UNIVERSITY OF BENGHAZI

FACULTY OF MEDICINE

MELASMA : Etiological factors clinical types and its relation to the disease severity and patients life quality

This Thesis is Submitted For Fulfillment Of The Requirement for the degree of Master (MSc) in dermatology and venereology

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CERTITFICATION

This thesis entitled **"MELASMA : Etiological factors clinical types and its relation to the disease severity and patients life quality"** prepared by Abdullatif .S.alghwel Under the supervision of prof. Gamal A. Duweb, has been approved for submission to the faculty of medicine, university of Benghazi , Benghazi, Libya in partial fulfilment for the certification of the degree of Master (MSc) in dermatology and venereology **.**

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DECLERATION

This is to declare that I have not submitted the research work embodied in this thesis **"MELASMA : etiological factors clinical types and its relation to the disease severity and patients life quality"** to any other university before.

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I wish to express my deepest gratitude and thanks To ALLAH, whose magnificent help was the main factor in accomplishing this work .

I am grateful to my supervisor, Prof. Gamal A . Duweb, for suggesting the original lines of this work and the many hours of fruitful discussion .

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DEDICATION

I dedicate this work to the soul of my father, and my family especially and my wife and my son eng .Mohamed Abdullatif

SUMMARY

1-Summary

Melasma is a very common skin disorder. It is most common in young women with brownish skin tane, but it can affect anyone. Melasma is often associated with the female hormones estrogen and progesterone. It is common in pregnant and women taking birth control pills (oral contraceptives).

Aim of the study: To know theclinico-epidemiological pattern and the precipitating or provocation factors in Libyan melasma patients, to assess the melasma areas and severity index(MASI) and the alteration of quality of life in melasma patients.

Materials and methods: In a cross-sectional study 100 patients with melasma attending out-patient clinic, dermatology department, Aljamhoria hospital, Benghazi-Libya. All patients were exposed to detailed disease history and complete dermatological examination. Woods light examination was done to every patient and MASI score was calculated and dermatology life quality index (DLQI) questionnaire was applied.

Results:The study included 100 patients , 89% were female and 11% were male. There was female preponderance with a female to male ratio of approximately 8.1:1, Age ranged from 18 to 64years, with mean age 30.7±7years , there was no significant difference between the mean age of male and female p value was 0.987.Duration of disease was ranged between one month and 6 years. Family history of melasma was recorded in 9% of the

patients. Outcome of treatment with Hydroquinon was 50.5% marked improvement. Regarding the site involved, 66% of the patients the site affected was centrofacial followed by malar that seen in 32%. Concerning the color of the lesions, dark brown / black color was presented in 58% and light brown in 42% of cases. Sun exposure plays an important aggravating factor and recorded in 55%, followed by oral contraceptive and pregnancy in female patients.Regarding the skin type and tanning intensity, the data showed 66.3% were type VI and 27% type III. Woods light examination showed that melasma was epidermal in 86% and dermal type in 11% of our cases. According to MASI score, it was mild in 26% of patients, moderate in 73% of cases and very severe in only 1% of the patients. MASI score for forehead darkness, normal skin was recorded in 46%, 45.5% of male and 46.1% of female. Quality of life was impaired in 67.4% of females patients and the DLQI score was ranging from mild to moderate while quality of life was not affected in 72.7% of male .

Conclusions: Melasma in men is definitely less common than in women, but shares the same clinico-histopathological characteristics as in women.Although the exact cause of melasma remains unknown, multiple factors seem to be contributing to its aetiopathogenesis in women, including genetic factors, exposure to sunlight, pregnancy, oral contraception, hormonal therapies.

INTRODUCTION

2-Introduction:

Melasma is an acquired hypermelanosis of sun-exposed areas.

Melasma present as symmetric hyperpegmented macules, which can be confluent or punctuate. The cheeks, the upper lip, the chin and the forehead are the most common locations , but melasma can occasional occur in other sun-exposed location.[1]

The pathophysiology of melasma is uncertain , in many cases a direct relationship with female hormonal activity appears to be present because melasma occurs with pregnancy and with the use of oral contraceptive pills. Other factors implicated in the etiopathogensis of melasma are photosensitizing medications, mild ovarian or thyroid dysfunction, and certain cosmetic .[2,3]

A genetic predisposition is major factor in the development of melasma. More than 30% of patients have a family history of melasma, identical twins have been reported to develop melasma while other siblings under similar condition did not.[2-6]

Hormonal influences play a role in some individuals. The mask of pregnancy is well known to obstetric patients. The exact mechanism by which pregnancy affects melasma is unknown.Estrogen, progesterone, and melanocyte- stimulating hormone (MSH)levels are normally increased during the third trimester of pregnancy .

One study found a 4 fold increase in thyroid disease in patients with melasma when compared with matched controls.[4-5]

Persons of any race can affected by melasma.However , melasma is much more common in constitutionally darker skin types than in lighter skin types and it may be more common in light brown skin types especially Hispanics and Asians , from areas of the world with intense sun exposure.[2-3]Melasma is much more common in women than in men, women are affected in90% of cases.[1]

The excess melanin can be visually localized to the epidermis or the dermis by use of a Wood lamp (wavelength 340-400nm). Epidermal pigment is enhanced during examination with Wood light, whereas dermal pigment is not .[3]

The Melasma Area and Severity Index (MASI) is common outcome measure used to assess melasma patients , however it previously had not been validated.[3]

REVIEW OF LITERATURE

3- Review of literature

3.1. Skin color:

Melanin is the major component of skin color, and melanocytes are the sole site of Melanin formation ; they are specialized dendritic cells present in normal akin only in The hair matrix and at the dermo-epidermal junction. Allmelanocytes are derived from The neural crest (melanblasts), with the single exception of melanocytes in the retinal Pigment epithelium (RPE), thes do notmigrate from the neural crest but arise from theOuter layer of the optic cup.Melanocytes are normally found in humans in the skin,the RPE, and in the striavascularis of the inner ear. Melanocytes produce two chemically Distinct types of melanin pigments:- eumelanin (brown-black melanin) isfound inEllipsoidal melanosomes, which impart brown-black color to the skin, eyes,and hair . Pheomelanin (yellow-red melanin), found in spherical melanosomes, is thebasis for Yellow-red hair and has also recently been found in basal layar melanocytes. Melanin Pigment is synthesized inspecialized cytoplasmic organelles calledmelanocytes Which contain theprincipal pigment-synthesizing enzyme tyrosinase. It is the presence Of melanizedmelanosomes within the keratinocytes thet imparts skin color. TheNumber, melanin content, and location of these melanosomes determine the various Hues of human skin and hair.color.[7]

Color of lesions was dark brown/black in 58% of patients and 42% light brown, in male 72.7% was dark brown/black and 27.3% light brown , while in female 56.2% dark brown/black and 43.8% light brown, but this difference in distribution between both sex was not significant difference p value was 0.468.

3.2. Melanogenesis.

Melanocytes possess the metabolic machinery for the synthesis of the melanogenic enzyme, tyrosinase, which is incorporated into melanosomes. The epidermal melanocytes are capable of transporting the fully mature melanosomes via dendrites into the neighboring keratinocytes. Melanosomes are highly organized ellipsoidal organelles that contain melanin inside a unit membrane and deposit it on an internal filamentous and/or microvesicular matrix. In melanosomes of normal skin, melanin is extremely dense, virtually insoluble polymer of high molecular weight and is always attached to the structural proteinMammalian melanin pigments have one of two chemical compositions

• eumelanin, a brown polymer derived from the conversion of the amino acid, tyrosine, to an alkali-soluble brown chromophore; or 2- pheomelanin, a yellow- reddish, alkali-soluble pigment derived from tyrosine but in which one of the intermediates in the tyrosine-melanin pathway (dopaquinone) combines with cysteine (or glutathione) to from cysteinyldopa; this leads to

the yellow pigment, pheomelanin. The conversion of tyrosine to dopa to dopaquinone is accomplished by an aerobic copper-containing oxidase, tyrosinase.

Despite evident differences in their structure and general properties, all types of melanins can be embraced by a unified biogenetic pathway in which dopaquinone is the crucial intermediate. Tyrosinase catalyzes the first step of eumelaninbiosynthesis,the hydroxylation of tyrosine to 3,4-dihydroxyphenylalanine (dopa). Dopa will be subsequently oxidized to dopaquinone by tyrosinase and then continue the to form dopachrome. Dopachrome, in turn, spontaneously decarboxylates to produce DHI, which is rapidly oxidized to produce indole-5,6-quinone. However, in the presence of certain divalent metal cations and the enzyme, the carboxylated intermediate DHICA will be produced. DHICA-oxidase can accelerate oxidation of DHICA to indole-5,6- quinone-2-carboxylic acid, which is autooxidized to become eumelanin. However, when dopaquinone encounters sulfhydryl compounds (e.g., cysteine or glutathione), cysteinyldopa is formed and eventually results in pheomelanin through the formation of benzothiazine metabolites [7].

Each epidermal melanocyte secretes melanosomes into a finite number of neighboring group of keratinocytes is called an epidermal melanocyte secretes melanosomes into a finite number of neighboring keratinocytes

(approximately 36); this partnership of a melanocyte and a neighboring group of keratinocytes is called an epidermal unit .

After melanosomes have been transferred to keratinocytes, they are surrounded by a membrane, becoming secondary lysosomes. In white skin, the melanosomes are relatively small and form groups within the secondary lysosomes. This iscalled a melanosomecomplex.Melanin is degraded during the ascent of the keratinocytes toward the outer surface of the epidermis. With the loss of the stratum corneum, the remaining melanin pigments are removed. Consequently, melanization of the epidermis is not static but requires constant renewal.[7]

3.3.melasma:

3.3.1. Definition of melasma:

Melasma (a term derived from the Greek word 'melas' meaning black) is a common, acquired hypermelanosis that occurs in sun-exposed areas, mostly on the face, occasionally on the neck, and rarely on the forearms. The term, 'chloasma' (from the Greek word, 'chloazein' meaning 'to be green') is often used to describe melasma developing during pregnancy; but the pigmentation never appears to be green, therefore the term, 'melasma' is preferred.[8]

3.3.2. Epidemiology of melasma:

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.[9,10] The disease affects all races, but there is a particular prominence among Hispanics and Asians.[11] Although women are predominantly affected, men are not excluded from melasma, representing approximately 10% of the cases.[12] It is rarely reported before puberty.

The study included 100 patients , 89% were female and 11% were male. There was female preponderance with a female to male ratio of approximately 8.1:1, which similar to other study were female to male ratio was 4:1.[13] Also in other study they foundfemales constituted almost 79% (127), while males constituted 21% (33), melasma is more common in women than men.The higher incidence of melasma in females may be attributable to a hormonal influence as in pregnancy, use of oral contraceptive pills, and the use of cosmetics.[14] Age ranged from 18 to 64years, with mean age 30.7±7 years, Mean age for male was 30.7±7, and for female was 30.7±7 years , there was no significant difference between the mean age of male and female p value was 0.987, in other study the mean age of onset was 29.99 years, with the youngest and oldest being 11 and 49 years, respectively.[13], compared to 42.3 years, reported in a study from Singapore.[15]

3.3.3. Causes of melasma:

The exact causes of melasma are unknown. However, multiple factors are implicated in its etiopathogenesis, mainly sunlight, genetic predisposition, and role of female hormonal activity. Exacerbation of melasma is almost inevitably seen after uncontrolled sun exposure and conversely melasma gradually fades during a period of sun avoidance. Genetic factors are also involved, as suggested by familial occurrence and the higher prevalence of the disease among Hispanics and Asians. Other factors incriminated in the pathogenesis of melasma include pregnancy, oral contraceptives, estrogen progesterone therapies, thyroid dysfunction, certain cosmetics, and phototoxic and anti-seizure drugs.[16]

Family history of melasma was recorded in 9% of the patients, in similar study a positive family history of melasma was observed in 104 (33.33%) patients , which is higher than this study[13],in other study family history of melasma in a first degree relative was reported by 56 (35%) of the patients.[14]which was in correlation with an earlier reported study, in which it varied from 20 to 70%.[17],[18], these findings suggest some genetic implication in the development of melasma.

3.3.4. Pattern of melasma:

The hyperpigmented patches may range from single to multiple, usually symmetrical on the face and occasionally V-neck area.

According to the distribution of lesions, three clinical patterns of melasma are recognized.[19]The centrofacial *pattern* is the most common pattern and involves the forehead, cheeks, upper lip, nose, and chin. The malarpattern involves the cheeks and nose. The mandibularpattern involves the ramus of the mandible.

The commonest site involved in melasma was centrofacial (66%) , followed by malar 32% and only 2% mandibular . centrofacial was the highest in both sex , it was 72.7% in male and 65.2% in female followed by malar 33.7% in female and 9.1% in male, this result was similar to the result of other study were centrofacial was the most common pattern (55.44%) observed.[20] However, studies from Singapore observed that malar distribution was the most common.[21] , also in other study 105 patients (65%) had malar distribution, 55 (35%) had centrofacial type, and none had mandibular type.[18] In similar study Chi-square test showed that the clinical pattern of melasma between men and women was statistically significant ($P < 0.001$).[9]This variation of results might be due to environmental or regional differences.The majority of the patients (58%) the type of lesion was presented as confluent macules followed by punctate macule in (20%) of patients , 13% was mixed and 9% was

longitudinal macules, also the highest in both sex was in confluent macules 81.8% in male and 55% in female.

3.3.5. Pathophysiology:

Melasma is caused by an increase in dermal and epidermal melanin production and retention. Skin biopsies from patients with melasma show an increase in the number of melanocytes and melanin-laden macrophages (melanophages). In addition, later-stage melanocytes containing greater numbers of melanosomes may be present; these are the cellular organelles responsible for melanin synthesis.[22] In keratinocytes, there is an overexpression of vascular endothelial growth factor (VEGF). It is thought that VEGF may be related to melanocyte behavior.[23]

3.3.6. Trigger- precipitating factors:

Melasma is thought to be the stimulation of melanocytes or pigment-producing cells by the female sex hormones estrogen and progesterone to produce more melanin pigments when the skin is exposed to sun. Women with a light brown skin type who are living in regions with intense sun exposure are particularly susceptible to developing this condition.

Genetic predisposition is also a major factor in determining whether someone will develop melasma.

The incidence of melasma also increases in patients with thyroid disease. It is thought that the overproduction of melanocyte-stimulating hormone (MSH) brought on by stress can cause outbreaks of this condition. Other rare causes of melasma include allergic reaction to medications and cosmetics.

