

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Kalf (Melasma): A Review of Unani Perspective and Therapeutic Interventions

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ABSTRACT

Melasma, also known as "Kalf" in Unani system of medicine, is a common pigmentary disorder, predominantly affecting sun-exposed areas of the skin, resulting from accumulation of Sauda (black bile) within the skin. The prevalence of melasma ranges widely between 3%-33% among different population. Melasma frequently results in a major psychological impact that negatively affects emotional health and quality of life.

Melasma's recurring recurrence, chronic character, and multi-factorial origin make management extremely difficult. Contemporary scientific treatments for melasma, including topical medications and lasers, often provide inconsistent results and can have adverse side effects. The Unani approach, however, emphasizes a holistic method, aimed at balancing humors, incorporating medicinal therapies, regimenal therapies and dietary adjustments.

This review explores the epidemiology, etiology, clinical presentation and management of melasma, highlighting the Unani system's perspective on its pathogenesis and treatment.

Keywords: Pigmentation disorders, Hormonal influence, Sun exposure, Sauda, Holistic approch.

INTRODUCTION

Melasma is a common chronic acquired pigmentary disorder predominantly affecting photo-exposed areas such as the cheeks, forehead, temples, nose, chin, periorbital regions, and upper lip in adults, especially women of reproductive age [1]. This condition is characterized by sharply demarcated, blotchy, brown maculae that are symmetrically distributed. The term melasma is derived from the Greek word "melas" meaning black, which reflects its brownish clinical appearance. Melasma is also known by other terms, including 'chloasma', 'mask of pregnancy', and 'liver spots' [2].

In Unani system of medicine, melasma is known as "*Kalf*" and it is defined as a blackish patch formed by the coalescing of many black spots called *'Barsh'* [3]. *Kalf* is caused by melancholic blood parts that ooze out of capillaries and get accumulated under the skin [4].

Melasma is a condition that affects people of all races and ethnicities, but it is more prevalent in Fitzpatrick skin types III to IV, especially in populations of Hispanic, Asian, and African people [5].

Melasma often causes a significant psychological impact with a negative effect on quality of life and emotional well-being [2,6]. Furthermore, the medical treatment and procedures are very expensive whose results are not always up-to patient's expectations [2].

The exact etiology of melasma is not clearly understood. Genetic predisposition, UV exposure, pregnancy, use of combined oral contraceptive (COC), ovarian tumors, hepatopathies, hormone replacement therapy, photo-sensitizing drugs, procedure and photo-toxic drugs are some of the predisposing factors [7].

In Unani system of medicine, kalf is considered as a humoural disease occurring due to any derangement in the quality and quantity of Khilte Sauda (black bile) [3,8]. Some other causes include Dam-e-Muharraq (charred blood), Sauda-e-Muharraq (charred melancholic blood), [9] Sauda producing Aghziya (foods) and Adviya (medicines), pregnancy, liver and spleen diseases. Risk factors for Kalf, include exposure to sun light, dyspepsia, unhygienic conditions, unhealthy diet and amenorrhoea [3,10,11,12].

Management of melasma is quite challenging due to its recurrent nature, chronicity of disease and multi-factorial etiology [13]. Contemporary scientific treatment includes topical medications such as hydroquinone, kojic acid, tranexamic acid, topical corticosteroid. Chemical peels, lasers, microdermabrasion, intense pulse therapy are also used but results are inconsistent or short lasting with associated adverse effects like erythema, skin irritation, post inflammatory hypermelanosis, contact dermatitis and skin atrophy [14].

An individual's temperament and humoural imbalances are taken into account in the Unani system of medicine for the management of kalf. In Unani system of medicine *kalf* is treated with topical application of drugs having *Jali* (Detergent), *Muhallil* (Resolvent), *Muhassine laun* (Color fearing agent) and *Muhammir* (Rubefacient) properties [4].

EPIDEMIOLOGY

Melasma is an extremely prevalent cutaneous disorder that affects 0.25 to 4% of patients seen in South East Asian dermatology clinics and is considered the most common pigment disorder among Indians.

Although it primarily impacts women, men may also develop melasma, accounting for about 10% of cases [15]. A larger disparity between men and women was seen in an Indian study: out of 120 melasma patients, 25.8% were men [16].

