MELASMA: UNDERSTANDING ITS COMPLEXITY AND ACCURATE THERAPEUTIC APPROACHES

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Abstract - Introduction: Melasma is an acquired pigmentary condition, primarily affecting the face, and predominantly occurs in women with darker skin phototypes. Objective: This literature review aims to explore the etiology, epidemiological characteristics, pathophysiology, pathogenesis, and treatments of melasma, with the purpose of deepening the understanding of this skin disorder and enhancing therapeutic approaches. Methodology: The study involves an analysis of relevant research on the topic, highlighting the influence of ultraviolet radiation, hormones, and genetic predisposition as the main etiological factors. Theoretical Framework: The review delves into the complex interaction between melanocytes, keratinocytes, and other cellular components in the pathogenesis of melasma. Estrogen plays a significant role, especially due to its increase in pregnant women, post-pubertal women, and users of oral contraceptives. Results and Discussion: Data reveal the high prevalence of melasma in women aged 20 to 40 years, particularly in Fitzpatrick skin types III to VI, with a predominance of the centrofacial and malar patterns. Additionally, treatments emphasize the use of chemical peels, hydroquinone, and retinoic acid, with a focus on combination therapies for greater efficacy. Conclusion: The need for personalized therapeutic strategies is emphasized, given the complexity of melasma and the diversity of factors influencing its development and persistence, underscoring the importance of ongoing studies to improve the clinical management of this condition.

Keywords - Melasma, melanin, Microphthalmia-associated Transcription Factor, Fitzpatrick.

Resumo - Introdução: O melasma é uma condição pigmentária adquirida, principalmente facial, que afeta predominantemente mulheres com fototipos mais escuros. Objetivo: Esta revisão literária visa explorar a etiologia, características epidemiológicas, fisiopatologia, patogênese e tratamentos do melasma, com o propósito de aprofundar o entendimento dessa desordem cutânea e aprimorar as abordagens terapêuticas. Metodologia: Consiste na análise de estudos relevantes sobre o tema, destacando a influência da radiação ultravioleta, hormônios e predisposição genética como principais fatores etiológicos. Referencial teórico: Envolve a complexa interação entre melanócitos, queratinócitos e outros componentes celulares na patogênese do melasma. O estrogênio desempenha um papel significativo, especialmente pelo seu aumento em mulheres grávidas, pós-púberes e usuárias de anticoncepcionais orais. Resultados e Discussões: Os dados revelam a alta prevalência do melasma em mulheres de 20 a 40 anos, particularmente em fototipos Fitzpatrick III a VI, com predomínio dos padrões centrofacial e malar. Adicionalmente, os tratamentos destacam o uso de peelings químicos, hidroquinona e ácido retinóico, com ênfase em terapias combinadas para maior eficácia. Conclusão: Enfatiza-se a necessidade de estratégias terapêuticas personalizadas, dada a complexidade do melasma e a diversidade de fatores que influenciam seu desenvolvimento e persistência, sublinhando a importância de estudos contínuos para aprimorar o manejo clínico dessa condição.

Palavras-chave: Melasma, melanina, Fator de Transcrição da Microftalmia, Fitzpatrick.

I. INTRODUCTION

Melasma, formerly known as chloasma, is an acquired pigmented condition that most frequently occurs on the face. This disorder, more prevalent in women and individuals with darker skin types, is primarily attributed to ultraviolet (UV) radiation exposure and hormonal influences. Melasma is generally diagnosed clinically and presents as symmetrical reticulated hypermelanosis in three predominant facial patterns: centrofacial, malar, and mandibular [1,2]. A more recent pattern, known as extrafacial melasma, may appear on body areas other than the face, including the neck, sternum, forearms, and upper limbs [3].