MelasmaSuprarenale(Latin - abovethekidneys) is a symptom of Addison's disease, particularly when caused by pressure or minor injury to the skin, as discovered by Dr. FJJ Schmidt of Rotterdam in 1859.[24 / 25 / 26]

Sun exposure was trigger factor for 55% of the patients, pregnancy was trigger factor in 30% of female, while using contraceptive pills was a trigger factor in 33% of female , in other study about 55.12% of our patients reported that their disease exacerbated during sun exposure. Among 250 female patients, 56 reported pregnancy and 46 reported oral contraceptive as the precipitating factors. Only 34 patients had given history of exacerbation of melasma during pregnancy[20],while in Tunisian study sun exposure was reported as a triggering factor by 51% of women and as an aggravating factor by 84%. Pregnancy was reported as an aggravating factor by 51% of women who had been pregnant, and oral contraceptive use reported by 38% of women exposed to oral contraceptives.[27]

3.3.7. Clinical features and diagnosis:

Patients with melasma exhibit splotchy areas of hyperpigmented macules on the face Three patterns of involvement are typically seen [22]:

- Centrofacial — involving the cheeks, forehead, upper lip, nose and chin
- Malar — involving the cheeks and nose
- Mandibular — involving the ramus of the mandible

There are two main histological patterns: epidermal and dermal. Both patterns have increased numbers of melanocytes. However, patients with the epidermal type will have pigmentary accentuation under a Wood's light, whereas those with dermal melasma will exhibit no enhancement. In addition, some women have a "mixed" picture on Wood's light examination, with enhancement in some areas and none in others[22]. In natural light, epidermal melasma appears light brown, the mixed type looks dark brown, and the dermal pattern is blue or ashen gray. Epidermal melasma seems to be the type most responsive to treatments such as bleaching cream, topical tretinoin, or chemical peels [22].

The diagnosis of melasma is based upon clinical appearance. Splotchy hyperpigmentation can also occur as a result of several inflammatory conditions, including acne, eczema, contact dermatitis, and superficial injuries; this may persist for months once the inciting event has resolved.

3.3.7.1. How is the diagnosis of melisma is made?

The characteristic appearance of melasma means diagnosis is usually straightforward and made clinically. Other disorders that may be considered include:

- Postinflammatory pigmentation
- Solar lentigines and other forms of lentigo
- Drug-induced pigmentation, e.g. due to minocycline
- Lichen planus
- Naevus of Ota.

Occasionally, skin biopsy may be performed to confirm the diagnosis. Histology varies with the type of melasma. But some degree of each of the following features is usually found.

- Melanin deposited in basal and suprabasal keratinocytes
- Highly dendritic (branched) deeply pigmented melanocytes
- Melanin in the dermis within melanophages

- Solar elastosis and elastic fibre fragmentation

The extent and severity of melasma can be described using the Melasma Area and Severity Index (MASI).

3.3.8. Classification:

Melasma presents as macules (freckle-like spots) and larger flat brown patches. There are several distinct patterns.

- Centrofacial pattern: forehead, cheeks, nose and upper lips
- Malar pattern: cheeks and nose
- Lateral cheek pattern
- Mandibular pattern: jawline
- Reddened or inflamed forms of melasma (also called erythrosispigmentosafaciei)
- Poikiloderma of Civatte: reddened, photoaging changes seen on the sides of the neck, mostly affecting patients older than 50 years
- Brachial type of melasma affecting shoulders and upper arms (also called acquired brachial cutaneous dyschromatosis).
- Melasma is sometimes separated into epidermal (skin surface), dermal (deeper) and mixed types. A Wood lamp may be used to identify the depth of the pigment and melasma was classified accordingly into : Epidermal

with well -defined border and dark brown color, appears more obvious under black light and responds well to treatment. Dermal which is the most common type, ill-defined border, light brown or bluish in color, unchanged under black light and responds poorly to treatment . Mixed with combination of bluish, light and dark brown patches , Mixed pattern seen under black light and partial improvement with treatment

3.3.8.1.Fitzpatrick skin type classification

- Type I: white, always burns easily, never tans
- Type II: white, always burns easily, tans minimally
- Type III: white, burns minimally, tans gradually
- Type IV: light brown, burns minimally, tans well
- Type V: brown, rarely burns, tans profusely
- Type VI: dark brown or black, never burns, tans profusely.

3.3.8.2. Histological subtypes :

The epidermal type, in which the pigmentation is intensified under Wood's light, is the most common type. Melanin is increased in all epidermal layers. In the dermaltype the pigmentation is not intensified. It has many melanophages throughout the entire dermis.[10] In the mixed type the pigmentation becomes more apparent in some areas, while in others there is no change. Indeterminate type is where

the pigment is apparent in the Wood's light, in individuals with skin type VI.[28,29]

Woods light examination results , epidermal was constitute to 86% , dermal 11% and mixed 3% , in male the results was 72.7% epidermal, 27.3% dermal and no one had mixed, while in female 87.6% epidermal, 9% dermal and 3.4% mixed, while in other study the Wood light examination showed the dermal type being the most common in 54.48% and epidermal and mixed were seen in 21.47% and 24.03% of the cases, respectively.[13]

3.3.9. Associations of melasma:

1- Association of melasma with thyroid autoimmunity and other thyroidal abnormalities and their relationship to the origin of the melasma.[30]

Melasma is localized hyperpigmentation over the forehead, upper lips, cheeks, and chin. In this study, evidence suggesting an association betweenautoimmune thyroid disorders and melasma and the relationship of thyroid disorders to the origin of melasma is presented. A total of 108 nonpregnant women, aged 20-56 yr, were divided into 2 groups for the purpose of this study: 1) melasma, 84 patients; 2) control group, 24 patients from the Dermatology Clinic matched for age and sex. Microsomal thyroid autoantibodies

(MCHA) were sought in all subjects. TRH-TSH tests were performed in patients with melasma and in those women with goiter and/or positive MCHA tests from the control group. Studies were completed with serum T4, T3, and antithyroglobulin antibody (TGHA) measurements in all patients with thyroid abnormalities. In patients with melasma, the frequency of thyroid disorders (58.3%) was 4 times greater than in the control group. The MCHA-negative patients had 1) simple goiter (13.1%), 2) Plummer's disease (2.4%), and 3) TSH hyperresponse to TRH in nongoitrous patients (10.7%). Patients with positive MCHA tests (32.1%) were divided into 2 subgroups. One comprised those women with an apparently normal thyroid gland and thyroid function (n = 7), while the other included all patients with goiter and/or subclinical hypothyroidism (n = 20). Regarding the origin of the melasma, it was found that 70% of women who developed melasma during pregnancy or while using oral contraceptives had thyroid abnormalities compared to 39.4% of patients with idiopathic melasma. Subjects from the control group had a 12.5% incidence of thyroid abnormalities, and only 8.3% had positive MCHA. Estrogen, progesterone, or both could be the triggering factor in the development of melasma in women who have a particular predisposition toward both melasma and thyroid autoimmunity.

Patients with idiopathic melasma had a lower frequency of thyroid abnormalities, suggesting that there may be different genetic patterns linked to autoimmune thyroid disease. We conclude that there is a true association between thyroid autoimmunity and melasma, mostly in women whose melasma develops during pregnancy or after ingestion of oral contraceptive drugs.[30]

2- Endocrinologic profile of patients with idiopathic melasma.[31] Complete endocrinologic evaluation of 9 women (ages 24-41) with idiopathic melasma (melasma not associated with pregnancy nor ingestion of oral contraceptives) was performed and compared to age- and sex-matched normal controls. Serum cortisol, adrenocorticotropin, plasma immunoreactive alpha and beta melanocyte-stimulating hormones, luteinizing hormone, follicular-stimulating hormone, estradiol and progesterone levels were performed in the basal state. Additionally, total T4, T3RU, FTI, prolactin, 2-h postprandial blood sugar, and 24-h urine for 17-hydroxysteroids and 17-ketosteroids were done and found to be normal. The melasma patients presented statistically significant increased levels of LH (p less than 0.001) and lower levels of serum estradiol (p less than 0.025) than normal controls. It is proposed that these hormonal alterations may represent subclinical evidence of a mild ovarian dysfunction which may underlie the pathogenesis of some casesof=idiopathicmelasma.[31]

3- Hormonal milieu in the maintenance of melasma in fertile women.[32]

Melasma is a specific type of facial hyperpigmentation seen in women taking oral contraceptives, in non-pregnant women who have not used oral contraceptives, and in some pregnant women during the progression of gestation, but rarely in men. Circulating LH, FSH, PRL, and E2-17 beta on day 5, 7, 9, and 11 of the menstrual cycle and progesterone (P) on day 17, 19, and 21 were measured in thirty-six ovulating women with melasma (study group) age 25-35 years and twelve healthy controls (control group). Twenty-seven subjects in the study group had normal pregnancies; 9 others were married or single and had no history of contraceptive pill use. Higher levels of FSH on day 7 ($p < 0.05$); E2-17 beta on 5, 7, 9 ($p < 0.05$) and LH on day 9 ($p < 0.002$) were observed in the study group than in the control group. There were no significant differences between the LH/FSH ratio in the two groups. Serum PRL was lower on day 9 in the study group ($p < 0.05$) than in the control group. Serum P was similar in the patients and the controls. These findings indicate a possible role of high E2-17 beta in the maintenance of melasma.[32]

4- Melasma in men. A clinical and histologic study.[33]

Melasma is characterized by a facial hypermelanosis of light to dark brown color, being more common in women of Hispanic origin. In this study, 27 men with melasma were evaluated clinically and histologically to compare their features with those of previous studies. Three patterns of localization were recognized, namely, centrofacial, malar, and mandibular. On the basis of Wood's light examination, an epidermal, a dermal, and a mixed type were identified. Epidermal hyperpigmentation only and epidermal and dermal hyperpigmentation were found in histologic analysis of the cases. Significant etiologic factors included exposure to sunlight in 66.6% as well as a familial predisposition in 70.4% of the cases. This study demonstrated that melasma in men shares the same clinicohistologic characteristics as in women, but hormonal factors do not seem to play major significant role[33]

5- Melasmain men: a hormonal profile.[34]

Melasma in men is much less common than in women. In the present communication, we evaluated circulating levels of LH, FSH, and testosterone in 15 men with idiopathic melasma. When compared with eleven age matched control men, the circulating LH was significantly higher and testosterone was markedly low in the

melasmic men. We conclude that male melasma involves subtle testicular resistance.

process that involves cumulative sun exposure as an important risk factor for its occurrence.[37] Some of the pathological changes found in the skin of melasma patients compared to nonaffectedperilesional skin include photodamage, vascularization, inflammation, and melanogenic activity. [34]

3.3.10. Treatment:

The treatment of melasma can be challenging because of the chronic and persistent nature of this condition. Intermittent long-term topical therapy and strict sun protection are often necessary to control the disease. Melasma due to pregnancy usually regresses within a year[35]; however, areas of hyperpigmentation may never completely resolve[36].

Bleaching agents and chemical peels are most often recommended for the treatment of melasma. Regardless of the method chosen, therapy must be combined with use of broad spectrum sunscreens (eg, Ombrelle, PreSun Ultra, Cetaphil 15) to maximize their effect; both ultraviolet B and ultraviolet A protection are essential[37].

3.3.10.1. Bleaching agents:

Hydroquinone (2% over the counter, 4% by prescription), azelaic acid, and tretinoin are common bleaching agents used to treat melasma.

- Hydroquinone exerts its effect by blocking the conversion of dopa to melanin via inhibition of the enzyme tyrosinase. It is applied twice daily for up to three months with subsequent tapering. Concentrations of hydroquinone vary from 2 to 4%; the higher concentration is most effective, but may be associated with more severe irritant or allergic contact dermatitis, hypopigmentation of surrounding skin, or rarely hyperpigmentation that resolves on cessation of therapy. The efficacy of hydroquinone may be improved by combining it with a keratolytic agent such as glycolic acid or tretinoin.

- Azelaic acid also inhibits tyrosinase and blocks the conversion of dopa to melanin. It is applied twice daily and appears to be better tolerated than hydroquinone. Adverse reactions include erythema, scaling, pruritus, and burning.

The efficacy of both hydroquinone and azelaic acid was demonstrated in a double-blind study involving 329 women with melasma[38].

Treatment with either 20% azelaic acid or 4% hydroquinone cream for 24 weeks resulted in good or excellent results in 65 percent of women.

- Tretinoin 0.1 percent (eg, microgel) is not a true "bleaching" agent, although it essentially acts in this manner in patients with melasma. It is applied once daily at bedtime. In a trial of 38 women with melasma who were randomly assigned to apply 0.1 percent tretinoin or vehicle cream once daily for 40 weeks, significantly more tretinoin-treated patients were clinically rated as improved or much improved than those using vehicle (68 versus 5 percent)[39]. Significant improvement first occurred after 24 weeks of tretinoin treatment. Histologically, epidermal pigment was reduced 36 percent following tretinoin treatment compared with a 50 percent increase with vehicle. Moderate cutaneous side effects, including erythema and desquamation, occurred more often in the tretinoin group (88 versus 29 percent). Thus, while tretinoin is effective, prolonged use is required.

Combinations of tretinoin and azelaic acid or hydroquinone also can be used. Kojic acid, a newer agent which, like hydroquinone and azelaic acid, blocks the conversion of tyrosine to melanin, also is effective[40 /41].

3.3.10.2. Chemical peels :

Referral to a dermatologist for chemical peels is indicated in patients with moderate to severe melasma that has not responded to bleaching agents. A chemical peel is a procedure in which a topically applied wounding agent creates smooth, rejuvenated skin by way of an organized repair process and exfoliation. A number of chemical peels are available; glycolic acid peels may be associated with the fewest adverse effects. Patients begin with application of low concentrations of the peeling agent and gradually titrate up on a weekly to monthly basis depending upon results. Topical bleaching agents are frequently used prior to and in between peels. Postinflammatory hyperpigmentation may result.

3.3.10.3. Laser therapy:

Some success with laser therapy for refractory melasma has been reported, but the technique is not yet in widespread use[42/43].

Outcome of treatment with Hydroquinon was 50.5% marked improvement, 40.4% moderate improvement , 8.1% mild improvement and only one no improvement. A study by Fulton *et al,*of 39 patients who applied hydroquinone 4% or 2% kojic acid on either cheek, revealed equal response in 20 (51%), to hydroquinone and kojic acid.[44]

Treatment with topical CS all patients had some degree of improvement ranged between 44.9% for marked improvement to 11.2% for mild improvement. One patient only treated with chemical peeling and had no improvement, 55% of patients treated with sunscreen , other study confirm the positive role of sun protection in the treatment of melasma.[45]

3.3.11. Melasma Area and Severity Index (MASI) Score :

This classification is primarily used in research and provides a quantitative index of the severity of melasma. Even though the MASI score is a subjective measure, a recent study showed reliability, stability, and consistency. [46]

Melasma area severity index (MASI) is developed by Kimbrough-Green et alfor the assessment of melasma.The severity of the melasma in each of the four regions (forehead, right malar region, left malar region and chin) is assessed based on three variables: percentage of the total area involved (A), darkness (D), and homogeneity (H).

