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The Profile and Triggering Factors of Melasma Patients: A Retrospective Study

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ABSTRACT

Background: Melasma is a skin pigmentation disorder characterized by brownish hyperpigmented lesions with symmetrical distribution and irregular borders. It becomes a cosmetic problem that causes a negative impact on quality of life and a lack of confidence in patients. The etiology of melasma is not completely understood, but several factors that trigger melasma can be explained. Yet, the profile and triggering factors associated with the prevalence of melasma patients in Surabaya are still unexplored. **Purpose**: To determine the profile and triggering factors of melasma patients in the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya from January to December 2019. **Methods**: A retrospective descriptive study using data from medical records with a total sampling technique. **Result**: In this study, most of the melasma patients were female (97.5%), dominated by the age group 46-55 years (49.4%), and worked as housewives (40.74%). The triggering factors found in patients were sun exposure (96.3%), cosmetics (67.9%), hormonal (49.4%), and family history (22.2%). The physical examinations of melasma lesions showed that they were mostly located in the malar area (72.8%), light brown colored (74.7%), and 2.0 – 4.0 cm in size (54.3%). Wood's lamp examination showed that most of the lesions had firm and indistinct borders (55.6%). **Conclusion**: The triggering factors of melasma are multifactorial, but we suspect that sun exposure plays an important role in affecting melasma.

Keywords: melasma, triggering factors, profile, human and health.

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BACKGROUND

Melasma is a skin pigmentation disorder that is quite common in Indonesia and is characterized by brownish to blackish patches with a symmetrical distribution and irregular borders on skin that is often exposed to sunlight. Melasma generally occurs on both cheeks, forehead, nose, chin, and sometimes on the neck.[1] Melasma can affect all skin types, but is more common in patients with Fitzpatrick skin types III-IV and often occurs many years after pregnancy.[2]

The prevalence of melasma in the population varies greatly according to ethnicity, skin type, and intensity of sun exposure. The prevalence of melasma in Southeast Asia has been reported to be as high as 40% in women and 20% in men.[3] A study in the Department of Dermatology and Venereology of Dr. Cipto Mangunkusumo Hospital (RSCM) Jakarta in 2014 showed that patients with hyperpigmentation disorders accounted for 33.6% of a total of 4,559 visits, with melasma accounting for 53.45% of all hyperpigmentation disorders.[4] Another study in the Dr. Soetomo General Academic Hospital Surabaya in 2014 showed that the number of new melasma patients was 1,313 patients, or 14.1% of all patients in the Medical Cosmetics Division of Outpatient Dermatology and

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Venereology Unit at Dr. Soetomo General Academic Hospital Surabaya.[5]

Melasma can cause a lack of confidence, a bad psychosocial impact, and affect the patient's quality of life due to black spots on the facial skin that cause aesthetic disturbances or an unfavorable appearance in the patient.[4] Melasma patients can feel shame and lack the motivation to go out. There was literature that reported suicidal ideas from patients with melasma.[2]

The etiology of melasma is still not completely understood, but several factors that trigger melasma can be explained, including sun exposure, hormonal influences, and genetics. Cosmetics selection, the use of oral contraceptives, and hormone replacement therapy can also trigger and worsen melasma.[2] Yet, the profile and triggering factors associated with prevalence of melasma patients in Surabaya are still unexplored. This study was conducted to determine the profile and triggering factors of melasma patients in the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya during January – December 2019. Knowledge of the profile and triggering factors associated with prevalence of melasma can be used as a preventive measure in the treatment of melasma.

METHODS

This study was a retrospective descriptive study using secondary data from medical records. The population of this study was melasma patients that met the inclusion criteria, which included all patients diagnosed with melasma at the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya from January to December 2019. Those were excluded if the medical records had missing, incomplete, or unknown data regarding age, gender, occupation, history, and physical examination. The variables of this study were age, sex, occupation, triggering factors, and physical examination. The materials and instruments used in this study were medical records of melasma patients in the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya. The data analysis of this study was descriptive using SPSS 23.0 and presented in tables. This study has received ethical approval from the Hospital Ethics Committee of Dr. Soetomo General Academic Hospital Surabaya (0598/LOE/301.4.2/IX/2021).

RESULT

Out of 82 patients, 81 were recruited for this study and one patient did not fulfill the inclusion criteria. Table 1 shows the description of the melasma cases that were recruited for the study. Most of the patients were female (97.5%, or 79 patients), and two were men (2.5%). Patients' ages ranged from the second until the sixth decade of life. The highest age group was 46-55 years (49.4%, or 40 patients), with no patients aged 0-25 years. Most of the patients worked as housewives (40.7%, or 33 patients).