The age at which melasma first appears varies. In some research, the average age of onset can vary between 20 to 30 years, however in others, it ranges from 36 to 40 years [17]. The major primary risk factors for men include family history (39.0%) and sun exposure (48.8%). Risk factors for women were using combined oral contraceptives (COC) (19.4%), pregnancy (45.3%), and being exposed to the sun (23.9%) [16].

ETIOPATHOGENESIS

Following factors play key role in the pathogenesis of Kalf :-

SUN EXPOSURE

In contemporary scientific literature, sun exposure is thought to be the most important extrinsic element in the pathophysiology underlying melasma since it only affects photo-exposed skin, develops later in darker phototypes, is worse after sun exposure, and is more common in intertropical nations [15].

Some effects of sun spectrum are described below;

Effects of UVB

UVB directly increases melanocytes migration, proliferation, and melanogenesis. Furthermore, it indirectly increases the secretion of cytokines such as interleukin-1 and endothelin-1, and peptides, particularly α -melanocyte-stimulating hormone, and adrenocorticotropic hormone that are produced by UV-stimulated keratinocytes. Tyrosinase activity and tyrosinase-related protein 1 get triggered by these peptides, which in consequence promote melanocyte proliferation and melanin formation. The process of melanogenesis is further aided by the increased expression of inducible nitric oxide synthase (iNOS) in keratinocytes in melasma [18].

Effects of UVA

UVA has a less direct effect on essential skin biomolecules than UVB. Chromophores convert the energy they absorb into reactive species, leading to produce oxidative stress. Exposure to UVA rays may lead to systemic oxidative stress in addition to skin damage [19].

Effects of Visible Light

When UV and visible light cause inflammation in the skin, dermal fibroblasts produce more stem cell factor (SCF), which binds to the tyrosine kinase receptor (c-kit). Melanogenesis is stimulated by the elevated expression of SCF in the dermis and c-kit in the epidermis [15].

Role of Sauda and Sun light in the pathogenesis of Kalf

According to Unani System of Medicine, the pathogenesis of Kalf (melasma), revolves around the ascent of Ghaleez Saudawi Bukharat (viscid melancholic vapors or fumes) towards the facial skin and pores [21]. Heat and sun exposure also contribute to this process, which causes revascularization in the skin's outer layers, blood sequestration, and the formation of Saudā' Damawī Muhtaraq (burnt melancholic blood) as a result of capillary damage [22].

HORMONAL INFLUENCE

It has been demonstrated that estrogen contributes to the pathophysiology of melasma, which explain why it is more common in pregnant women, postpubescent women, and those who use oral contraceptives. Researches indicates that melasma lesions have more estrogen receptors in the dermis and progesterone receptors in epidermis [23]. Tyrosinase and Microphthalmia-associated transcription factor (MITF) pathways can be activated to cause the synthesis of melanin when estrogen binds to its receptors on melanocytes and kerationocytes. Furthermore, elevated expression of the ion exchanger-regulating PDZ domain protein kidney 1 (PDZK1) in melasma lesion may aid in mediating the interactions between ion exchangers and estrogen to promote melanosome transfer and melanogenesis [1,2,24].

Hormonal Infulence is associated with disruption of Saudā

Unani System of Medicine also mentioned that the condition of kalf may develop during pregnancy or postpartum, when there is Ihtibās-i Tams (menstrual retention) or cessation of purpureal blood. This cessation can lead to the collection of blood and waste materials in the body, as well as to the production and disruption of Saudā, resulting in Ghaleez Saudawi Bukharat (viscid melancholic vapors) formation [21,25].

VASCULARIZATION AND MELASMA

Studies have confirmed that the number of blood vessels, vessels size, and vessel density is more in melasma lesions than in perilesional normal skin [26]. Immunohistochemical analysis of factor VIIIa-related antigen revealed a significant increase in the quantity, size, and density of enlarged blood vessels [27]. Because functional vascular endothelial growth factor (VEGF) receptors were shown in melanocytes in vitro, the increased expression of VEGF in keratinocytes has given rise to the theory that VEGF may influence the behavior of melanocytes in the skin. There have also been reports of increases in c-kit, stem cell factor (SCF), and inducible nitric oxide synthase levels, which may have an impact on vascularization [26,27,28].