A numerical value assigned for the corresponding percentage area involved is as follows: 0=no involvement; 1=< 10% involvement; 2=10-29% involvement; 3=30-49% involvement; 4=50-69%

involvement; 5=70-89% involvement; and 6=90-100% involvement. The darkness of the melasma (D) is compared to the normal skin and graded on a scale of 0 to 4 as follows: 0=normal skin color without evidence of hyperpigmentation; 1=barely visible hyperpigmentation; 2=mild hyperpigmentation; 3=moderate hyperpigmentation; 4=severe hyperpigmentation. Homogeneity of the hyperpigmentation (H) is also graded on a scale of 0 to 4 as follows: 0=normal skin color without evidence of hyperpigmentation; 1=specks of involvement; 2=small patchy areas of involvement < 1.5 cm diameter; 3=patches of involvement> 2 cm diameter; 4=uniform skin involvement without any clear areas).To calculate the MASI score, the sum of the severity grade for darkness (D) and homogeneity (H) is multiplied by the numerical value of the areas (A) involved and by the percentages of the four facial areas (10-30%).

Total MASI score: Forehead 0.3 (D+H)A + right malar 0.3 (D+H)A + left malar 0.3 (D+H)A + chin 0.1 (D+H)A .[47]

3.3.12. Dermatology Life Quality Index(DLQI):

The Dermatology Life Quality Index, the first dermatology-specific health-related quality of life (HRQoL) questionnaire, was published in 1994 (Finlay and Khan, 1994)

The DLQI was designed to be simple and easy to use in a busy clinical setting: wide experience of its use has confirmed the appropriateness of this concept. Although the DLQI was created in the United Kingdom, it has been used in at least 20 countries and it is currently being used in several others. The concepts described in the 10 questions are very simple and ask about very basic human concerns. The questions have consequently been found to be appropriate across many different cultures. One should not, however, assume that the questions are necessarily universally appropriate: for example, the question about sexual difficulties may not be acceptable in some cultures.

There are several reasons for trying to measure the impact of skin disease on patients' lives. HRQoL measures provide a patient orientated and relevant outcome measure in the assessment of new therapies and in comparing different ways of delivering health care. They provide a way of being able to compare the impact of different skin diseases, and compare the impact of skin diseases to diseases affecting other organs. This information may be important to inform decision taking concerning resource allocation in health care systems and for political purposes in emphasizing the importance of skin disease. The DLQI has been used for all of these purposes. In the

direct clinical consultation allowing patients to express the issues in their lives caused by their skin disease can enhance the quality of care provided. HRQoL measures may in the future be helpful in informing clinical decision taking where consideration is being given to using expensive or potentially harmful therapies.

These studies indicate that melasma is common in Latino men. The overall rateof 14.5% is somewhat higher than a recently published prevalence of 8.8% inLatina women.[48] Among the male population with the highest prevalence of melasma, we observed a moderate association with quality of life. Latinos associate melasma with ill health and poor nutrition, and melasmaisconsidered disfiguring.[49]Melasma is more common in older men compared toyounger men. The oldest age group (31 years and older) in each of the three studies had a higher prevalence of melasma than the younger two age groups (18–24 years and 25–30 years). One limitation of this study is the use of the DLQI to assess the impact of melasma on quality of life. It is possible that the DLQI scores of participants in these studies may have been affected by other skin conditions. Further, the version of the DLQI used was developed for Mexican Spanish, and this version may not be completely appropriate for those who speak Guatemalan Spanish or whose primary language

is an indigenous language. Despite these limitations, we found a significant impact of melasma in the poultry worker sample.Several options are available for treatingmelasma. A simple and effective option for women is a cosmetic camouflage make up. This effective treatment for melasma improves QOL in women [11]. For men who are bothered by melasma, this approach is generally not practice

AIM OF THE STUDY

4. Aim of the study:

1-To know the clinico-epidemiological pattern and the precipitating or provocation factors in melasma, in Libyan patients.

2-To assess the melasma areas and severity index(MASI) and the

alteration of quality of life in melasma patients.

PATIENTS &METHODS

5- Patients and methods

One hundred Libyan patients with the clinical diagnosis of melasma attending out- patient clinic at Aljamhoria hospital, Benghazi-Libya during the period from January 2012 to December 2012 were included in this study.All patients were exposed to detailed disease history including the demographic data regarding age of patient, age of onset of melasma, sex, duration of the disease, and family history were noted according to the prepared proforma (Appendix-I). The data of different predisposing factors like sun-exposure, pregnancy, cosmetics, ovarian tumor, and other endocrinal diseases and history of different treatment used by the patients were also included. In addition, complete dermatological examination was carried to every patient in order to confirm the diagnosis clinically and to determine clinical type of the disease depending upon the distributions of lesions, they were divided into centrofacial, malar, or mandibular.

The clinical type of melasma weather it is epidermal, dermal or mixed was determined by using Wood lamp examination. Severity was measured by using melasma area and severity index scoring system (MASI) and the alteration of life was rated using five point of ordinal scale (Appendix II) .

The Dermatology Life Quality Index (DLQI) [8] was used to measure quality of life. The DLQI was originally developed in English and has been translated and validated in multiple languages. A Mexican Spanish version of

the DLQI, which was translated using methods approved by Dr. Finlay, was used. Total DLQI was computed as recommended [8]. The total scale score has a range of 0 to 30. A score of 0–1 is generally recognized as demonstrating that the patient has experienced no effect on quality of life due to skin conditions. A score of 2–5 represents a small effect, 6–10 a moderate effect, 11–20 a very large effect, and 21–30 an extremely large effect (Appendix III and IV).

Type of the study: Cross-sectional study.

Statistical analysis:

The data were entered into SPSS version 18 for analysis.

Descriptive statistics: were as mean , standard deviation , minimum and maximum were calculated for quantitative variables like age.

For qualitative variables like gender, frequency and percentage were calculated.

Inferential statistics: t- test was used to compare the mean between two group like male and female , chi- square (x^2) was used to know if there is difference between the distribution of variables , test was considered significant when p value < 0.05.

Data presentation:Data was presented in tables and figures were figures done by Microsoft Excel 2007**.**

RESULTS

6- Results:

Among 100 patients of melasma enrolled in this cross –sectional study , 89 patients (89%) were females and 11 patients (11%) were males. The age of the study group was ranging from 18 years to 46 years (mean: 30.7 years). Majority of the patients affected by the disease (57%) were aged between 21 years and 35 years (Table.1, Fig. 1).

The duration of the disease was ranging from 1 month to 6 years (Mean 2.1 years) and in most of the cases (66%) the duration was 2 years or less (Table .2, Fig. 2). There was no significant difference between males and females in relation to age groups and duration of the disease and P. value was 0.987 and 0.746 respectively.

Family history of melasma in our patients was recorded in only 9 patients.

Regarding the site involved by the disease in our study cases, 66% of the patients the site affected was centrofacial followed by malar that seen in 32% with no significant difference between both sexes (Fig. 3).

Clinically, confluent macules were the most presenting picture in our melasma cases followed by punctate type of macules and seen in 58% and 20% respectively, which presented in 81.9% of the males and in 55% of the female patients (Fig. 4).

Concerning the color of the lesions, dark brown / black color was presented in 58% and light brown in 42% of cases. Although, there is significant statistical difference between males and females (p.0.468), dark brown/black color was seen more in males while light brown color was seen more in females (Fig.5).

Sun exposure plays an important aggravating factor in our patients condition and recorded in 55% of all patients followed by oral contraceptive and pregnancy in female patients and recorded in 33% of each (Fig. 6). Majority of our cases were dark skin patients (72%), with no significant difference between both gender (p.0.442).

In addition to the color of the skin, both color of the patient hair and the eyes were assessed, and the results showed that black hair was seen in 67% , brown color in 29% and blond/chestnut hair in only 4%. Black hair color was seen in 90.9% of male patients and in 64% of females. Also the color of the eyes showed black color was the popular among our patients and seen in 68% of cases followed by brown in 29% while the green/chestnut was seen in only 3% of patients.

Observation of the presence of freckles among the total study patients, detected that 81 patients (81%) had no freckles, and 18% had some freckles

(Fig 7). Regarding the skin type and tanning intensity, the data showed 66.3% were type IV and 27% type III with no statistically significant

difference between males and females, p.0736 whereas tanning intensity was dark in 64% and light in 30% with significant difference between males and females (p. 0.004) (Fig.8, 9). According to the Woods light examination, melasma was epidermal in 86% and dermal in 11% of our cases (Fig. 10). The outcome of treatment to different topicals were assessed regarding response and our results showed that among the total patients, 50% of the patient had marked improvement to hydroquinone (Fig. 11), The use of topical steroids 89 patients, 40 patients had marked improvement and 49 patients had moderate improvement.55 patients used sunscreens in addition to other treatments. Chemical peeling had been used only in one case.

Melasma Area Severity Index (MASI) scores was calculated to all patients which pointed out that 73% had moderate severity and more males had moderate scores (Fig. 13). MASI score for forehead darkness showed that 46% had normal skin and 39% had barely visible hyperpigmentation with no difference between genders (Fig.12) whereas for forehead homogeneity equal percentage of normal skin and 41% of specks of involvement (Fig. 14). In forehead area of MASI score, 45% had none and 42 patients (42%) had less 10% (Fig 15). MASI for the right malar area darkness showed moderate hyperpigmentation in 60% (Fig. 16) , homogeneity with patches < 1.5 cm in 45.5% (Fig.17) and the area was 10-29 % in 56 patients (56%) , (Fig.18). The left malar region darkness showed the same percentage of

moderate hyperpigmentaion (Fig. 19) while for homogeneity more speckes of involvement that seen in 45% (Fig.20) and in 50% of cases the area was 10-29 % (Fig. 21). There is significant difference in both right and left malar region darkness between males and females.

MASI for chin region darkness presented that 64% of patients had normal skin and 26% of them had barely visible hyperpigmentation with no difference between males and females (Fig. 22). while homogeneity and with the same percentage of normal skin and almost equal percentage of non involved area and non significant difference in both sexes (Fig.23,24).

Quality of life index was impaired in more than 60% of the cases and the mean DLQI scores were ranging from mild to moderate effect on patient life. There was statistically significant difference between males and females

(Fig.25).

Table -1: Distribution of patients according to sex and age .

Age /years	Male		Female		Total	
	No.	%	No.	%	No.	%
≤ 20	0	0	11	12.4	11	11
21 – 25	0	0	17	19.1	17	17
26 - 30	5	45.5	18	20.2	23	23
31 - 35	1	9	26	29.2	27	27
36 – 40	5	45.5	12	13.5	17	17
>40	0	0	5	5.6	5	5
Total	11	100	89	100	100	100

Mean= 30.7years. Standard deviation = 7 years. Median =30 years. Mode = 30 years. Minimum age=18 years. Maximum age =46 years.

For male :Mean= 30.8years . Standard deviation =7.1 years. Median =29.5 years. Mode =40 years. Minimum age= 20 years. Maximum age = 40 years .

For female :Mean=30.7 . Standard deviation = 7 years. Median = 30 years. Mode =30 years. Minimum age=18 years. Maximum age = 46years.

t = 0.016 with 98 degrees of freedom; P = 0.987 (not significant).

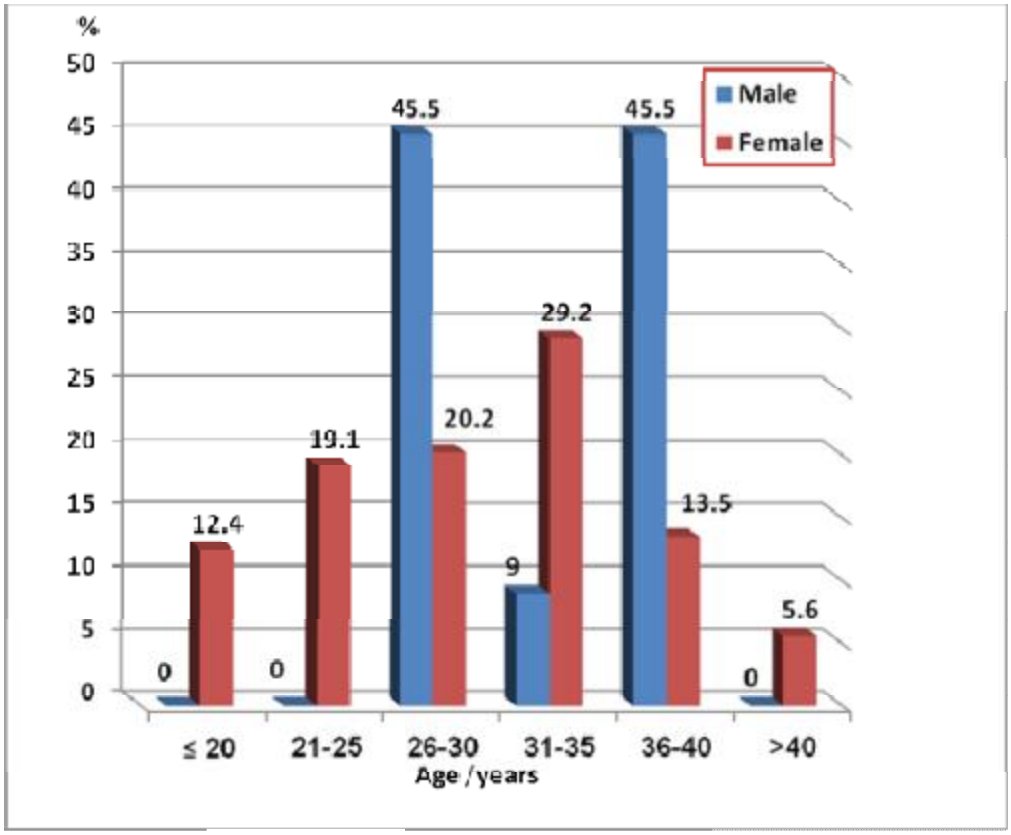

Fig.1: Distribution of patients according to sex and age .

Table -2: Distribution of patients according to sex and duration of the disease .

Duration of the disease/year	Male		Female		Total	
	No.	%	No.	%	No.	%
≤1	4	36.4	36	40.6	40	40
2	5	45.5	18	20.2	23	23
3	2	18.1	19	21.3	21	21
4	0	0	9	10.1	9	9
5	0	0	6	6.7	6	6
6	0	0	1	1.1	1	1
Total	11	100	89	100	100	100

Mean=2.1years. Standard deviation =1.4 years. Median = 2 years. Mode = 2 years. Minimum =one month. Maximum = 6 years.

For male: Mean=1.7years. Standard deviation =0.86 years. Median =2 years. Mode =2 years. Minimum =5months. Maximum = 3 years.

For female: Mean=2.1years. Standard deviation = 1.4years. Median =2 years. Mode = 2 years. Minimum =one month. Maximum =6 years.

t = -0.325 with 98 degrees of freedom; P = 0.746 (Not significant).