Table 1. The characteristics of melasma cases in the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya during January – December 2019

Characteristic	Total (%)
Gender	
Male	2 (2.5)
Female	79 (97.5)
Age (years)	
0-5	0 (0)
6-11	0 (0)
12-16	0 (0)
17-25	0 (0)
26-35	4 (4.9)
36-45	26 (32.1)
46-55	40 (49.4)
56-65	10 (12.3)
≥65	1 (1.2)
Occupation	
Housewives	33 (40.7)
Government employees	7 (8.6)
Private employees	16 (19.8)
Entrepreneurs	10 (12.3)
Others	15 (18.5)

The precipitating factors found in melasma patients are shown in Table 2, and there can be more than one factor for each patient. Sun exposure was the most precipitating factor found in patients (96.3%, or 78 patients), followed by cosmetic usage in 55 patients (67.9%). 49.4% of patients had hormonal factors, which were caused by contraception (45.7%), gravidity (3.7%), and others caused by myoma (2.5%). Family history was found in 18 patients (22.2%) and in 6 patients with medication history (7.4%). Sun exposure with cosmetic usage was the most multifactor found in patients (25.8%, or 21 patients), followed by sun exposure with cosmetic usage and hormonal (22.2%, or 18 patients).

Table 3 shows the physical examination of melasma cases that were recruited for this study. According to the lesion location, malar was the most common (72.8%, or 59 patients), and some patients had more than one location. The color of lesions was mostly light brown (74.1%, or 61 patients). The lesion

size found in patients was 2.0 – 4.0 cm (54.3% or 44 patients), 0.1 – 2.0 cm (40.7% or 33 patients), >4.0 cm (3.7% or 3 patients), and <0.1 cm (1.2% or 1 patient). Wood's lamp examination performed on patients showed that most lesions had a firm and indistinct border (55.6%, or 45 patients). According to the wood's lamp examination, the most common types of melasma were mixed types, followed by epidermal and dermal types.

Table 2. The precipitating factors of melasma cases in the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Academic Hospital Surabaya during January – December 2019

Precipitating Factors	Total (%)	
Sun exposure	78 (96.3)	
Hormonal		
Contraception	37 (45.7)	40 (49.4)
Gravidity	3 (3.7)	
Others	2 (2.5)	
Medication		
Chlorpromazine (CPZ)	0 (0)	
Klorokuin	0 (0)	
Minosiklin	0 (0)	
Others	6 (7.4)	
Cosmetics	55 (67.9)	
Family history	18 (22.2)	

Table 3. The physical examination results of melasma cases in the Outpatient Dermatology and Venereology Unit of Dr. Soetomo General Academic Hospital Surabaya during January – December 2019

Physical Examination	Total (%)
Location of lesion	
Centrofacial	27 (33.3)
Malar	59 (72.8)
Mandibular	1 (1.2)
Color of lesion	
Same color as the surrounding skin	0 (0)
Light brown	60 (74.1)
Dark brown	39 (48.1)
Bluish brown/black	1 (1.2)
Size of lesion	
Ø <0,1 cm	1 (1.2)
Ø 0,1 – 2,0 cm	33 (40.74)
Ø 2,0 – 4,0 cm	44 (54.3)
Ø >4,0 cm	3 (3.7)
Wood's lamp examination	
Firm border	24 (29.6)
Indistinct border	12 (14.8)
Firm and indistinct border	45 (55.6)

DISCUSSION

Melasma is a common skin pigmentation disorder characterized by brownish to blackish patches on the skin that is often exposed to sunlight.[1] The highest age group of melasma patients in this study was 46-55 years (49.4%), similar to the previous study by Tamarina et al., with the highest age group being 45-54 years (71.43%).[6] Another study by Novarina et al. showed that 80% of melasma patients were aged 45-64 years old.[7] This may be due to hormonal changes in the premenopause period.[8] Premenopause is a transitional period between the reproductive and senium periods. It generally occurs at the age of 47-51 years.[9] Melasma generally appears in premenopausal women and rarely occurs before puberty.[1,10]

The result of this study showed that melasma is more common in women (97.5%) than men (2.5%). A previous study by Oktaviana et al. showed that 96.61% of melasma patients were women.[11] Another study by Umborowati and Rahmadewi also showed that most melasma patients were female (99.2%) and only 0.8% were male patients.[5] A study by Kumar et al. showed that 173 melasma patients were female and 27 were male, with a 6.4:1 ratio.[12] The prevalence of melasma in Southeast Asia is as high as 40% in women and 20% in men.[3] These results show that melasma is more common in women.

