efficacy. All these limitations have driven the search for alternatives, yet till now, very few compounds with comparable efficacy or superior safety profiles have been found.

- **Research Gaps Limiting Evidence-**

Based Management-

Incomplete genetic and molecular understanding: Despite centuries of clinical observation and decades of laboratory investigation, the fundamental genetic basis of melasma has yet to be fully understood. As of today, no genome-wide association study has been conducted to date, thus keeping important genetic mechanisms unexplored. Single-gene approaches have implicated numerous pathways such as the genes for tyrosine-melanin synthesis (TYR, TYRP1), lipid metabolism pathways (PPAR), the H19/microRNA-675 axis, and Wnt/AKT signaling; however, there is still no comprehensive functional validation. Melanocortin-1 receptor, required for melanin synthesis pathway activation, demonstrates several polymorphisms-the most relevant for showing the genetic association between nucleotide variants and susceptibility to melasma. The Val92Met MC1R variant was found at the highest allelic frequency in South Asian populations, and melasma statistical risk was associated with this allele, although population specific genetic studies are still few. Large-scale, ethnically diverse GWAS studies with functional investigations will shed light on the genetic architecture of melasma and identify novel therapeutic targets for treatment.

- **Emerging therapeutic directions:-**



It involves the use of nanotechnology and advanced drug delivery systems. Nanotechnology is one of the most promising frontiers for improving the efficacy of melasma treatment. The stratum corneum barrier poses a significant limitation to skin penetration and bioavailability for most current topical agents. Topical drug delivery through nanotechnology can bypass this limitation by offering improved skin permeation, selective delivery to the site of action, prolonged deposition at the targeted area, and limited systemic absorption.

Nanostructured lipid carriers and transferosomes demonstrate particular promise, offering flexible structures that enhance skin penetration while maintaining drug stability. Still, another emerging approach is microneedle patches, which allow for convenient physical delivery of multiple medications with targeted drug delivery and minimal invasiveness, associated with fewer adverse effects compared to traditional energy-based methods. Dissolvable microneedles eliminate the safety concern of needle fragments remaining in the skin and offer a particularly attractive option for long-term maintenance therapy.

• Prevention Focus and Future Strategies-

Occupational Prevention Programs:

Occupational populations have a vastly increased burden of melasma, with 41% prevalence among Indian paddy field workers, far greater than in the overall population. There are no broad occupational sun protection guidelines or prevention programs for these susceptible workers. Future directions should involve employer-sponsored sun protection programs, provision of high-SPF sunscreens and protective clothing, scheduling modifications that minimize

peak-hour exposure, and paid occupational dermatology screening for early detection.

CONCLUSION:-

Melasma as a Global Health Burden and Path Forward, melasma represents one of the most prevalent yet therapeutically challenging pigmentary disorders worldwide, affecting an estimated 0.025–50% of the global population depending on ethnicity, geography, and environmental factors. This wide prevalence range reflects the profound ethnic and phototype disparities in disease burden: while Southeast Asian populations experience prevalence ranging from 0.025–4%, Brazilian women show 15–35%, Iranian women 39.5%, and paddy field workers in India reach 41%. In North America, Arab-Americans demonstrate 13.4–15.5% prevalence, Latino populations 8.2–8.8%, and Hispanic populations 2.5%.

These striking epidemiological variations underscore melasma's fundamental connection to skin phototype, sun exposure intensity, and genetic predisposition, highlighting how global inequities in dermatological burden concentrate in dark-skinned populations residing in equatorial and tropical regions or engaging in outdoor occupational activities.

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