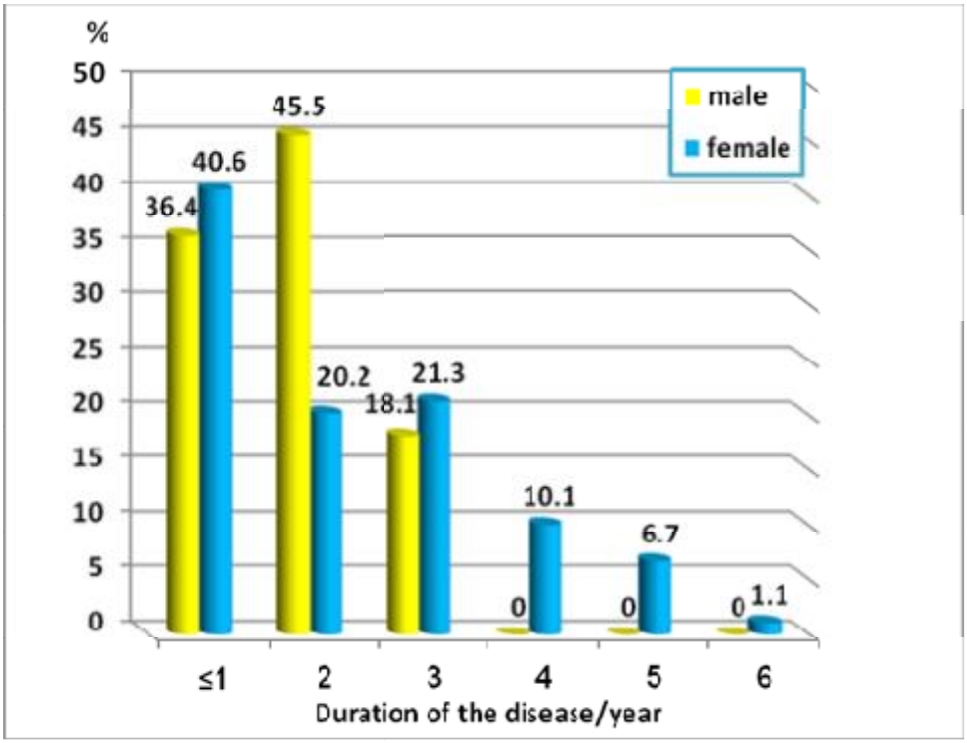

Fig.2: Distribution of patients according to sex and duration of the disease

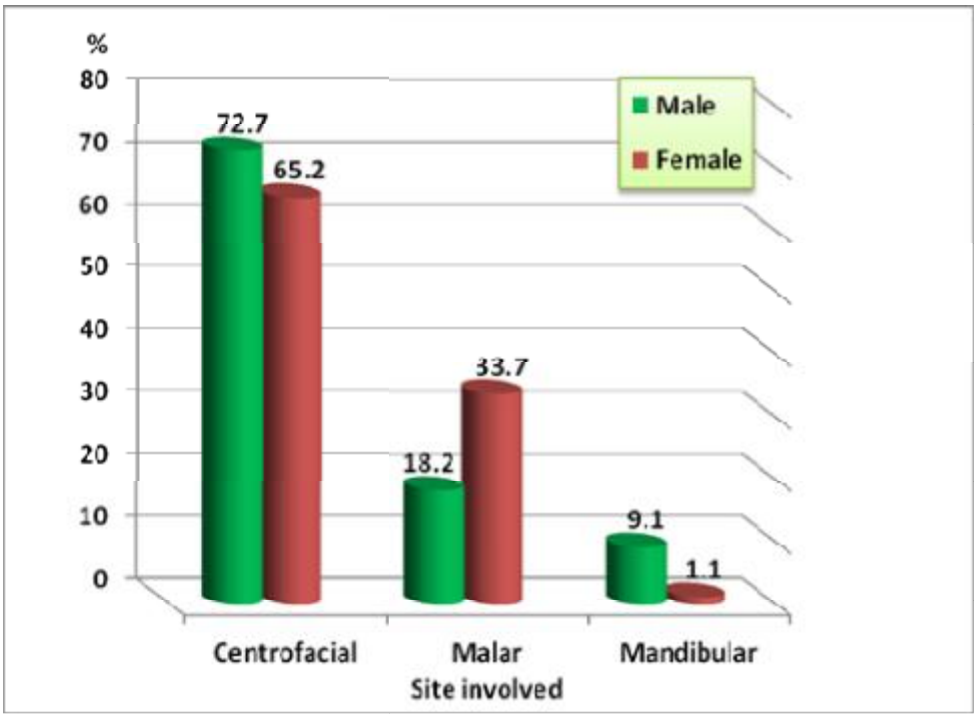

Fig. 3: Distribution of patients according to sex and site involved

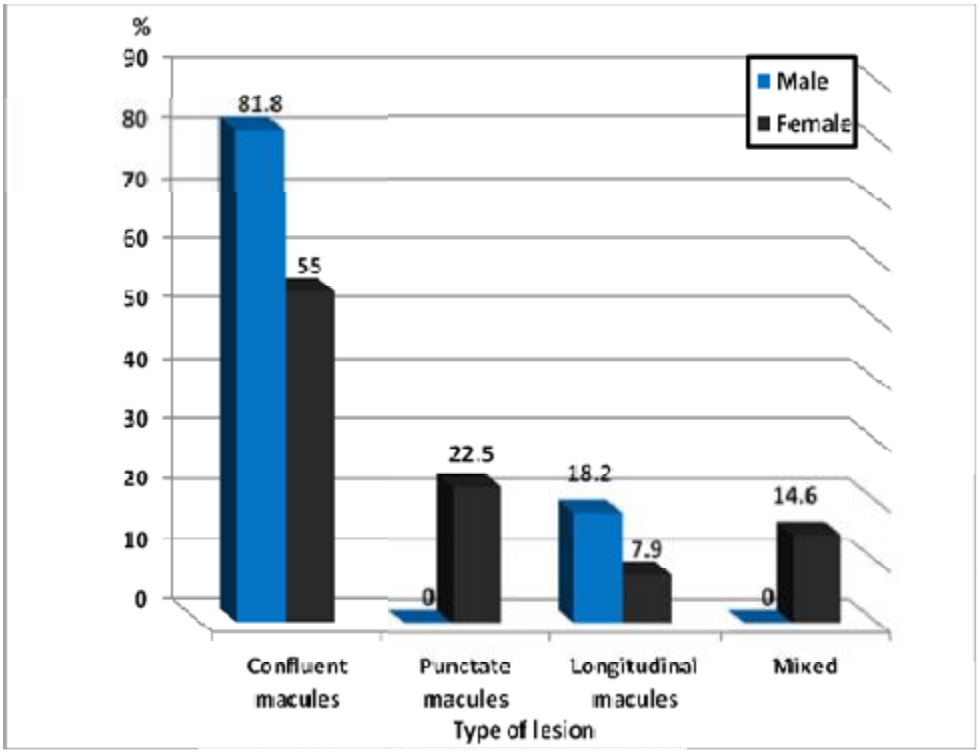

Fig.4: Distribution of patients according to sex and type of lesion.

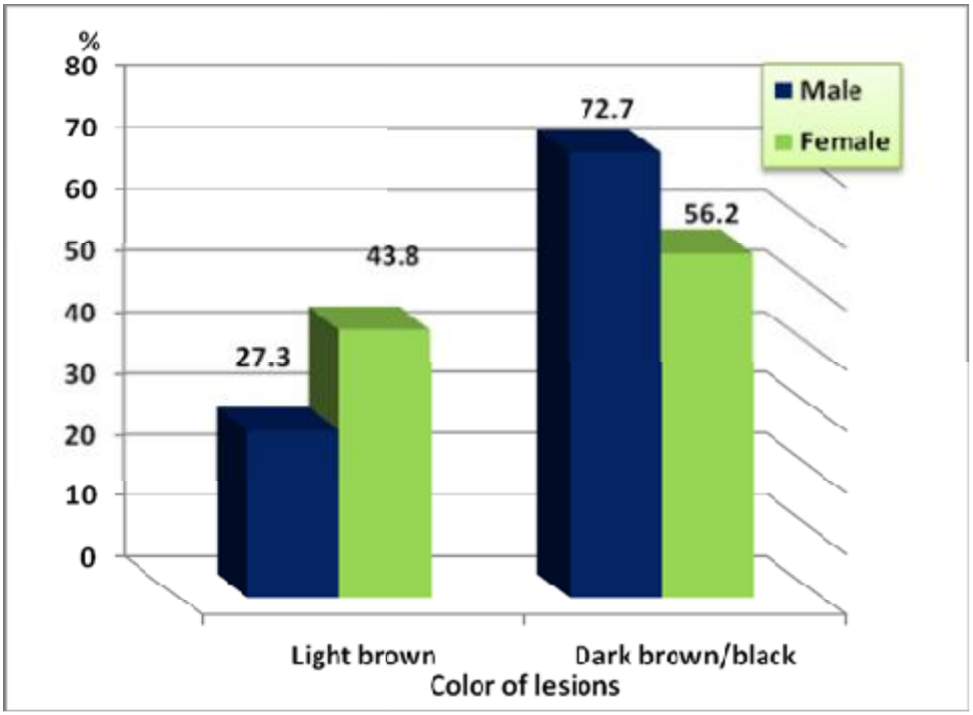

Fig. 5: Distribution of patients according to sex and color of lesions.

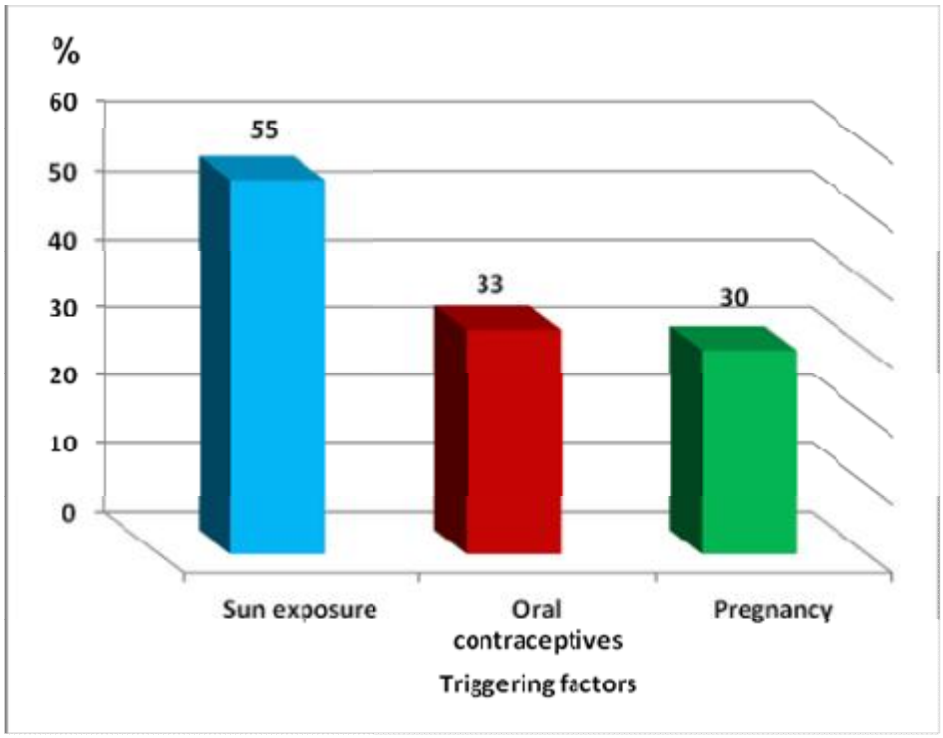

Fig. 6: Distribution of patients according to triggering factors.

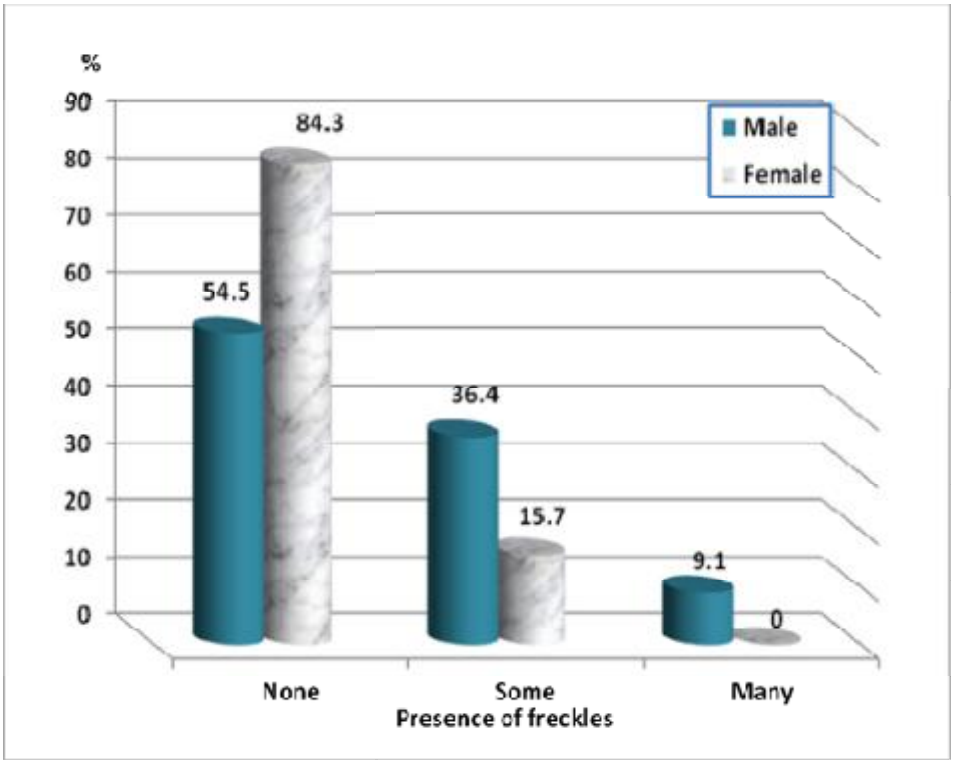

Fig.7: Distribution of patients according to sex and presence of freckles.

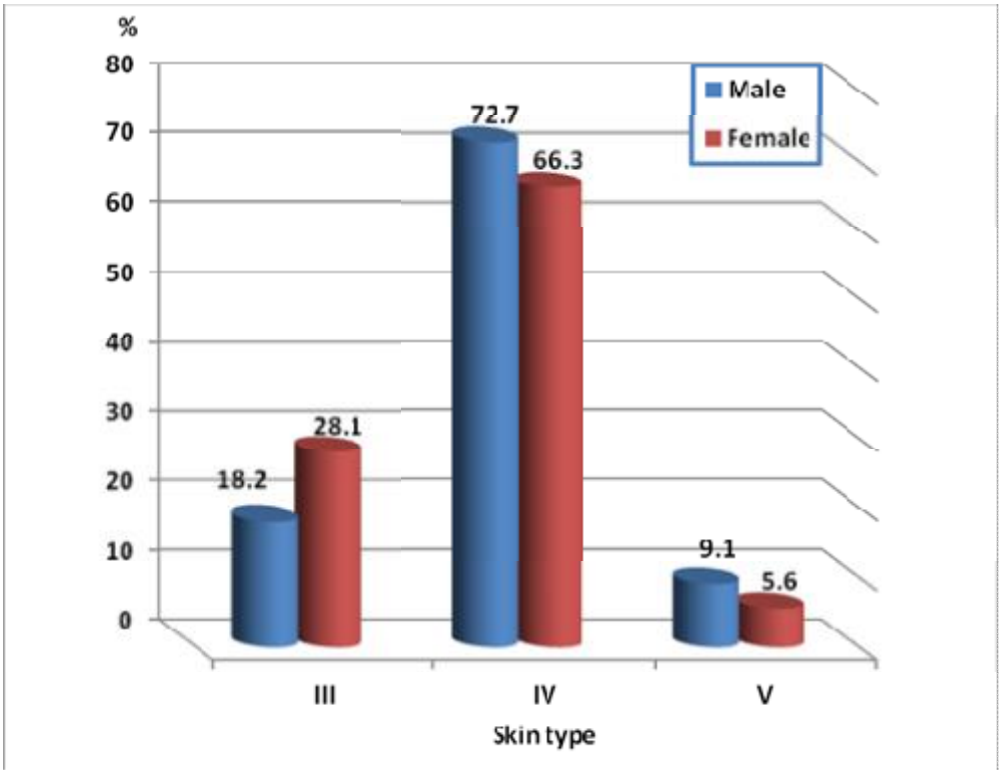

Fig. 8: Distribution of patients according to sex and skin type.