Melasma presents significant treatment challenges due to its unpredictable nature, with frequent recurrences. It is typically characterized by dark brown, symmetrical spots with irregular borders, most commonly on the face, in centrofacial and malar patterns [4]. This condition is more

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prevalent in Fitzpatrick skin types III to VI, in ethnic groups such as Hispanics, African-Americans, Asians, or women from the Middle East, and tends to emerge in patients between 20 and 40 years of age [5]. Although less common, men account for 10% of cases, usually presenting with malar distribution patterns. The exact pathogenesis of melasma is not yet fully understood [6]. However, it is known that sun exposure, oral contraceptives, pregnancy, certain medications, genetic predisposition, some cosmetics, and autoimmune diseases can exacerbate and contribute to the clinical signs of melasma [7,8].

Skin pigmentation, which is determined by the amount of melanin produced by the body, defines skin color. The two main types of melanin, eumelanin and pheomelanin, are synthesized by melanocytes in the epidermal layer of the skin. Pheomelanin contributes to lighter skin tones, while eumelanin is responsible for darker skin tones [9,10]. The skin is protected from sunburn by the presence of eumelanin, a dark brown pigment that absorbs UV rays from the sun. Darker skin tones are associated with higher levels of eumelanin, while lighter skin tones are related to lower levels [11]. In addition to its protective function against skin cancer, eumelanin also contributes to temperature regulation by absorbing solar heat and helping to keep the body cool. Studies have shown that individuals with higher levels of eumelanin are less likely to develop skin cancer compared to those with lower levels [11,12].

Wood's lamp examination has been used to categorize melasma based on the depth of melanin in the skin: the epidermal form is characterized by light brown coloration, while the dermal form exhibits gray-blue or mixed coloration, observed in dark brown tones [13]. However, in vivo confocal reflection microscopy has revealed a heterogeneous distribution of melanophages, suggesting that all melasma is "mixed" [14]. It is currently believed that melasma results from a complex interaction between epidermal melanocytes, keratinocytes, dermal fibroblasts, mast cells, vascular endothelial cells, and hormonal, genetic, and UV influences [15].

Understanding the pathogenesis of melasma remains incomplete, but a complex interaction between various cellular elements, hormonal, genetic, and UV influences is recognized as essential. The diversity in melanin depth in the skin, revealed by diagnostic methods such as Wood's lamp examination and in vivo confocal reflection microscopy, suggests a complexity greater than previously considered. In this context, this literature review study aims to extensively investigate the multiple facets of melasma, from its etiology to its clinical presentation and accurate diagnosis, with the ultimate goal of developing more effective and personalized therapeutic approaches for this challenging skin condition.

II. METHODOLOGY

This study was conducted through a literature review using recognized databases such as PubMed, Scopus, Web of Science, and Google Scholar to identify relevant scientific articles on melasma. A broad range of relevant terms, such as "melasma," "melasma etiology," "melasma pathophysiology," and "melasma treatment," was employed in the search. Studies published in the last 20 years were included, covering various aspects of the condition, such as etiology, clinical presentation, diagnosis, and therapeutic approaches. The selection of studies was based on inclusion criteria that considered articles in English that presented relevant data on melasma. Studies that did not directly address the investigated aspects or had internal methodological issues were excluded. Data analysis was performed qualitatively, identifying recurring patterns in the findings of the selected studies.

III. THEORETICAL FRAMEWORK

a. Etiology

The origin of melasma does not have a single cause but is influenced by several factors, including the intake of exogenous hormones, stress, genetic factors, photosensitizing drugs, and primarily exposure to UV radiation [16]. Recurrences are common in subsequent pregnancies, and melasma has a negative impact on quality of life, especially due to its effect on the face and body image. It usually resolves completely within a year postpartum; however, about 30% of pregnant women experience some degree of unwanted pigmentation [17]. Given this, melasma is more prevalent in darker skin types, as the amount of melanin in the epidermis is higher compared to lighter skin. Eumelanin (the darker pigment) is predominant in skin types IV to VI, which explains the brown color of melasma [18].

b. Epidemiological Characteristics

Factors determining and influencing the frequency of melasma presentation include age, sex, ethnicity, use of hormonal contraceptives, use of cosmetics, use of other medications, sun exposure, family history of melasma, history of thyroid disorders, use of sunscreen, and emotional factors [19]. In the Andean population, which lives at altitudes above 2,000 meters, melasma occurs in the majority of the Amerindian population, including males, due to constitutional melanodermic type and higher UV intensity [20]. In Brazilian patients, melasma was more prevalent in women (97.5%) and in Fitzpatrick skin types II (12.8%), III (36.3%), and IV (39.7%). Skin types II and III and a family history of melasma had an earlier onset of the disease compared to skin types IV, V, and VI [21].

c. Pathophysiology and Risk Factors

Factors contributing to the development of melasma include gender, with an increased prevalence in women.

