Profile Of Melasma Patients In Dermatology And Venerology Outpatient Clinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

by Budi Utomo

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ABSTRACT

Background: Melasma is characterized by symmetrical brownish macules with well-defined borders. The etiology of melasma is still unknown, but factors that are thought to influence include genetic predisposition, ultraviolet radiation, hormonal factors, thyroid disorders, use of cosmetics, and drugs. This study aimed to determine the epidemiological data, evaluate risk factors, management, and follow-up in new melasma patients.

Methods: The medical records of patients with melasma attending Dermatology and Venereology Outpatient Clinic over a 4-year period from 2015 to 2018 were analyzed retrospectively for this descriptive, observational study. Data were analyzed using SPSS version 23 for Windows.

Results: This study found 739 new melasma patients from January 2015 to December 2018, with the proportion of women 734 patients (99.3%) more than men only 5 patients (0,7%). The age of most patients who were treated was 46-55 years in 320 patients (43.3%), with the highest age of onset being 37-45 years in 308 patients (41.7%). About 561 patients (75.9%) had a melasma duration of more than 1 year. The most common job of melasma patients was housewives in 366 patients (49.5%). The most frequent risk factor for melasma was ultraviolet radiation in 258 patients (34.9%). The most common melasma was malar type in 482 patients (65.2%) and mixed melasma in 617 patients (83.4%). The most widely administered therapy was sunscreen in 735 patients (99.5%) and Tretinoin 0.05% in 235 patients (31.8%). Most patients did not make repeat visits as many as 448 patients (60.6%).

Conclusion: The most common disease in women of childbearing age with ultraviolet radiation is the most precipitating risk factor. The low number of patient repeat visits can be caused by a lack of doctor education or a lack of patient adherence to treatment due to chronic and recurrent diseases.

Keywords: Melasma, Epidemiology, Risk Factors, Therapy, Human and Disease.
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INTRODUCTION

Melasma is a hyperpigmentation disorder often experienced by millions of people worldwide. Melasma manifestations are symmetrical brownish macules with a well-defined border, especially in the forehead, zygomatic area, upper lip, nose, and chin.[1] The etiology of melasma is still unclear. Factors that influence include ultraviolet radiation, genetic predisposition, hormonal factors, thyroid disorders, drugs, cosmetics, and stress, but the most contributing factor to melasma is sun exposure.[2] UV light induces reactive oxygen species (ROS) by activating nitric oxide and causing melanogenesis. A positive family history of melasma confirms the hypothesis of a genetic predisposition. Hormonal factors have a role in melasma pathogenesis; there is an increased prevalence of melasma in pregnancy, oral contraceptives, and hormonal therapy.[3]

Melasma is estimated to be around 0.25-4% of all skin diseases in Indonesia.[4] The diagnosis of melasma is usually made clinically because of its characteristic appearance. The use of Woods lamp, dermoscopy, and Reflectance Confocal Microscopy (RCM) can assist in melasma classification into epidermal, dermal, mixed, and indeterminate subtypes.[5] Research evaluating the current treatment for melasma is still inadequate and the available treatments are still unsatisfactory.[6] Most existing treatments can temporarily relieve melasma, but the condition usually recurs. Many factors influence the occurrence and recurrence of melasma, so a complete history is needed regarding the risk factors that cause and trigger melasma again.

A retrospective study on the profile of melasma patients had previously been carried out in 2012-2014 at the Cosmetic Division of the Dermatology and Venereology Outpatient Clinic Dr. Soetomo General Academic Hospital Surabaya.[7] This research will continue a retrospective study of the profile of new melasma patients for the period January 2015 to December 2018. This retrospective study will provide an overview of new melasma patients in 2015-2018, evaluate

the risk factors of melasma, the treatment given to melasma patients, as well as repeat visits so that it is expected to provide advice to improve the management of melasma patients in the Cosmetic Division of the Dermatology and Venereology Outpatient Clinic Dr. Soetomo General Academic Hospital Surabaya.