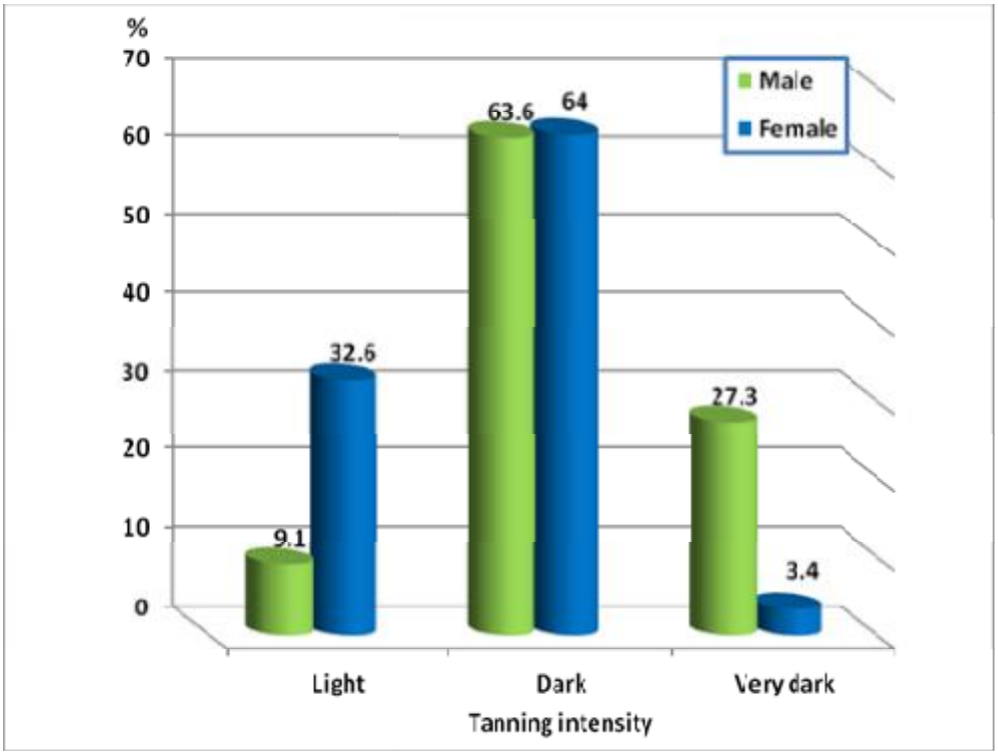

Fig. 9: Distribution of patients according to sex and tanning intensity.

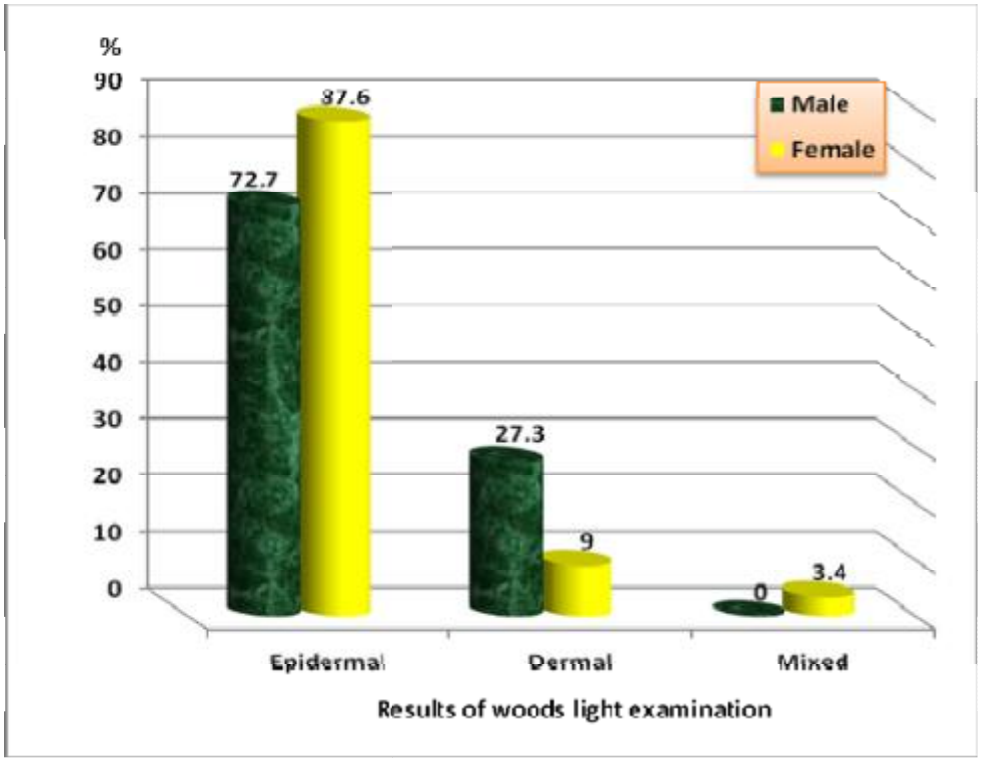

Fig. 10: Distribution of patients according to sex and results of woods light

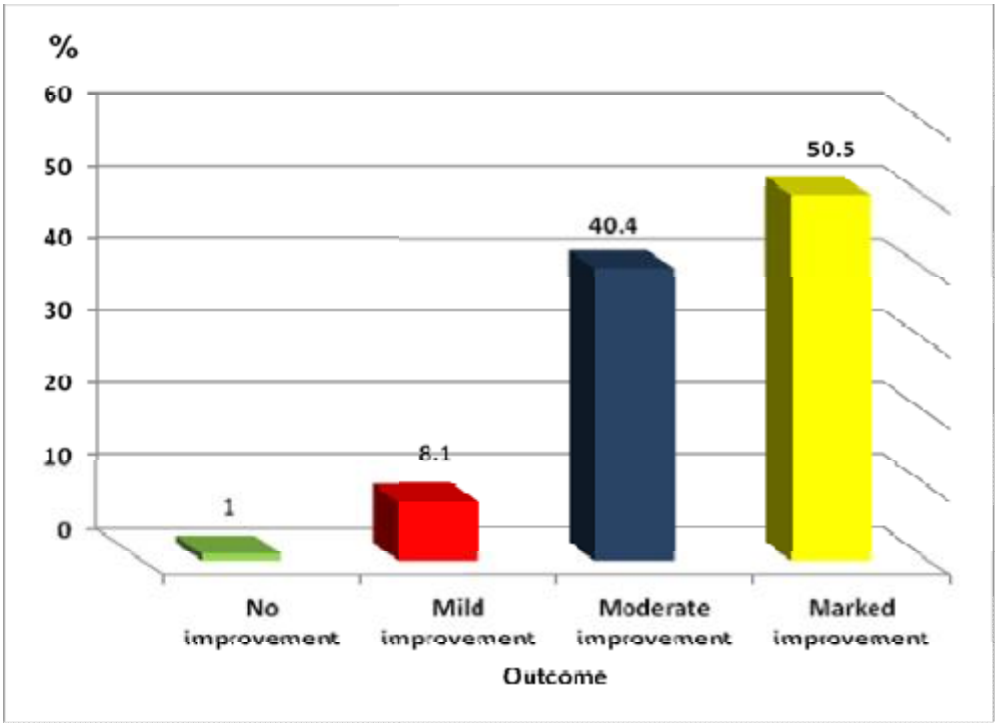

Fig. 11: Outcome of treatment with Hydroquinon.

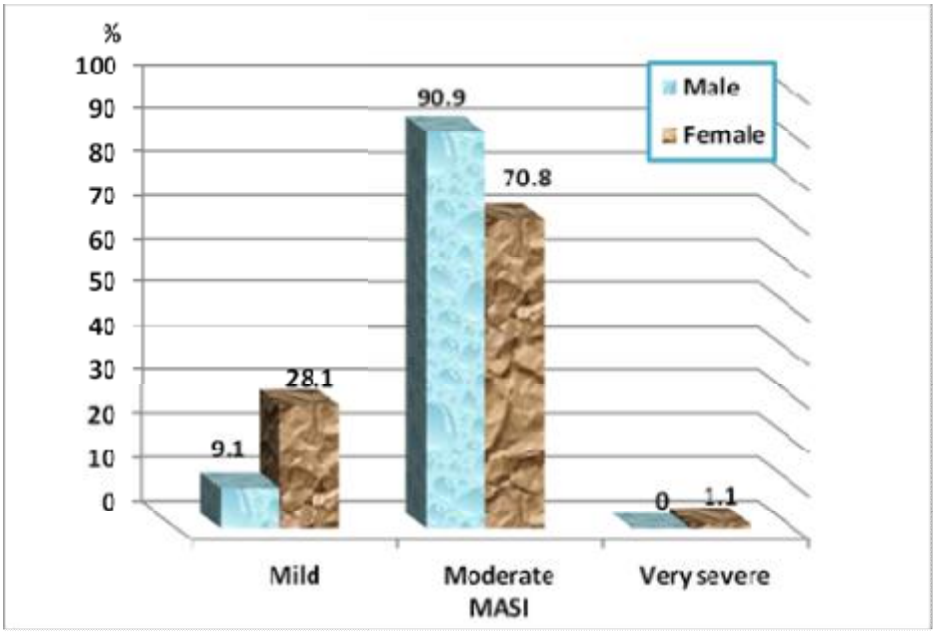

Fig. 12: Distribution of patients according to sex and MASI.

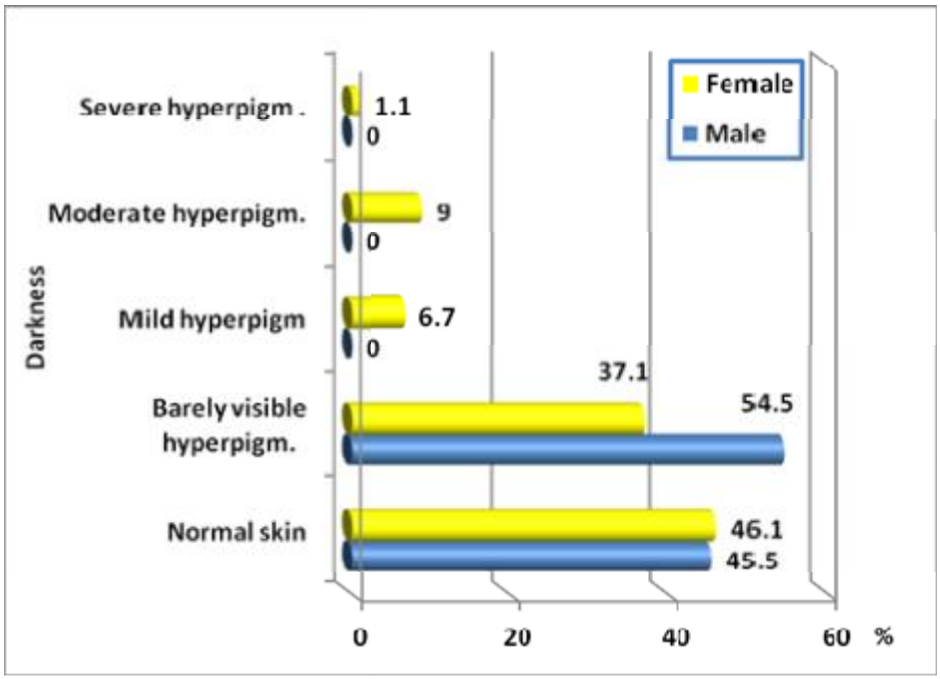

Fig. 13:Distribution of patients according to sex and MASI score for forehead darkness.

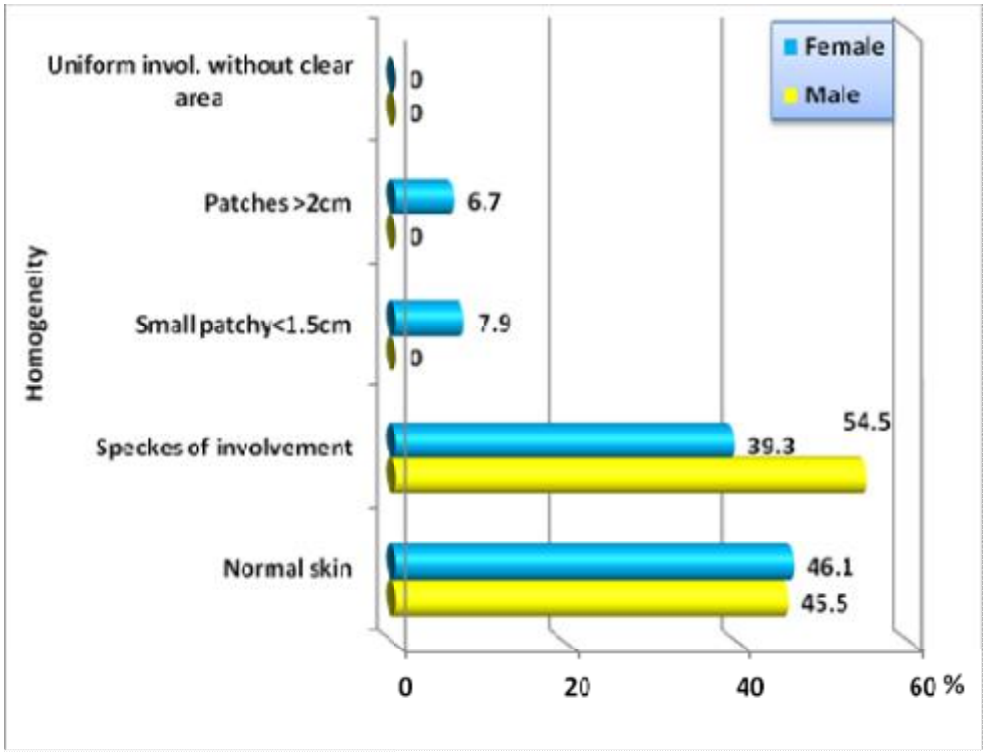

Fig. 14: Distribution of patients according to sex and MASI score for forehead homogeneity

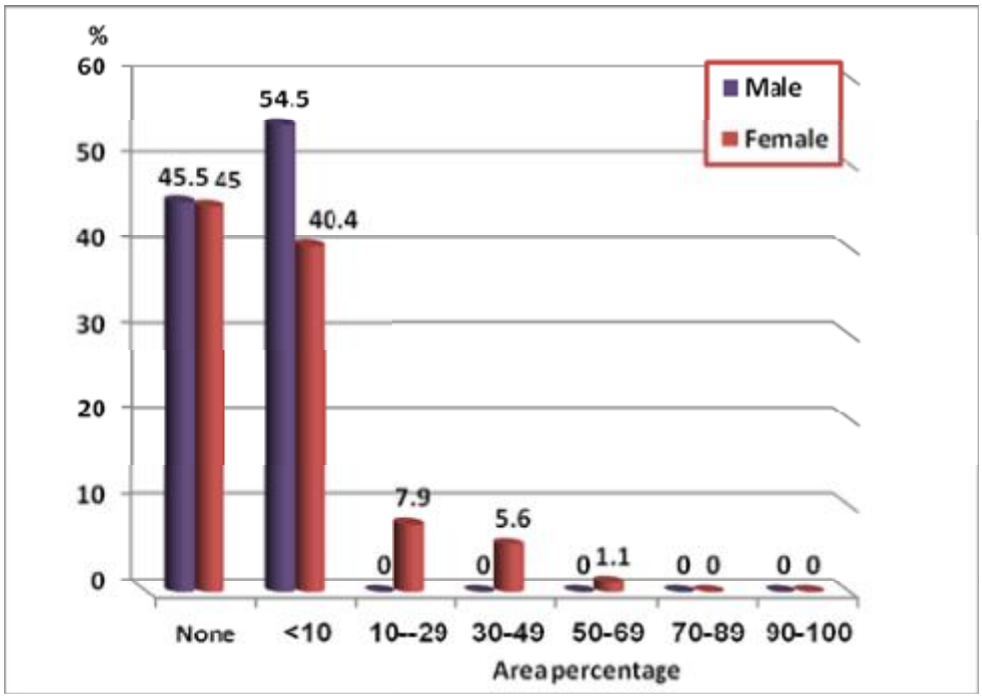

Fig. 15: Distribution of patients according to sex and MASI score for forehead area.