Another risk factor is darker skin types, such as African, Hispanic, Asian, and Indian individuals, who are more likely to develop the condition due to having more active melanocytes for melanin production [22]. The pathophysiology of melasma involves both dermal and epidermal origins. This disorder extends beyond the melanocytes, with affected skin showing signs of photoaging due to UV exposure, an increase in mast cells and sebaceous glands, changes in the basal membrane, solar elastosis, and increased blood flow [23]. Some authors describe the pathophysiology of melasma as follows: There are three patterns of melasma lesion distribution: Centrofacial pattern, which corresponds to the most common presentation of the disease, occurring in about two-thirds of melasma patients [24].

d. Pathogenesis of Melasma

Estrogen plays a role in the pathogenesis of melasma, as its levels increase in pregnant women, postpubertal women, and women using oral contraceptives. Several studies have demonstrated a large number of estrogen receptors present in the dermis and progesterone receptors in the epidermis over melasma lesions [25]. When estrogen interacts with its receptors on melanocytes and keratinocytes, it can stimulate the Microphthalmia Transcription Factor (MITF) pathways, as well as tyrosinase, to initiate melanin production [26].

The pathogenesis of melasma, particularly the role of keratinocytes and fibroblasts in the development and maintenance of the disease, is not well understood [27]. Its pathogenesis remains unclear, but factors involved in the disease include ultraviolet (UV) radiation, which is the primary environmental factor affecting melasma pigmentation by inducing melanogenesis through the stimulation of melanogenic factors released by keratinocytes [28].

e. Melanin Synthesis Pathway

The melanocyte is a specialized cell responsible for the synthesis and transport of melanin, distributed throughout the skin, with high concentration on the face [29]. Melanins are synthesized in specialized epithelial cells called melanocytes, derived from melanoblasts (cells originating from the embryonic neural crest), which differentiate into various cell types, including pigment cells [30]. Inside melanocytes are the organelles responsible for the property and storage of melanin, called melanosomes, which produce the pigment during their maturation [30]. Physiologically, α-MSH is the most relevant hormonal pigment, stimulating the translocation of pigment collectors and melanin properties, as well as cellular sedative effects [86].

f. Genetics

Genetic predisposition is associated with a high familial incidence in certain racial groups. Although there are no studies indicating the association of a specific gene with melasma, epidemiological studies have shown that this pigmentary disorder is common among Hispanics and Asians with Fitzpatrick classifications III to V, and among African-Americans [35]. Despite the high frequency of familial cases, the genetic segregation pattern has not yet been defined. There is also evidence that European admixture with certain ethnic groups, such as Indigenous and African populations, may favor the development of melasma, but the genetic ancestry of these patients has not been explored to date [80]. Tyrosine is the limiting factor in melanin synthesis; the conversion of dopaquinone (DOPA) to dopaquinone occurs spontaneously at physiological pH and the entire process is under genetic control [81].

g. Alterations

There are three types of melasma: dermal, epidermal, and mixed, with mixed being the most prevalent. The location of pigment deposition differentiates one type of melasma from another. In epidermal melasma, melanocytes and melanin are concentrated more in the basal layer and the epidermis, giving the skin a brown coloration due to increased melanin in the epidermal melanocytes and keratinocytes [41]. Skin alterations that may be related to the development and progression of the disease have been identified. Abnormalities in the extracellular matrix of the affected melasma area have been observed. Solar elastosis, an abnormal accumulation of elastic tissue in the dermis due to prolonged sun exposure, a process known as photoaging, is a frequently described feature in melasma-affected skin [70]. One of the skin's functions is to ensure pigmentation or coloration of the tissue, a process known as melanogenesis, in which melanin is synthesized [92]. Melasma also brings emotional and psychological alterations. Healthy, intact skin allows people to interact in various aspects; however, the presence of dermatological changes can significantly impact the individual. In terms of quality of life, melasma causes changes in various areas, such as social issues, activity and leisure, and particularly emotional well-being [71].