METHODS

The research design used in this study was a retrospective descriptive study in patients diagnosed with melasma at the Cosmetic Division Dermatology and Venereology Outpatient Clinic Dr. Soetomo General Academic Hospital Surabaya for 2015-2018. The sample of this study was calculated using total sampling sourced from secondary data for the period January 2015 – December 2018. The inclusions criteria were all patients recorded in medical records with a diagnosis of new melasma at the Dermatology and Venereology Outpatient Clinic Dr. Soetomo General Academic Hospital Surabaya for January 2015 – December 2018. The exclusions criteria were if the patient medical record was not found. The study data were entered into and analyzed using Statistical Package for Social Sciences (SPSS) version 23 for Windows. Clinical characteristics of participant (patients age, gender, employment status, melasma duration, follow-up frequency), characteristics of melasma lesion (melasma location, color of melasma, lesion size, wood lamp examination, diagnosis), risk factors, and therapy were summarized using descriptive statistics. The categorical data were presented using frequencies and proportions.

RESULTS

Melasma occurred in adults aged 17 to 25 years in 1 patient (0.1%), in adults aged 26-36 years in 60 patients (8.1%), in adults aged 37-45 years in 241 patients (32.6%), in adults aged 46-55 years in 320 patients (43.3%), in adults aged 56-65 years in 94 patients (12.7%), and occurred in more than 65 years in 23 patients (3.1%). Since the 2015-2018 visit, female patients visits were more than male. Total female patients visit were 734 patients (99.3%), and male were 5 patients (0.7%) (Table 1).

Melasma occurred mostly in housewives as many as 366 patients (49.5%), private employees with 219 patients (29.7%), and civil servants at least 154 patients (20.8%). The most common duration of melasma was ≥ 1 year in 561 patients (75.9%) and less than 1 year in 178 patients (24%). Patients who made 1-time repeat visits were 127 patients (17.2%), 2 visits by 84 patients (11.4%), 3 visits by 34 patients (4.6%), 4 visits by 27 patients (3.7%), 5 visits by 16 patients (2.2%), and 6 visits by 3 patients (0.4%). Patients who did not make repeat visits were the most, as many as 448 patients (60.6%) (Table 1).

Malar was the most common location distribution of melasma as many as 482 patients (65.2%), followed by centrofacial 202 patients (27.63%), at least in the centrofacial and mandibular in 3 patients (0.4%) (Table 2). One participant may have more than one melasma location. The color of the most melasma lesions was light brown in 397 patients (53.7%), followed by dark brown in 319 patients (43.2%), blue-black brown in 16 patients (2.2%), the same as the surrounding skin in 7 patients. (0.9%). The largest distribution of melasma lesion size was 0.1-2 cm in 335 patients (45.3%), followed by a lesion area of 2-4 cm in 290 patients (39.2%). The smallest distribution of melasma lesion size was <0.1 cm (5%). The size of the melasma lesion is the total area of the lesion on the face. From the results of Woods lamp examination, from all patients, 617 patients (83.4%) had lesions with well-defined and indistinct borders, 69 patients (9.3%) had lesions with well-defined borders and 53 patients (7.2%) with indistinct borders. If the Woods lamp shows a well-defined lesion, the melanin pigment is present in the epidermis. The most common type of melasma was mixed melasma in 617 patients (83.4%), epidermal melasma in 69 patients (9.3%), and dermal type melasma in 53 patients (7.2%) (Table 2).

Types of factors that most often caused melasma in subjects were sun exposure in 258 patients (34.9%), sun exposure and contraception in 128 patients (17.3%), sun exposure and family history in 97 patients (13.1%), at least only in gravidity as many as 1 patient (0.1%) (Table 3).

Table 1. The clinical characteristic of participants (N=739).

Variable	Year			
	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)
Patient Age (Years Old)				
17-25	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
26-36	20 (7.4)	19 (10.3)	15 (7.9)	6 (6.3)
37-45	89 (33.1)	57 (30.8)	64 (33.7)	31 (32.6)
46-55	125 (46.5)	77 (41.6)	78 (41,1)	40 (42.1)
56-65	26 (9.7)	28 (15.1)	23 (12.1)	17 (17.9)
>65	8 (3)	4 (2.2)	10 (5.3)	1 (1.1)
Gender				
Male	1 (0.4)	2 (1.1)	1 (0.5)	1 (1.1)
Female	268 (99.6)	183 (98.9)	189 (99.5)	94 (98.9)
Employment status				
Housewife	129 (48.0)	86 (46.5)	94 (49.5)	57 (60)
Civil servant	79 (29.4)	31 (16.8)	32 (16.8)	12 (12.6)
Private employee	61 (22.7)	68 (36.8)	64 (33.7)	26 (27.4)
Melasma duration (Years)				
< 1	59 (21.9)	55 (29.7)	36 (18.9)	28 (29.4)
≥ 1	210 (78)	130 (70.2)	154 (81)	67 (70.5)
Follow-Up Frequency				
Once	50 (6.8)	33 (4.5)	21 (2.8)	23 (3.1)
Twice	27 (3.7)	14 (1.9)	30 (4.1)	13 (1.8)
Three times	9 (1.2)	10 (1.4)	9 (1.2)	6 (0.8)
Four times	8 (1.1)	7 (0.9)	11 (1.5)	1 (0.1)
Five times	6 (0.8)	6 (0.8)	1 (0.1)	3 (0.4)
Six times	1 (0.1)	1 (0.1)	1 (0.1)	0 (0)
None	168 (22.7)	114 (15.4)	117 (15.8)	49 (6.6)