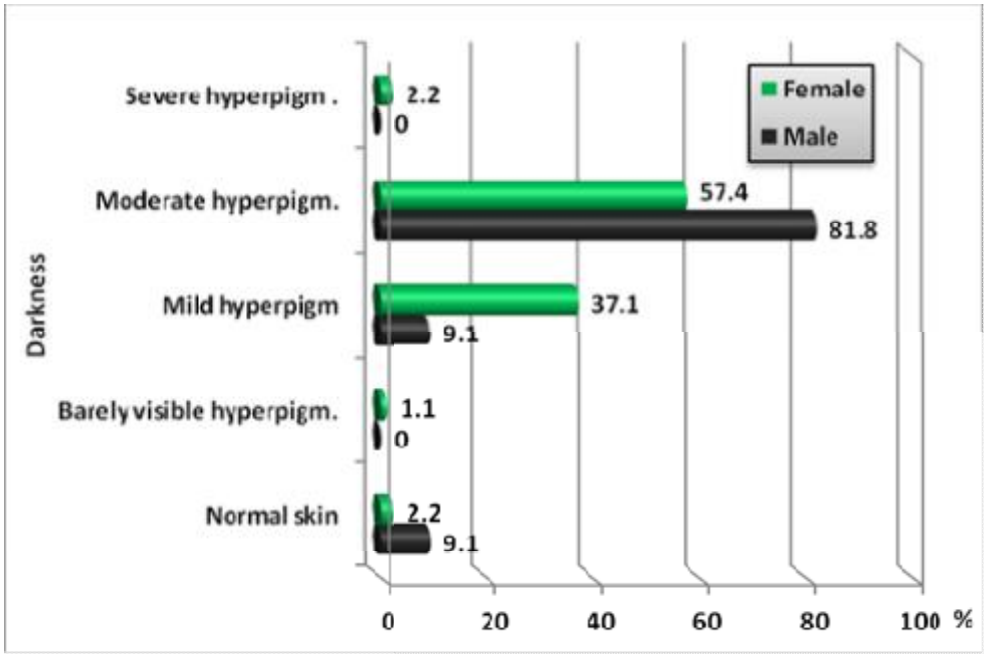

Fig.16: Distribution of patients according to sex and MASI score for right malar region darkness.

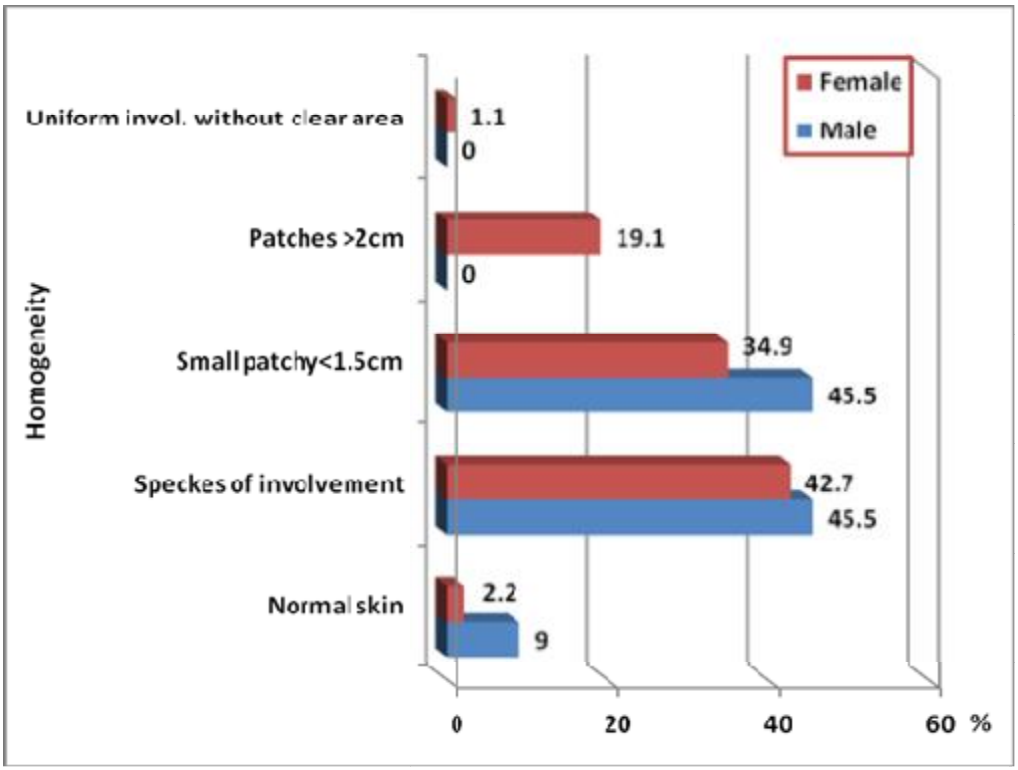

Fig.17: Distribution of patients according to sex and MASI score for right malar region homogeneity.

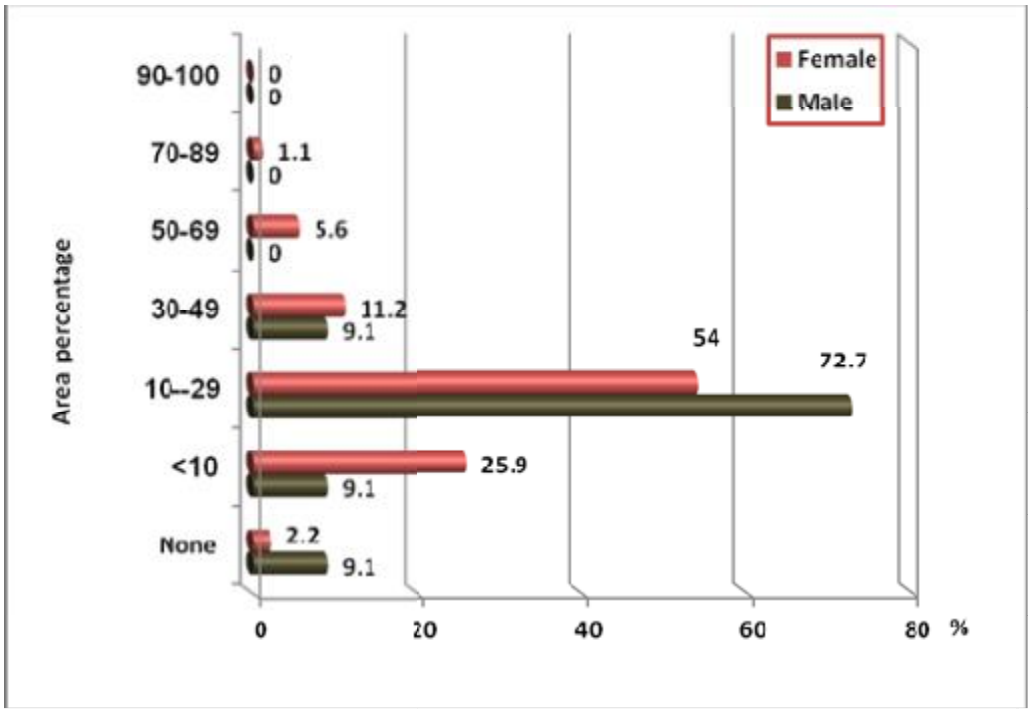

Fig. 18: Distribution of patients according to sex and MASI score for right malar region area.

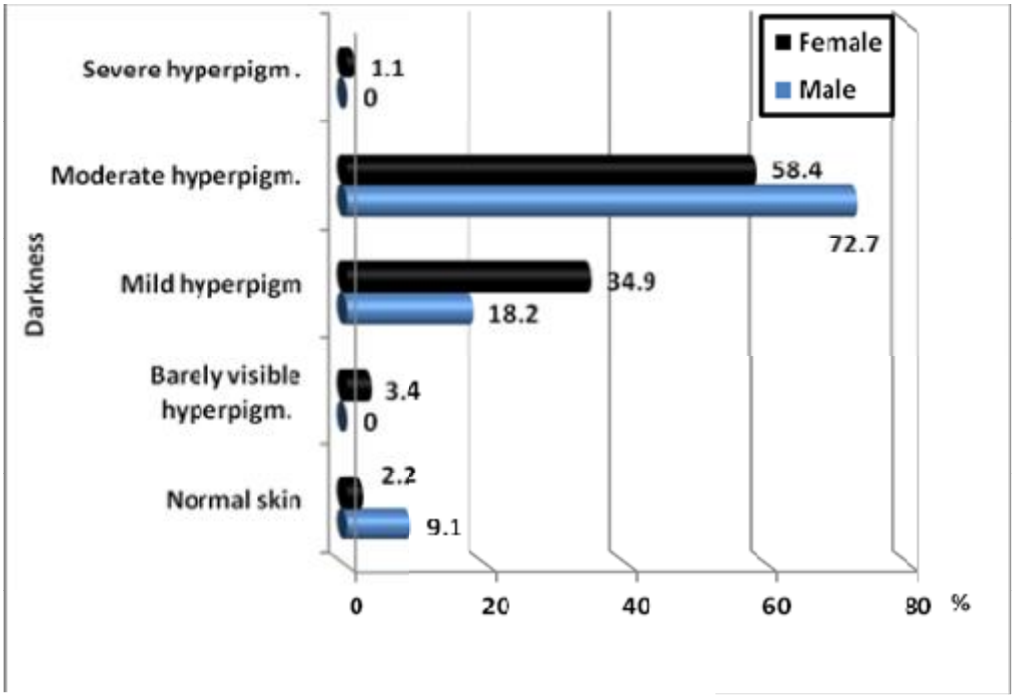

Fig.19: Distribution of patients according to sex and melsma area and severity index (MASI) score for left malar region darkness.

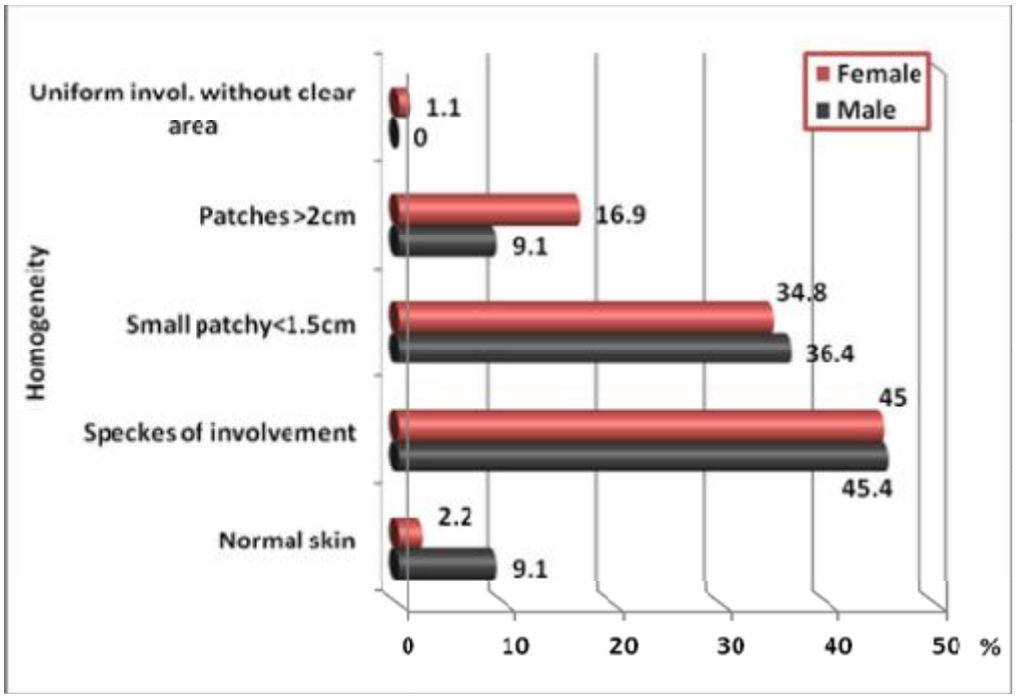

Fig. 20: Distribution of patients according to sex and MASI score for left malar region homogeneity.

