"A CLINICO-EPIDEMIOLOGICAL STUDY OF MELASMA IN MEN"

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ABSTRACT

BACKGROUND: Melasma is one of the most common and distressing pigmentary disorder presenting to dermatology clinics. It is more common in women, in Indians men seems to be frequently involved. The precise cause of melasma remains unknown, but genetic or hormonal influences with UV radiation are important. It is notably difficult to treat and has a tendency to relapse. Its population prevalence varies according to ethnic composition, skin phototype, and intensity of sun exposure. There are hardly any studies delineating the clinical and etiological factors of melasma in men and the present study was taken up to fill this lacuna.

OBJECTIVES: To study the clinical pattern and the types of melasma in men.

To study the age of onset and different etiological factors of melasma in men.

MATERIAL AND METHODS: The study was undertaken from January 2015 to July 2016. All men between 20 -50yrs of age, having melasma attending to the Department of Dermatology, Sri R.L.Jalappa Hospital and Research centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar were enrolled in the study. A written consent was taken from patient. A detailed history including occupation, onset, duration and evolution of melasma, predisposing factors like sun exposure, genetic factors, drug intake and cosmetic usage was taken followed by general physical examination, cutaneous examination and Woods lamp examination was done and recorded in a proforma. Laboratory investigations like complete haemogram, hormonal profile, liver function tests were done whenever necessary depending on the presenting condition.

RESULTS: Of 72 patients, the youngest age was 22 years and eldest was 50 years. The mean age of onset was 31.48 years. The duration of melasma varied from 3 months to 6.5 years with average mean of 2.33 years. The etiological factors identified were, sun exposure in 42 patients (58.33%), family history in 29 (40.27%), cosmetic usage in 8 (11.11%), phenytoin drug intake in 3 patients (4.16%). Laboratory investigations revealed hepatic disorders in 5 patients(6.94%), increased luteinizing hormone (LH) and low testosterone in 2 (2.77%) and hypothyroidism in 4 patients (5.55%). According to clinical patterns, malar pattern is seen in 65.27% of patients, centro-facial in 31.94% and mandibular in 2.77% of patients. The commonest skin type found to be type IV (63.88%) followed by type III (30.55%) and type V (5.55%). Wood's lamp examination showed epidermal type in 35 patients (48.1%), dermal type in 24 (33.33%) and mixed type in 13 (18.06%) patients. Their MASI scores ranged from 1.2 to 24, with mean score of 11.61.

CONCLUSION: Melasma is more frequently observed in Indian men, but definitely less common than in women even though only male patients with melasma were analyzed. Although melasma has multifactorial etiology, the main aggravating factors appeared to be sun exposure and family history. Early reporting of patients for treatment, reflects the concern regarding their facial appearance. Here in we have tried to elucidate the epidemiology, clinical patterns, and etiological factors in the causation of this pigmentary imperfection.

KEY WORDS: Melasma, Men, Clinical, Epidemiology.

LIST OF ABBREVIATIONS

UVR	Ultra Violet Radiation
ACTH	Adrenocorticotropic hormone
MSH	Melanocyte stimulating hormone
PPAR	Peroxisome proliferator activated receptor
NGFR	Nerve growth factor receptor
OCP	Oral contraceptives pills
LH	Luteinizing hormone
FSH	Follicle stimulating hormone
TSH	Thyroid stimulating hormone
VEGF	Vascular endothelial growth factor
MASI	Melasma area and severity index
MSI	Melasma severity index
MAMI	Melasma area and melanin index
SCF	Stem cell factor
RCM	Reflectance confocal microscopy
DEJ	Dermo-epidermal junction
PIH	Post inflammatory hyperpigmentation
HQ	Hydroquinone
NAG	N-acetylglucosamine
TXA	Tranexamic acid
PDGF	Platelet derived growth factor
TGF	Transforming growth factor

PRP	Platelet rich plasma
GA	Glycolic acid
SA	Salicylic acid
TCA	Trichloroacetic acid
IPL	Intense Pulse Light
Q-S Nd:YAG	Q-Switched Neodymium doped Yttrium aluminum garnet
Er:YAG	Erbium –Yttrium aluminum garnet
PDL	Pulsed dye laser

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INTRODUCTION

Melasma is an acquired increased pigmentation of the skin characterized by symmetrical and confluent grey-brown patches mostly on the areas of the face exposed to the sun, such as the cheeks, forehead, and chin. It rarely affect other areas such as the neck and forearms.[1,2]

The exact prevalence of melasma is unknown in most of the countries. Melasma is a very common cutaneous disorder, accounting for 0.25 to 4% of the patients seen in Dermatology Clinics in South East Asia, and is the most common pigment disorder among Indians.[3,4] The disease affects all races, but there is a particular prominence among Hispanics and Asians. Although women are predominantly affected, men are not excluded from melasma, representing approximately 10% of the cases.[5]

The exact underlying etiology for melasma remains unknown while several well known risk factors exist. Melasma is more common in darker skin types, particularly Fitzpatrick's skin types III and IV. Other reported risk factors include genetic predisposition, exposure to ultraviolet light, pregnancy, and exogenous hormones (i.e. oral contraceptives and hormone replacement therapy), hepatic dysfunction, use of cosmetics and photosensitizing drugs, procedures and inflammatory processes of the skin and stressful events.[6]

According to their clinical distribution, facial melasma lesions can be categorized into three types such as,1) Centro-facial pattern 2) Malar pattern and 3) Mandibular pattern. Under Wood's light examination, melasma is classified into four major histological types depending upon the depth of pigment deposition like 1) epidermal type, 2) dermal type, 3) mixed type and 4) intermediate type.[7,8]

Most of the previous studies were done on clinico- epidemiological profile of melasma in general population [3,9,10,11]. Except for few studies [12,13,14] paucity of data available in the literature on male patient with melasma. With this background, the present was undertaken to find out the clinico-epidemiological profile of melasma in male population of southern part of the Karnataka, India.

AIMS AND OBJECTIVES

1. To study the clinical pattern and the types of melasma in men.

2. To study the age of onset and different etiological factors of melasma in men.

DEFINITION

Melasma (from the Greek word, 'melas' meaning black) is a common, acquired, circumscribed pigmentary disorder which is characterized by more or less symmetrically distributed, medium to dark brown macular lesions with defined geographic borders, affecting sun exposed areas particularly forehead, cheeks, temples and upper lip.[15,16]

EPIDEMIOLOGY

Incidence

The exact incidence of melasma is unknown.[7] But it is relatively common acquired pigmentary disorder observed in all cultures and ethnicities. A survey conducted by Halder et al of 2000 black patients seeking dermatologic care in a private practice in Washington DC, revealed that the third most commonly cited skin disorders were pigmentary problems. [17]

Race

Melasma affects all racial groups but it is more prevalent in dark skin people (skin type IV to VI) such as of Hispanic, East Asians, Middle Eastern, Mediterranean- Africans including Indians who live in areas with intense UV (Ultra violet) radiation.[16,18] It is the most common pigmentary disorder among Indians. [17]

Sex

Melasma is most commonly observed in women, whereas men represent only 10% of cases and demonstrate same clinical and histopathologic characteristics as do women.[16] Pregnant women are most commonly affected than non-pregnant women. The term

"chloasma" is used to describe melasma developed during pregnancy. It is also described as 'mask of pregnancy'.[15]

Age

It is most common in second and fourth decade of life and in women of child bearing age. A study done on age incidence in men, found most common age group involvement in men is similar to as in females.[12]

Seasonal variation

Studies have shown that it worsens in summer and improves during winter season. An exacerbation of melasma is seen after a period of sun exposure and gradually fades during periods of sun avoidance.[7]

SKIN TYPE

Melasma is most common among people of skin types IV to VI, and Hispanics, Asian, Middle Eastern, and also in India.[18] The onset of the melasma lesions were found to be earlier in light skin types, when compare to dark skin types (V and VI) which is associated with late onset of melasma lesions.[19] There are six sun-reactive skin types, which was shown in table 1, among them melasma is more common in individuals of Fitzpatrick's skin types IV-VI. [16]

Table-1: Fitzpatrick's skin types

Skin type	Sun sensitivity	Pigmentary response
I	Very sensitive, always burn easily	Little or no tan
II	Very sensitive, always burn	Minimal tan
III	Sensitive, burn moderately	Tan gradually (light brown)
IV	Moderately sensitive, burn minimally	Tan easily (brown)
V	Minimally sensitive, rarely burn	Tan darkly (dark brown)
VI	Insensitive, never burn	Deeply pigmented (black)

Color of melasma macule:

Under normal light, color of the melasma lesions varies depending upon the depth of melanin pigment deposition. Epidermal shows- light brown color, dermal shows bluish grey, and mixed showed dark brown or black.[2]

ETIOPATHOGENESIS

Melanin is produced in melanocytes and stored in melanosomes within the keratinocytes. The number, melanin content, and location of these melanized cells (along with oxygenated and deoxygenated hemoglobin) helps to determine the color of the skin.[20] Melanosomes contain tyrosinase, a copper-containing enzyme that catalyzes the conversion of L-tyrosine to L-dopa and L-dopa to L-dopaquinone in melanin synthesis. Melasma is dysfunction of this pigmentary system.[21] The exact cause of melasma is unknown. Multiple factors have been implicated in the etiopathogenesis of this condition. These include genetic influences, racial, exposure to UV radiation, pregnancy, oral contraceptives, hormonal replacement therapies, thyroid dysfunction,

cosmetics, phototoxic and anti-seizure drugs. However, these associated factors are mostly reported in women. Little is known about the etiology of melasma in men.[6]

Sun exposure

Ultraviolet exposure is a major triggering and aggravating factor in the development of melasma. UVR on human skin induces production of α-MSH (Melanocyte stimulating hormone) and ACTH (Adrenocorticotropic hormone) in melanocytes and keratinocytes. α-MSH stimulates the activity of tyrosinase and increases melanin synthesis. These peptides also stimulate proliferation of melanocytes through MC1-R (Melanocortin-1 receptor).[22]

Very recently, it was suggested that visible light also induces hyperpigmentation on skin types IV-VI, but the pigmentation after visible light exposure is more intense and more stable as compared with UVA exposure. Thus the use of tinted mineral sunscreens protects both against UV and visible light and more effective in preventing melasma relapses.[19]

The role of mast cells in the development of melasma has not been definitively elucidated. Repetitive UV irradiation induces production of mast cell tryptase, which degrades type IV collagen and weaken the basement membrane in melasma skin. Mast cells also induce vascular proliferation by secreting angiogenic factors, including VEGF (Vascular endothelial growth factor), fibroblast growth factor-2, and transforming growth factor-ß. Elevated numbers of mast cells together with the presence of infiltrating leukocytes and dilated blood vessels might reflect the chronic skin inflammation that underlies the development of melasma.[23,24]

Prolonged UV exposure induces dermal inflammation and fibroblast activation leading to upregulation of stem cell factors causing increased melanogenesis.[2] The enhanced expression of iNOS (inducible Nitric oxide synthase) within keratinocytes also contributes to melanogenesis process in melasma after UV radiation.[19] Lesional melasma skin also showed significant cytoplasmic expression of c-kit protein with different intensities in all types of melasma.[25]

Chronic UV exposure down regulates the genes involved in lipid metabolism such as PPAR (Peroxisome proliferator activated receptor) alpha, PPAR gamma coactivator 1 alpha, diacylglycerol o-acyltransferase 2,[26] thus lipid metabolism seems to be the most affected biological process in the pathogenesis of melasma.[2] Several other genes involved in biological pathways were found to be affected such as genes involved in prostaglandin synthesis.

H19 gene also plays a minor role in the pathogenesis. It transcribes a noncoding RNA and is downregulated in melasma lesions leading to stimulation of melanogenesis and increased transfer of melanin from melanocytes to keratinocytes.[2,27]

Prostaglandins and COX2 (Cyclooxygenase 2) are synthesized or upregulated in the skin during UV irradiation and affect melanocytes and pigmentation. So role of steroids in treating melasma may include blocking this process.[26]

Neural involvement also plays a role in the pathogenesis of pigmentation. Increase in number of keratinocytes expressing NGFR and neural endopeptidase which are the crucial factors leading to pathogenesis were found in diseased skin.[28]

Genetic influences

Genetic predisposition plays a major role in the etiology of melasma. Skin phototypes III, IV or V and female gender are the most common genetic predisposing factors for the development of melasma. However, several studies suggest the possible role of other inheritable characters, probably multigenic.[29] Higher reported incidence of genetic predisposition is seen in certain racial groups. It has ranged from 10-70% in studies from Iran, Singapore and in Latin men.[1] statistically significant higher frequency of family history was found in Indian male patients with melasma when compared with females.[12]

Hormonal factors

Pregnancy

During pregnancy estrogens, progesterones and MSH are elevated especially in the third trimester.[30] Estrogens and progesterone increases transcription of tyrosinase and dopachrome tautomerase, which are involved in the development of pigmentation. Environmental factors, photosensitizing drugs or other clinical conditions like hyperthyroidism may exacerbate the pre-existing condition.[31] Sex steroids increase transcripts of genes for enzymes of melanogenesis in normal melanocytes. After delivery, melasma regress but never disappears and recurrence and aggravation of melasma during subsequent pregnancies are common. The most effective way to prevent the occurrence of melasma during pregnancy is to avoid sun exposure.[32,33]

Hormonal replacement therapy

There is a significant link between severity of melasma and current use of OCP (Oral contraceptives pills) due to stimulation of melanogenesis by estrogens and

progesterone. Melasma generally appears 1-3 years after its use and recedes more slowly than pregnancy related melasma, but never disappears completely. Similar development of melasma is seen in post- menopausal women on HRT (Hormone replacement therapy). Again the most effective way to prevent melasma in women taking OCP is to avoid sun exposure. Melanocytes express estrogen receptors with higher expression in the facial areas as compare with other regions, which explains the preferential location of melasma. Cases of melasma in men were reported who had taken exogenous estrogens for prostatic carcinoma and also seen in oral therapy with stimulators of testosterone production, a compound including DHEA (Dehydroepiandrosterone), androstenedione, indole-3-carbinol and Tribulus terrestres, a gonadotropic stimulator that increases LH (Luteinizing hormone) secretion.[34,35,36]

Hormonal profile in women

Hormonal profile in women with melasma has found significant rise of LH and lower levels of serum estradiol suggesting subclinical evidence of mild ovarian dysfunction.

Hormonal profile in men

Hormonal profile in men with melasma has found high circulating LH with low testosterone and an LH/FSH ratio indicating subtle testicular resistance.[13]

Thyroid disorders

Significant association between thyroid autoimmunity and melasma has been found. 4 times greater frequency of thyroid disorders both autoimmune and non-autoimmune, in patients with melasma compared to controls in a study suggests an association. Another study reported no differences in levels of autoantibodies to thyroid peroxidase, T3, T4 or

TSH in patients with melasma and controls. Thus there was no strong evidence between melasma and thyroid disorders. Further studies will be needed to clarify this.[37,38]

Others

Studies carried out in men having melasma pointed out some minor factors for the development of melasma such as infections and hepatic disorders.[12]

Drugs

Certain drugs have been reported as a possible etiology in some men. Diethylstilboestrol therapy for prostate cancer develops melasma as a side effect.[13] It increases tyrosinase- related protein 2, an enzyme involved in melanogenesis by 20 fold. Phenytoin therapy causes melasma like pigmentation as a side effect by exerting direct action on melanocytes causing dispersion of melanin granules and also induces increased pigmentation in basal epidermis.[2,12] Finasteride-induced melasma in the treatment of men for androgenetic alopecia was also reported.[39] Likewise, a wide variety of chemicals such as arsenic, iron, copper, bismuth, silver, gold and sdrugs like photosensitizing substances, antimalarials, tetracyclines, anticonvulsants, amiodarone and sulfonylureas can cause hyperpigmentation of the skin, by depositing in the surface layers or by stimulating melanogenesis.[40]

Cosmetics

Cosmetics have been one of the factors considered in the etiology of melasma. This consideration is further strengthened by the fact that most of the patients are healthy young adults and would have used a wide variety of available cosmetics; in addition, the disease is confined to the area which generally receives the greater part of cosmetic attention- the face and neck. Use of heavy cosmetics, perfumes, etc., that contain

psoralen derivatives or hexachlophane which are photodynamic and may cause hyper-pigmentation of face. Photoactive contaminants of mineral oils, petroleum, beeswax, some dyes, para-phenylenediamine and perfume ingredients are also been involved.[40, 41]

Mustard oil

Of all cosmetics used by men, mustard oil application is the common one. Mustard oil is derived from seeds of mustard plant, which belongs to family Brassicaceae. It is composed of fatty acids such as oleic acid, linoleic acid and crucic acid, which are toxic. Contact hypersensitivity occurs because of allyl isothio-cyanate, a chief antigen in oil, capable of inciting contact dermatitis. It is also a common photosensitizer which can lead to appearance of facial pigmentation. Role of mustard oil in the causation of melasma is still unclear and needs to be substantiated by more clinical evidence.[12,42]

Vascular factors

Besides neural and hormonal factors, blood vessels also play a role. UV radiation induces angiogenesis with up-regulation of proangiogenic factors like VEGF, basic fibroblast growth factor and interleukin-8. VEGF is a major angiogenic factor which enhances melanogenesis by interaction with its receptors present in the epidermal keratinocytes. Efficacy of two newer treatment modalities that is tranexamic acid and pulsed dye laser , lend support to the vascular theory of melasma.[19]

Stress

Stressful events and affective disorders were considered as triggers in the development. ACTH and MSH, produced as organic respose to stress, activate melanocortin receptors in melanocytes, inducing melanogenesis. Some authors consider melasma as the mask of stress.[43]

QUALITY OF LIFE

Melasma can have a severe impact on the quality of life by undermining a patient's psychological and emotional well-being.[44] Disfiguring facial lesions can lead to decreased social functioning, lowered productivity and reduced self-esteem. Clinicians should be aware that melasma may be a concern for the male patients also.[45]

CLINICAL FEATURES

Melasma is characterized by the insidious development of asymptomatic light to dark brown (in fairer skin) or dark pigmented (in darker skin) macules, predominantly seen over the forehead and malar eminences and to lesser degree sometimes on the lower portions of the cheeks, the chin, upper lip and the sides of the neck. The morphology of melasma lesion is blotchy, irregular, arcuate, or polycyclic and also can be linear, or evolve into an starburst distribution. The scalp, ears, eyelids are usually spared. Also other sites such as mucous membranes areolae of the breasts, axillary regions or external genitalia are not involved.[46,47]

Unusual presentations of melasma have been reported. A unilateral involvement of melasma over right side of the face with the other half being normal has been reported.[48] Tabata et al reported a case of band like melasma on the median line of the forehead of a middle aged woman. Melasma has also been reported over the forearm of the patient and over nape of the neck.[49,50] A study done by Sarkar et al found 43.9% of the patients were presented with melasma in the superciliary location.[51]

Classification

Melasma is classified into three patterns based on the distribution of lesion which was shown in the figure 1.