h. Solar Radiation

Exposure to UV rays affects skin pigmentation, leading to disorders such as hyperpigmentation and Fitzpatrick skin types I-IV. UVB rays (290-320 nm), the most intense, cause DNA damage through the production of pyrimidine dimers, cyclobutane, and photoproducts. UVA rays (320-400 nm) generate reactive oxygen species, causing DNA damage. UVA rays penetrate the skin and reach both the basal layer and the epidermis [40]. Variations in skin color are believed to be evolutionary gains related to the regulation of ultraviolet (UV) radiation penetration [78]. Increased melanin production in response to stimulation is a defensive occurrence of the skin against solar damage.

After irradiation, melanosomes regroup around the nucleus to protect the cell's genetic material. Thus, in addition to providing coloration and pigmentation, melanin acts as a sunscreen by absorbing or reflecting solar radiation [79].

i. Endocrine Stimuli

Hormones are regulatory chemical substances secreted by endocrine glands, released into the bloodstream, and respond to their stimuli. The amount of hormones released by endocrine glands or cells is determined by the body's needs at a given time, and their effects are varied [36]. Hormonal fluctuations can trigger or exacerbate a range of dermatological conditions, such as acne, hirsutism, melasma, and seborrheic dermatitis [37]. Endocrine disruptors are synthetic substances that alter the functioning of the endocrine system by mimicking sex hormones, especially estrogens [77].

j. Oxidative State

Stress increases the production of free radicals and attacks the body's antioxidants, leading to an imbalance between oxidative stress and the body's antioxidant defense capacity, thus generating oxidative stress [38]. Free radicals are often synthesized in the body and are atoms or molecules with one or more unpaired electrons in their outermost layer, making them reactive. They achieve stability by pairing electrons with natural molecules in healthy cells and cause harmful changes to DNA and proteins, while also provoking lipid peroxidation [76]. Superoxide dismutase is an intracellular enzyme complex, and serum levels of superoxide dismutase are higher in patients with melasma compared to controls, indicating increased systemic oxidative stress and supporting the use of antioxidants in the treatment of melasma [75].

k. Morphological Changes (Epidermis)

Morphological changes in melasma appear to be related to an increase in the number and activity of melanocytes. Examination of melanocytes in melasma lesions has shown higher melanogenic activity in the affected epidermis compared to adjacent areas, highlighting a local functional disturbance of the epidermal-melanin unit [39]. The most important morphological element in melasma is the increased epidermal density of eumelanin in all layers, including the stratum corneum, where there is greater manipulation of melanin compared to adjacent skin [74].

l. Pigmentation Disorders

Skin color is generally a combination according to the Fitzpatrick scale, created in 1975 [33]. According to the Fitzpatrick classification, 13% of the population had skin type II, 36% had skin type III, 40% had skin type IV, and 10% had skin type V, with skin types III, IV, and V being statistically more prevalent in people with melasma [70]. The etiology of these changes may be related to altered melanocyte density, inadequate melanin production, or a combination of both scenarios [33]. Melasma is a pigmentation disorder that primarily affects women of reproductive age with higher Fitzpatrick skin types due to the hyperactivation of dermal melanocytes [84].

m. Diagnosis

To diagnose melasma, several procedures are available. The diagnosis involves investigating the patient's family and personal history of the disorder, with laboratory tests generally not required [90]. Four types of melasma can be identified: epidermal, dermal, mixed, and the less visible Wood's light examination for individuals with darker skin. Hormonal assays (evaluating hormonal levels), microscopic histopathology, electron microscopy, immunohistochemistry, and dermatoscopy are also used [23].