In the Cosmetic Division of the Dermatology and Venereology Outpatient Clinic, Dr. Soetomo General Academic Hospital Surabaya, one melasma patient can be given more than one type of therapy. The most given topical therapy was sunscreen in 735 patients (99.5%), Tretinoin 0.05% in 235 patients (31.8%), Kligman formula and Tretinoin 0.025% in 155 patients (21%) and a combination of Kligman formula, tretinoin 0.025%, alpha hydroxy acid (AHA) 8% and vitamin C

Table 2. Characteristic of melasma lesion.

Variables	Year			
	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)
Melasma location				
Centrofacial	77 (28.7)	56 (30.3)	41 (21.6)	28 (29.4)
Malar	149 (55.4)	124(67.0)	144 (75.8)	65 (68.4)
Mandibular	2 (0.7)	2 (1.1)	3 (1.6)	0 (0)
Centrofacial and mandibular	2 (0.7)	0 (0)	0 (0)	1 (1.1)
Malar and mandibular	24 (8.9)	3 (1.6)	2 (1.1)	1 (1.1)
Centrofacial, malar, and mandibular	15 (5.6)	0 (0)	0 (0)	0 (0)
Color of melasma				
Bluish black-brown	8 (3.0)	5 (2.7)	3 (1.6)	0 (0)
Light brown	140 (52)	109 (58.9)	99 (52.1)	49 (51.6)
Dark brown	120 (44.6)	69 (37.3)	84 (44.2)	46 (48.4)
Same as skin color	1 (0.4)	2 (1.1)	4 (2.1)	0 (0)
Lesion size (cm)				
< 0.1	10 (3.7)	9 (4.9)	17 (8.9)	1(1.1)
0.1-2	110 (40.9)	98 (53)	88 (46.3)	39 (41.1)
2-4	110 (40.9)	64 (34.6)	73 (38.4)	43 (45.3)
> 4	39 (14.5)	14 (7.6)	12 (6.3)	12 (12.6)
Wood lamp examination				
Indistinct border	20 (7.4)	13 (7)	12 (6.3)	8 (8.4)
Well-defined border	17 (6.3)	19 (10.3)	12 (6.3)	21 (22.1)
Well-defined and indistinct border	232 (86.2)	153 (82.7)	166 (87.4)	66 (69.6)
Diagnosis				
Mixed melasma	232 (86.2)	153 (82.7)	166 (87.4)	66 (69.5)
Dermal melasma	20 (7.4)	13 (7)	12 (6.3)	8 (8.4)
Epidermal melasma	17 (6.3)	19 (10.3)	12 (6.3)	21 (22.1)

Table 3. Risk factors of melasma patients in 2015 – 2018.