1. Centro- facial pattern (63%): commonest form, affecting cheeks, forehead, upper lip, nose and chin. The centro-facial pattern has been reported to be the most common one, accounting for nearly two-thirds of cases of melasma. However in dark skinned individuals, malar type appears to be the commonest type.[7]

2. Malar pattern (21%): involvement of the cheeks and nose. Among Indians it has been observed that malar type is the commonest type.[7]

3. Mandibular pattern (16%): involvement of the rami of the mandible.[7]

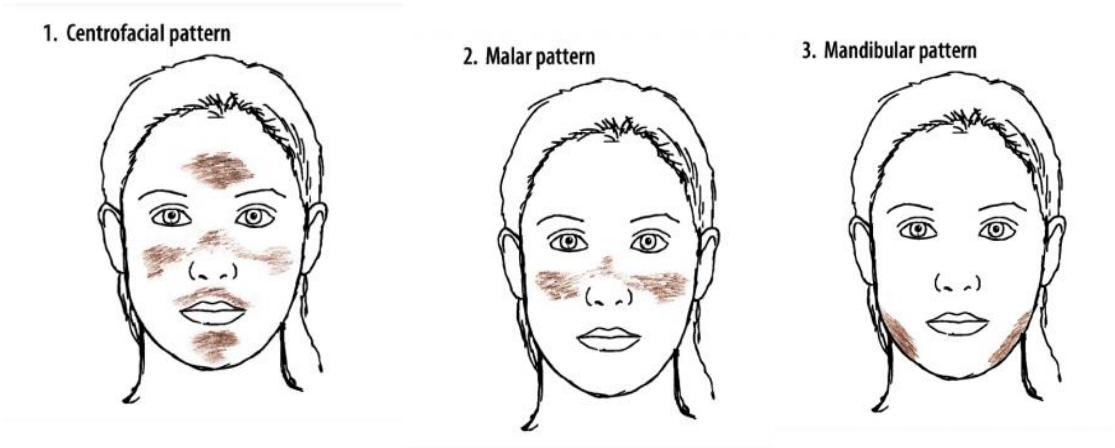


Figure 1- Clinical patterns of melasma

ASSESSMENT OF SEVERITY OF MELASMA

Melasma Area and Severity Index (MASI) SCORE

To quantify the severity of melasma and response to treatment, a Melasma Area and Severity Index (MASI) score was devised. The face is divided into 4 areas – forehead (F), right malar region (MR), left malar region (ML) and chin (C) corresponding to 30%, 30%, 30% and 10% of the face respectively (figure 2). The melasma in each of these four areas (Af, Amr, Aml, Ac) is given a numerical value. 0 – absent, 1 – < 10%, 2 – 10-29%, 3 – 30-49%, 4 – 50-69%, 5 – 70-89%, 6 – 90-100%. Severity of melasma

is based on two factors, Darkness (D) of melasma compared with normal skin and Homogeneity (H) of hyper pigmentation.[52] These are assessed on a scale from 0 through 4. The rating scale for darkness of melasma is as follows:

0 – Normal skin color without any hyper pigmentation

1 – Specks of involvement

2 – Small patchy areas of involvement <1.5 cm in diameter

3 – Patches of involvement >2 cm in diameter

4 – Uniform skin color without any clear areas

The rating scale for homogeneity of melasma is as follows:

0 – Normal skin color without any hyper pigmentation

1 – Barely visible hyper pigmentation

2 – Mild hyper pigmentation

3 – Moderate hyper pigmentation

4 – Severe hyper pigmentation

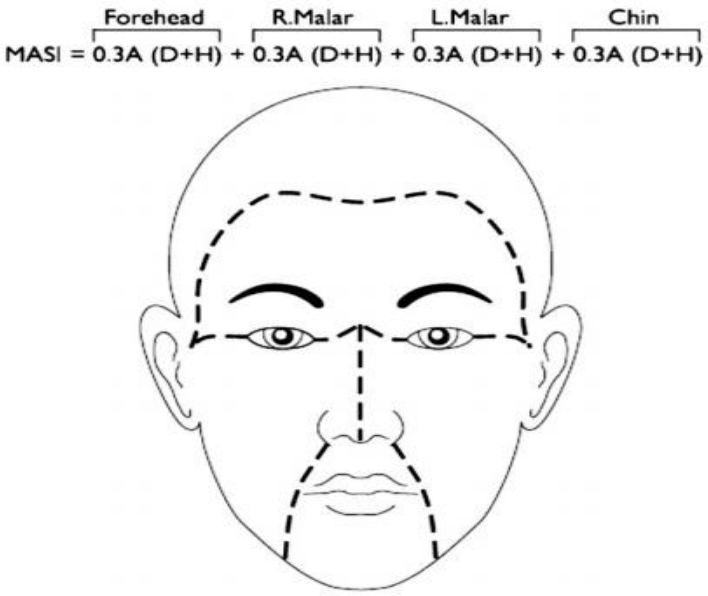


Figure 2: scoring of melasma area severity index (MASI)

To calculate the MASI score, the sum of the severity rating for Darkness (D), and Homogeneity (H) is multiplied by the numerical value of the areas involved (A) and by the percentages of the four facial areas. These values are added to obtain the MASI score and therefore,

MASI = 0.3 (Df + Hf) Af + 0.3 (Dmr + Hmr)Amr + 0.3 (Dml + Hml) Aml + 0.3 (Dc + Hc) Ac Where, "f" is forehead, "rm" is right malar, "lm" is left malar, and "c" is chin. The maximum score of MASI is 48 with minimum 0.[52]

Modified MASI (Melasma Area Severity Index) score

Modified MASI (modified Melasma Area and Severity Index) was proposed to learn and perform easily, and is scored as follows:[53]

Modified MASI total score:

0.3 A(f) D(f) + 0.3 A(lm) D(lm) +0.3 A(rm) D (rm) +0.1A(c) D(c)

The range of the total score is 0 to 24.

Area and darkness are scored as follows:

Area of involvement:

0 = absent, 1 = 10%, 2 = 10%-29%, 3 = 30%-49%, 4 = 50%-69%, 5 = 70%-89%, and

6 = 90% 100%;

darkness:

0 = absent, 1 = slight, 2 = mild, 3 = marked, and 4 = severe.

Melasma Severity Index score (MSI score): The proposed MSI score is calculated by multiplying the area of involvement with the square of pigmentation as follows:

MSI = 0.4 (a × p2) l + 0.4 (a × p2) r + 0.2 (a × p2) n

Where, “a” stands for “area of involvement,” “p” for “severity of pigmentation,” “l” for left face, “r” for right face, and “n” for nose.

In cases with uniform pigmentation, score can be simplified as,

MSI = a×p2

Scoring of pigmentation

Score 0: No visible pigmentation

Score 1: Barely visible pigmentation

Score 2: Mild pigmentation

Score 3: Moderate pigmentation

Score 4: Severe pigmentation

Scoring for area of involvement

≤10% area involved - score 1

11-30% - score 2

31-60% - score 3

>60% - score 4

The area involved, as well as the severity of pigmentation is scored from 0 to 4.[54]

Melasma Area and Melanin Index (MAMI): MAMI score is calculated in the same way as MASI score which was described above, but darkness and homogeneity are replaced by the single variable of the melanin index. This melanin index is measured at involved sites, using reflectance spectrophotometer. [55]

HISTOPATHOLOGY

Generally, histopathological features of melasma are subtle, so control skin biopsies are needed for comparison and diagnosis. Melasma was formerly classified histopathologically as epidermal dermal and mixed type by the location of pigments. Histopathological features of melasma showed flattening of rete ridges with epidermal thinning. Melanocytes in the epidermis are more active with increased melanin, is pathological hallmark seen mainly in the basal and suprabasal cells (figure 3). In some cases, it is seen in all layers of the epidermis. Stratum corneum of epidermis is thinned, and in some cases, a degraded molecule of the melanin is observed. [27,56,57]

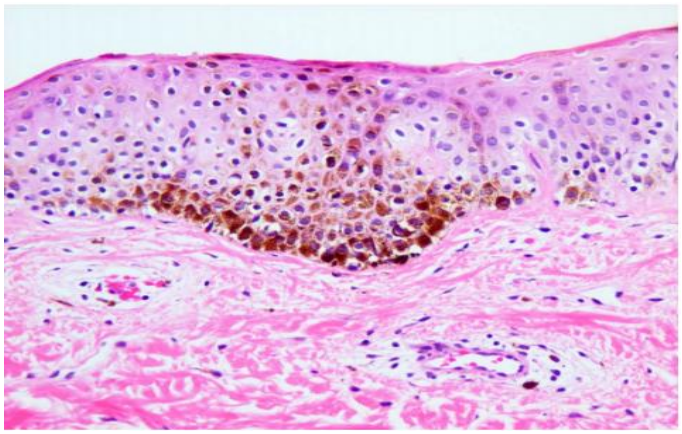


Figure 3: Histopathology of epidermal melasma lesion

In dermis, melanin pigments are seen mainly in macrophages or melanophages around superficial and deep dermal vascular plexus. Melanophages were present both in melasma skin and in some cases of normal skin also, so it is not considered as a hallmark of dermal type of melasma and suggested there is no true dermal type of melasma. Some non-specific changes are also seen such as solar elastosis, increased vasculature, telangiectasia and mild perivascular lymphohistiocytic infiltrate. [27,58]

In men

The immunohistochemical findings of male melasma lesions showed higher ER (estrogen receptor) and PR (progesterone receptor) expression than non lesional epidermis. Further investigation is needed to clarify the exact role of sex hormones and their receptors in male melasma.[59] Melasma skin in men showed prominent solar elastosis compare to non lesional skin,[58] which suggests that significant associated factor of melasma in men was sun induced aggravation.[42] Chronic UV radiation associates with signaling of paracrine cytokines and increased vascularity also play an essential role in the development of male melasma.[59]

Increased SCF (stem cell factor) expression is observed in the epidermis of male melasma compared with female melasma skin. The c-kit expression is also increased in male melasma epidermis compare with non lesional epidermis. (Figure 4a & 4b) Hence, SCF in the dermis and its receptor c-kit in the epidermis play an important role in the pathogenesis of hyperpigmentation of melasma in men.[59]Clinically and histologically, melasma in men is similar to women.[12]

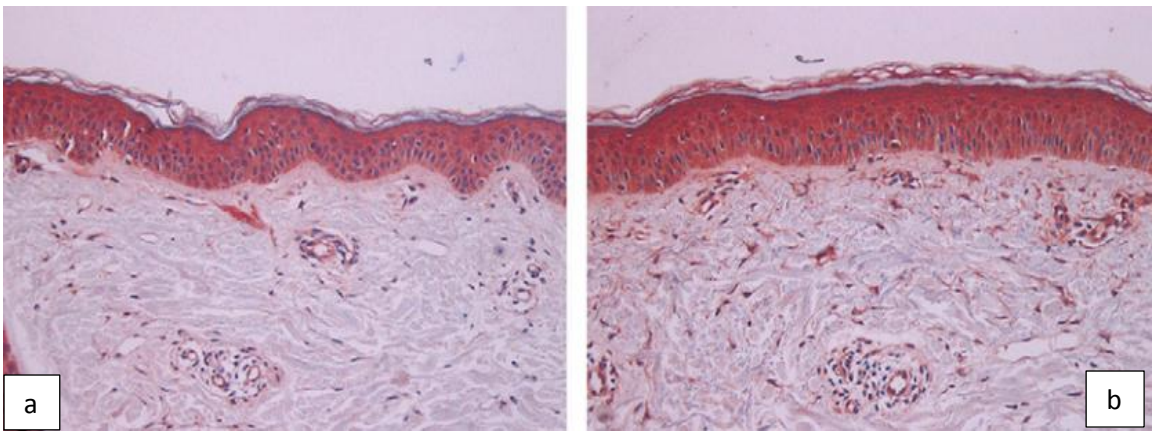


Figure 4: histopathology of (a) non lesional (b) lesional epidermis of male melasma

ELECTRON MICROSCOPY

In the stratum corneum, melanosomes were more in the melasma skin than in the non lesional skin. Melanosomes which were transferred into keratinocytes are arranged in a single array or sometimes membrane bound complexes. Melanocytes are filled with more mitochondria, Golgi apparatus, rough endoplasmic reticulum and ribosomes in the perikaryon of melasma skin indicating its increased cell activity than in normal skin. (Figure 5). More melanosomes are also found in membrane-bound clusters in basal and suprabasal keratinocytes in lesional skin than in normal skin.Dermal melanophages are present in both.[58]

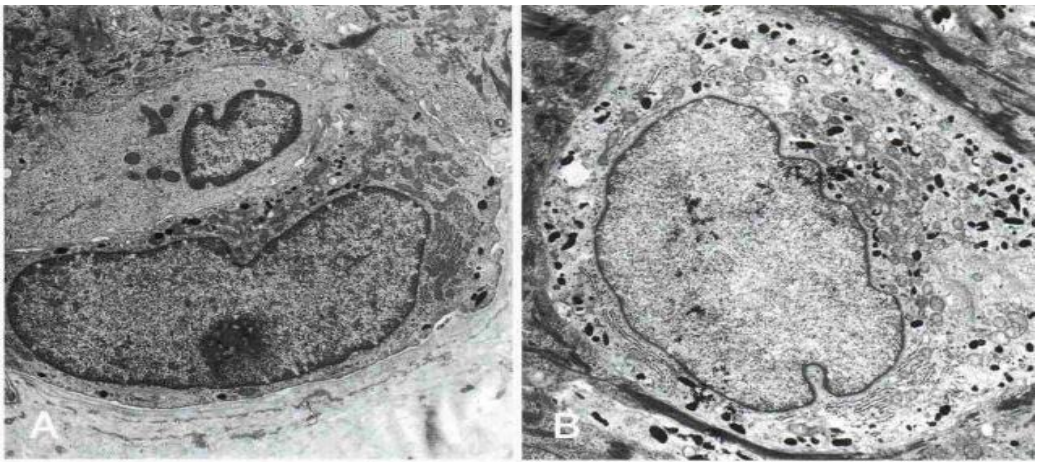


Figure 5- electron microscopy of perilesional skin (a) and melasma skin (b)

DERMOSCOPY

A dermatoscope is a non-invasive, diagnostic tool which magnifies subtle clinical surface features of skin as well as subsurface skin structures not normally visible even with a magnifying lens.[8] The dermoscopic diagnosis of pigmented lesions is based on both global and local features. Reticular pattern is the global feature seen in all melasma lesions. Lesions of melasma show diffuse reticular pigmentation in various

shades of brown sparing the follicles and sweat gland openings producing exaggerated pseudonetwork pattern with concave borders called the "jelly sign".[60] By examination, the color of melanin depends on the quantity or density and the location; going from black when localized in the stratum corneum, through shades of brown in the lower layers of the skin, to blue or bluish-gray in the dermis.[61]

Well-defined small patches of melasma (epidermal) demonstrate more diffuse blotchy brownish reticular pattern showing multiple granules and globules of dark brown color superimposed on reticular pattern[8] which is shown in figure 6.

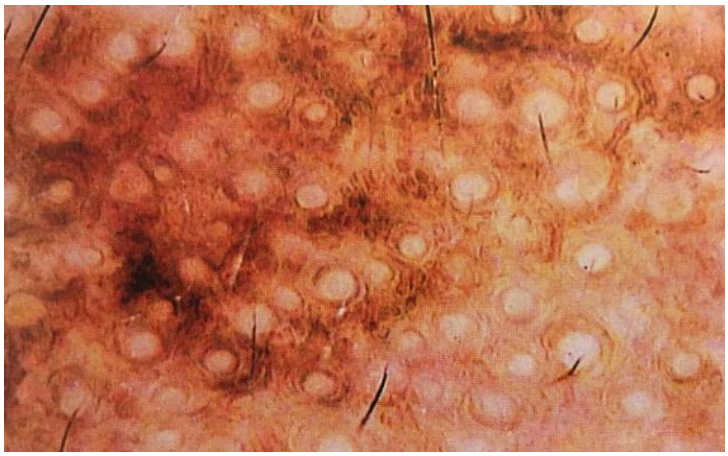


Figure 6: Dermoscopy of epidermal melasma

Melasma with uniform skin involvement and no areas of sparing with dark brown to grey hyperpigmented lesions depending on the depth of the pigment location (dermal melasma) show greyish brown or greyish black pigmented specks or arcuate, star-shaped, honeycomb and annular structures mainly in perifollicular location but sparing the follicles[8] (Figure-7).

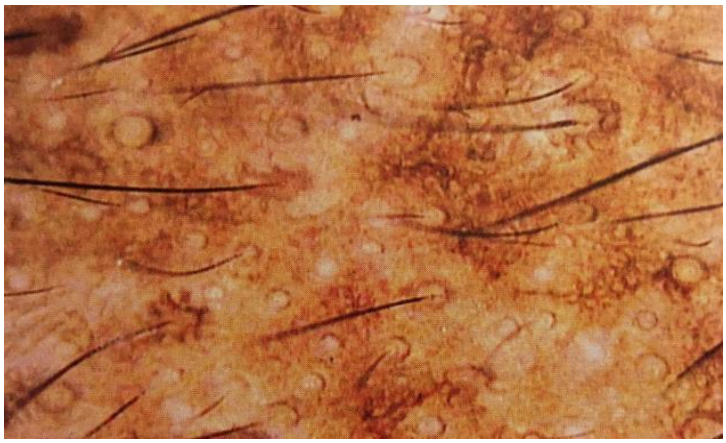


Figure 7: Dermoscopy of dermal melasma

Mixed melasma show diffuse reticular pigmentation of blotches of irregularly shaped, dark brown or blackish pigmentation with surface showing varying morphologies like arcuate, star-like, annular. Granules and globules of dark brown color are also seen especially in the perifollicular regions but sparing the follicles (Figure 8).

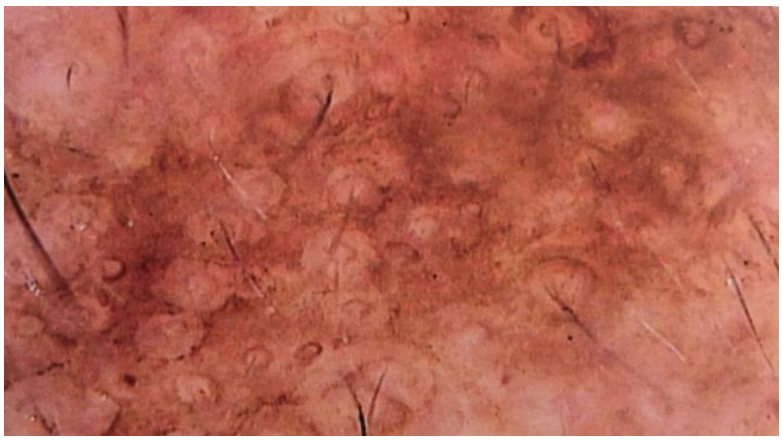


Figure 8: Dermoscopy of mixed melasma

Dermatoscopy helps in differentiating melasma from other conditions with facial hyperpigmentation, i.e. lichen planus pigmentosus, photomelanosis, seborrheic melanosis, nevus of Ota, ochronosis, lentigines and so on especially doing biopsy on face is best avoided.[60] As epidermal and dermal melanin gives different shades of color on dermatoscopy, it assists in differentiating epidermal from dermal melasma, in dark skinned in in whom Wood's lamp is of little help.

REFLECTANCE CONFOCAL MICROSCOPY

Reflectance Confocal microscopy (RCM) is a novel technique that allows the non-invasive imaging of epidermis and upper dermis at a cellular level resolution. RCM is widely used for the diagnosis of pigmented tumor and inflammatory skin diseases. RCM can detect melanocytes, pigmented keratinocytes and melanophages within epidermis and superficial dermis and helps in management of melasma.[26,62]

RCM features of epidermal melasma

RCM Shows characteristic hyper refractile cobblestone pattern in the basal layer and sometimes in the lower stratum spinosum of epidermis. The dermal papillary rings are usually not visible in the lesional melasma skin (Figure 9). RCM at the level of DEJ (dermo epidermal junction) shows bright dendritic cells in the lesional melasma skin[26,62] (Figure 10).