Hyperpigmentation can also be caused by medications, including antibiotics such as cyclophosphamide and tetracycline, antimalarials, and amiodarone hydrochloride. In these cases, the lesions are usually not symmetrical [61]. Melasma is clinically classified based on its topographic distribution into: central facial (affecting the central forehead, zygomatic, nasal, buccal, labial, supralabial, and mental regions) and peripheral (affecting the temporal, parotid, and mandibular regions) [62].

n. Treatments

Treatment Agents

Treatment agents for melasma emphasize the effectiveness of combined therapies for lightening lesions and reducing affected areas [58]. One of the most effective treatments for melasma is chemical peels, such as Tranexamic Acid, Mandelic Acid, Kojic Acid, and Glycolic Acid, which work by depigmenting and inhibiting melanocyte activity [26]. Among the available treatments, mandelic acid peels stand out for being milder than other acids and showing impressive results in lightening spots, treating acne through antibacterial and antiseptic actions, and anti-aging effects. Mandelic acid induces a gentler exfoliation, accelerates tissue regeneration, and stimulates collagen production [59].

Hydroquinone

Hydroquinone has been the most commonly used therapeutic option for melasma for over 50 years. It inhibits tyrosinase, reducing the conversion of Dopa to melanin. Other possible mechanisms of action include destruction of melanocytes, manipulation of melanosomes, and inhibition of DNA and RNA synthesis. When combined with tretinoin and corticosteroids, its potency is enhanced or diminished [18]. Hydroquinone is a skin-lightening agent that decreases melanin synthesis (the

endogenous pigment considered the primary determinant of color) by inhibiting the enzyme tyrosinase [44]. Hydroquinone, considered a first-line topical treatment, has been described for its lightening ability since 1936 by Oettel [45].

Azelaic Acid

Formulations containing azelaic acid are among the most commonly used in melasma therapy. Its mechanism of action involves competitive, non-permanent inhibition of the enzyme tyrosinase and modulation of growth factors [88]. Other possible mechanisms of action include destruction of melanocytes, manipulation of melanosomes, and inhibition of DNA and RNA synthesis. When combined with tretinoin and corticosteroids, its potency can be increased or decreased [18]. Azelaic acid is known for its skin-lightening properties, affecting melanin synthesis by inhibiting tyrosinase [44]. Its lightening ability has been described since 1936 by Oettel [45].

Retinoic Acid

Retinoic acid is an active metabolite of vitamin A that regulates the growth and differentiation rates of various cell types due to the possible cis-trans configurations of its side chain [48]. It promotes the separation of pigment grains present in keratinocytes and causes their displacement by inducing the movement of melanosomes, leading to a loss of color in the affected area. It has also been identified that this acid can inhibit the synthesis of tyrosinase in the melanin formation process [32]. Retinoids generally repair skin damage primarily caused by solar rays through restorative mechanisms and by limiting existing damage. Retinoic acid blocks UV induction in the matrix of metalloproteinases, a family of enzymes responsible for breaking down collagen, the primary constituent of the dermis. It also stimulates keratinocytes and controls fibroblasts, resulting in smoother skin and increased collagen production, making the skin thicker and more resistant to trauma [49].

Glycolic Acid

Glycolic acid works by exfoliating, thinning the epidermal layer of the skin, and minimizing the attraction between corneocytes. Thus, age-related changes cause alterations in the epidermis, leading to rapid dispersion of the pigment in melasma lesions [32]. Glycolic acid peels stimulate the synthesis of collagen and elastin, reduce the stratum corneum layer and expression lines, diminish the appearance of hyperchromic spots, and improve skin texture. It has keratolytic and antioxidant potential [50].

Chemical peels involve applying acidic substances to the skin, aiming for controlled exfoliation of the epidermis (the outer layer of skin), followed by regeneration, which enhances the natural process of skin restructuring [89]. Glycolic acid is one of the most commonly used acids for this purpose; chemically, it is a very small molecule, which means it penetrates the skin easily, reaching deeper layers and providing intense, visible effects. It is of natural origin, derived from sugarcane, and belongs to the alpha-hydroxy acid family [51].