Risk Factors	Year			
	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)
Gravidity	0 (0.0)	0 (0)	1 (0.1)	0 (0.0)
Contraceptives	13 (1.8)	11(1.5)	3 (0.4)	5 (0.7)
Contraceptives, cosmetic	2 (0.3)	0(0)	1 (0.1)	2(0.3)
Contraceptives, cosmetic, family history	3 (0.4)	0(0)	1 (0.1)	0(0)
Contraceptives, family history	6 (0.8)	2 (0.3)	0(0)	1 (0.1)
Contraceptives, family history, gravidity	2 (0.3)	0 (0)	0(0)	0(0)
Cosmetic	3 (0.4)	6 (0.8)	5 (0.7)	3 (0.4)
Family history	7 (0.9)	2 (0.3)	4 (0.5)	2 (0.3)
Family history, cosmetic	2 (0.3)	1 (0.1)	0 (0)	0 (0)
Sun exposure	70 (9.5)	66 (8.9)	79 (10.7)	43 (5.8)
Sun exposure, contraceptives	46 (6.2)	31 (4.2)	39 (5.3)	12 (1.6)
Sun exposure, contraceptives, cosmetic	10 (1.4)	13 (1.8)	3 (0.4)	1 (0.1)
Sun exposure, contraceptives, cosmetic, family history	1 (0.1)	1 (0.1)	1 (0.1)	0 (0)
Sun exposure, contraceptives, family history	21 (2.8)	10 (1.4)	6 (0.8)	4 (0.5)
Sun exposure, contraceptives, family history, gravidity	1 (0.1)	0 (0.0)	0 (0)	0 (0)
Sun exposure, contraceptives, cosmetic, family history, gravidity	1 (0.1)	0 (0.0)	0 (0)	0 (0)
Sun exposure, cosmetic	21 (2.8)	20 (2.7)	21 (2.8)	10 (1.4)
Sun exposure, cosmetic, family history	9 (1.2)	1 (0.1)	2 (0.3)	3 (0.4)
Sun exposure, drug	1 (0.1)	2 (0.3)	1 (0.1)	1 (0.1)
Sun exposure, family history	48 (6.5)	19 (2.6)	22 (3)	8 (1.1)
No data	2 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)

Table 4. The therapy of melasma patients in 2015–2018.

Therapy	Year			
	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)
Sunscreen	267 (36.1)	185 (25)	188 (25.4)	95 (12.9)
Tretinoin 0.025%	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)
Tretinoin 0.025%, Vitamin C	2 (0.7)	14(7.6)	1 (0.5)	1(1.1)
Tretinoin 0.05%	12 (4.5)	81(43.8)	102 (53.7)	40 (42.1)
AHA 8%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0)
Kligman	1 (0.4)	0 (0.0)	0 (0.0)	1(1.1)
Kligman, Vitamin C	1 (0.4)	0 (0.0)	1 (0.5)	1 (1.1)
Kligman, AHA 8%	2 (0.7)	0 (0.0)	0 (0.0)	10 (10.5)
Kligman, Tretinoin 0.025%	54 (20.1)	23 (12.4)	47 (24.7)	31 (32.6)
Kligman, Tretinoin 0.025%, Vitamin C	77 (28.6)	38 (20.5)	11 (5.8)	3 (3.2)
Kligman, Tretinoin 0.025%, Vitamin E	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Kligman, Tretinoin 0.025%, AHA 8%	10 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
Kligman, Tretinoin 0.025%, AHA 8%, Vitamin C	104 (38.7)	24 (13)	20 (10.5)	2 (2.1)
Kligman, Tretinoin 0.025%, AHA 8%, Vitamin E	2 (0.7)	1 (0.5)	0 (0.0)	0 (0.0)
Kligman, Tretinoin 0.025%, AHA 8%, Vitamin A and E	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)
AHA 8%, Tretinoin 0.025%	0 (0.0)	4 (2.2)	5 (2.6)	3 (3.2)
AHA 8%, Tretinoin 0.025%, Vitamin C	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vitamin A and E	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

in 150 patients (20.3%). Oral therapy includes vitamin A, vitamin C, and vitamin E (Table 4).

DISCUSSION

This retrospective study in the Cosmetic Division of Dermatology and Venereology Outpatient Clinic Dr. Soetomo General Academic Hospital in 2015-2018 as many as 739 patients, namely 27.9% of all Cosmetic Dermatology Division patients and 7% of all Dermatology and Venereology Outpatients Clinic. The results of this study indicate that the number of new melasma patient visits in the Cosmetic Division for the 2015-2018 period decreased in 2016 (185 patients) and 2018 (95 patients) when compared to 2015 (269 patients), with a total of 739 patients over 4 years. This finding indicates a decrease in the average number of new melasma patients per year compared to a previous retrospective study at Dr. Soetomo General Academic Hospital in the 2012-2014 period with 869 patients within 3 years.[7] The decrease in the number of melasma patient visits can be caused because melasma is a cosmetic problem not covered by the National Health System and, currently, several beauty clinics that offer various services for skin problems. Hence, patients likely prefer to seek treatment at a beauty clinic rather than a hospital.