RCM features of dermal melasma

Shows plump bright cells in the papillary dermis which corresponds to melanophages. Also shows ragged, less refractile lacy structures corresponding to solar elastosis and dark round to tubular structures which corresponds to blood vessels in the upper reticular dermis which shown in the figure 11. [26,62]

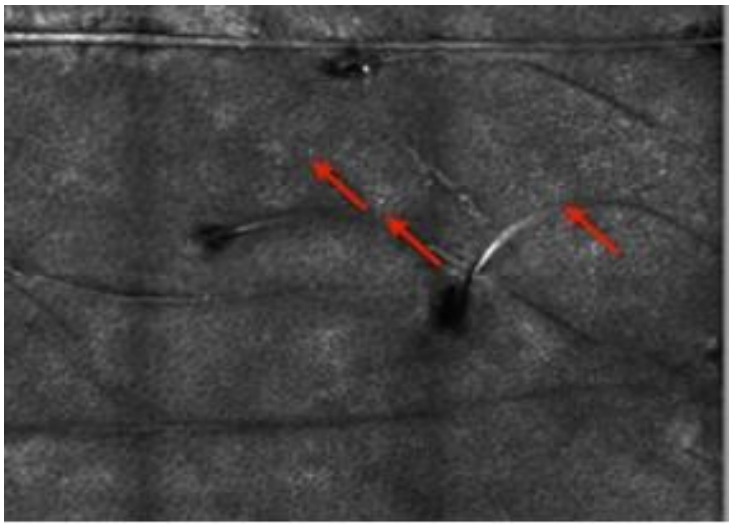


Figure 9: Reflectance confocal microscopy at the level of stratum spinosum- pattern of mottled pigmentation composed of clusters of bright keratinocytes (red arrows)

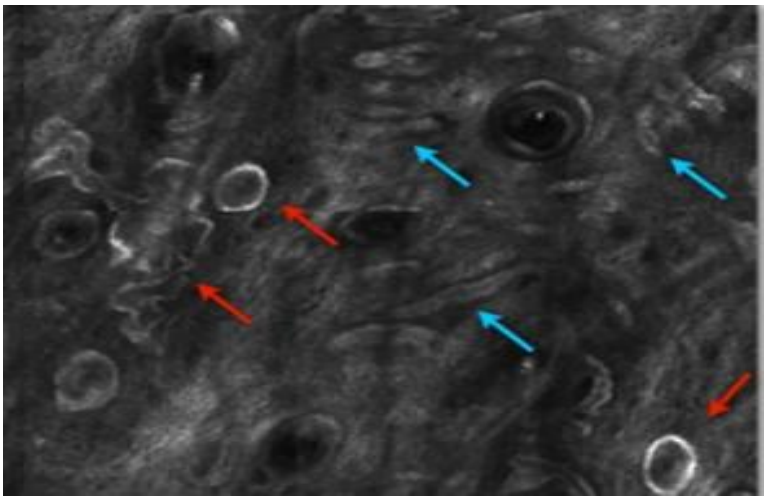


Figure 10: Reflectance confocal microscopy at the level of DEJ- shows bright rings (red arrows) and bright polycyclic papillary contours (blue arrows) due to pigmented keratinocytes and melanin rich melanocytes.

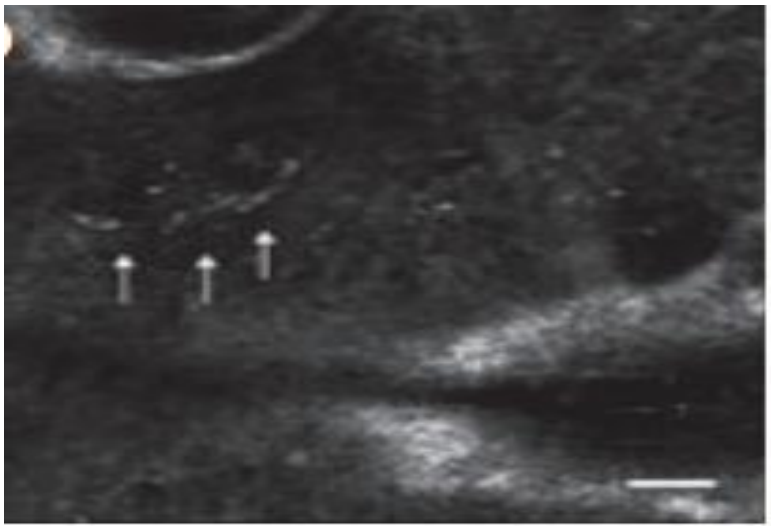


Figure11: Reflectance confocal microscopy of dermis showing plump brighter cells (arrow)

WOOD'S LAMP EXAMINATION

Wood's lamp examination of the affected skin helps distinguish whether the pigment is mainly localized in the epidermis, or in the dermis or both. Based on Wood's light examination of the skin, melasma can be divided into 4 types [8]:

Epidermal type

It is the most common type of melasma seen in about 70% of patients. There is color accentuation in this type as light is absorbed by the excess of melanin in the basal or suprabasal layers as shown in the figure 12a and 12b.

Dermal type

The pigmentation is not enhanced under wood's light examination, as most of the melanophages are seen in dermis as shown in the figure 13a and 13b. This type is seen in 10-15% of the cases.[8]

Mixed type

In this type, deposition of melanin is seen in both epidermis and dermis. Wood's light examination reveals both enhancement of lesions in some areas and no enhancement of lesions in other areas (Figure 14a & 14b). This type comprised 5% of melasma.[8]

Indeterminate type

This type goes unnoticed under wood's lamp, because melanin in these patients is abundant and most of the light is absorbed by this pigment. Only a small amount returns to eyes and the skin appears as dark and usually seen in individuals with phototype V and VI. However clinico-pathological findings of melasma and findings obtained by Wood's lamp examination are controversial because Wood's lamp underestimates the melanin deposition in the dermis.[63]

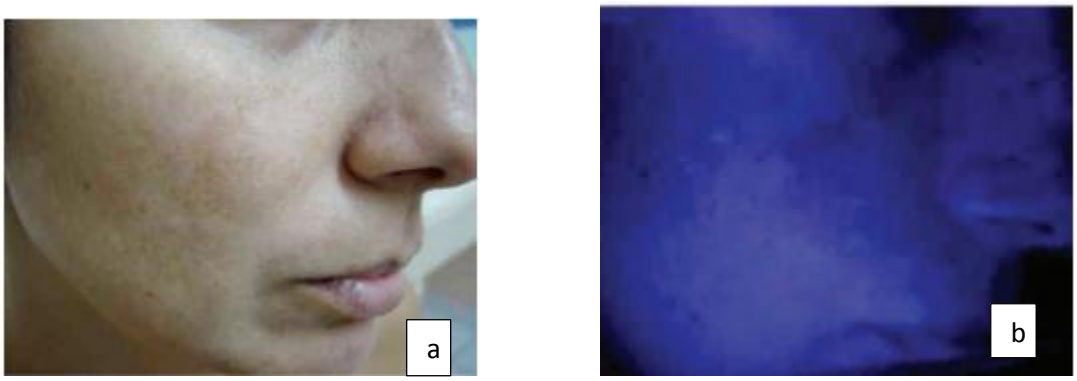


Figure 12: (a) epidermal melasma (b) Wood's lamp examination of epidermal melasma showing accentuation of lesions

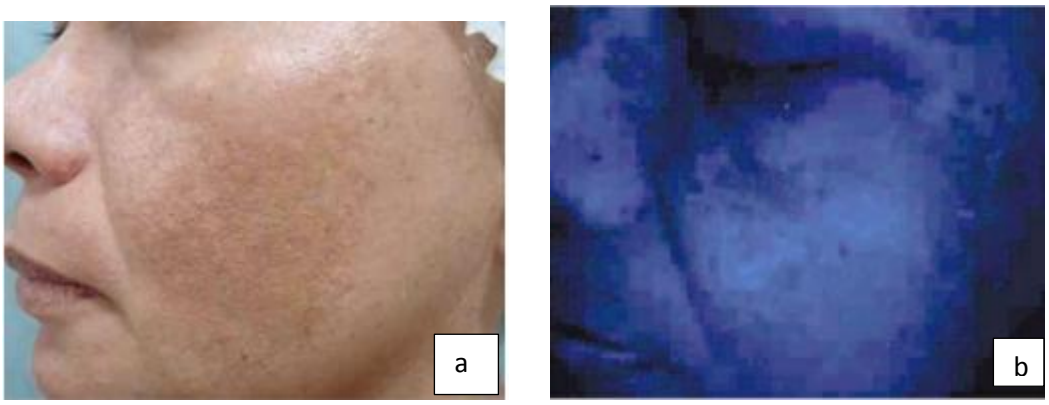


Figure 13: (a) dermal melasma (b) Wood's lamp examination of dermal melasma showing no enhancement of lesions

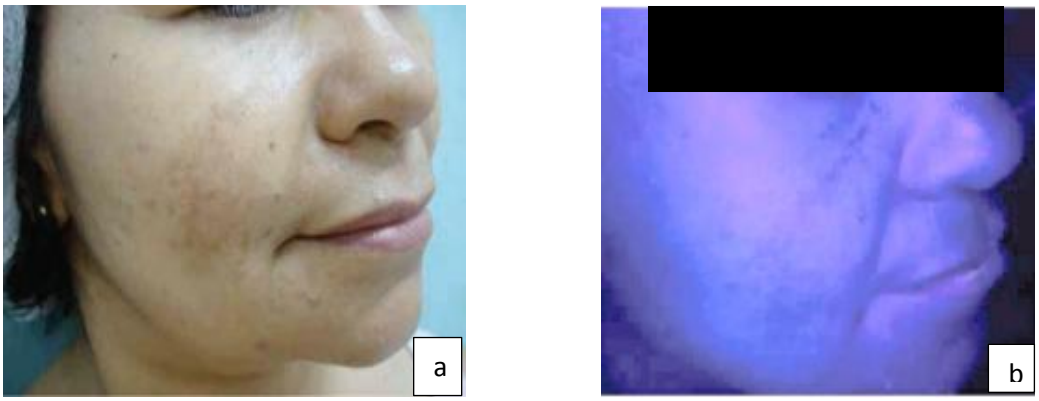


Figure 14: (a) mixed melasma (b) Wood's lamp examination of mixed melasma showing both enhancement and no enhancement of lesions.

DIAGNOSIS

Diagnosis of melasma is mostly made clinically, but many pigmentary disorders clinically mimic melasma. These are the few conditions that should be differentiated from melasma such as post inflammatory hyperpigmentation, riehl's melanosis, poikiloderma of civatte, facial acanthosis nigricans, bilateral nevus of Ota, nevus of hori, lichen planus pigmentosus, exogenous ochronosis, erythema dyschromicum perstans, freckles, solar lentigo.

DIFFERENTIAL DIAGNOSIS

Post inflammatory hyperpigmentation

Post inflammatory hyperpigmentation (PIH) is an acquired hypermelanosis, which develops following inflammation or injury. Very common causes of PIH are acne vulgaris, atopic dermatitis, and impetigo. Clinically PIH is characterized by brownish or bluish grey macules or patches in the same area of initial inflammatory process.[6,15,56]

Riehl's melanosis

It is usually caused by the allergens present in the cosmetics, fragnances, kumkum, henna, and coal tar dyes. This condition is characterized by patches of brownish grey pigmentation present over the temples, forehead, scalp and neck.[15,56]

Piokiloderma of Civatte

Genetic factors, sun exposure, and photosensitizing chemicals play a role in its pathogenesis. It is characterized by reddish brown reticulate pigmentation, and atrophy, present symmetrically over cheeks, sides of neck with sparing the area under chin.[15,56]

Facial Acanthosis nigricans

Most commonly seen over nape of neck and flexural areas of the body and less commonly seen on face, back of hands and fingers. Clinically it is presented as bilaterally symmetrical hyperpigmented, velvety thickening of the skin.[6,56]

Bilateral nevus of Ota

Genetic factors play a role in its etiology and exclusively seen in Asians. Clinically it is characterized by bluish grey mottled or speckled pigmentation over the face with bluish discoloration of oral mucosa and eye.[6,56]

Hori nevus

It is an acquired condition usually seen in elderly women. Clinically it is seen as bluish brown or slate grey patches, over malar, cheeks, forehead and temple areas of face. Oral and ocular mucous membranes are not involved in hori's nevus.[6,15,56]

Lichen planus pigmentosus

It is one of the variant of Lichen planus. Exact etiology is unknown. Characterized by bilaterally, symmetrical dark brown to slate grey patches with lacking of erythematous border present over sun exposed areas and flexures.[6,56]

Exogenous ochronosis

Usually occur in patients after prolonged use of high percentage of hydroquinone. Characterized by tiny, sooty, reticulated and rippled bluish pigmentation over the face. Biopsy shows banana shaped yellowish brown granules in the papillary dermis. [64]

Erythema dyschromicum perstans

Exact cause is not known, but intake of radio contrast media or hiv, hepatitis C infection has suggested. It is characterized by asymptomatic, bluish grey patches with raised erythematous border over trunk and extremities.[65,66]

Freckles

It is most commonly seen in sun exposed areas, such as malar and nose and characterized by small, discrete, irregular hyperpigmented macules which intensified with sun exposure.[6,66]

Solar lentigo (Actinic lentigo)

Prolonged exposure to ultra violet radiation induces chronic inflammation of skin which is clinically characterized by hyperpigmented macules over sun exposed areas such as hands, arms and face.[6,65]

TREATMENT

Melasma is often difficult to treat because of its refractory and recurrent nature. Careful history about possible precipitating or aggravating factors must be taken with special attention to intake of OCP or other hormonal preparations. Discontinuation of oral pills and avoidance of scented cosmetics is advised.[16]

The goals of the treatment

- Prevention or reduction in severity, recurrence, reduction of the affected area.
- Improvement in cosmetic defect.
- To reduce time of clearance with few side effects.

Depigmentation is achieved by regulating the following pathways in three levels.[67]

(i) Transcription and tyrosinase activity, tyrosinase related protein1 (TRP-1), tyrosinase related protein 2 (TRP-2), and peroxidases.

(ii) Uptake and distribution of melanosomes in the recipient keratinocytes

(iii) Melanin and melanosomes degradation and the turnover of the pigmented keratinocytes.

Usually, it takes up to 2 months to initiate the response and up to 6 months to complete the process with depigmenting agents.[66] Epidermal melasma respond well to topical modalities of treatment, but dermal melasma doesnot respond, so other therapies like chemical peels, laser therapy, dermabrasion are needed.[68]

STRATEGIES

General measures

Women developing melasma during pregnancy should avoid excessive exposure to sunlight and should use an appropriate sunscreen throughout pregnancy. The likelihood of spontaneous clearance after delivery should be explained to the patient. The treatment for the melasma during the period of pregnancy or breast feeding is usually not advisable. Women taking oral contraceptive pills are advised to discontinue the drugs. Patients should be explained about the nature of response to treatment as long as OCP is continued. [66]

Sun screens

The ideal sunscreen should completely block the transmission of both UVA (280-315nm) and UVB (315-400nm). Additional important properties are durability on the skin and water resistance. The use of noncomedogenic, oil-free base formula with SPF (Sun protection factor) > 15 is effective.[69] The types of sunscreens that have been used are-

Reflecting or physical or inorganic sunscreens

Opaque preparations act by reflecting and scattering ultraviolet and visible radiation. The effectiveness depends on thickness of film. The reflectors are titanium dioxide (5-20%), zinc oxide (most effective), talc (magnesium trisilicate), magnesium oxide, kaolin, calcium carbonate, ferric chloride, and icthammol. They are not easily washed off.[69]

Absorbing substances or chemical or organic sunscreens

These are colorless, easily washable, cosmetically more acceptable chemicals. These are two types- those which absorb only UVB and those absorb both UVA and UVB. The former group consists of PABA (Para aminobenzoic acid) and its esters,

cinnamates, salicylates, and camphor derivates. Benzophenones and anthranilates constitute the latter group.[69]

Systemic photoprotective agents

There are several compounds that has systemic photoprotective effect, referred as "systemic sunscreens" which includes beta-carotene, antimalarials, ascorbic acid, selenium, alpha tocopherols (vitamins A, C, and E) and green tea polyphenols.[69]

Topicals

Hydroquinone

Hydroquinone (HQ) is one of the most prescribed topical agents in the treatment of melasma, and is considered the gold standard therapy. HQ inhibits the conversion of dopa to melanin by inhibiting the tyrosinase enzyme. It also inhibits the formation of melanosomes and also increases its degradation. It is commonly used at concentration ranging from 2% to 10% either alone or in combinations. It is easily oxidized and loses its efficacy. To maintain its potency, antioxidants should be used such as 0.1% sodium bisulfate or 0.15% ascorbic acid. Adverse effects of HQ include allergic and irritant contact dermatitis, nail discoloration and guttate hypomelanosis. These side effects are temporary and usually resolve on discontinuation of drug. The rare side effect noticed on prolonged usage of HQ is, ochronosis. Ochronosis is characterized by greyish brown or bluish black pigmentation over the HQ applied area, most commonly seen in dark skinned individuals. [47,70]

Combination of HQ and other topical agents

Hydroquinone has been combined with other various topical agents like corticosteroids and retinoids to increase the efficacy and to decrease the side effects. [47]

Various formulations

Kligman and Will 86 have proposed the combination of hydroquinone 5%, tretinoin 0.1% and dexamethasone 0.1% in ethanol and propylene glycol 1:1 or in hydrophilic ointment. The most commonly used topical retinoid is tretinoin in the treatment of melasma. It acts by stimulating the cell turnover and promotes the rapid pigment loss through epidermopoiesis. It increases the epidermal penetration of HQ, and also prevents its oxidation. It also suppresses the atrophic side effect of corticosteroids. Corticosteroids inhibit the melanin production and eliminate the irritation caused by the tretinoin and HQ.This formula is advised to apply twice daily for not more than 5-7 weeks, because the depigmentation process usually begins within 3 weeks. This formulation is is not preserved by antioxidants and thus should not be used after 30 days time.[15,47]

In a modified Kligman and Willis (Katsamba's) formula, is composed of hydroquinone 4%, tretinoin 0.05% and hydrocortisone acetate 1% in ethanol and propylene glycol 1:1 or in hydrophilic ointment. The main purpose of this formulation is to eliminate the tretinoin's irritation and possible side effects by lowering the its concentration and by using non fluorinated steroid. Both formulations should keep in the refrigerator at 2-4^{0}C.[47]

Westerhof's formulation is a combination of N-acetylcystein 4.7%, HQ2% and triamcinolone acetonide and this formulation shows significant response in 4-8 weeks. [15]

Pathak and colleagues believe that rapid clearance of melasma can be achieved without addition of topical steroid. Their formulation contains hydroquinone 2% and tretinoin 0.05% to 0.1% and suggested that steroid should be added when only irritation occurs from HQ and tretinoin. [15,47]

Gano and Garcia's formulation is a combination of hydroquinone 2%, tretinoin 0.05% and betamethasone valerate 0.1%.[15,47]

One of the most recent and successful combination of formulation is HQ 2%, tretinoin 0.05%, and fluocinolone acetonide 0.01%. These triple combination topical therapies are the most effective treatment modality in the management of melasma.[71]

In the United States, the triple combination formula consists of HQ 4%, tretinoin 0.05% and fluocinolone acetonide 0.01%. This is the only HQ containing drug that is FDA approved for the treatment of melasma.[72]

Azelaic acid

It is one of the topical agents used in the treatment of melasma. It is produced naturally as a byproduct in the metabolism of pityrosporum ovale and is associated with hypopigmentation seen in tinea versicolor. The mechanism of action includes: (1) inhibits tyrosinase enzyme activity reversibly (2) interferes the mitochondrial oxidoreductase activity. (3) anti-proliferative effect on abnormal melanocytes.[73]

Azelaic acid is used in the concentration of 10-20%, applied twice daily. Shows minimal side effects like transient irritation at the beginning of treatment, pruritis, mild erythema, scaling and burning. A study suggests that azelaic acid 20% twice daily application is found to be more effective than HQ 4% in the cases of mild melasma. [74]

Kojic acid

Kojic acid (5-hydroxy-2-hydroxymethyl-4H-pyran-4-one) is a fungal metabolite produced by Penicillium species and Aspergillus oryzae. It is one of the last depigmentary agents preferred in treating melasma. It is used in the concentration of 1-

4%, alone or in the combination with tretinoin, HQ or corticosteroids. It inhibits the tyrosinase enzyme by chelating copper at the enzyme's active site. It has anti-inflammatory and antioxidant properties. Adverse effects includes contact dermatitis, irritation, and erythema.[75]

In a split face trial, a gel containing HQ, glycolic acid and kojic acid showed more improvement (60%) when compared to a gel containing only glycolic acid and HQ (47%). [76]

Ascorbic acid

It is also known as vitamin C. It acts as a depigmenting agent by interacting with copper at the active site of tyrosinase enzyme and also by reducing dopaquinone. Various forms in 5-10% concentrations are used to treat melasma. Ascorbic acid is usually combined with licorice extracts and soy to increase its potency. It is a good adjuvant in those who cannot tolerate HQ as it causes less irritation than HQ.[77]

In a randomized trial, where 4% HQ cream is compared with 5% ascorbic acid, showed significant improvement with HQ (93%) than ascorbic acid (62.5%).[78]