Tranexamic Acid

Tranexamic acid interferes with plasminogen, whose activator is affected by UV radiation, inhibiting plasminogen action and preventing melanogenesis [32]. Plasmin activates the release of phospholipase A2 precursors, which acts in the production of arachidonic acid and induces the release of fibroblast growth factor. It is a potent factor for melanocyte growth [52]. Tranexamic acid has emerged as a significant alternative for treating melasma, given its ability to alter abnormal dermal changes related to melasma, such as increased vascularization [91]. A study aimed at evaluating the efficacy and safety of tranexamic acid in treating melasma compared localized microinjection versus topical treatment, with subjective clinical evaluation declaring injectable treatment superior [53].

Ascorbic Acid (Vitamin C)

Ascorbic acid inhibits melanin formation. It plays a role in protecting cells, acting on melanocytes to help even out skin tone [32]. The present review found beneficial effects of topical AA in scar healing, such as improved wound closure and depth, better colorimetry of spots, improved hydration, enhanced firmness, improved correction, reduced erythema, and decreased occurrence of revealed scars [54]. One of the beneficial actions of vitamin C is related to skin lightening, primarily due to the indirect stimulation of tyrosinase, specific inhibition of melanosomes, tyrosinase inhibition, and detrimental effects on melanocytes [55].

Kojic Acid

Kojic acid holds a prominent position among substances used for lightening various types of apparent hyperchromia. However, aside from its topical activity, there are no studies demonstrating systemic effects or side effects resulting from its use [56]. It is a fungal derivative from Acetobacter sp, Aspergillus sp, and Penicillium sp, obtained through carbohydrate fermentation. It exerts its effect by non-competitively inhibiting tyrosinase through chelation of copper ions, preventing the formation of the copper-protein enzyme complex, blocking oxidative processes, and suppressing melanin formation, leading to skin depigmentation. Kojic acid is used in concentrations of 1 to 4%, but its effectiveness can be increased by raising the concentration in formulations [22]. Despite its proven efficacy, kojic acid is a compound with low stability, sensitivity to light and heat, and a risk of oxidation [57].

Mandelic Acid

Mandelic acid causes mild exfoliation, thus inducing depigmentation of melasma lesions. It prevents melanin formation [23]. Mandelic acid provides gentle responses in facial rejuvenation, being effective in treating hyperpigmentation, acne scars, and hyperchromic spots [58]. It has gained popularity among dermatology and aesthetics professionals as an effective and minimally invasive treatment for signs of skin aging and hyperchromia, primarily due to its ability to accelerate cell renewal, removing dead cells [60].

o. Technology

Among aesthetic treatments, phototherapy stands out, performed with Light Emitting Diodes (LEDs), and can be applied to all skin types and age groups, where the visible light from LEDs varies according to wavelength techniques [1]. Light phototherapy is highlighted as a method of photobiostimulation for tissue repair, which increases local circulation, cellular control, and collagen extension [29]. Intense pulsed light targets the pigment. Emitting light pulses against the skin evaporates the pigment, causing a brownish discoloration on the skin [27].

Laser therapy is based on the principle of selective photothermolysis. Lasers emit light at a specific wavelength suited to the target chromophores. The target chromophore for pigmented lesions is melanin. The laser light absorbed by melanin generates a rapid burst of light, corresponding to the thermal relaxation time of melanin, thus effectively destroying the pigment [27].

Microneedling is a completely manual and simple technique that has proven capable of reducing hyperchromia caused by visible pigment changes, whether through the introduction of cosmetics or alone, facilitating fibroblast protection and subsequent new collagen fibers, as it induces exfoliation, cellular regeneration, resulting in firmer, more consistent skin with fewer spots, according to pre- and post-procedure treatment [28].

A variety of laser therapies have been studied in numerous clinical trials to date, demonstrating a wide range of effectiveness and adverse events. The five major categories of laser and light therapy include intense pulsed light (IPL), Q-switched lasers, picosecond lasers, non-ablative fractional resurfacing lasers, and ablative fractional resurfacing lasers [32].