Avicenna and Rhazes first introduced the hypothesis of vascularization. Revascularization beneath the upper layer of skin induces skin darkness attributed to their explanation. They recognized that abnormal vascular diameter expansion of the affected area could lead to vascular rupture, intensifying the situation [3,4,22].

GASTRIC DISORDERS AND MELASMA

Studies suggests that, digestive ailments, such as stomach complaints, are common among melasma patients (307 per 100,000 population/year) [29,30]. One study suggests that cirrhosis of the liver may produce melasma.

Atrophic gastritis is a digestive illness that leads to zinc deficiency. Zinc deficiency could eventually result in increased estrogen levels [31]. Excess estrogen elevates alpha melanocyte-stimulating hormone (α -MSH) [32]. α -MSH may ultimately result in melasma.

Atrophic gastritis symptoms comprise pain [33]. Dyspepsia results in pain [34]. Pain triggers stress [30]. Stress boosts estrogen levels [35]. High estrogen levels increases α -MSH, resulting in mealsma.

Gastro Esophageal Reflux Disease (GERD) is associated with elevated ghrelin levels, a peptide released by the stomach that regulates secretion and motility [36]. Ghrelin promotes corticotropin-releasing hormone (CRH) [36]. CRH stimulates adrenocorticotropic hormone (ACTH) [37]. ACTH results in melasma [30].

Role of Amraz-e-Mi'da in the pathogenesis of Kalf

Unani scholars have also described that kalf develops after the consumption of Saudawi foods or due to the presence of Saudawi fuzlat (melancholic wastes) in the body, which in turn generate contaminated stomach gases, leading to the formation of Bukharat-i Sokhta (burned vapors) and subsequent viscid melancholic vapors. These vapors or fumes ascend towards the facial skin and pores, resulting in kalf [3,22].

LIVER DISORDER AND MELASMA

Chronic liver disease patients commonly have muddy gray hyperpigmentation, particularly in sun-exposed areas [38]. Hemochromatosis is characterized by hyperpigmentation in sun-exposed areas, which can also indicate iron deposition in other organs [39]. Iron deposition in skin activates melanocytes, leading to increased melanin formation [40]. Sun exposure exacerbates this process.

Role of Amraz-e-Jigar in the pathogenesis of Kalf

According to Unani scholars also, kalf is associated with Saudawi (melancholic) disorders of the liver and spleen which lead to predominance of ghalbae-Sauda (black bile) in the blood [3].

CLINICAL PRESENTATION

Melasma is characterized by symmetrical brownish macules with uneven outlines and distinct boundaries. It mostly affects sun-exposed areas, such as the face and cervical region, although it can also affect the arms and sternum [2,17].

CLASSIFICATION

Melasma is categorized into three clinical categories based on the distribution of its macules. [5]. The centrofacial pattern affects the central face, the forehead, nose, cheekbones, upper lip, and chin all are involved [17]. The malar pattern is distinguished by the involvement of the cheekbones and nose. The mandibular pattern focuses primarily on the mandibular dermatome [17].

Historically, melasma has been classified as having three histologic variants: epidermal, dermal, and mixed [5]. In the epidermal type, melanocytes in the epidermis are generally enlarged, have prominent dendrites, and increased melanosomes [15]. The dermal subtype comprises melanophages in both the superficial and deep dermis. Melasma with mixed histology can have both epidermal and dermal characteristics [15,41].

DIAGNOSIS

Melasma is usually diagnosed clinically, and the dermatologist encounters no further challenges in this regard [2].

Wood's lamp examination - To ascertain the type of melasma (epidermal, dermal, or mixed) and the depth of melanin pigmentation, a wood's lamp examination can be beneficial. When examined under a wood's lamp, epidermal melasma typically appears light brown and exhibits enhanced color contrast. On the other hand, dermal melasma frequently appears somewhat bluish or grey and has less color contrast with wood lamps [42].