Topical retinoids

Topical retinoids increase the cell turn over and also increase the rapid loss of melanin through epidermopoiesis. It facilitates the penetration of other depigmenting agents in the epidermis, thereby increasing its efficacy of depigmentation. Most commonly used topical retinoid is tretinoin, is so effective as monotherapy. Used at 0.05-0.1% concentration daily once at night time, requires 20 to 40 week treatment periods. The

common side effects are burning, scaling, and erythema. In dark skin type individuals, retinoid dermatitis may lead to post inflammatory hyperpigmentation.[77]

Another topical retinoid used in the treatment of melasma is Adapalene, in the concentration of 0.1%. It is found to be safe and effective in the epidermal melasma with lower irritation. In a study done, adapalene 0.1% showed 41% improvement in MASI score when compared with 0.05% tretinoin which showed only 37% improvement.[79]

Topical steroids

Various types of topical corticosteroids are used in the treatment of melasma. Mild potency steroids like hydrocortisone 1% shows poor response, whereas high potency steroids like betamethasone 2% and very potent steroids like clobetasol propionate 0.05% showed better results. Rapid relapse is noticed on discontinuation of drug. Corticosteroids have better efficacy when combine with HQ or tretinoin. The common side effects noticed are itching, atrophy, acne and telangiectasia. The potent steroids should not be used continuously for more than 4 weeks, and later it has to be tapered to low potent steroids which should also be stopped after 2 months of usage.[80]

Glycolic acid (GA)

Is an alpha-hydroxy acid, used as an depigmenting agent at the concentration of 5-10%. It acts by directly inhibiting tyosinase enzyme thereby decreasing the melanin synthesis in the melanocytes. It also accelerates the desquamation of epidermis resulting in rapid dispersion of pigment. Most common side effect noted is irritation which resolves with temporary stoppage of application and application of moisturizers.[80]

A study was conducted by Garcia et al, to evaluate two formulations that is glycolic acid (GA) plus HQ and glycolic acid plus kojic acid in 39 melasma patients. The results were not statistically different in the both formulations after 3 months of therapy. [81]

Arbutin

Arbutin is a natural plant product. It acts by inhibiting tyrosinase enzyme and thereby decreasing the melanin synthesis. The hydrolysed form of arbutin is more effective in inhibiting the tyrosinase enzyme and also acts as a free radical scavenger. Recently, deoxyarbutin has been developed, a derivative of arbutin by removing hydroxyl group. It directly inhibits the tyrosinase enzyme.[75]

Mequinol (4-hydroxyanisole, 4-methoxyphenol)

It is a phenolic compound derived from HQ. It is available as 2% solution with added 0.01% retinoic acid. It acts by competitively inhibiting the precursors of melanin formation. In India, it is still not marketed.[75]

N-acetyl-4-S-cysteaminylphenol

It is a phenolic compound that acts as a substrate for tyrosinase enzyme and inhibits it leading to decreased melanogenesis. It is more stable and less irritating than HQ, shows improvement in 2-4 weeks.[77]

Niacinamide

Niacinamide is the biologically active amide form of niacin (vitamin B3). Its mechanism of action in depigmentation is by preventing the transfer of melanosomes from melanocytes to keratinocytes. It has no effect on the tyrosinase enzyme.[77]

Soy:

It is a plant derivative found in tofu products and also in soya beans and soy milk. It reversibly inhibits protease activated receptor-2 (PAR-2) pathway thereby interfering with melanin transfer. It can also inhibit both base-line and ultraviolet radiation induced pigmentation.[82]

Liquorice

It is obtained from the root of a herb, Glycyrrhiza glabra. Glabridin and Liquiritin are both derivatives of liquorice. Glabridin acts by inhibiting tyrosinase enzyme and by dispersing melanin pigment. It aslo has anti-inflammatory properties.[80]

Flavonoids

Flavonoids are naturally occurring polyphenolic compounds. Many plant derived flavonoid compounds have hypopigmentary effects and their role is still under investigation. These include catechin conjugated with gallic acid (from green tea leaves), ellagic acid (from green tea, strawberry, eucalyptus) and aloesin (from aloe tree). [16]

Alpha Tocopheryl ferulate

Alpha-tocopherol prevents lipid peroxidation induced by UV irradiation and also inhibits tyrosinase at a posttranslational level. Compared with kojic acid and arbutin, alpha tocopheryl ferulate has exhibited the same ability to reduce melanin formation.[20]

Beta carotene

It is a structural analog of vitamin A. It acts as agonist to vitamin A, saturates the receptors present on the melanocytes and reduces the melanin synthesis. Prolong duration of treatment is required with few side effects.[75]

Tranexamic acid

Tranexamic acid is a plasmin inhibitor, used topically in 5% base. Presently studies are going on in various places with good initial reports. In the latest studies, intralesional injection of tranexamic preparation of 0.05ml (4mg/ml) once a week for 12 weeks showed effective improvement.[83]

Silymarin

Silymarin is derived from milk thistle plant silybum marianum. Silybin is the main component present in it, found to have antioxidant properties. It inhibits melanin synthesis in a dose dependent manner. It also reduces the harmful effects of ultraviolet radiation. No adverse effects were seen. In a study conducted by Altaei, showed excellent improvement in all patients treated with silymarin cream. [84]

Zinc

Zinc is an oral antioxidant; anti-inflammatory agent which is used extensively in pigmentation disorders.It has peeling and exfoliating property and also reduces the synthesis of melasma. A double –blind randomized comparative study was conducted by Yousefi et al. to compare the efficacy of topical zinc sulfate 10% with 4%HQ. Results showed that significant fall of MASI score is seen with HQ than with topical zinc sulphate.[85]

Methimazole

It is an oral antithyroid drug. Recently found that topical 5% preparation has a depigmenting effect. It is a potent peroxidase inhibitor, showed improvement in the melasma lesions over a period of 6 weeks without affecting thyroid hormone levels in the blood.

Metformin

Metformin is widely used in the treatment of type 2 diabetes. Metformin led to reduced melanin in the melanocytes by decreasing cAMP accumulation and cAMP-responsive element binding protein phosphorylation. It also decreases the expression of genes that involved in the melanogenesis. Topical application of metformin showed depigmenting effect by removal of already present melanin in the epidermis and dermis.[86]

Linoleic acid

New liposomal formulations (0.1%) have been developed with increase solubility and also with increased efficacy at lower concentrations. Linoleic acid 2% plus 2% lincomycin with 0.05% betamethasone valerate improved pigmentation in 47 melasma patients in a 6 week randomized controlled trial. A clear efficacy in the treatment of melasma has not been demonstrated. [65]

N-Acetylglucosamine (NAG)

It is an amino- monosaccharide that inhibits enzymatic glycosylation, which is required for the conversation of inactive prothyrosinase to active tyrosinase. It decreases the melanin production and also downregulates the genes that are involved in melanosome transport.[73]In a double blind, placebo controlled trial of 8 week period, 2% NAG showed improvement in depigmenting the lesions. In an another study of 10 week period, combination of 2% NAG and 4% of niacinamide showed good results in reducing the facial spots and appearance of hyperpigmentation.[87]

4-n-Butylresorcinol

It is a derivative of resorcinol that inhibits tyrosinase enzyme and tyrosinase related protein leading to decreased melanin synthesis. Studies have shown good efficacy and safety with 4-n-butylresorcinol in patients with melasma.[2]

Aloesin

Aloesin is a C glycosylated compound, derived from aloe vera. It competitively inhibits the hydroxylation of tyrosinase to DOPA and oxidation of DOPA to dopachrome thereby decreasing melanin synthesis.[77]

Orchid extracts

Orchid extracts contain various flavonoids that act as antioxidant. Tadokoro et al. performed a study to compare the efficacy of formulation containing plant extracts including orchid extracts, with topical 3% vitamin C derivative in patients with melasma, found similar significant improvement in both groups.[77]

Hydroxycoumarins

Coumarins are lactones of phenyl propanoic acid with benzopyranone nucleus. They have alpha tocopherol like structure. Hydroxycoumarins are antioxidant, and strongly inhibit tyrosinase enzyme. The natural derivatives of coumarins includes aloesin, which has tyrosinase inhibitory properties.[77]

Gentisic acid

It is a safe, effective skin depigmenting topical agent and less cytotoxic than HQ. It is derived from Gentian roots. It has the ability to inhibit melanogenesis without cytotoxicity and mutagenesis.[77]

Thiotic acid

Thiotic acid, antioxidant agent has proven to be slightly less effective than 2%HQ. It is derived from octanoic acid and prevents UV-induced oxidative injury and inhibits tyrosinase by chelating copper and suppresses the formation of dopaquinone derivatives.[77]

Table-2: Other botanical extracts used for treatment of melasma

Plant extract	Active component	Mechanism of action
Grape seed extract	Proanthocyanidin	Antioxidant
Marine algae extract		Inhibition of tyrosinase
Cinnamic acid		Inhibition of tyrosinase
Green tea extracts	Epigallocatechin-3-gallate	Antioxidant? Inhibition of tyrosinase
Coffee berry	Chlorogenic acid Proanthocyanidins	Antioxidant
Mulberry extract	Contain methanolic extracts	Inhibition of dopa oxidase Superoxide scavenging activity
Umbelliferone	7-hydroxycoumarin	Absorbs UV light, antioxidant
Boswellia	Boswellic acid	Anti-inflammatory, pro apoptotic

Dioic acid

It is a dicarboxylic acid, derived by fermentation of oleic acid. It interrupts with melanin production by binding to nuclear peroxisome receptor which regulates the tyrosinase transcription. 1% dioic acid application for 12 weeks showed good results in some studies.

SYSTEMIC THERAPY

Tranexamic acid (TXA)

Now recently oral TXA has been successfully using in the treatment of melasma. Traditionally it is used for bleeding disorders and menorrhagia. It decreases the tyrosinase activity in the melanocytes and increases in vascular endothelial growth

factor and alpha- melanocyte stimulating hormone. It also acts mainly via the plasminogen activator-plasmin system to prevent UV radiation induced pigmentation in melasma.It is used as topical, intradermal and oral forms. Oral TXA is a potent and convenient modality for the treatment of melasma. The common side effects noted are headaches, menstrual irregularities and back pain.[88]

A pilot study was conducted by Aamir et al. to assess the efficacy of oral TXA, were given oral TXA 250mg twice daily for 6 months in 65 melasma patients. The results showed good improvement in 41, excellent in 15 and fair improvement in eight patients.[89]

Antioxidants

In a randomized, double bind, placebo-controlled trial, a combination of oral procyanidin with vitamin A,C and E was assessed in 60 Filipino melasma patients. The antioxidants were taken twice daily for 8 weeks and the results showed significant reduction in the pigmentation and improvement in MASI scores.[90]

A double blind placebo controlled trial was conducted by Teo et al, to evaluate the effectiveness of dietary supplement rich in carotenoids as adjuvant to topical lightening creams for the treatment of melasma. Results showed greater improvement in the group on oral supplements, compared to placebo.[91]

Pycnogenol

Pycnogenol are procyanidins, consists of catechin and epicatechin. It has antioxidant and anti-inflammatory properties. It aslo causes regeneration and protection of vitamin C and E. Main advantage of pycnogenol is its high bioavailability and low side effects with oral intake. Side effects observed were fatigue, constipation, body pains and anxiety.[77]

Dermabrasion

Another adjuvant therapy in the treatment of hyperpigmentary disorders is dermabrasion. Epidermal melasma responds to most of the topical therapies, but dermal melasma is very hard to treat and is resistant to treatment. In such cases, local or full face dermabrasion with 16-mm diameter coarse grit diamond fraise, up to the upper or mid dermis showed successful response. The common side effects noted are pain, edema, exudation, discomfort, crusting and hyperpigmentation.[17]

Microdermabrasion

Microdermabrasion is also known as micro-resurfacing procedure, used for mechanical exfoliation of skin. It uses aluminum oxide crystals at high pressure to remove the outermost layer of stratum corneum. It is contraindicated in skin ulcers, erosions and active infections. Little data are available regarding its efficacy in the treatment of melasma. Microdermabrasion can be combining with other modalities like chemical peels and lasers to increase its efficacy.[66]

Platelet rich plasma

The most important contents of platelets are contained in the α-granules. The bioactive substances present in the α-granules include PDGF (platelet derived growth factor), TGF-β1, β2 (transforming growth factor) and mitogenic growth factors. PDGF present in PRP (platelet rich plasma) are mainly involved in hyaluronic acid production which increases skin volume and tone, thereby reducing the pigmentation. TGF β1 is also being investigated in relation to melanogenesis.[75]In one patient of epidermal melasma, 1.5ml of PRP is injected into dermis of the face at each session with 2 weeks interval, showed 80% improvement at the end of third session.[92]

Cosmetic camouflage

Cosmetic camouflage is a technique using makeup to disguise the hyperpigmented skin lesions immediately, with the intention of normalizing the appearance of the skin. So it is considered as one of the therapy that offers rapid and dramatic results. This technique uses specialized products such as cover creams, liquids and powders to be applied in a systematic way, so it can rapidly disguise melasma affected areas. These products are different from conventional cosmetics, as they are waterproof and opaque, allowing adherence to the skin.[65]

Most of the products are low allergenic potential. The main advantage is, the immediate results and instant gratification. Many products exist for the patients suffering from melasma like Dermablend, Cover FX, Covermark and Microskin. The hyperpigmented patches are always difficult to conceal than depigmented or hypopigmented areas.[65]

CHEMICAL PEELS

Chemical peeling or chemoexfoliation is the application of chemical agent to the skin, which causes controlled destruction of a part of or the entire epidermis, with or without dermis, leading to exfoliation and removal of superficial lesions, followed by regeneration of new epidermal and dermal tissues.

Pre-peel Priming

It is essential to do pre-peel priming of the skin with sunscreens, HQ, Glycolic acid 10%, and tretinoin to enhance peeling effects. Priming is essential for at least 2-4 weeks prior to the procedure. Priming helps to reduce wound healing time, facilitates uniform penetration of peeling agent and reduces the risk of complications. [26]

Chemical Peeling in melasma

Chemical peels are most commonly used in epidermal type of melasma, where dermal type is almost resistant to the effect of peel. It causes inflammation and induces macrophages to phagocyte stagnant melanin in the dermal type. The commonly used peels in the treatment of melasma are Glycolic acid (GA), trichloroacetic acid (TCA), salicylic acid (SA), lactic acid (LA), mandelic acid and arginine. They are combined with the medical treatment for rapid clearance of the pigmentation. [93]

Glycolic acid peel

It is an alpha hydroxy acid, commonly used for chemical peeling. For melasma peeling, 20-70% concentrations are used. They are very safe and are repeated once in 3-4 weeks for a minimum of 4-5 peels. It acts on epidermis by causing corneocyte dysadhesion, leading to epidermal desiccation and shedding. It also stimulates epidermal growth and smoothening of the skin. The advantages are well tolerated, safe and effective at low concentration, no systemic toxicity and long shelf life. Disadvantages includes, results not always predictable, great variability in reactivity and efficacy, tendency to penetrate unevenly, expensive.[94]

Trichloroacetic acid peel

Used as superficial depth peel for pigmentary dyschromias and medium depth peel to combat wrinkles and other haringers of aging. The peel depth achieved with TCA correlates very well with the intensity of skin frost. TCA does not need to be neutralized; only dilution with water is enough.TCA precipitates the epidermal proteins, causing necrosis and sloughing. It can be combined with CO2 laser and liquid nitrogen to get deeper penetration, creating medium depth peel.[65]

Salicylic acid peel

SA is a beta-hydroxy acid, on application, the vehicle evaporates leaving a precipitate of SA, which is seen as a white pseudofrost. The initial concentration is 20%-30%, going up to 70%. It causes stinging sensation when applied. The peel is terminated by washing with water. SA reduces corneocyte adhesion, thus acts as a keratolytic agent. Because of its lipophilic nature, SA has a strong comedolytic effect. SA affects the arachidonic cascade and thus exhibits anti-inflammatory capabilities. The advantage is safe in all skin types and inexpensive.[93]

Tretinoin peels

Tretinoin in lower concentration has been used as a component in kligman's formula for the treatment of pigmentary disorders. However, in higher concentrations (1%) has been used as a peeling agent (yellow peel) for the treatment of melasma. The advantages are that it is well tolerated, causes no burning when applied. The disadvantages are that it is yellow in color and has to be left on for at least 4 hours.[65]

Lactic acid (LA)

Lactic acid is used as a peeling agent in its full strength of 92% and PH of 3.5. It improves superficial pigmentation by inhibiting tyrosinase in the treatment of melasma. Is a relative cheap and safer agent for chemical peeling.[75]

Kojic acid

Kojic acid inhibits the catecholase activity of tyrosinase and is used as a lightening agent. A study reported the use of a gel solution composed of 50% glycolic acid and 10% kojic acid in the treatment of hyperpigmentation.

Pyruvic acid

It is an alpha keto acid. It is used in the concentration of 40% to 70%, acts a s a superficial peel in the treatment of melasma. Intense burning is the side effect reported, which limited its use.[56]

Mandelic acid

It is an aromatic alpha-hydroxy acid, extracted from bitter almond, which shows satisfactory results in the treatment of melasma even in dermal types. It is less irritating because of its larger molecular weight and slow penetration into the skin.[56]

Lipohydroxy acid

It is a salicylic acid derivative, with an extra fatty acid chain, has increased lipophilicity and keratolytic effect. Its penetration is less than GA peel. Its PH is close to skin PH, and does not require any neutralization.[56]

Phytic acid peel

It is an alpha hydroxyl peel, which requires low PH for efficiency. This peel does not require neutralization. There are no studies about its efficacy in the treatment of melasma.[56]

Combination of peels

A combination of peeling agents increases the depth of the peel without using a higher concentration of the peeling agent. [93] The combinations include:

- Glycolic acid 70% combined with TCA 20%
- Solid carbon dioxide (CO_2) combined with 20% TCA
- Jessner's solution with 20% TCA.

LASER THERAPIES

Laser therapy in melasma is usually not recommended as first line therapy because of high incidences of relapses, high cost and modest efficacy. The mechanism of lasers in treating melasma, is by decreasing the number of melanocytes and eliminating the melanin in the surrounding keratinocytes. It also targets the blood vessels along with the melanin pigment and leads to lower recurrence rate of melasma after the cessation of therapy. Intense pulse light (IPL), Q-switched Neodymium-doped Yttrium Aluminum Garnet (Nd:YAG; 1064nm), Q-switch alexandrite, Qswitched ruby [694 nm], Erbium:Yttrium-Aluminum-Garnet(Er:YAG), diode [840 nm], PDL (Pulsed dye laser) [595 nm], non-ablative fractioned 1550- nm erbium (Er)-doped and ultra-pulsed CO2 lasers are used successfully for treatment of melasma. [77,93]

Intense Pulse Light (IPL)

This laser shows moderate results in melasma refractory to topical therapy. It works over wavelengths of 515-1200nm. Cut off filters will delivery specific wavelengths and reduces the side effects. The sessions are repeated every 3-4 weeks with downtime of 1-2 weeks.[75]

Q-Switched Lasers (QS)

Q-switched Nd:YAG

The Q-switched Nd:YAG laser is effective in treating melasma by inducing sub-lethal injury to the melanosomes, leading to the fragmentation and rupture of the melanin granules. It also causes damage to the upper dermal vascular plexus. "Laser toning" or "laser facial" is a technique using large spot size (6-8 mm), low fluence, multiple passed of Q- switched Nd:YAG laser, done every 1-2 weeks for several weeks. Studies

have shown that the topical triple combination creams before this technique improves its efficacy and decreases the side effects.[95]

Vachiramon et al. conducted a study, to compare the efficacy of low fluence Q-switched Nd:YAG laser to combined laser and glycolic peel in 15 mixed type male melasma patients. At the end of 12th week, showed statistical improvement in MASI score with combined therapy than laser therapy alone.[96]

Q Switched alexandrite laser

The Q-switched alexandrite laser (755 nm) is an appropriate laser for the treatment of mixed- type melasma over the face. In a comparative study, Fabi et al. showed that both the low-fluence Q-switched Nd:YAG and low-fluence Q-switched alexandrite laser were equally effective in the treatment of facial melasma.[97]

Q Switched ruby Laser

In comparison with Q-switched Nd:YAG lasers, Q Switched ruby laser (694 nm) is more selective for melanin, but its efficacy in treating melasma is still controversial. Its mechanism of action in the treatment of melasma is similar to that of the Q-switched Nd:YAG laser.[98]

Er:YAG laser

The Er:YAG laser (2940 nm) used successfully in the treatment of melasma, but its effectiveness is temporary. Its light is highly absorbed by water, resulting in ablating the skin with the minimal thermal damage and with low risk of hyperpigmentation.