Research shows that melasma is more dominant in women. The ratio of women to men with melasma is 9:1, but a recent multicenter study in Brazil with 953 melasma patients found a ratio of 39:1.[6] A study in India with 312 melasma patients found a 4:1 ratio between women and men. In this study, new melasma patients were dominated by women, and the results of this study were the same as Asditya A et al. previous studiy, namely 98.6%.[7]

Melasma most often occurs in women of childbearing age, ranging in age from 17-45 years, although melasma can also occur in men.[8] The youngest melasma patient was 19 years old and the oldest was 75 years old in this research. New melasma patients were commonly found in the 46–55-year age group. This is in accordance with this study; the onset of melasma was mostly at 37-45 years. Melasma onset is found earlier in light skin, whereas dark skin is associated with late-onset melasma.[9] Melasma often occurs in adult women with darker skin (Fitzpatrick skin types III-IV) who live in intense sun exposure areas, so Fitzpatrick's skin type should be listed in the medical records of melasma patients.[10]

Study subjects with longer exposure to heat while cooking had more severe illness or higher Melasma Area and Severity Index (MASI) scores. There is a mild positive correlation between disease severity and duration of exposure to cooking heat. A link between cooking or heat exposure at work and the severity of melasma was found by Sarkar and colleagues in their research. The melanogenic potential of the infrared and visible light spectrum is much lower than that of UVA and UVB, but some authors report worsening melasma after prolonged exposure to oven heat and high-intensity light.[11] In this research, housewives are the most suffering from melasma compared to other occupations. This is in accordance with the resuts of a previous study where new melasma patients have work types such as housewives, civil servants, or the private sector are listed, so this does not describe the patient's exposure to UV rays.[11] It is important to know the specific type of work, especially for evaluating melasma cases associated with outdoor activities, which are usually susceptible to exposure to sunlight.

The duration of having melasma is likely to affect the success of therapy. Sarkar R et al., suggested that chemical peels gave good results on epidermal melasma with a duration of less than 1 year.[11] About 561 patients (75.9%) had melasma duration ≥ 1 year in this research. This shows that in most patients, chemical peels will not give satisfactory results.

Most of the patients did not make repeat visits in this research. This shows the disobedience of patients or ignorance about melasma treatment which takes

quite a long time. A lack of knowledge about melasma can cause a one-time visit or because they can't wait for melasma to heal. Low visit rates may also occur due to lack of education provided by doctors, and it should be explained that evaluation of therapy is usually carried out after 2 months and may take longer, especially if the patient has moderate to severe melasma.

Melasma is generally a clinical diagnosis of symmetric reticulated hyper melanosis in three predominant facial patterns: centrofacial, malar, and mandibular.[1,2] In one patient can be found more than one location of melasma. These data are in accordance with research by Asditya A et al., which states that the most common melasma lesions are located in malar, but not in accordance with some literature which says that the most common location for melasma is centrofacial.[7]

The color assessment of melasma lesions is carried out during physical examination and can be clarified with dermoscopy. The color of the most melasma lesions in this study was light brown. This is different from Asditya's previous study, where dark brown was more abundant than other lesion colors.[7] A dermoscopy study conducted by Nanjundaswamy and colleagues on 100 melasma patients found a significant relationship between dermoscopy analysis and color in melasma lesions. Epidermal melasma is associated with a light brown color of the lesions, dermal melasma is associated with a gray color, and mixed melasma is related to dark brown lesions.[12] If the lesion color is blue-black, it is necessary to consider other differential diagnoses such as exogenous ochronosis, especially if the patient has a history of using hydroquinone for a long time or using creams of unknown composition.[13]

The size of the melasma lesion is the total area of the lesion on the face. This data is also in accordance with a previous study where the size of melasma lesions of 0.1-2 cm was the most common found in this research.[7] Based on the literature, there is no melasma classification based on this size. The size of the melasma lesion should be calculated based on the percentage of the area involved to facilitate the total MASI.

The type of melasma lesion is more accurately determined by Woods lamp than physical examination. Woods lamp examination helps identify the location of the melanin pigment in melasma lesions. A well-defined lesion indicates the pigment in the epidermis on a wood lamp. In contrast, melanin deposits are present in the dermis if the lesion appears with an indistinct border. The lesions that show both features are of mixed type. In this research, well-defined and indistinct boundaries were the most commonly found.