This is due to the influence of estrogen and progesterone as female sex hormones, which can stimulate tyrosinase through its receptors on melanocytes and keratinocytes that increase melanogenesis.[13] Pregnancy, contraception usage, and cosmetics also affect the high incidence of melasma in women. Fragrance substances, dyes, and certain chemicals in cosmetics can increase the formation of Reactive Oxygen Species (ROS), which trigger melanocyte activity through photosensitivity reactions.[14] The incidence of melasma is lower in men because of fewer cosmetics usage.[15] The trigger factor for all male patients in this study was sun exposure.

Most patients in this study worked as housewives (40.7%), followed by private employees (19.8%), others (18.5%), entrepreneurs (12.3%), and government employees (8.6%). Others job categories in this study include traders, teachers, retirees, nurses, and chefs. A study by Alifa et al. showed that 44.1% of melasma patients were housewife, followed by private employees, government employees, and others.[15] A study by Rao and Rao also showed that most occupations in melasma patients were housewife (52%), followed by daily laborers, teachers and nurses, private employees, advocates, and tailors.[16] The patient's occupation affects their activities outside the

house, so there is more sun exposure and cosmetic usage, which was the triggering factor of melasma.

The etiology of melasma is multifactorial, but some factors trigger and worsen melasma.[2] Several clinical and laboratory studies in Surabaya, Bandung, and India have shown that sun exposure is the most precipitating factor causing melasma in patients.[5,7,12,15] In this study, sun exposure was found in 96.3% of patients. Ultraviolet light from sun exposure can stimulate the proliferation and migration of melanocytes. This will increase the melanogenesis process.[17] Ultraviolet light exposure also causes lipid peroxidation of the cell membrane, leading to free radical formation.[15] This induces keratinocytes to release various cytokines, including α-melanocyte stimulating hormone (α-MSH) and adrenocorticotropic hormone (ACTH). Increased levels of MSH and ACTH that bind the melanocortin 1 receptor (MC1R) will stimulate melanocyte tyrosinase activity. This results in the proliferation of melanocytes and increased melanin production.[5,10,12,13]

Hormonal factors are thought to be one of the main factors causing melasma due to the high incidence of melasma in pregnant women, oral contraception usage, and hormone replacement therapy.[18] In this study, hormonal factors were found in 49.4% of melasma patients, consisting of contraception usage (45.7%), gravidity (3.7%), and others (2.5%). A study by Alifa et al. showed that 31.8% of patients used oral contraception and 27.9% were pregnant.[15] Another study by Syamsinar et al. showed that 18.9% of the subjects used hormonal contraception.[19] In this study, most of the patients were in the 46-55-year age group which is the premenopausal age, so it is possible to be a cause of fewer patients with gravidity or pregnancy.

Hormonal contraception usage like contraception pills, injections, and implants affects the onset of melasma with different degrees of severity. Contraception can lead to melanogenesis because it contains estrogen and progesterone hormones.[20] Estrogen acts directly on melanocytes as their receptors and causes an increased amount of melanin in cells, while progesterone causes the spread of melanin in keratinocyte cells raising.[15,20] These mechanisms are mediated by the peptide hormones (peptides and glycoproteins) and involve the activity of cyclic adenosine monophosphate (c-AMP) on cell membranes.[15]

Increased estrogen and progesterone hormones in pregnancy will increase melanocyte-stimulating hormone (MSH). This induces the melanogenesis process by stimulating tyrosinase and tyrosinase-related protein-2 (TRP-2) and leads to the formation of melasma lesions. Especially in the third trimester of pregnancy, melasma usually arises and expands due to increased levels of hormones produced by the ovaries, pituitary, and placenta.[2,15] In this study, 2.5% of patients had another hormonal factor, a myoma. Hormonal diseases, such as ovarian tumors, uterine myomas, ovarian cysts, and breast tumors, cause an imbalance of sex hormones, especially estrogen and progesterone, which allows melasma to develop.[15]

About 10-20% of acquired hyperpigmentation cases are caused by medications.[21] Medications that trigger melasma are psychotropic medications such as phenothiazine (chlorpromazine), amiodarone, tetracycline, minocycline, chloroquine, cytostatics, heavy metals, inorganic arsenic, and anticonvulsant drugs such as hydantoin, dilantin, phenytoin, and barbiturates.[21] These act directly on melanocytes, causing the dispersion of melanin granules and inducing pigmentation in the basal epidermis. It stimulates melanocyte activity and increases skin pigmentation, especially in the sun-exposed area.[22] In this study, 7.4% of patients had a medication history that was not involved in the formation of melasma. It was amoxicillin, amlodipine, methylprednisolone, dexamethasone, levothyroxine, and cardiovascular medications such as bisoprolol, spironolactone, and furosemide.