Pulsed dye laser (PDL)

The efficacy of PDL in the treatment of melasma is based on the skin vascularization, which plays an role in the pathogenesis of melasma. This laser targets the vascular component in melasma lesions, there by decreases the melanocyte stimulation and subsequent relapses.[97]

Fractional Lasers

Fractional technology is a technique, where microscopic thermal damage or microscopic holes are created in the skin, so that neighboring keratinocytes will rapidly correct the defects. Marije et al. compared the use of non-ablative fractional laser therapy to triple topical therapy (HQ 4%, tretinoin 0.05% and triamcinolone 0.1% cream) in 20 moderate to severe melasma patients. Laser treatment was performed every 2weeks for a total of 4 times. At the end of 3 week, mean treatment satisfaction was significantly higher in the laser group compared to topical therapy group.[99]

Copper bromide lasers

Copper bromide lasers emit green beam with wavelength at 511nm. The advantage of this laser is that the melanin absorbs this spectrum to greater extents producing a more selective damage. Transient hyperpigmentation is seen in about 10% of patients treated.

Ghorbel et al. conducted a comparative study between copper bromide laser and triple combination cream (HQ 5%, dexamethasone 0.1% and retinoic acid 0.1%) in the treatment of 20 melasma patients, which showed no significant difference in the mean MASI score between the two groups at the end of 6 months.[100]

COURSE AND PROGNOSIS

Once established, the disease tends to be persistent unless treatment is instituted early. As the disease becomes chronic, response to treatment is usually poor. The prognosis also depends on whether the pigmentation is epidermal, dermal or mixed. It is only the epidermal pigmentation that is treatable and dermal pigment responds poorly to therapy. Still it is worthwhile to treat all patients, with any one, or several of the therapeutic options available, as it is impossible to be certain about the nature of the pigmentation.

MATERIALS AND METHODS

The present descriptive study was undertaken in 72 male patients aged between 20 to 50 years, having melasma, reporting to the department of Dermatology, Venereology and Leprosy in R L Jalappa Hospital and Research centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from January 2015 to July 2016.

Inclusion criteria

Men having melasma aged between 20-50yrs irrespective of treatment taken.

Exclusion criteria

Men with other dermatological conditions but were not seeking treatment for co-existing melasma.

Based on inclusion and exclusion criteria, a total number of 72 male patients with a clinical diagnosis of melasma were enrolled in the study. A written and informed consent was taken from all the patients who were willing to participate in the study. A detailed history, including name, age, occupation of the patient, onset and duration of melasma, aggravating factors like sun exposure, family history, cosmetic usage (such as mustard oil, dyes, perfumes and aftershave lotion application), drug intake (such as anti- convulsants, anti malarials, tetracyclines and any other drugs which are phototoxic) and chronic illness (such as thyroid disorders, hepatic disorders, bowel disorders any other hormonal imbalance) was taken from each patient and documented. History related to treatment taken by patients pertaining to the presenting condition was taken. A general physical examination including signs of endocrinological disturbances was performed. Then detailed cutaneous examination was performed which includes skin type, as per Fitzpatrick's skin type (as shown in table-1), pattern of melasma

whether centro-facial, malar or mandibular pattern and color of melasma macule whether light or dark brown, or bluish grey and the details of examination findings were documented. Melasma Area and Severity Index (MASI) score was calculated according to the formula as shown in the figure 2 and documented. Wood's lamp examination was performed in all patients to find the type of melasma whether epidermal, dermal or mixed type. Laboratory investigations such as complete blood picture, liver function tests, hormonal assay (T3, T4, TSH, LH and testosterone) and stool examination were done where ever necessary based on patient's history and clinical examination. All the methods carried out were in accordance with ethical standards of the institute and approval.

Sample size:

Based on a study[12], proportion of melasma in men was 20.5%. At 95% confidence interval and 10% non-responsive, a total of 72 subjects have to be studied.

Statistical analysis

Data were recorded on a pre-designed proforma and managed using Microsoft Excel 2010 (Microsoft Corp, Redmond, USA). The statistical software IBM SPSS Statistics Version 20 was used for all mathematical computations and statistical calculations. All the data were presented as frequency, percentage or number of patients.

OBSERVATIONS AND RESULTS

Age distribution

In the present study of 72 patients, 8 patients (11.11%) belongs to age group 20-25 years, 14 patients (19.44%) belongs to 26-30 years, 27 (37.5%) patients belongs to 31 to 35 years, 13 patients (18.05%) in 36 to 40 years, 7 (9.72%) patients were in 41to 45 years and 3 (4.16%) patients were in age group between 46 to 50 years and the details were shown in table 3 and figure 15.

Table 3: Age distribution in patients with melasma

Age of patients in years	No. of patients	Percentage
20-25	8	11.11
26-30	14	19.44
31-35	27	37.50
36-40	13	18.05
41-45	7	9.72
46-50	3	4.16

Age of onset in patients with melasma

In this study of 72 patients, age of onset of melasma were found to be between 31-35 years in 28 (38.88%) patients followed by 22 (30.55%) patients between 26-30 years, 8 patients (11.11%) were between 36-40years, 7 patients (9.72%) between 21-25 years, 5 patients (6.94%) between 41-45years and 1 patient (1.38%) each in group of <20 years and >50 years and the data was shown in table 4 and figure 16.

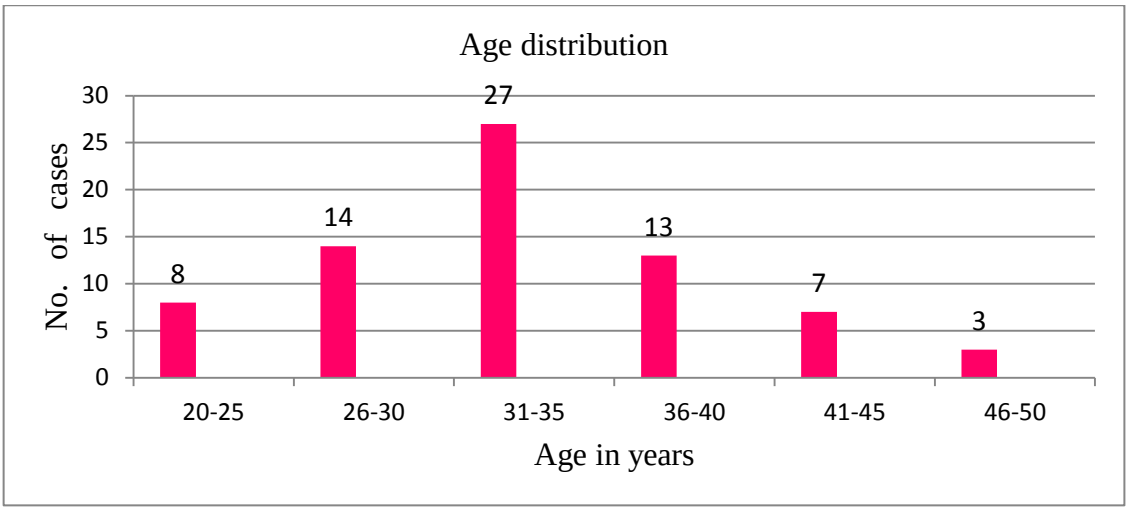


Figure 15: Diagram showing age distribution

Table 4: Age of onset in patients with melasma

Age of onset of melasma in years	No. of cases	Percentage
<20	1	1.38
21-25	7	9.72
26-30	22	30.55
31-35	28	38.88
36-40	8	11.11
41-45	5	6.94
>45	1	1.38

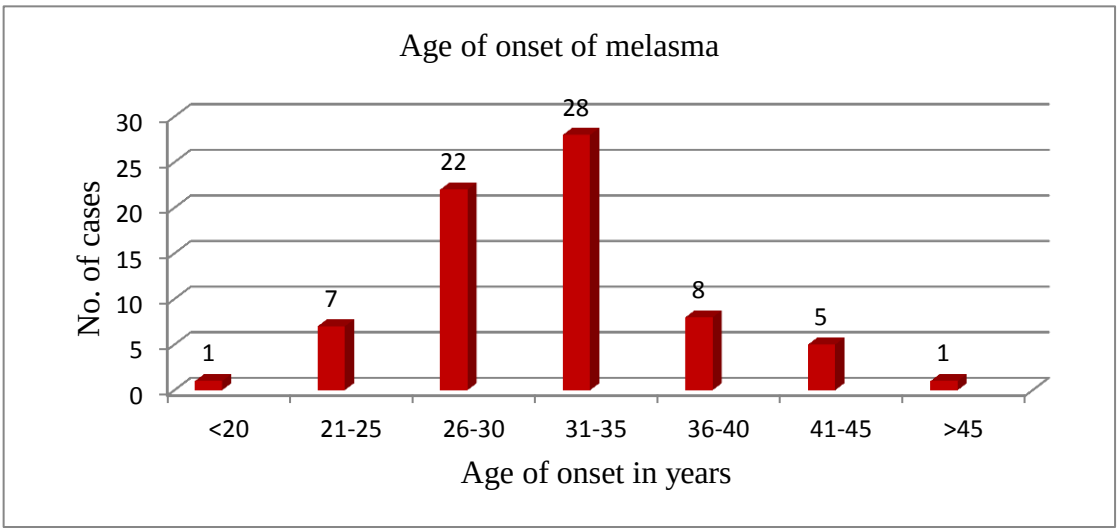


Figure 16: Diagram showing age of onset of melasma

Duration of melasma lesions

In the present study 14 patients had duration of lesion less than 1 year (19.44%), 30 patients had of duration 1-2 year (41.66%), 21 patients had 2-5 year (29.16%) and 7 patients had duration of more than 5 years (9.72%) as shown in table 5 and figure 17.

Table 5: Duration of melasma lesions

Duration of lesions	No. of patients	Percentage
Less than 1 year	14	19.44
1year- 2year	30	41.66
2 year- 5year	21	29.16
More than 5 years	7	9.72

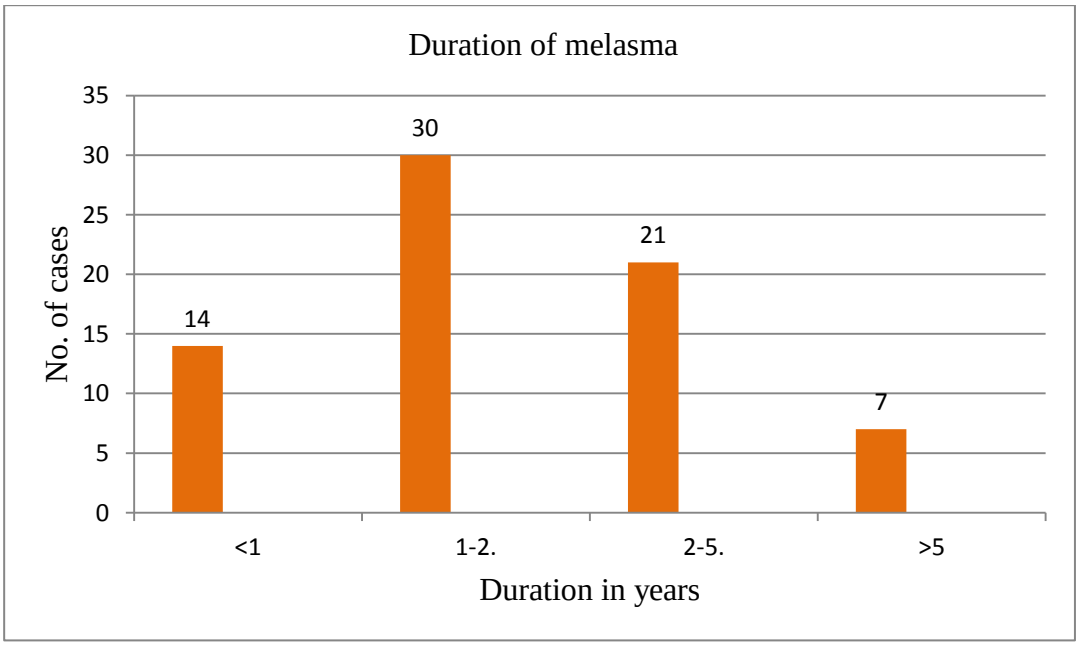


Figure 17: Diagram showing duration of melasma lesions

Family history

A positive family history of melasma in the relatives was noted in 29 (40.27%) patients in the present study and no family history in 43 patients (59.72%) and details were showed in table 6 and figure 18.

Table 6: Family history

Family history	No. of Patients	Percentage
Yes	29	40.27
No	43	59.72

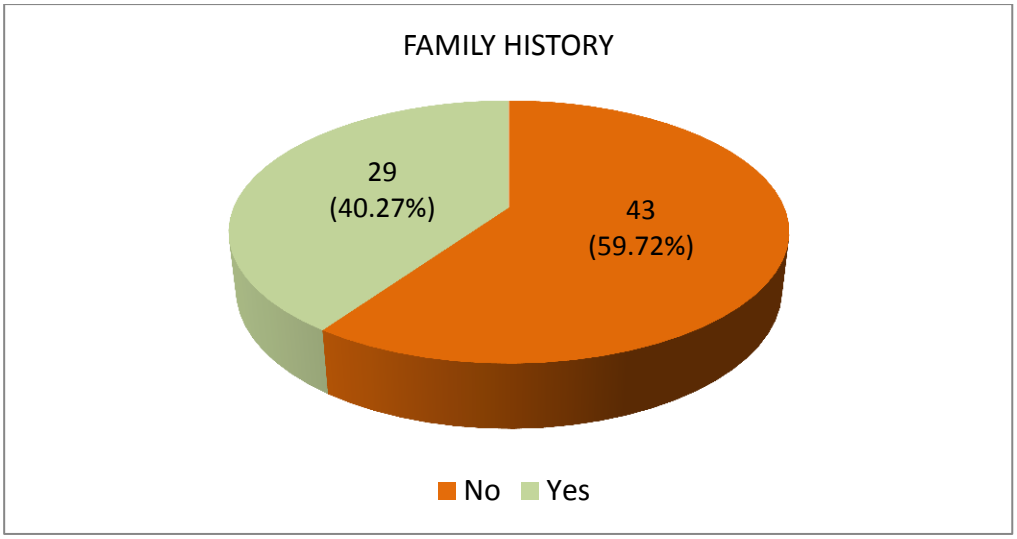


Figure 18: Diagram showing cases according family history

Sun exposure

42 (58.33%) patients had history of sun exposure as a precipitating factor in the present study because majority of our patients were outdoor workers and remaining 30 patients (41.66%) had no history of sun exposure as shown in table 7 and figure 19.

Table 7: Sun exposure

Sun exposure	No. of Patients	Percentage
Yes	42	58.33
No	30	41.66

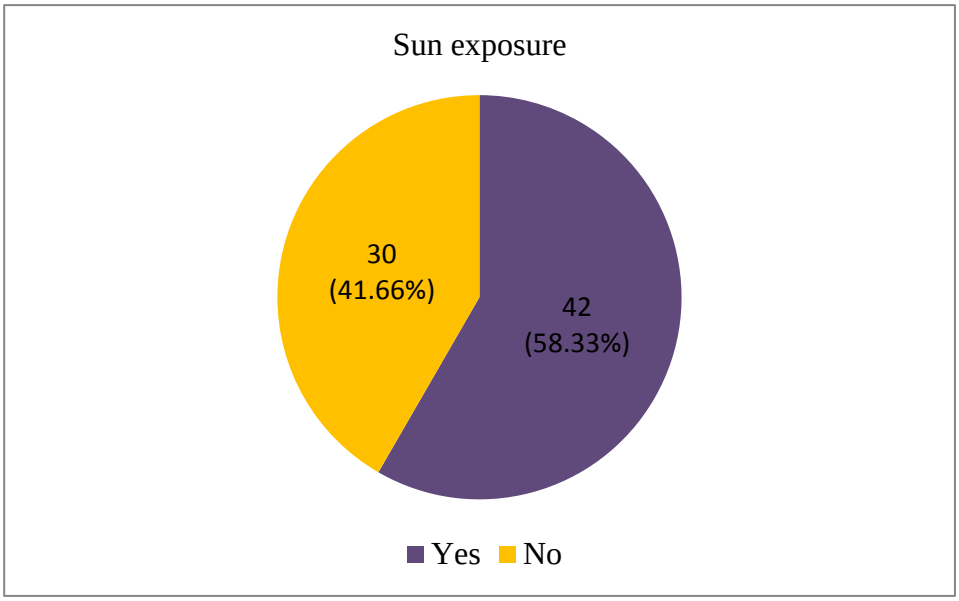


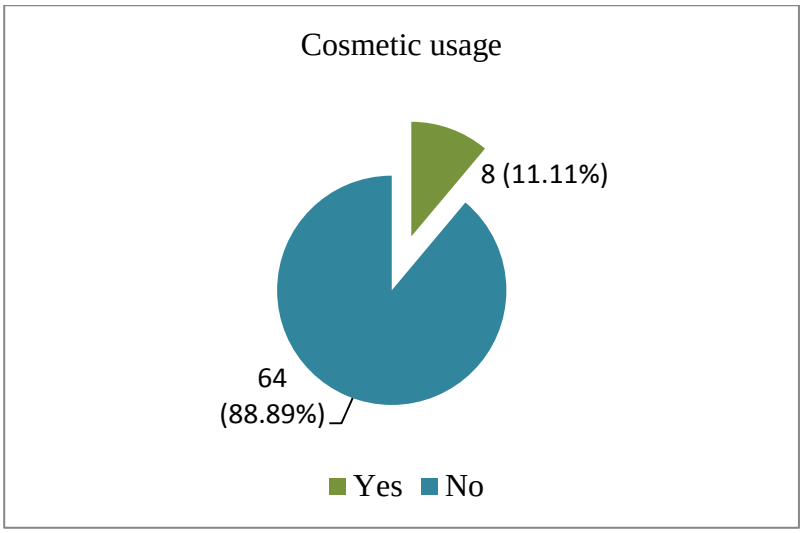
Figure 19: Diagram showing patients according to sun exposure

Cosmetic usage

In the present study, 8 (11.11%) patients gave history of application of cosmetics and remaining 64 patients (8.89%) has no history of cosmetic usage and details were shown in table 8 and figure 20.

Table 8: Cosmetic usage

Cosmetic usage	No. of Patients	Percentage
Yes	8	11.11
No	64	88.89



Graph 20: Diagram showing cases according to cosmetic usage

Type of cosmetic usage

In the present study, 8 (11.11%) patients given history of application of cosmetics, among them 5 patients (6.94%) were using mustard oil and remaining 3 patients (4.16%) were using after shave lotion and data was shown in table 9 and figure 21

Table 9: Type of cosmetic usage

Type of Cosmetic usage	No. of Patients	Percentage
Mustard oil	5	6.94
Aftershave lotion	3	4.16

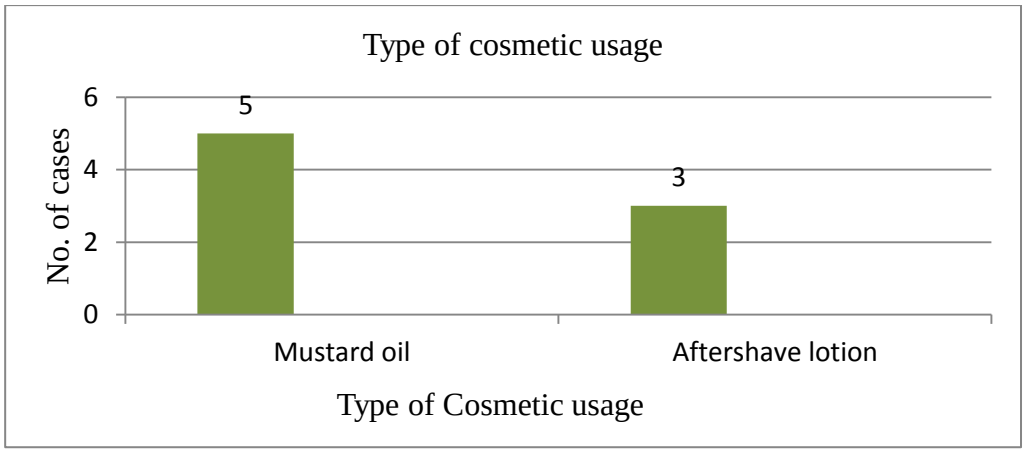


Figure 21: Diagram showing type of cosmetic usage

Drug intake

In our study 3(4.16%) patients gave history of drug intake of phenytoin and remaining 69 patients (95.84%) had no history of any drug intake and the data was shown in table 10 and figure 22.