Studies have shown that most patients treated with superficial and deep intradermal injections (intradermotherapy) of the compound were quite satisfied with the treatment. Notably, several patients with melasma reported improvements with the treatment [83]. Epidermal and dermal melasma can be addressed. With strategy, both types are treatable with a HyaluronPen Pressurized Pen. The active ingredients used include mandelic acid, kojic acid, phytic acid, tranexamic acid, among others. To avoid intense inflammatory processes and minimize the risk of melasma hyperpigmentation [82].

IV. RESULTS AND DISCUSSION

The use of exogenous hormones, such as estrogen and progesterone, is associated with the development of melasma, a condition characterized by skin hyperpigmentation. These hormones stimulate melanin production, especially during pregnancy when their levels are higher than normal. This makes women more susceptible to developing this dermatological condition (95). About 40 to 50% of women experience melasma during pregnancy or when using combined hormonal contraceptives, with cases also reported following hormone replacement therapy (96). Table 1 below summarizes data from a study analyzing the prevalence of melasma in women using hormonal contraceptives, as extracted from the studies.

Table 1: Data on the Prevalence of Melasma in Women Using Hormonal Contraceptives.

Study	Number of Patients	Melasma Prevalence (%)	Hormone Type
Handel et al. (2021)	250	8 to 34%	Oral Contraceptives, Sun Exposure
Sarkar et al. (2003)	200	19 to 40%	Sun Exposure, Family History
Hexsel et al. (2009)	224	10 to 27%	Pregnancy
Study in Iran	200	16%	Pregnancy
Study in Morocco	150	37%	Pregnancy
Study in Pakistan	300	46%	Pregnancy

The data show a high prevalence of melasma in women using oral contraceptives, reflecting both hormonal and environmental factors that significantly contribute to this hyperpigmentation condition. Melasma in patients using oral contraceptives ranges from 8% to 34%, as indicated in the table. Sun exposure, a common environmental factor, also plays a significant role and shows considerable results in the development of melasma. Additionally, melasma during pregnancy is quite evident, with percentages ranging from 16% to 46%, again highlighting the crucial role of hormonal factors in the onset of this condition.

The predisposition to melasma is directly related to the amount of eumelanin in the skin, varying with different phototypes (97). Melasma, characterized by increased hyperpigmentation, is more prevalent in individuals with darker skin phototypes, such as Fitzpatrick phototypes IV, V, and VI (98). It is observed that the incidence of melasma varies between ethnic groups and phototypes. As illustrated in the graph, this condition is more common in women with medium skin tones of phototypes III and IV, affecting between 50% and 70% in some populations (Fig. 1). In individuals with lighter skin, phototypes I and II, the prevalence is lower; however, sun exposure increases the risk of developing melasma in these groups.

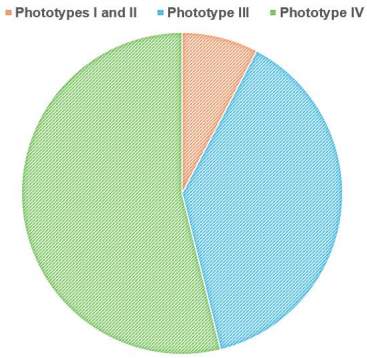

Figure 1: Percentage of melasma occurrence in women, categorized by phototypes. Phototypes I and ll (10%); phototypes Ill (50%) and phototypes IV (70%).

V. CONCLUSION

This work highlights the complexity of melasma, a chronic dermatological condition with a multifactorial etiology involving genetic, hormonal, and environmental factors. The therapeutic approach to melasma requires a detailed understanding of the underlying processes of skin pigmentation, particularly concerning the regulation of melanogenesis. The variability in the effectiveness of currently available treatments suggests the need for combined and individualized strategies that integrate advancements in topical, oral, and technological therapies. Future research should focus on interventions that not only address the symptoms but also target the causal mechanisms to prevent recurrence.

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