Dermoscopy - Using dermoscopy, melasma can be diagnosed. There is sparing of follicular apertures and diffuse reticular pigmentation in different shades of brown in melasma lesions [43].

Reflectance confocal microscopy - RCM provides a direct, noninvasive method of evaluating vast regions of melasma in vivo. Melanin is consistently observed in all layers of the epithelium and dermis, and hypertrophied melanocytes are seen in high resolution [2,43].

DIFFERENTIAL DIAGNOSIS

Kalf must be distinguished from a number of skin conditions. The clinical characteristics of these differential diagnoses have been thoroughly described by the Unani scholars, making it easier to identify and distinguish them.

Barash (freckle, lentigo): It is characterized by the appearance of several tiny black spots on the skin of the face, which are frequently reddish or bluish in color [3,10]. It has been proposed that Barash and freckle lentigo may be comparable, highlighting the necessity of close monitoring during the diagnostic procedure [44].

Namash (Naevus): It often manifests from birth as reddish, blackish, or violet patches that can occasionally take on a circular shape [3]. What distinguishes it from Kalaf is its unique congenital nature. Researchers have suggested that Naevus could be a Namash substitute, requiring careful clinical testing [44].

Khīlān/Til (Moles): It is characterized by an appearance of round, black spots that are slightly raised from the skin's surface [3]. A potential correspondence has been suggested between Khīlān/Til and moles [44].

Bahaq-e-Aswad (Pityriasis Nigra): This disorder causes the skin to darken, especially in areas like the back, chest, abdomen, and forelimbs. Essential indicators for differentiating Bahaq Aswad from Kalaf include the skin's rough texture and microscopic scales [3,10]. It has been proposed that Bahaq Aswad and Pityriasis Nigra could possibly be related [44].

Baras Aswad (Tinea): Regarding Baras Aswad, the skin exhibits roughened skin with darker areas and scaling. It is crucial to distinguish between Baras Aswad and Qūbā (tinea), as some Unani academics have regarded them as interchangeable terms [3,10].

MANAGEMENT

Topical, oral, laser, and chemical peels are commonly used conventional medical therapies for melasma. For melasma, topical medications such as hydroquinone, corticosteroids, retinoids, and photoprotection tend to be the first line of treatment [5,29]. Adverse reactions might occur following conventional melasma treatment options. Commonly used hydroquinone is associated with erythema, stinging, and paradoxical post-inflammatory hypermelanosis, along with additional dose and time-related side effects [45]. Topical corticosteroids, which are used to lessen discomfort, can lighten the skin and eventually induce atrophy [46]. Given these possible drawbacks and restrictions, it is now more important than ever to investigate and provide alternate therapeutic solutions.

The Unani medical system has identified a number of therapeutic modalities for melasma, including risk factor modification, Ilaj bi'l ghiza (dietotherapy), Ilaj bi'l dawa (medication therapy), and Ilaj bil-tadbeer (regimenal therapy).

- 1. **Risk factor modifications -** Avoiding excessive sun exposure, treating stomach issues, and treating irregular menstruation in women are crucial steps in modifying risk factors because they can cause or exacerbate Kalf [21].
- 2. Ilaj bi'l Dawa (Medication therapy) Ilaj bi'l dawa invovles the following steps:
- **Tanqiya-i-sauda** The initial therapeutic approach for managing Kalaf is Tanqiya-i Sauda (evacuation of black bile), which specifically targets Sauda (black bile) through Munzij (purgative) and Mushil (laxative) and Tabrid interventions [47].
- For munzij these drugs can be used such as Bādranjboya (Melissa axillaris), Bisfā'ij (Polypodium vulgare L.), Halīla Siyāh (Terminalia chebula Retz.), Usţūkhudūs (Lavendula stoechas L.), Aftīmūn (Cuscuta reflexa L.), Mā al-Jubn (whey) [8].