Epidermal melasma is histologically characterized by an increase in melanin in the epidermis.[3,11] Epidermal melasma responds better to treatment than dermal and mixed types of melasma. Dermal-type melasma is less responsive to conventional therapy and characterized by melanin-laden macrophages, especially in the dermis, whereas mixed-type melasma partially responds to therapy.[14,15] The most common types of melasma in this study were mixed-types in accordance with a previous study by Asditya A et al., in melasma patients at the Cosmetic Division of Dermatology and Venereology Dr. Soetomo General Academic Hospital Surabaya in 2012-2014.[7] This suggests that most patients will likely respond partially to therapy.

The exact cause of melasma is unclear, but melasma is thought to be caused by various factors such as sun exposure, contraceptive use, pregnancy conditions, use of drugs or cosmetics, and genetic factors, which are described by a family history of melasma. In one patient, the influencing factor can be more than one.[11] In clinical and laboratory studies, UV light has been shown to trigger and exacerbate the condition. According to the literature, UVA and UVB play an important role in triggering melasma. Sun exposure is the most common factor causing melasma in new patients at the Cosmetic Division of the Dermatology and Venereology Dr. Soetomo General Academic Hospital Surabaya in 2015-2018. In the medical record of a new patient with melasma, only sun exposure was written as the triggering factor without the duration of sun exposure, so a complete history and recording of sun exposure (hours/day) and history of sunscreen used before should be done. Visible light can induce pigmentation, so it is important to add a physical sunscreen to control melasma.[11]

Sun exposure and contraception are the second most common cause of melasma in this research.[16] Melasma is thought to arise from the use of the synthetic progestin levonorgestrel. Progesterone can stimulate melanogenesis in epidermal melanocytes. In contrast, other investigators suggested the prevention of melasma with a progesterone component in oral contraceptives because progesterone reduces melanocyte proliferation without a significant effect on tyrosinase activity.[9] Women are affected more often, and the onset of melasma usually occurs after adolescence, during pregnancy, or while using oral contraceptives supports the fact that there is an association between melasma and hormonal activity. In addition, melasma prevalence decreases after menopause and rarely manifests before puberty-estrogen and progesterone increase tyrosinase activity. Levels of circulating luteinizing hormone are higher in male patients, whereas testosterone concentrations are lower in men with melasma when compared to controls, suggesting a role for mild testicular resistance.[16] This is in accordance with the research of Filoni and colleagues, who stated that based on epidemiological data, melasma occurs in 11.3%-46% of individuals who use contraception in various countries.[9] The types of contraception used by the patient included oral contraceptives, injections, implants, and spirals, but the type of contraception and the composition of the contents were not written in the medical record. If contraception is thought to be the trigger for melasma, it is advisable to do a complete record of the type of contraception and the contraceptive content used.

Sun exposure and family history were the third most common risk factors experienced in this study. The high incidence in melasma patients with a family history suggests that genetic factors are important in the development of melasma. Evidence from a study by Griffiths and colleagues among melasma patients, where 47% had a positive family history of melasma and first-degree relatives were

affected. The high incidence of melasma also occurs in Latin America, Hispanics, and Asia with Fitzpatrick III–V skin types.[11,17] Melasma patients were found to have downregulation of the H19 gene in hyperpigmented and normally pigmented skin. Other related genes are those involved in melanin biosynthesis, the Gene Encoding Tyrosinase (TYR), tyrosinase-related proteins TRP1 and TRP2, And Microphthalmia-Associated Transcription Factor (MITF), which are responsible for transcriptional regulation.[17] This research showed positive family history in 13.1% of melasma patients.

Sun exposure and cosmetics were the fourth most common risk factors suspected of triggering in this study. Cosmetics are thought to be a minor factor associated with melasma. Cosmetics that are believed to trigger melasma include those containing photoactive contaminants such as petrolatum mineral oil, some dyes, beeswax, para-phenylenediamine, and perfume ingredients.[18] The cosmetics used by patients previously included facial soap, moisturizers, day or night creams obtained from doctors at the clinic, purchased online, and cosmetic products that could be bought freely in the market. Therefore, the names of cosmetic products that have been used or are being used by the patient should be recorded in the medical record. Cosmetics rarely cause melasma, but melasma patients have shown a high prevalence of contact sensitivity to cosmetics. When melasma is not associated with pregnancy, breastfeeding, or hormone therapy, Riehl melanosis and cosmetic contact sensitivity should be considered as etiologic factors. The use of vegetable oil (mustard oil) on the face can affect the appearance of pigmentation due to sun exposure, as it is a common photosensitizer in India.[16]