Table- 10: Drug intake

Drug intake	No. of Patients	Percentage
Yes	3	4.16
No	69	95.84

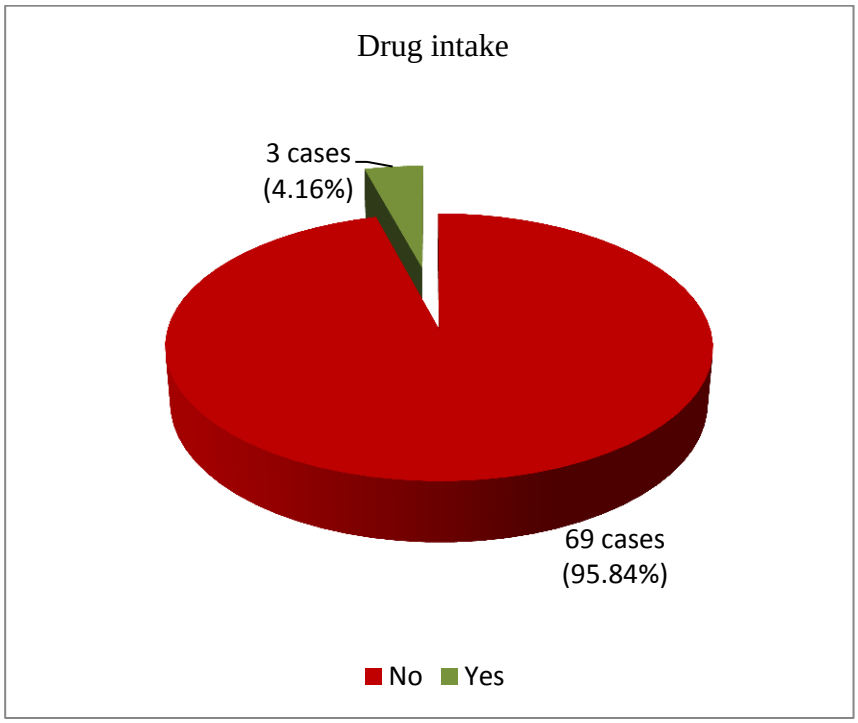


Figure 22: Diagram showing cases according to drug intake

Endocrine disorders

In our study, 4 (5.55%) patients showed thyroid abnormality (hypothyroidism) with raised TSH levels and low T3, T4 levels. 2 (2.77%) patients showed low levels of testosterone with elevated levels of luteinizing hormones and 5 patients (6.94%) showed hepatic dysfunction with raised aminotransferases and details were shown in table 11 and figure 23.

Table 11: Endocrine disorders

Endocrine disorders	No. of cases	Percentage
Thyroid abnormality	4	5.55
Testosterone hormone imbalance	2	2.77
Hepatic disorders	5	6.94

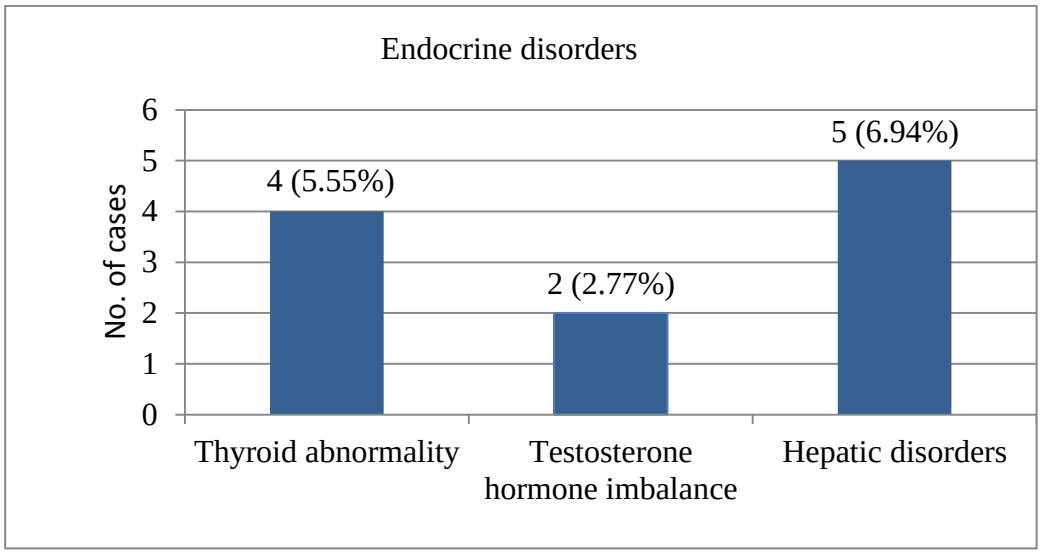


Figure 23: Diagram showing endocrine disorder

Treatment history

In the present study four patients (5.55%) had history of treatment taken in the past, of them three patients used triple combination (hydroquinone, steroid and retinoid) and the other one patient had undergone 2 sessions of 35% Glycolic acid peel. The remaining 68 (94.44%) patients were not taken any treatment related to melasma in the past and data was shown in the table 12 and figure 24.

Table 12: Treatment history

Previous history of treatment taken	No. of cases	Percentage
Yes	4	5.55
No	68	94.44

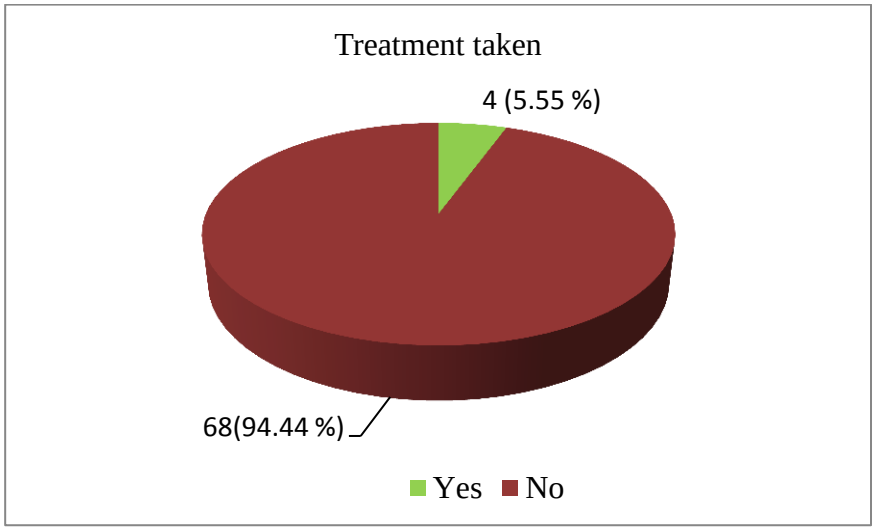


Figure24: Diagram showing previous treatment history

Skin type of patients

The most common skin type (Fitzpatrick's skin type) in the present study was found to be type IV (brown colour) seen in 44 patients (61.12%) followed by type III (light brown) in 18 (25%) and type V (dark brown) in 10 patients (13.88%) as shown in the table 13 and figure 25.

Table 13: Skin type of patients

Skin type of Patients	No. of Patients	Percentage
Type I	0	0
Type II	0	0
Type III	22	30.55
Type IV	46	63.88
Type V	4	5.55
Type IV	0	0

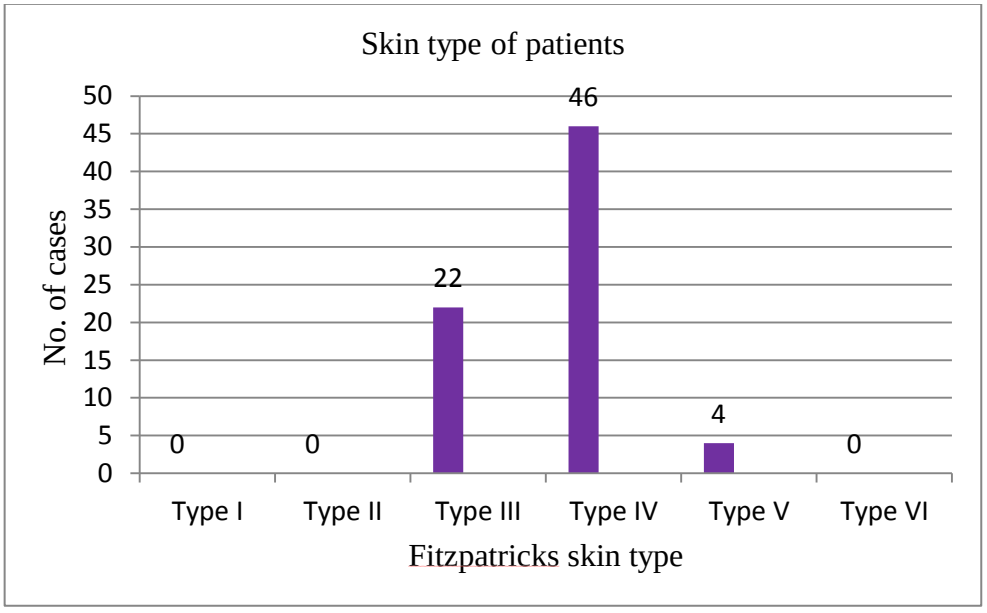


Figure 25: Diagram showing skin type of patients

Colour of the melasma macule

In the present study, the colour of the melasma macule was light brown in 38 patients (52.77%), bluish grey in 19 (26.38%) and dark brown or black in 15 (20.83%) patients was observed and data was shown in table 14 and figure 26.

Table 14: Colour of the melasma macule

Color of the macule	No. of Patients	Percentage
Light brown	38	52.77
Bluish grey	19	26.38
Dark brown/Black	15	20.83

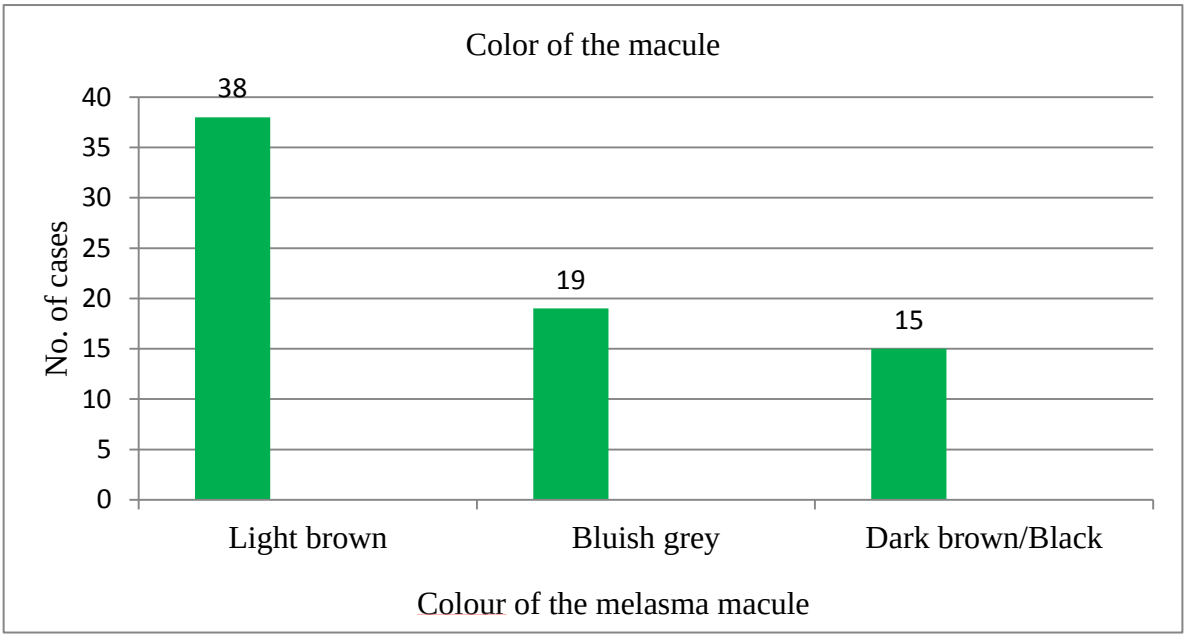


Figure 26: Diagram showing colour of melasma macule

Type of melasma pattern

In the present study, 21 patients (29.16%) had Centro-facial pattern, 45 patients (62.51%) had malar type of pattern and 6 patients (8.33%) had mandibular type of pattern and the data was shown in the table 15 and figure 27.

Table 15: Type of melasma pattern

Type of melasma pattern	No. of Patients	Percentage
Centro-facial	23	31.94
Malar	47	65.27
Mandibular	2	2.77

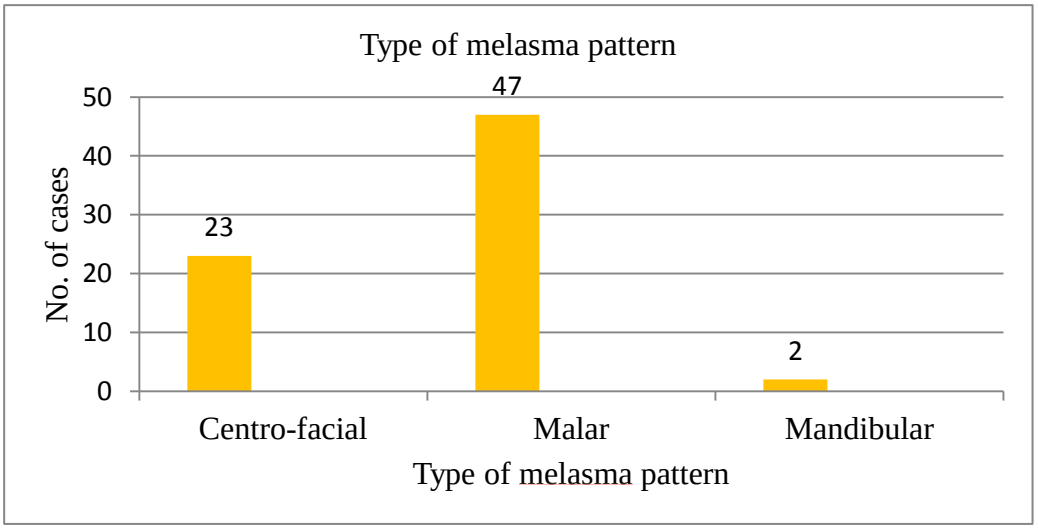


Figure 27: Diagram showing types of melasma patterns

Wood's lamp examination

In the present study, Wood's lamp examination of melasma lesions revealed epidermal type in 35 patients(48.61%), dermal type in 24 (33.33%) and mixed type in 13 (18.06%) patients and the data was shown in the table 16 and figure 28.

Table 16: Wood's lamp examination

Wood's lamp examination	No. of Patients	Percentage
Epidermal type	35	48.61
Dermal type	24	33.33
Mixed type	13	18.06

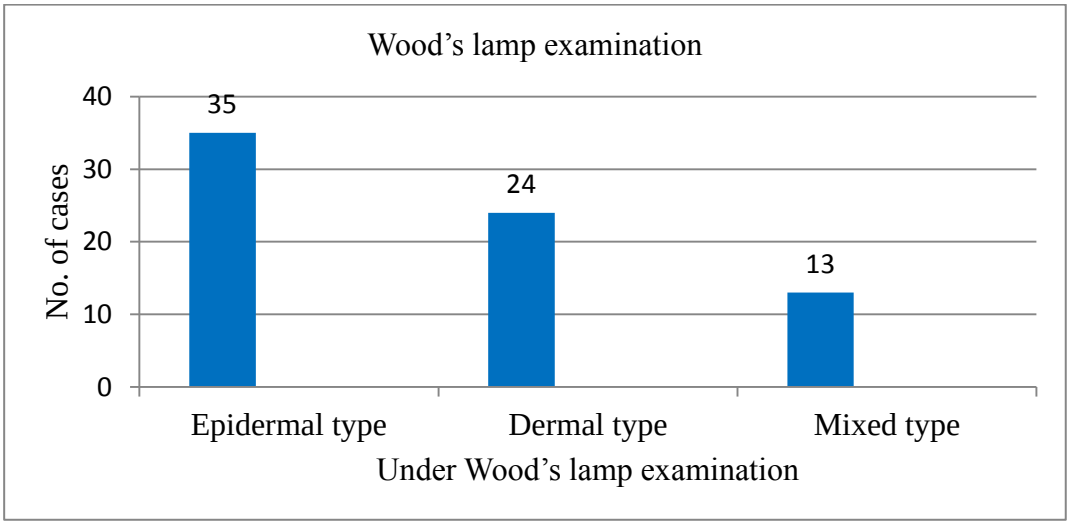


Figure 28: Diagram showing features of Wood's lamp examination

Melasma Area and Severity Index (MASI) score in patients with melasma

In our study, majority 24 (33.33%) patients had a MASI score ranging between 11 to 15 followed by 6 to 10 in 18 patients (25%), less than 5 in 13 patients (18.05%), 16 to 20 in 12 patients (16.66%) and greater than 20 in 5 patients(6.94%) and the results were shown in table 17 and figure 29.