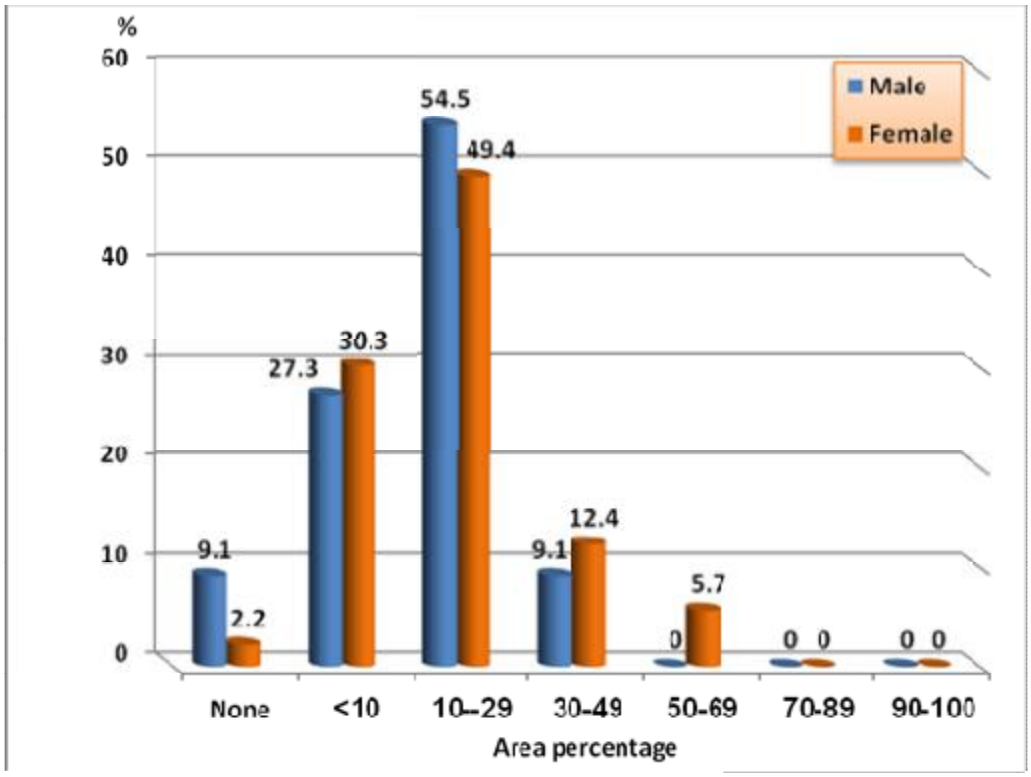

Fig.21: Distribution of patients according to sex and MASI score for left malar region area.

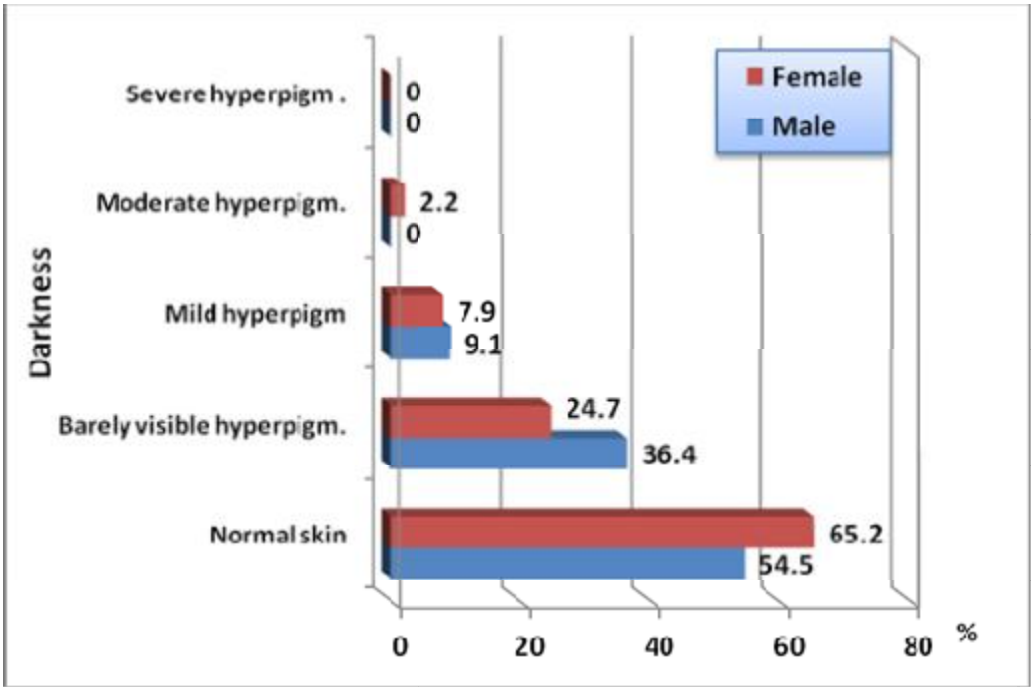

Fig. 22: Distribution of patients according to sex and MASI score for chin region darkness.

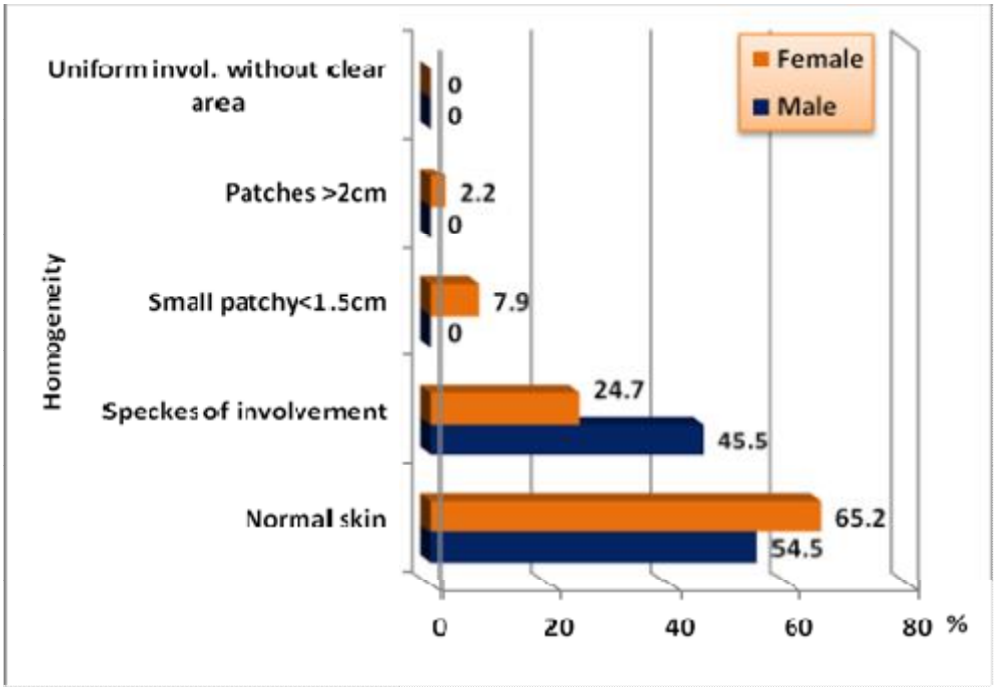

Fig. 23: Distribution of patients according to sex and MASI score for chin region homogeneity.

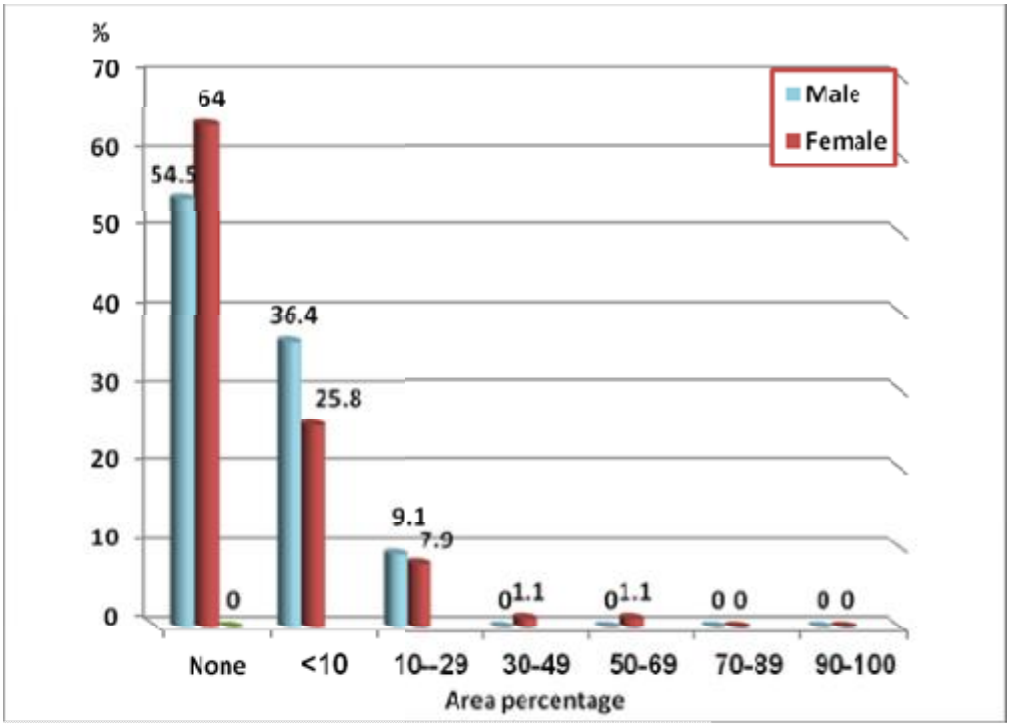

Fig. 24: Distribution of patients according to sex and MASI score for chin region area .

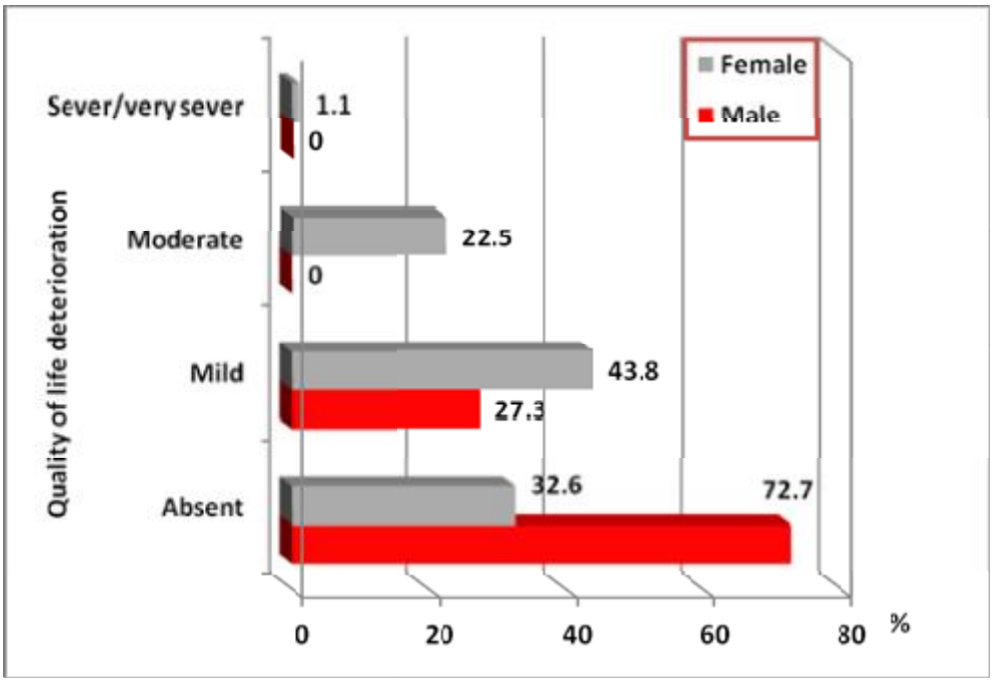

Fig.25: Distribution of patients according to sex and Quality of life deterioration .

DISCUSSION

7-Discussion:

Melasma is an acquired hypermelanosis of sun-exposed areas. Melasma presents as symmetric hyperpigmented macules, which can be confluent or punctate. The cheeks, the upper lip, the chin, and the forehead are the most common locations,

Among the total patients enrolled in our study, 89% were females and 11% were males. There was female preponderance with a female to male ratio of approximately 8.1:1, which was similar to other study where female to male ratio was 4:1.[20]The overall rate of 14.5% is somewhat higher than a recently published prevalence of 8.8% in Latina women.[49] Among the male population with the highest prevalence of melasma, we observed a moderate association with quality of life. Latinos associate melasma with ill health and poor nutrition, and melasma is considered disfiguring.[50]Also in other study they found females constituted almost 79% (127), while males constituted 21% (33), so it is noted that melasma is more common in women than men. Melasma is more common in older men compared to younger men. The oldest age group (31 years and older) in each of the three studies had a higher prevalence of melasma than the younger two age groups (18–24 years and 25–30.(a). The higher incidence of melasma in females may be attributable to a hormonal influence as in pregnancy, use of oral contraceptive pills, and the use of cosmetics.[51] Age ranged from 18 to 64years, with mean age

30.7±7 years, Mean age for male was 30.8±7, and for female was 30.7±7 years , there was no significant difference between the mean age of male and female p value was 0.987, in other study the mean age of onset was 29.99 years, with the youngest and oldest being 11 and 49 years, respectively.[20], compared to 42.3 years, reported in a study from Singapore.[21]

The female in age group ≤20 was 12.4% and in age group 21-25 yeas was 19.1% , but no male in these age groups, which seem to be that the females affected in age group younger than men,45.5% of male was in age group 26-30years , which was similar to age group 36-40years, 29.2% of female was in age group 31-35years and the lowest in age group >40years, in other study about 60% developed melasma before thirty.[24]

In combination of three similar study about one-half of the participants in all three studies were aged 30 years or younger.[52]

The duration of the disease was ranged from 1month to 6 years with means 2.1 ±1.4years , in male the mean was 2.7±0.86years, and in female the mean was 2.1± 1.4years , and this slight difference was not statistically significant p value was =0.746.Duration of disease in male all are 3 years or less and 45.5% was 2years duration , while in female 82.1% had the disease since 3 years or less 17.9% had duration 4years or more .In similar study the patients with a disease duration of less than 6 months were 3%, those between 6

months to 2 years 29%, 3-5 years 23%, 6-10 years 25% and >10 years were 20%.[8]

In similar study the average age and mean duration of disease were tested by independent sample t-test and were not statistically significant.[9]

Family history of melasma was recorded in 9% of the patients, in similar study a positive family history of melasma was observed in 104 (33.33%) patients , which is higher than this study[20],in other study family history of melasma in a first degree relative was reported by 56 (35%) of the patients.[18]which was in correlation with an earlier reported study, in which it varied from 20 to 70%.[53],[54], these findings suggest some genetic implication in the development of melasma.

The commonest site involved in melasma was centrofacial (66%) , followed by malar 32% and only 2% mandibular . centrofacial was the highest in both sex , it was 72.7% in male and 65.2% in female followed by malar 33.7% in female and 9.1% in male, this result was similar to the result of other study were centrofacial was the most common pattern (55.44%) observed.[20]However, studies from Singapore observed that malar distribution was the most common.[21] , also in other study 105 patients (65%) had malar distribution, 55 (35%) had centrofacial type, and none had mandibular type.[53] In similar study Chi-square test showed that the clinical pattern of melasma between men and women was statistically significant ($P < 0.001$).[9]This

variation of results might be due to environmental or regional differences.The majority of the patients (58%) the type of lesion was presented as confluent macules followed by punctate macule in (20%) of patients , 13% was mixed and 9% was longitudinal macules, also the highest in both sex was in confluent macules 81.8% in male and 55% in female.

Color of lesions was dark brown/black in 58% of patients and 42% light brown, in male 72.7% was dark brown/black and 27.3% light brown , while in female 56.2% dark brown/black and 43.8% light brown, but this difference in distribution between both sex was not significant difference p value was 0.468.