Cosmetics usage was the second-largest triggering factor causing melasma in this study (67.9%). The cosmetics used by patients were moisturizers, various creams without a doctor's prescription, and compact powder. A previous study by Umborowati and Rahmadewi also showed cosmetics as the second-largest triggering factor, with a 40.6% percentage.[5] Perfumes, dyes, or certain chemical ingredients in cosmetics cause photosensitivity that increases the formation of ROS and triggers melanocyte activity. This will result in hyperpigmentation on the sun-exposed face.[14] However, further research is needed to explain how melasma is induced by cosmetics.[16]

Various epidemiological studies have shown a correlation between family history or genetic factors with melasma. Positive family history of melasma reported varies from 20-70% in different studies.[20] As much as 22.2% of patients in this study had a positive family history, slightly more than the previous study by Umborowati and Rahmadewi, which had 21% of the percentage.[5] Another study by Kumar et al. showed that 29.07% of women and 14.28% of men had a positive family history of melasma.[12] Familial predisposing factors in melasma are genetically important, although the pattern is non-Mendelian.[10]

A transcriptional analysis study conducted by Kang et al. showed that a total of 279 genes were modulated in melasma skin lesions. Melanogenesis-related genes expression was increased, mainly the tyrosinase-

related protein-1 (TRP-1) gene and 3 Wnt pathway modulators, including Wnt5a, secreted frizzled-related protein 2 (SFRP2), and Wnt inhibitory factor 1 (WIF1). Those had a role in the development of melanocytes (Kang et al., 2011). Another interesting finding demonstrated the role of the H19 gene in the pathogenesis of melasma. Microarray analysis performed on hyperpigmented lesions in melasma patients showed a downregulation of the H19 gene.[23] Downregulation of the H19 gene can stimulate melanogenesis and increase the transfer of melanin from melanocytes to keratinocytes in melasma patients.[3]

The location of melasma lesions on the face was classified into 3 patterns including centrofacial (63%), malar (21%), and mandibular (16%) pattern.[1] In this study, malar was the most common location observed in 72.8% of patients, and several patients had more than one location of melasma lesions. A previous study by Umborowati and Rahmadewi showed that most common location of melasma lesions was malar.[5] Another study by Salim et al. also showed that the malar type (48.4%) was the most common.[24] Melasma mainly occurs in the malar area, forehead, and upper lip because these areas are more exposed to sunlight. These also have more sebaceous glands capable of synthesizing vitamin D and secreting various cytokines, including interleukin 1 alpha (IL1α) and interleukin 6 (IL6). The increase in growth factors secretion, such as angiopoietin and adipokines, can modulate melanocyte function. Sebocytes are under the control of MSH, so overexpression of this factor can affect sebocytes and melanocytes.[25]

Melasma is characterized by brownish to blackish lesions. Color differentiation is caused by differences in the location of melanin pigment.[4] In this study, the most common lesions were light brown (74.1%). Light brown lesions indicate melanin deposition in the basal and suprabasal layers of the epidermis. In contrast, bluish gray indicates melanin in melanophages in the dermis, and dark brown indicates melanin deposition in the epidermis and dermis.[2,26]

The largest lesion size found in patients was 2.0 – 4.0 cm (54.3%). The lesion size is the total area of all melasma lesions on the face. This can be used to measure the severity of melasma based on the Melasma Area Severity Index (MASI) score, a validated scale used to measure the level of hyperpigmentation on the face.[2] The MASI assessment consists of 3 components, including the area of involvement (A), darkness (D), and homogeneity (H) of the melasma lesion. The MASI score can also evaluate the melasma's response to treatment.[27]

The result of Wood's lamp examination showed that a firm and indistinct border was the most common (55.6%). 29.6% of patients had a firm border, and 14.8% had an indistinct border. The firm border on Wood's lamp examination shows melanin pigment deposition in the epidermis, while the indistinct border shows melanin deposition in the dermis. Lesions that have firm and indistinct borders are mixed type melasma with melanin deposition in the epidermis and dermis layers.[5,7] According to Wood's lamp examination data in this study, the most common types of melasma were mixed types, followed by epidermal and dermal types.

In conclusion, melasma cases at the Dermatology and Venereology Outpatient Unit of Dr. Soetomo General Hospital from January to December 2019 were predominately females, ages 46 to 55, and housewives. The triggering factors for melasma are multifactorial; there was more than one factor for each patient, and sun exposure was the most common. The lesion was typically malar, light brown in color, 2.0 – 4.0 cm, and had a firm and indistinct border. Knowing the triggering factors of melasma is helpful for prevention. Thus, identifying the type of melasma is important for future therapy planning.

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