Table 17: MASI score in patients with melasma

MASI Score	No. of Patients	Percentage
Less than 5	13	18.05
6-10	18	25.0
11-15	24	33.33
16-20	12	16.66
More than 20	5	6.94

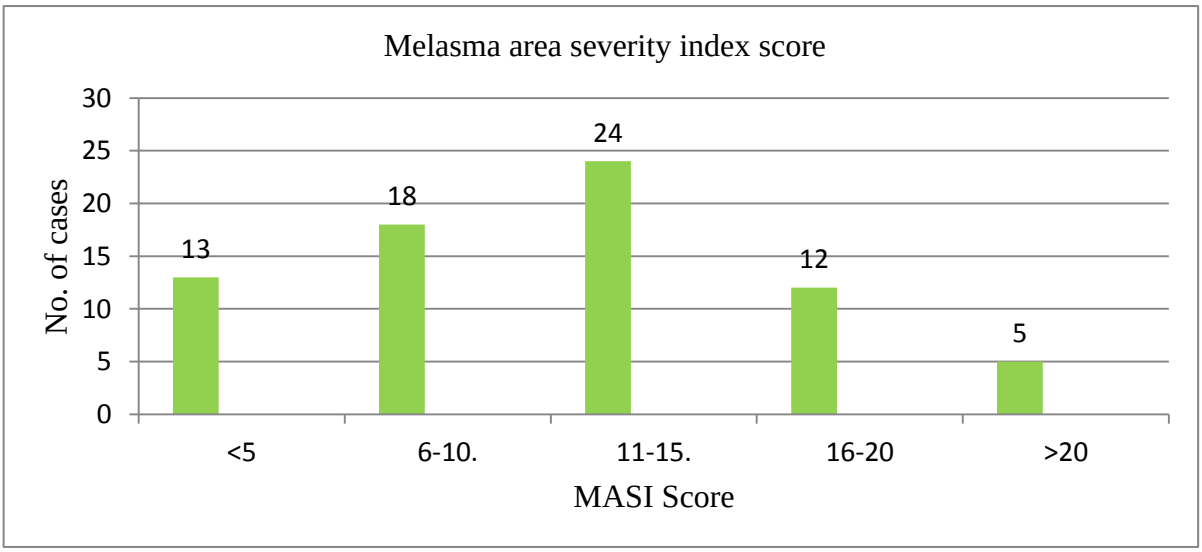


Figure 29: Diagram showing melasma area severity index (MASI) score

PHOTOGRAPHS

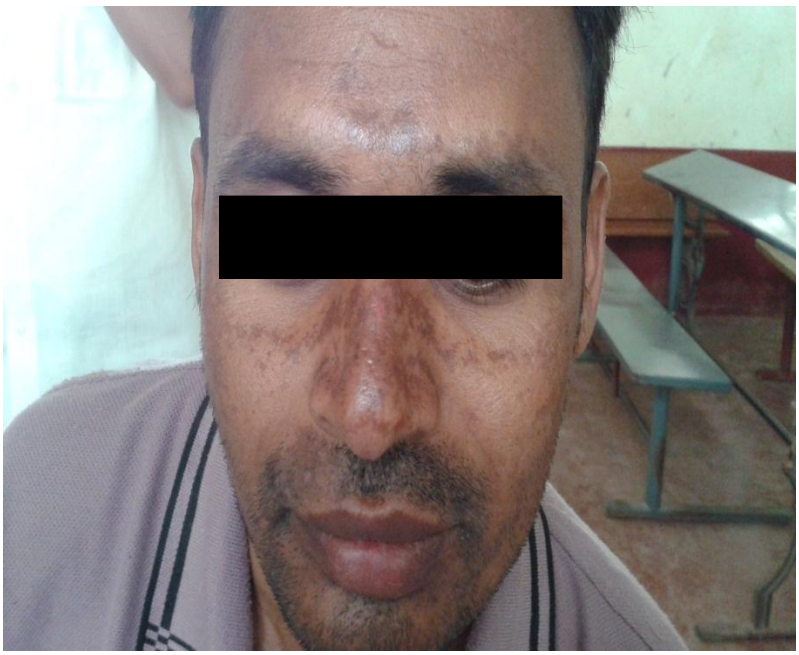


Figure 30: Centro-facial pattern of melasma

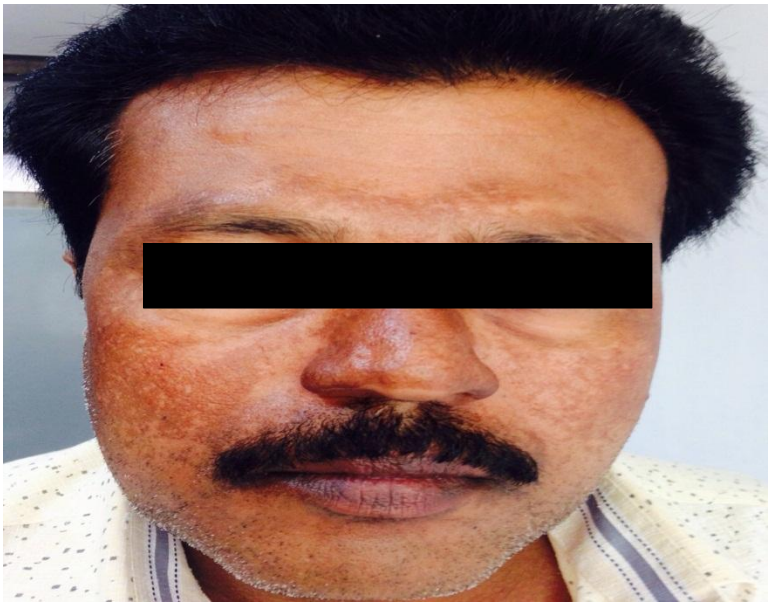


Figure 31: Centro-facial pattern of melasma

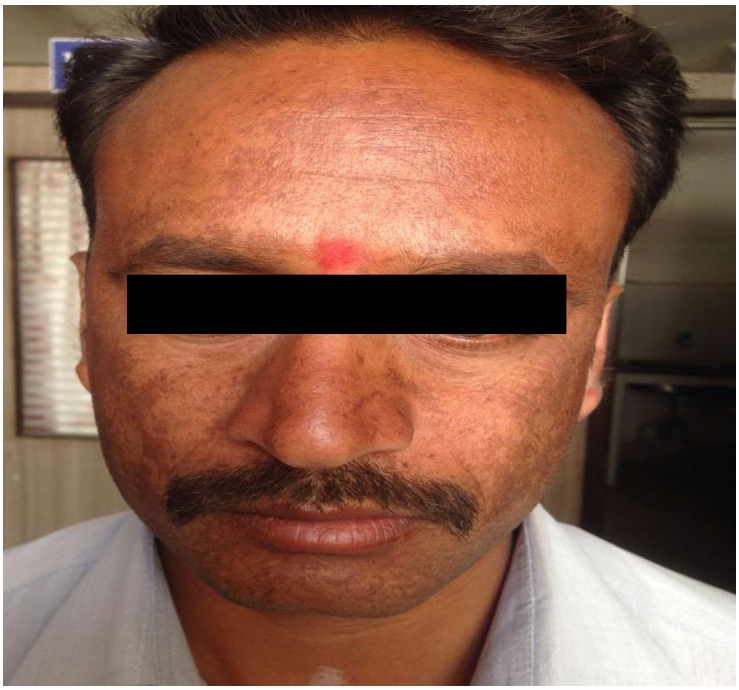


Figure 32: Centro-facial pattern of melasma

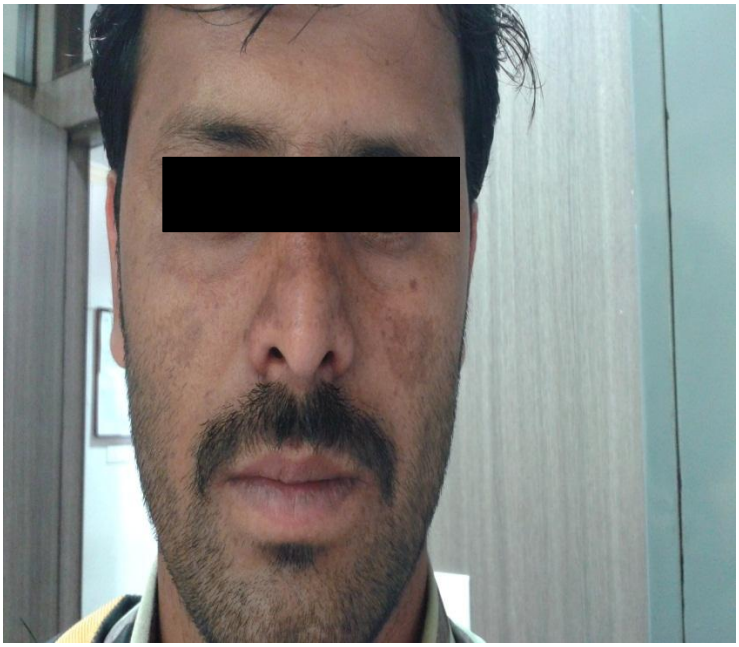


Figure 33: Malar pattern of melasma

Figure 34: Malar pattern of melasma

Figure 35: Malar pattern of melasma

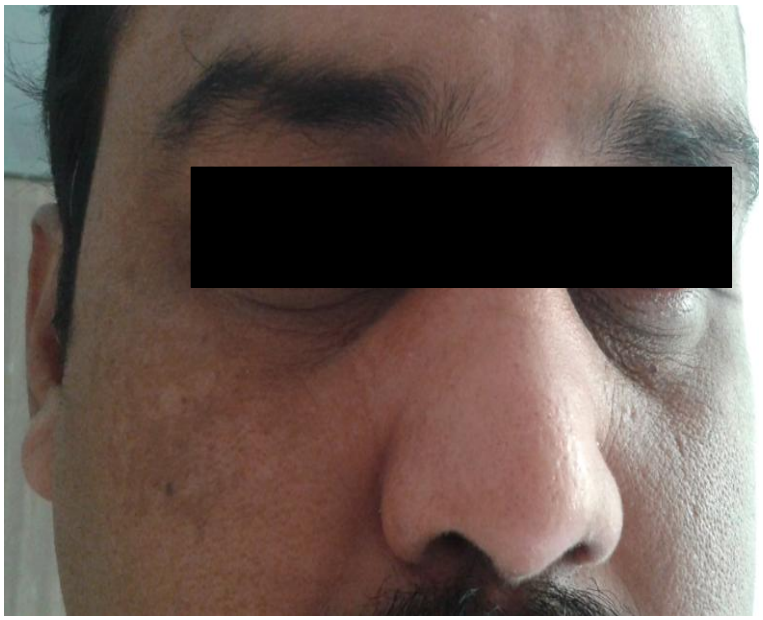


Figure 36: Light brown color of melasma lesion

Figure 37: Bluish grey color of melasma lesion

Figure 38: Dark brown color of melasma lesion

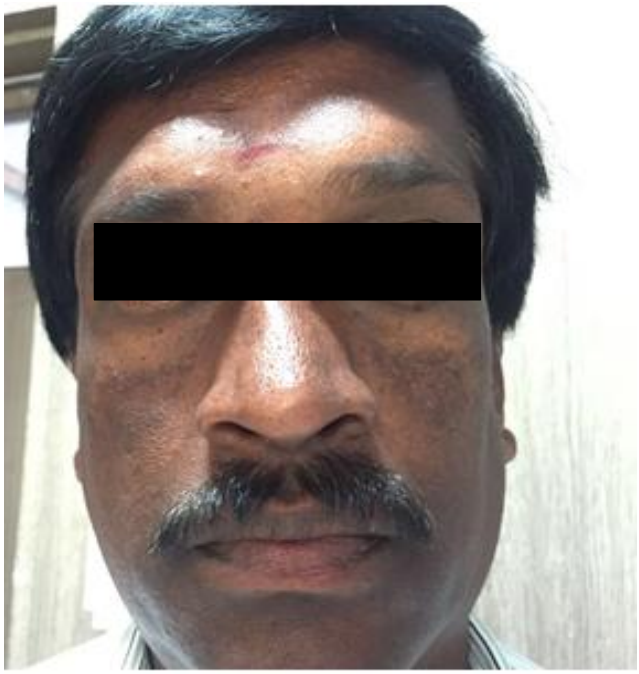


Figure 39: Black color of melasma lesion

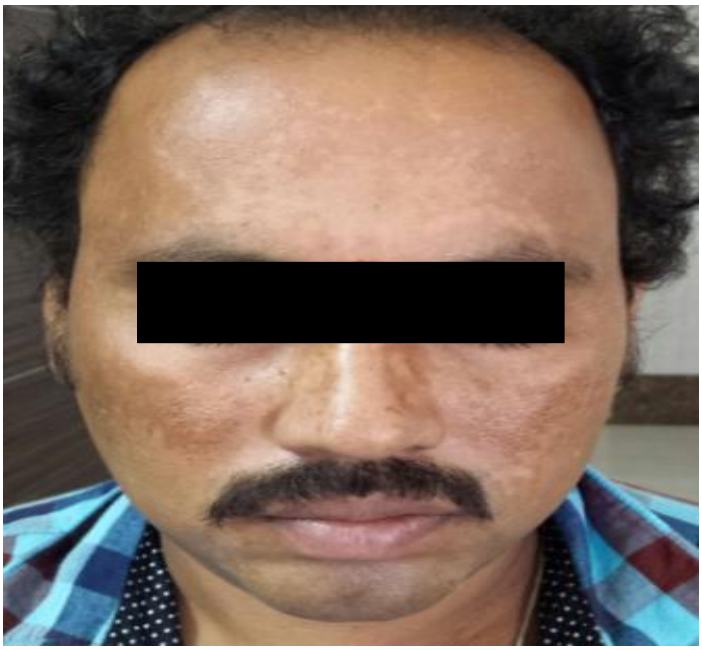


Figure 40(a): Centro-facial pattern of melasma

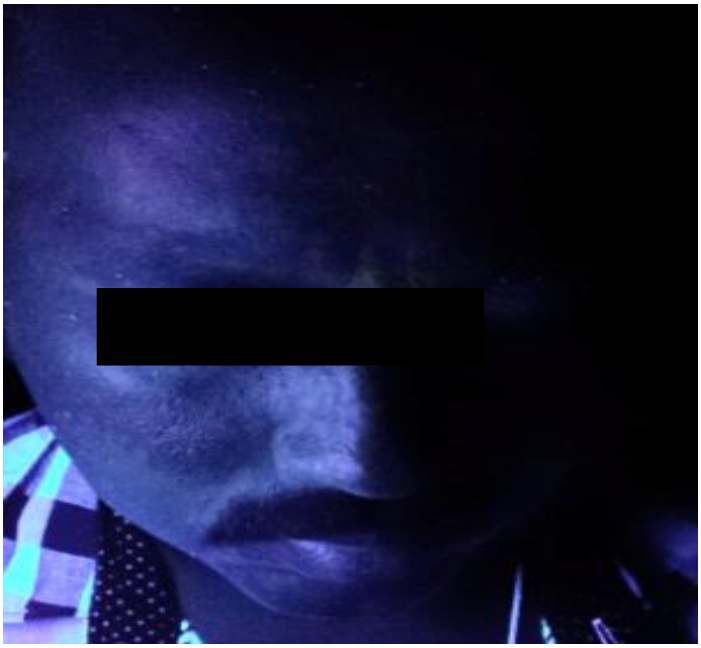


Figure: 40(b) Wood's lamp examination showing accentuation of lesion (epidermal type)

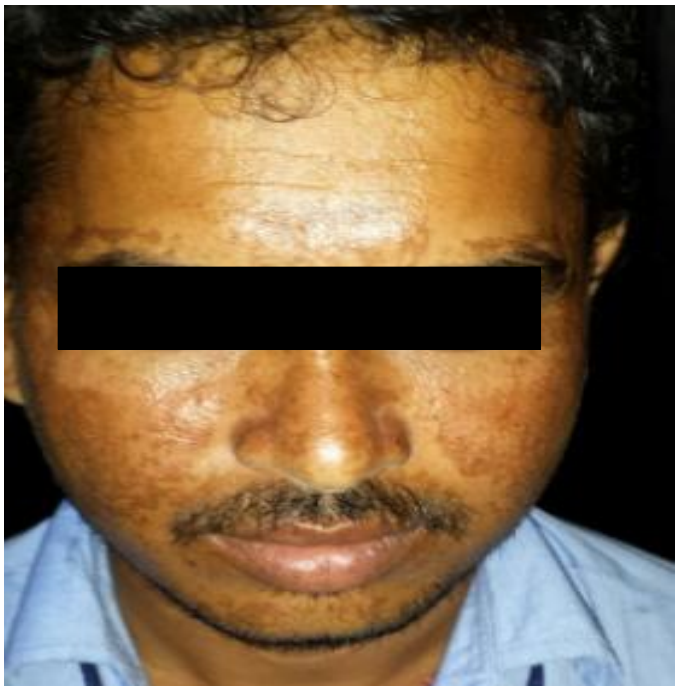


Figure: 41(a) centro-facial pattern of melasma

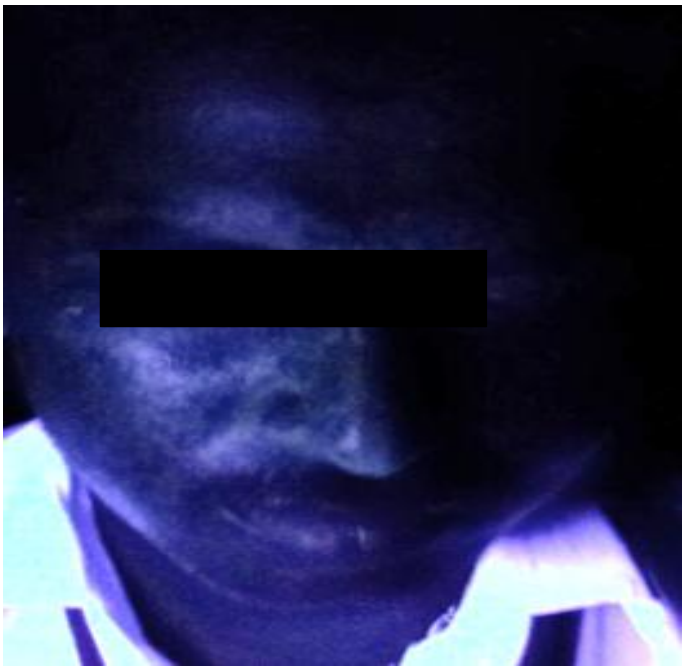


Figure: 41(b) Wood's lamp examination showing mixed type of both accentuation and no accentuation areas

DISCUSSION

Melasma is an acquired hyper-pigmentary disorder of the skin. It is the most common pigmentary disorder in Indian population. In a survey of 2000 black patients seeking dermatologic care in private practice, the third most commonly cited skin disorder was pigmentary problem of which post inflammatory hyperpigmentation, melasma and vitiligo were diagnosed most often.[17]

Although women are predominantly affected, men are not excluded from melasma, representing approximately 20% of the cases.[3] It can be a source of embarrassment in men because of its unsightly appearance and the social stigma of being categorized as a disease in pregnant women.[6] The exact cause of melasma although remains unknown, multiple factors seem to be contributing to its etiopathogenesis in woman such as pregnancy, use of hormone replacement therapy, oral contraceptive-pills, sun exposure, family history and drugs intake, where as in men etiological factors includes sun exposure, genetic factors, chronic illness, anti-seizure drugs and cosmetic usage. Melasma in men, has not been adequately studied.[12]

In the present study, a total of 72 male melasma patients of age between 20-50years were enrolled. Detailed history was taken, general physical examination, cutaneous examination, Wood's lamp examination was done along with appropriate investigations. The following observations were made and are compared with other similar studies.

The youngest age of the patient with melasma in our study was 22 years and eldest was 50 years. The mean age distribution was 33.83 years. In the two different studies done

by Sarkar et al, [12,42] the mean age distribution of melasma in men was 33.5 years and 34.5 years respectively, which is similar to our study.

In this study of 72 patients, majority of them (37.5%) were in the age group between 31 - 35 years, 14 patients (19.44%) were in age group of 26 - 30 years followed by 13 patients (18.05%) in between 36 - 40 years, indicating most common age distribution in our study was in the age group of 31 to 40 years (55.5%) which is similar to the other study[12] in which it was 51.2% and in contrast to other studies [11,34] which showed 42% and 33.3% respectively.

With regard to age of onset of melasma in the present study, the mean was found to be 31.48 years, which is similar to the previous studies.[14,45]

The duration of melasma varied from 3 months to 6.5 years in the present study. The mean duration of melasma was 2.33 years. In the other studies done by Sarkar et al,[42] Achar et al [3]and Vachiramon et al.[6] the mean duration of melasma was found to be 1.4 years, 3.59 years and 7 years respectively. Comparatively early reporting of patients for treatment in the present study, reflects the concern of our patients regarding their facial appearance.

In the present study, 42 (58.33%) patients had history of sun exposure as a precipitating factor because majority of our patients were agriculturists, laborers, security guards, auto drivers etc . All these patients had 4-6 hours of sun exposure per day. Melasma and other pigmentary conditions are more common in dark-complexioned individuals and in those who have greater exposure to the sun caused by their occupation, as observed in the present group of patients. The various studies[9,14,42,101] conducted in men

with melasma suggested prolonged sun exposure can be a precipitating factor, which is consistent with our study.

A positive family history of melasma in the relatives was noted in 29 (40.27%) patients in this study. Vazquez et al, [14] Guinot et al [34] and Kumar et al [9] reported 70.4%, 33.3% and 14.28% of men with melasma in their studies had family history of melasma respectively. In a study done by Keeling et al[101] showed all patients had family history, while two patients acknowledged of having an affected male relative. The studies[102], which show remarkable differences even between populations living in similar environmental conditions, suggest that susceptibility of melasma is polygenic in nature.