Sun exposure was trigger factor for 55% of the patients, pregnancy was trigger factor in 30% of female, while using contraceptive pills was a trigger factor in 33% of female , in other study about 55.12% of our patients reported that their disease exacerbated during sun exposure. Among 250 female patients, 56 reported pregnancy and 46 reported oral contraceptive as the precipitating factors. Only 34 patients had given history of exacerbation of melasma during pregnancy[20],while in Tunisian study sun exposure was reported as a triggering factor by 51% of women and as an aggravating factor by 84%. Pregnancy was reported as an aggravating factor by 51% of women who had been pregnant, and oral contraceptive use reported by 38% of women exposed to oral contraceptives.[24]

Dark color skin was recorded in 72% of the patients and 28% had fair skin, there was no significant difference between both sex in the distribution of skin color, p value was 0.442.

67% of the patients had black hair ,29% had brown color and only 4% had blond/chestnut , 90.9% of male had black hair color and 9.1% brown , while in female 4.5% had blond/chestnut color , 31.5% brown and 64% had black hair color.

Black eye color constitute to 68% , 29% was brown color and green/chestnut was 3%.

Black eyes in male constitute 81.8% , brown 18.2% and no male had green/chestnut color, in female 66.3% had black eyes , 30.3% had brown eyes and 3.4% had green/chestnut eyes.

Freckles was not present in 81% of the patients , some freckles was present in 18% and only one male (1%)had many freckles.

Skin type IV constitute to 67%, type III 27% and 6% type V, no significant difference between both sex p value = 0.736.

In other study done in Tunisia 14% presented phototype III, 45% phototype IV and 41% phototype V; 76% presented a centrofacialmelasma phenotype [24], also in similar study they found that skin phototypes II (12.8%), III (36.3%), and IV (39.7%).[55]

Degree of tanning intensity , dark constitute 64% , 30% was light and 6% was very dark. The distribution of degree of tanning intensity was statistically significant difference between male and female p value =0.004.

Woods light examination results , epidermal constitute 86% , dermal 11% and mixed 3% , in male the results was 72.7% epidermal, 27.3% dermal and no one had mixed, while in female 87.6% epidermal, 9% dermal and 3.4% mixed, while in other study the Wood light examination showed the dermal type being the most common in 54.48% and epidermal and mixed were seen in 21.47% and 24.03% of the cases, respectively.[20]

Outcome of treatment with Hydroquinon was 50.5% marked improvement, 40.4% moderate improvement , 8.1% mild improvement and only one no improvement. A study by Fulton *et al,*of 39 patients who applied hydroquinone 4% or 2% kojic acid on either cheek, revealed equal response in 20 (51%), to hydroquinone and kojic acid.[44]

Treatment with topical CS all patients had some degree of improvement ranged between 44.9% for marked improvement to 11.2% for mild improvement. One patient only treated with chemical peeling and had no improvement, 55% of patients treated with sunscreen , other study confirm the positive role of sun protection in the treatment of melasma.[45]

According to MASI , 26% was mild, 73% moderate and 1% very sever ,in male 90.9% moderate , 9.1% mild and no one had very sever, while in female 70.8% was moderate , 28.1% mild and only 1% very sever.

MASI score for forehead darkness, normal skin was normal in 46%, 45.5% of male and 46.1% of female, Barely visible hyperpigm. , was 39% , 54.5% of male and 37.1% of female, Mild hyperpigm 6%, no male had mild or moderate or severe hyperpigm, while 6.7% of female had mild hyperpigm., 9% had moderate hyperpigm.,and only one (1%) female had severe hyperpigm.

MASI score for forehead homogeneity, 46% of patients had normal skin, 45.5% of male and 46.1% of female , Speckes of involvement was 41% , in male as 54.5% and in female 39.3% , Small patchy<1.5cm, was 7.9% of female , Patches >2cm in female was 6.7% , for male no one had the last two type while no one had uniform involvement without clear area.

MASI score for forehead area ,45% none ,>10 was 42%. 10-29 was 7%, 30-49 was 5% , 50-69% was 1% and no one had areas of more than 69.

MASI score for right malar region darkness, 3% had normal skin, 1% was barely visible hyperpigmentation, 34% was mild hyperpigmentation, 60% was moderate hyperpigmentation and 2% was severe hyperpigmentation .

MASI score for right malar region homogeneity, 3% was normal, 43% was speckes of involvement , 36% was small patchy<1.5cm , 17% was patches >2cm and only one % was uniform involvement without clear area.

MASI score for right malar region area, 3% was none , 24% <10, 56% was 1-29, 11% was 3-49 , 5% was 50-69, 1% was 70-89, and no one had 90-100.

MASI score for left malar region darkness, 3% had normal skin, 3 % barely visible hyperpigmentation , 33% mild hyperpigmentation, 60% moderate hyperpigmentatiuon, and only1% had severe hyperpigmentation.

MASI score for left malar region homogeneity, normal skin was in 3% of the patients, 45% had speckes of involvement, 35% had small patchy<1.5cm, 16% had patches >2cm and 1% had uniform involvement without clear area .

MASI score for left malar region area, none was 3 % , <10 was 30%, 10-29 was 50%, 3-49 was 12% , 50-69 was 5% and no one had more than 69%.

MASI score for the chin region darkness normal skin was constitute to 64%, Barely visible hyperpigmentation was 26% , mild hyperpigmentation was 8%, moderate hyperpigmentation was only 2% and no one had Severe hyperpigmentation .

MASI score for chin region homogeneity, normal skin was constitute to 64%, speckes of involvement was 27%, small patchy<1.5cm was 7%, patches >2cm was 2 patches >2cm% and no one had uniform involvement without clear area.

MASI score for chin region area, none constitute to 63%, 10-29 was 8%, 30-49 was 1% , 50-69 was 1% and no one had more than 69.

The DLQI questions were designed to be specific to skin disease, with all 10 questions mentioning skin. There is a very high specificity of the DLQI when compared with the normal population, confirmed in seven studies. The mean DLQI scores (maximum 30) in normal populations ranged from 0 to 0.5.

. In our study majority of our female patient were affected by the disease There was impairment of their life ranging from mild to moderate which expressed on their work and social engagement 72.7 had no Quality life impairment which indicate that Libyan female are much more concerning with their cosmetic appearance than males. The questions have consequently been found to be appropriate across many different cultures. One should not, however, assume that the questions are necessarily universally appropriate: for example, the question about sexual difficulties may not be acceptable in some cultures as our Libyan culture especially in non-educated patients who can not fill the questionnaire independently.

CONCLUSION

8- Conclusions:

1) Melasma is an important health and cosmetic problem, affecting mainly females with age ranging between 21 and 35 years.
2) The mean duration of the disease was 2.1 years with no statistically significant difference among age groups between genders family history of the disease was recorded in only 9% . Sun exposure plays an important aggravating factor in our patients followed by oral contraceptive and pregnancy among female patients.
3) Confluent macules was the most frequent clinical presentation, centrofacial was the common site involved and the common observed patient skin lesions color was darkbrown/ black whereas common color of both patient hair and eyes was black.
4) Freckles was seen in only 19% of cases , the common skin type was type IV. Only 4% had H/O sunburn and 64% had dark tanning intensity. In majority of patients with Woods light examination the disease was epidermal type.
5) Concerning treatment, most of our patients received hydroquinone and topical steroids with moderate to marked improvement. Less commonly used drugs and less response were tretinoin and azeilic acid. Along with treatment more than 50% of patients used sunscreens.

6) Majority of our patients had moderate MASI. MASI sores for darkness in majority of our patients, both right and left malar regions showed moderate hyperpigmentation , while both forehead and chin showed normal skin or barely visible hyperpigmentation.

7) MASI scores for forehead and chin homogeneity, both showed normal skin and specks of involvement, while both right and left malar regions showed specks of involvement and small patchy <1.5 cm. MASI scores for the area of forehead and chin regions both showed in most of the patient had none or < 10% area whereas in both right and left malar regions, majority of the patient , the area was ,<10 % and 10-29%. .

8) Quality of life index was impaired in 60% of patients and DQLI scores was ranging from mild to moderate effect which was more statistically significant difference in females and males with more predominance in females.

RECOMMENDATION

9-Recommendations:

1) Since sun exposure considered an important aggravating and etiological factor in melasma, it is recommended that all patients should avoid exposure to sunlight and the use of sunscreens whenever the patients are outdoors and consider it as essential part of treatment.
2) More studies on a large scale and in different skin centers concerning the etiological factors , clinical types , skin types and response to different modalities of treatments.
3) More studies are required to determine the MASI scores in Libyan patients and to study the impact of the disease on patients life and the relationship between MASI scores and Dermatology life quality index in those patients,.

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APPENDIX

APPENDIX – I:

Proforma

SN : ..... Name : ..... Age :.....Sex :.....

Clinincal diagnosis:.....Duration:.....

Site involved: Centrofacial ( ) Malar ( ) Mandibular( ) Others: .....

Type of lesion: Confluent macules( )Punctate macules( ) Longitudinal macules( )

Mixed ( ) .

Color of lesions : Light brown ( ) Dark brown / black ( )

Triggering factors : Pregnancy ( ) Sun exposure ( ) Oral contraceptives ( )

Skin color : Fair ( ) Dark ( )

Hair color : Blond/ chestnut ( ) Brown ( ) Black ( )

Eye color : Green/chestnut ( ) Brown ( ) Black ( )

Freckles : None ( ) Some ( ) Many ( )

Skin type: III ( ), IV ( ) V ( ) Others :----------

Sunburn : Yes ( ) No ( ).

Tanning intensity : Light ( ) Dark ( ) Very dark ( )

Family history : Yes ( ) No ( ) Relation :----------

Woods light examination :Eqidermal ( ) dermal ( ) mixed ( )

Treatment received:

Hydroquinon( ) duration :------Improv . None ( ) Mild ( ) Moderate ( ) Marked ( )

Topical tretinoin : duration :------ Improv. None ( ) Mild ( ) Moderate ( ) Marked ( )

Topical CS : duration :------ Improv. None ( ) Mild ( ) Moderate ( ) Marked ( )

Chemical peeling : duration :------ Improv. None ( ) Mild ( ) Moderate ( ) Marked ( )

Azellicacid : duration :------ Improv. None ( ) Mild ( ) Moderate ( ) Marked ( )

Others :----------

MASI : Mild ( ) Moderate ( ) Very severe ( )

Quality of life deterioration : Absent ( ) Mild ( ) Moderate ( ) severe/Very severe ( )

Investigations :Hb:---------- FBS:---------- LFT:---------- RFT:----------

Stool Examination :----------

Hormonal profile : Progesterone :----------Testosterone:----------LH:---------FSH:------

Prolactin:---------- TSH:----------T3:----------T4:----------

APPENDIX – II :

MASI Score:

Forehead:

Darkness	0:Normal skin	1:barely Visible hyperpigm	2:mild hyperpigm	3:Moderate hyperpigm	4:Severe hyperpigm
Homogeneity:	0:Normal skin	1:speckes of involvement	2:small Patchy<1.5cm	3:patches >2cm	4:uniform Invol. Without Clear area

Area	0:none	1:<10%	2:10-29%	3:30-49%	4:50-69%	5:70-89%	6:90-100%

Right malar region

Darkness	0:Normal skin	1:barely Visible hyperpigm	2:mild hyperpigm	3:Moderate hyperpigm	4:Severe hyperpigm
Homogeneity:	0:Normal skin	1:speckes of involvement	2:small Patchy<1.5cm	3:patches >2cm	4:uniform Invol. Without Clear area

Area	0:none	1:<10%	2:10-29%	3:30-49%	4:50-69%	5:70-89%	6:90-100%

Left malar region

Darkness	0:Normal skin	1:barely Visible hyperpigm	2:mild hyperpigm	3:Moderate hyperpigm	4:Severe hyperpigm
Homogeneity:	0:Normal skin	1:speckes of involvement	2:small Patchy<1.5cm	3:patches >2cm	4:uniform Invol. Without Clear area

Area	0:none	1:<10%	2:10-29%	3:30-49%	4:50-69%	5:70-89%	6:90-100%

Chin

Darkness	0:Normal skin		1:barely Visible hyperpigm		2:mild hyperpigm	3:Moderate hyperpigm	4:Severe hyperpigm
Homogeneity:	0:Normal skin		1:speckes of involvement		2:small Patchy<1.5cm	3:patches >2cm	4:uniform Invol. Without Clear area
Area	0:none	1:<10%	2:10-29%	3:30-49%	4:50-69%	5:70-89%	6:90-100%

Total MASI score: Forehead 0.3 (D+H) A +right malar 0.3 (D+H) A +left malar 0.3 (D+H)A+ Chin 0.1 (D+H) A

APPENDIX – III :

DERMATOLOGY LIFE QUALITY INDEX

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ☑ one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	 Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	 Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	 Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	 Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	 Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	

8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

APPENDIX – IV :

المقياسالجلدي لجودة الحياة

التاريخ رقم المستشفى
التشخيص الاسم
مجموع النقاط

خلال هذه الأسئلة نسعى إلى قياس الحجم الحقيقي لمشكلتك الجلدية خلال الأسبوع الماضي .الرجاء اختيار حقل واحد من الأجوبة لكل سؤال .

1. 1خلال الأسبوع الما ضي ، ما مقدارالحكه، الألم بأشكاله المختلفه أو الإحساس بالوخز أو اللسع بسبب جلدك ؟

*كثير جدا ، *كثير ، *قليل ، *معدوم

2.خلال الأسبوع الماضي ، ما مقدار إحراجك أو ارتباكك بسبب جلدك ؟

*كثير جدا ، *كثير ، *قليل ، *معدوم

3.خلال الأسبوع الماضي ، ما مدى ما أعاقك جلدك في تأدية بعض أعمالك مثل التسوق أو العمل المنزلي أو العمل في حديقة الدار؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

4.خلال الأسبوع الماضي ما مدى تأثير جلدك على أسلوب اختيارك لملابسك التي ترتديها؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

5.خلال الأسبوع الماضي هل أثر جلدك على أي نشاط اجتماعي أو نشاط تقوم به في وقت فراغك ؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

6.خلال الأسبوع الماضي ما مدى صعوبة القيام بأي نشاط رياضي بسبب جلدك؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

7 .خلال الأسبوع الماضي هل منعك جلدك من العمل أو الدراسة ؟

*نعم ، لا ، *ليس له أي صلة بالموضوع

إذا كان الجواب بالنفي ، فخلال الأسبوع الماضي ما مقدار المشكلة التي سببها لك جلدك في العمل والدراسة ؟

*كثير ، قليل ، *معدوم

8.خلال الأسبوع الماضي ، ما مقدار المشكلة التي سببها لك جلدك مـــع شـــــريكك او مع أصدقاءك المقربين أو أقاربك ؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

9.خلال الاسبوع الماضي،مامقدار الصعوبات الجنسية بسبب جلدك؟

***كثير جدا، كثير، قليل** ، *معدوم، *ليس له أي صلة بالموضوع

10.خلال الأسبوع الماضي ،ما مقدار ما سبب لك العلاج الجلدي من مشاكل على سبيل المثال كم كان مقدار الفوضى التي حدثت في منزلك أو كم من الوقت استهلكت ؟

*كثير جدا ، *كثير ، قليل ، *معدوم ، *ليس له أي صلة بالموضوع

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