- For mushil drugs such as Maghz Amaltās (Cassia fistula L.), Barg-i- Sanā (Senna alexandrina Mill.), Turbud (Operculina turpethum), Ghārīqūn (Agaricus alba L.) can be used [8].
- For tabrid drugs such as Luāb-i Resha Khatmi (Althaea officinalis L.), Shira Bādiyan (Foeniculum vulgare Mill.), Shīra Luāb-i Behīdāna (Plantago ovata Forssk.), Shīra Unnāb (Zizyphus sativa Gaertn.), Tukhme Kasni (Cichorium intybus L), Arq-i Shāhtara (Fumaria parviflora Lam) can be used [8].
- Taqwiyat-i-Mi'da Following tanqiya-i-sauda, Taqwiyat-i Mi'da, which involves the administration of Muqawwi-i Mi'da (stomach-tonic) medications such as Mastagi (Pistacia lentiscus Linn), Heel Khurd (Elettaria cardomomum L.), Saleekha (Cinnamomum cassia Blume), Darchini (Cinnamomum zeylannicum), Qaranfal (Syzygium aromaticum L.), Zanjabeel (Zingiber officinale Roscoe), Filfil Daraz (Piper longum Linn.), Filfil Siyah (Piper nigrum Linn.), Oode Balsan (Commiphora opobalsamum L.), Habbul Aas (Myrtus communis Linn.), Chiraita Shirin (Swertia chirayta Buch. Ham.), are implemented [48,49].
- **Tasfiya-i-Jild** It is achieved by using medicine which exhibit different pharmacological properties such as Jali (detergent), Qashir (scaling), Ghassal (irrigator), Muhammir (rubefient), Muhallil (Resolvent), Muhassine laun (Color fearing agent) [4].
- 3. Ilaj bil-Tadbeer (Regimenal therapy) Tanqiya-i Mawād (expulsion of toxic material) is the basic concept underlying Unani therapy for the treatment of chronic ailments like kalf (melasma). Harmful humors are removed from the body through a series of systemic processes. A few of these include Ishāl (purgation), Fasd (venesection), Hijāma (cupping), Irsāl-i 'Alaq (leeching), Qay (emesis), Huqna (enema), Riyāzat (exercise) and Dalk (massage) [21].
- 4. Ilaj bi'l ghiza (Dietotherapy) Unani system of medicine holds that kalf can be cured or can be improved with the help of certain dietary plans dependent on the temperament. Therefore, some foods like water peas, grape juice, rice milk, almond porridge, lamb steak, can help lower melasma. Ma'al-Jubn is also recommended, as it has tremendous benefits in treating melasma. It is possible to reduce melasma and lighten the skin or treat hyperpigmented areas by avoiding foods that produce sauda, such as eggplant, dates, cow's meat, salty food [4,50,51].

DISCUSSION

Melasma is a common skin condition and it recalcitrant to available treatment. In classical literature of Unani system of medicine, some predisposing factors such as sunlight, hormones, pregnancy, gastric disorders and liver disorders are mentioned as probable reason for this disorder. These factors are also validated by modern scientific literature. Melasma remains a complex condition with significant psychological and cosmetic impact. Exploring the molecular pathways underlying the vascular changes, hormonal influences, and melanocytes activation in melasma may offer novel therapeutic targets for more effective treatments with fewer side effects. The current medical approach, though effective in some cases, leaves much to be desired in terms of long-term results and minimizing side effects. Traditional Unani systems of medicine, offer valuable insights into holistic, patient-centered care that may complement contemporary scientific interventions such as topical agents, chemical peels, and laser therapies and improve outcomes for patients with melasma. While contemporary treatments focuses on symptomatic relief, Unani system of medicine, with its holistic approach focuses on balancing the body's humors. It offers a promising alternative by addressing underlying imbalances through polyherbal Unani formulations, dietary modifications and lifestyle modification. Investigating the synergy between contemporary treatments and Unani therapies could provide a more comprehensive treatment paradigm, combining the strengths of both systems.

CONCLUSION

Kalf (Melasma) has been vastly discussed in Unani system of medicine including its etiopathogenesis and treatment approaches. Contemporary treatments like topical agents, chemical peels, and laser therapies can offer short-term improvements, their inconsistent results and potential side effects highlight the need for more effective, long-lasting solutions. While Unani medicine provides a promising complementary approach, further clinical research and clinical trials are needed to validate its effectiveness in managing melasma. Future research should focus on bridging the gap between these systems to create more comprehensive, individualized, and effective treatment strategies for this challenging condition.

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