In the present study, 8 (11.11%) patients had history of application of cosmetics, among them five used mustard oil and remaining three used aftershave lotion. In a study by Guinot et al[34], three out of nine patients used aftershave lotion as cosmetic usage. In the studies conducted by Sarkar et al,[12] and Kumar et al,[9] reported 43.9% and 32.14% of male patients with melasma used mustard oil as cosmetic respectively. Although mustard oil was used by large number of patients, its role in the causation of melasma is still unclear and needs to be substantiated by further studies.[102]

In our study, 3(4.16%) patients had history of intake of phenytoin drug for seizure disorders. Melasma-like pigmentation is a known side effect of phenytoin therapy. Sarkar et al. in their study reported that 3 of 41 Indian men with melasma used phenytoin.[12]

Hormonal changes, although different from women, may analogously play a role in the development of melasma in men.[6] In the present study two (2.77%) patients showed low levels of testosterone and elevated levels of luteinizing hormones. Sialy et al,[13]

conducted a study in 15 Indian male melasma patients and found higher level of luteinizing hormone and lower level of testosterone when compared with 11 male controls. A similar finding has been reported in another study[12] from India, although seen in only 9.7% of patients. This finding indicated that subtle testicular resistance may be involved in the pathogenesis of melasma in men.[12,13]

In our study, four (5.55%) patients found to have hypothyroidism. Sarkar et al,[12] conducted similar study in 41 males with melasma, noticed hypothyroidism in three (7.33%) patients. Lutfi et al, [37] found that thyroid disorders are four times more frequent in melasma patients than controls, and significant differences were also reported by another study done by Perez et al.[103] However, the matter is still controversial, a study conducted by Yazdanfar et al,[38] showed no difference in thyroid levels between melasma patients and controls, and similar results were also reported by Sacre et al.[104] Further larger studies are needed to clarify this association.

Five patients (6.94%) showed hepatic dysfunction in the present study. There is no solid supporting evidence for other causative factors such as, nutritional disorder, hepatic disorders and parasitic infestations[12] suggests that the development of melasma is influenced by many factors, and depends on the interaction of environmental and hormonal influences in a genetically predisposed individuals.[18]

The commonest skin type of patients (Fitzpatricks skin type) in the present study was found to be type IV (brown colour) seen in 46 patients (63.88%) followed by type III (light brown) in 22 patients (30.55%) and type V (dark brown) in four (5.55%), which was similar to a study done in male melasma patients by Vachiramon et al.[6] In another

study done by Guinot et al,[34] skin type IV (55.5%) was the most common followed by skin type V (44.4%).

In the present study, the colour of the melasma macule was light brown in 38 patients (52.77%), bluish grey in 19 patients (26.38%) and dark brown/black in 15 (20.83%) patients. Dark brown or black colored melasma macules were seen in 66.66% of patients and 33.33% showed light brown color melasma macule, in a study[34] done in Tunisian male population.

Malar type of pattern, in 47 patients (65.27%) is most common pattern seen in our study followed by centro-facial pattern in 23 (31.94%) and mandibular pattern in two patients (2.77%) which is consistent with other studies.[9,12,39] In a similar study by Sialy et al,[13] conducted in male melasma patients showed centro-facial pattern in 80% followed by malar pattern in 13.33% and mandibular pattern in 6.66% patients which is in contrast to our study. This variation in results might be due to regional and environmental differences.

In the present study, Wood's lamp examination of melasma showed epidermal type in 48.61% of patients followed by dermal type in 33.33% and mixed type in 18.06% of patients which is similar to other studies.[14,42]

In our study, majority of the patients (33.33%) had a MASI score range between 11 - 15 followed by 6 - 10 in 18 patients (25%), less than 5 in 13 patients (18.05%). In the present study, MASI score ranged from 1.2 to 24, with mean score of 11.61. Pandya et al, [53] stated that MASI has face validity, as it attempts to measure the size and darkness of pigmentation associated with melasma, which are the most frequent symptoms of patients with this disorder.

SUMMARY

- A total of 72 male melasma patients who presented to the department of Dermatology at R.L. Jalappa hospital and research centre, attached to Sri Devaraj Urs Medical College, Tamaka, Kolar between January 2015 to September 2016 were studied.

- The youngest age in our study was 22 years and eldest was 50 years. The mean age distribution was 33.83 years. The mean age of onset of melasma was 31.48 years.

- Majority of the patients 37.5% were in age group of 31 to 35 years, followed by 14 patients (19.44%) were in between 26 to 30 years, 13 patients (18.05%) in between 36 to 40 years, 8 patients (11.11%) in between 20 to 25 years, 7 patients (9.72%) in between 41 to 45 years and least 3 patients (4.16%) were in between 46 to 50 years.

- The duration of disorder between 1 to 2 years was found majority in 41.66% of patients followed by 29.16% of patients with the duration of 2-5 years, 19.44% of patients with the duration of less than 1 year and 9.72% with duration greater than 5 years.

- The duration of melasma varied from 3 months to 6.5 years. The average duration of melasma in this study was 2.33 years.

- 42 (58.33%) patients had history of sun exposure as a precipitating factor because majority of our patients were agriculturists, laborers, security guards and auto drivers etc. All these patients had 4-6hrs/day of sun exposure.

- A positive family history of melasma in relatives was noted in 29 (40.27%) patients.
- Eight (11.11%) patients gave history of application of cosmetics. Among them five were using mustard oil and remaining three was using after shave lotions.
- Three (4.16%) patients gave history of intake of phenytoin as anti-seizure drug.
- Laboratory investigation revealed, hypothyroidism in 4 patients (5.55%), hepatic disorder with raised amino transaminases in 5 patients (6.94%), and 2 patients (2.77%) showed low levels of testosterone with elevated levels of luteinizing hormones.
- The most common skin type of patients was found to be type IV seen in 63.88% of patients followed by type III in 30.55% and type V in 5.55% of patients.
- The colour of the melasma macules were light brown in 52.77% of patients, bluish grey in 26.38% of patients and dark brown/black in 20.83% of patients.
- Malar type of pattern was the most common type seen in 65.27% of patients followed by centro-facial pattern in 31.94% and mandibular pattern in 2.77% of patients.
- Wood's lamp examination showed epidermal type in 48.61% of patients followed by dermal type in 33.33% and mixed type in 18.06% of patients.
- Majority of the patients (33.33%) had a MASI score range between 11 to 15 followed by 6 to 10 in 25% of patients , less than 5 in 18.05%, 16 to 20 in 16.66% and greater than 20 in 6.94% patients. MASI score ranged from 1.2 to 24, with mean score of 11.61.

CONCLUSION

Melasma is a common pigmentary disorder that often motivates the search for dermatological care. It is more frequently observed in Indian men, but definitely less common than in women even though only male patients with melasma were analyzed. Although melasma has multifactorial etiology, the main aggravating factors appeared to be sun exposure and family history. Early reporting of patients for treatment reflects the concern of our patients regarding their facial appearance. Although the current study is a source of new relevant data on the etiopathogenesis and epidemiology of melasma in men, prospective studies would be needed to improve knowledge of this frequent skin disease.

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ANNEXURE - I

PROFORMA

SL No: Date:

Name:

Age:

Occupation:

Address:

OP/ IP No:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

1. Onset : sudden/insidious
2. Duration :
3. Progression : stationary/ gradual spread/ rapid spread/ regression
4. Aggravating factors:

   a) Sun exposure : present/absent

   b) Cosmetic usage : mustard oil/ dyes/ perfumes/ after shave lotions

   c) Drugs : Anticonvulsants/ antimalarials/ tetracyclines/ sulfonylureas

   d) Chronic illness : Thyroid dysfunction, hepatic disorders, nutritional disorders, inflammatory bowel disorders

PAST HISTORY:

TREATMENT HISTORY:

1. Treatment taken to the presenting condition: Yes/No

2. Type of treatment : topical/ systemic/ chemical Peels/ lasers

3. Duration :

FAMILY HISTORY : history of similar complaints in the family members

PERSONAL HISTORY:

ON EXAMINATION:

GENERAL PHYSICAL EXAMINATION:

CUTANEOUS EXAMINATION:

1. Skin type :

Black / Dark brown/ Brown / Light brown/ Fair

Type-VI Type-V Type-IV Type-III Type-I,II

2.Distribution : Malar / Centrofacial /Mandibular

3.Colour of the macule : Light Brown / Bluish grey/ Dark brown or black

4. MASI score : $0.3\ (D_F+H_F)A_F + 0.3(D_{MR}+H_{MR})A_{MR} +0.3(D_{ML}+H_{ML})A_{ML} +0.1(D_C+H_C)A_C$

5.Wood's lamp examination: Accentuation / No accentuation / equivocal

SYSTEMIC EXAMINATION : RS: CVS:

GIT: CNS:

INVESTIGATIONS: (where ever necessary)

1. Complete haemogram : Hb,WBC, TC, DC
2. Liver function tests : SGOT, SGPT, ALP
3. Hormonal assay : T3, T4, TSH, LH, Testosterone
4. Stool examination : ova, cyst

PROVISIONAL DIAGNOSIS:

ANNEXURE - II

PATIENT INFORMATION SHEET

Study title: A clinico-epidemiological study of melasma in men.

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Aim: To study the clinical pattern, types and different etiological factors of melasma in men.

Hyperpigmentation of the skin is a very common problem .Such pigmentary changes can be present since birth or can be acquired later in the life. One such acquired condition is melasma. Melasma will have an impact on the quality of life of patients because, cosmetically un- acceptable facial lesions can significantly affect a person's psychological and social wellbeing.

This study will help to know the common presentations, types and different etiological factors of melasma. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study we will collect information (as per proforma) from you. Relevant investigations (complete blood picture, liver function tests, stool examination, hormonal profile) will be carried out if required. This information collected will be used for dissertation and publication only.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above investigations will be funded by the study investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

ANNEXURE - III

CONSENT FORM

Study title: A CLINICO-EPIDEMIOLOGICAL STUDY OF MELASMA IN MEN.

Chief researcher/ PG guide's name: Dr. RAJASHEKAR T.S

Principal investigator: Dr. KEERTHI C

a) I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.

b) I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.

c) I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.

d) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

e) I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature…….

Date……

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature……..

Date……

ANNEXURE - IV

KEY TO MASTER CHART

1. SL NO. : Serial number
2. OP NO. : Outpatient number
3. AGE (YRS): age in years
4. PLACE:
5. OCCUPATION:
6. AGE OF ONSET: age in years
7. DURATION(YRS): Duration of melasma in years
8. ETIOLOGY: a) Sun exposure: P-Present A-Absent
   b) Family history: P-Present A-Absent
   c) Cosmetic usage: P-Present A-Absent
   d) Drugs intake: P-Present A-Absent
   e) Endocrine disorders: P-Present A-Absent
9. TREATMENT TAKEN: P-Present A-Absent
10. SKIN TYPE: (Fitzpatricks skin type)
    III: light brown IV: brown V: dark brown
11. CLINICAL PATTERN: CF- Centro-facial type Mlr- Malar type
    Man- Mandibular type
12. COLOUR OF MACULE: LB- Light brown BG- bluish grey
    DB-dark brown
13. WOOD'S LAMP EXAMINATION: Acc- Accentuated Equ- Equivocal
    LA- Less Apparent
14. MASI SCORE: Melasma area severity index score

ANNEXURE - V

MASTER CHART

Sl No.	OP.No	Age (yrs)	Place	Occupation	Age of onset (yrs)	Duration of melasma (yrs)	Etiology							Treatment history	Skin type	Clinical pattern	Colour of macule	Wood's lamp	MASI score
							Sun exposure	Family history	Cosmetic usage	Drugs intake	Endocrine disorders								
											Thyroid imbalance	Testosterone imbalance	Hepatic disorders						
1	169363	50	srinivaspura	agriculturist	44	6	P	A	P	A	A	A	A	A	III	CF	LB	Acc	16
2	173090	33	kolar	clerk	30	3	A	P	A	A	A	A	P	A	IV	Mlr	DB	Equ	14.4
3	173876	36	chintamani	policemen	31.5	4.5	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	12
4	173919	35	malur	car driver	33	2	A	P	A	A	P	A	A	P	III	CF	BG	LA	24
5	59320	34	sidlaghatta	clerk	32.5	1.5	A	A	P	A	A	A	A	A	III	Mlr	BG	LA	7
6	2426	31	kolar	accountant	30.5	0.5	A	P	A	A	A	A	A	A	IV	Mlr	DB	Equ	14.4
7	61340	29	kolar	gar.worker	26.5	2.5	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	12
8	36166	41	nangali	watchman	39	2	P	P	A	A	A	A	P	A	V	CF	LB	Acc	24
9	65231	25	bagepalli	teacher	24.5	0.5	A	A	A	A	A	A	A	A	IV	CF	LB	Acc	20
10	71650	34	koalr	pharmacist	33	1	A	A	P	A	A	P	A	A	IV	Mlr	DB	Equ	12.8
11	11734	31	KGF	business	29	2	A	A	A	P	A	A	A	A	III	Mlr	BG	LA	11.6
12	103512	35	kolar	doctor	32	3	A	P	A	A	A	A	A	A	IV	CF	LB	Acc	20
13	138329	34	kolar	labourer	32.5	1.5	P	A	A	A	A	A	A	A	IV	Mlr	LB	LA	14.4
14	164301	32	malur	officeattender	31.5	0.5	A	P	P	A	A	A	A	A	IV	CF	LB	Acc	16
15	65347	35	sidlaghatta	conductor	32	3	P	A	A	A	A	A	A	A	III	CF	LB	Acc	9.8
16	95379	40	kolar	bank manager	36	4	A	P	A	A	A	A	A	P	III	Mlr	DB	Equ	16.8
17	97369	45	srinivaspura	agriculturist	39.5	5.5	P	A	A	A	A	A	A	A	IV	CF	BG	LA	12
18	62998	50	bangarpet	labourer	46	4	P	A	A	A	A	A	P	A	IV	Mlr	LB	Acc	15
19	97174	33	hoskote	business	30	3	A	A	A	A	P	A	A	A	IV	Mlr	LB	Acc	9
20	67873	25	kolar	technician	24.75	0.25	P	P	A	A	A	A	A	A	V	CF	LB	Acc	18
21	98504	35	malur	vendor	31	4	P	A	A	A	A	A	A	A	IV	Mlr	DB	Equ	15
22	164633	42	kolar	business	41	1	A	A	A	P	P	A	A	A	IV	Mlr	LB	Acc	18
23	155986	30	tamaka	business	28	2	A	P	A	A	A	A	A	A	III	Mlr	BG	LA	9.6
24	179402	36	kolar	bus driver	34	2	P	A	A	A	A	A	A	A	IV	Man	LB	Acc	8.4
25	14111	45	tamaka	agriculturist	42	3	P	A	P	A	A	A	A	A	IV	Mlr	BG	LA	9
26	195699	33	kolar	bank employe	29.5	3.5	A	A	A	A	A	P	A	A	IV	Mlr	BG	LA	15
27	195782	24	malur	student	23.5	0.5	A	P	A	A	A	A	A	A	IV	Mlr	LB	Acc	18
28	201348	38	chintamani	agriculturist	32.5	5.5	P	A	A	A	A	A	A	A	III	Mlr	DB	Equ	4.8
29	202770	28	sidlaghatta	mechanic	27.5	0.5	P	A	A	A	A	A	A	A	IV	CF	LB	LA	9
30	927084	30	bangarpet	agriculturist	29	1	P	P	A	A	A	A	A	A	IV	Mlr	LB	Acc	2.4
31	928308	32	nangali	beedi worker	30	2	A	A	P	A	A	A	A	A	III	Mlr	LB	Acc	3.6
32	926453	37	kolar	labourer	35	2	P	A	A	A	A	A	A	A	IV	Mlr	BG	LA	8.4
33	921987	35	bagepalli	agriculturist	31.5	3.5	P	P	A	A	A	A	A	A	IV	Mlr	LB	Acc	6

34	900313	35	tamaka	mechanic	34	1	A	P	A	A	A	A	A	A	III	CF	BG	LA	4.8
35	901083	39	kolar	auto driver	34	5	P	A	A	A	A	A	A	A	IV	CF	DB	Equ	15
36	982918	35	hoskote	vendor	34.5	0.5	P	A	A	A	A	A	A	A	III	CF	LB	Acc	9
37	962787	30	tamaka	business	28.5	1.5	A	P	A	A	A	A	A	A	IV	Mlr	BG	LA	4.8
38	959287	26	srinivaspura	electrician	25.5	0.5	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	18
39	964849	30	chintamani	mechanic	29	1	P	P	A	A	A	A	A	A	III	Mlr	LB	Acc	11.2
40	931959	28	kolar	clerk	26	2	A	P	A	A	A	A	A	A	IV	Mlr	BG	LA	3.6
41	901099	39	mulbagal	veg.seller	32.5	6.5	P	A	A	A	A	A	A	A	IV	Mlr	BG	LA	14.4
42	982947	36	tamaka	auto driver	34	2	P	A	A	A	A	A	A	A	IV	Mlr	DB	Equ	12
43	924651	39	kolar	constable	36	3	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	21
44	188217	29	nangali	carpenter	28.5	0.5	P	P	A	A	A	A	A	A	III	Mlr	BG	LA	12.8
45	923555	28	tamaka	technician	27	1	A	A	A	A	A	A	A	P	IV	CF	LB	Acc	15
46	921411	35	malur	sales man	33	2	P	A	A	A	A	A	A	A	V	Mlr	LB	Acc	15
47	958341	43	kolar	teacher	41.5	1.5	A	P	A	A	P	A	A	A	III	CF	BG	LA	8.4
48	188936	24	tamaka	student	23.75	0.25	A	P	A	A	A	A	A	A	IV	Mlr	DB	Equ	12
49	188815	33	bagepalli	agriculturist	27.5	5.5	P	A	P	A	A	A	A	A	IV	Mlr	LB	Acc	3.6
50	175660	22	sidlaghatta	student	21.5	0.5	A	A	A	A	A	A	P	A	III	CF	LB	Acc	18
51	227424	24	nangali	student	23	1	P	A	A	P	A	A	A	A	IV	Mlr	BG	LA	1.2
52	223706	32	kolar	accountant	31.5	0.5	A	P	A	A	A	A	A	A	IV	Mlr	LB	Acc	9
53	223228	42	mulbagal	agriculturist	36.5	5.5	P	P	A	A	A	A	A	A	IV	CF	DB	Equ	11.2
54	227408	39	bagepalli	labourer	36	3	P	A	A	A	A	A	A	A	III	Mlr	BG	LA	24
55	318432	28	hoskote	fruit seller	26.5	1.5	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	1.8
56	224684	33	KGF	bank employe	31	2	A	P	A	A	A	A	A	P	IV	CF	LB	Acc	18
57	318163	29	tamaka	labourer	26	3	P	A	A	A	A	A	A	A	IV	Mlr	DB	LA	6
58	250792	37	kolar	agriculturist	34	3	P	P	A	A	A	A	A	A	III	CF	LB	Acc	12
59	223709	32	kolar	agriculturist	28	4	P	A	A	A	A	A	A	A	IV	Mlr	BG	LA	8.4
60	227397	22	bangarpet	student	19.5	2.5	A	A	A	A	A	A	A	A	IV	Mlr	DB	Equ	4.8
61	223176	44	kolar	plumber	39	5	P	P	A	A	A	A	P	A	V	CF	BG	LA	16
62	198591	38	sidlaghatta	teacher	37	1	P	A	A	A	A	A	A	A	IV	Mlr	LB	Acc	2.4
63	318466	27	mulbagal	student	26.5	0.5	A	P	A	A	A	A	A	A	III	Mlr	BG	LA	9.6
64	225498	31	hoskote	sales man	29	2	P	A	A	A	A	A	A	A	IV	Mlr	DB	Equ	7
65	226981	36	kolar	conductor	32.5	3.5	P	A	A	A	A	A	A	A	III	CF	LB	Acc	12.8
66	223210	23	nangali	student	22.5	0.5	A	P	A	A	A	A	A	A	IV	Mlr	LB	Acc	21
67	227745	39	bagepalli	agriculturist	33.5	5.5	P	A	P	A	A	A	A	A	III	Mlr	LB	Acc	8.4
68	226855	33	srinivaspura	business	31.5	1.5	A	P	A	A	A	A	A	A	IV	Man	DB	Equ	4.2
69	227872	46	mulbagal	labourer	42	4	P	P	A	A	A	A	A	A	IV	Mlr	LB	LA	6
70	220853	34	malur	business	32	2	A	P	A	A	A	A	A	A	III	CF	LB	Acc	11.6
71	226882	28	kolar	agriculturist	26.5	1.5	P	A	A	A	A	A	A	A	IV	Mlr	DB	LA	3.6
72	227280	35	hoskote	car driver	34	1	P	A	A	A	A	A	A	A	III	CF	LB	Acc	12