Melasma occurs in 75% of pregnancies and 26-29% of women report its onset during pregnancy. In the third trimester, the stimulus for melanogenesis occurs and can be explained by an increase in placental, ovarian, and pituitary hormones.[16] A previous study found that 10.70% of melasma sufferers out of 224 pregnant women.[11] This study only reported 5 patients (0.6%) with pregnancy as a risk factor for melasma. This low rate may be due to incomplete history taking regarding the early onset of melasma in patients who have had melasma for a long time or in patients unaware that melasma occurred during a previous pregnancy.

Drugs can also cause melasma. Photosensitizing drugs can activate melasma or preexisting dark lesions, and the mechanism could be similar to exacerbations after cosmetic procedures. In 10% of patients taking phenytoin, melasma-like pigmentation appears. This drug causes the dispersion of melanin granules and induces increased pigmentation in the basal epidermis.[16] In this study, there were 5 people (0.7%) with drug use as a factor influencing the occurrence of melasma. 3 data from medical records did not mention the name of the drug, while 2 other medical records mentioned the use of euthyrox and chloroquine as triggers for melasma. Euthyrox drug may not be a drug that triggers the occurrence of melasma but occurs because of thyroid disorder of the patient. Chloroquine is one of the antimalarial agents that can cause drug-induced pigmentation in 25% of patients receiving antimalarial therapy.[19]

Sunscreen is used in the treatment of and as protection against pigmentary disorder. Several studies document the role of visible light in inducing pigmentation in individuals with darker skin types. Chemical and mineral broad-spectrum sunscreens (zinc oxide and titanium dioxide) do not provide optimal protection from visible light. Sunscreens that offer better protection against visible light contain iron oxide in concentrations above 3%.[20] Sunscreen was the most widely used therapy in new melasma patients in this study. This follows Perdoski guidelines where every melasma patient must use a sunscreen with SPF 30. At the same time, Grimes and colleagues recommend using a broad-spectrum sunscreen every day with an SPF of 50 or higher. Sunscreen is applied in the morning and can be reapplied every two to three hours when outdoors.

Tretinoin is a retinoid that targets multiple melanin synthesis and dispersion pathways in the skin and has been widely used in several studies on melasma. Griffiths and colleagues compared a 0.1% tretinoin cream with a vehicle over a 40-week. Sixty-eight percent of the treatment group showed improvement. The therapeutic effect was not seen for 24 weeks and 88% of the treatment group experienced side effects from this high concentration of Tretinoin.[21] In our research, Tretinoin 0.05% was the second most widely used therapy after sunscreen. Based on the PERDOSKI guidelines, this therapy is appropriate, where tretinoin 0.05-0.1% in creams and gels can be used as a topical therapy for melasma. Follow-up is done after 3 or 6 months.[22] If there is an improvement, therapy can be continued, but if there is no improvement, other actions are recommended, such as peeling, laser, ESR mesotherapy, and others. Based on Grimes and colleagues' algorithm, therapy with Tretinoin is not used as a therapy for melasma. The use of 0.1% Tretinoin can improve melasma, but the improvement process is quite long.

Kligman formula is a combination cream consisting of 4% hydroquinone, 0.05% tretinoin, and 0.1% dexamethasone is safe and effective for melasma.[21,22] The Kligman formula is usually used for 3 months to avoid side effects. A previous multicenter study and the randomized controlled trial concluded that the Kligman formula was more effective than multiple combinations of three active ingredients.[21] Seventy-seven percent of patients achieved cure or near cure versus a maximum of 47% in the numerous combination group. 26% of patients taking the Kligman formula achieved a complete treatment within 8 weeks.[21] Kligman formula and 0.025% tretinoin were the third most widely used therapy in this study. Based on the Perdoski guidelines, Tretinoin at a dose of 0.025% was not used as a topical therapy for melasma.[22] Tretinoin was used at 0.5% and 0.01%, while the Kligman formula was not described as one of the therapies for melasma. Based on the Grimes algorithm, Tretinoin is not used as a topical therapy for melasma. At the same time, the Kligman formula is the first-line therapy for moderate (MASI 17-32.9) to severe (MASI 33-48) melasma.[22]

RCT study evaluated GA cream as an adjuvant to 4% hydroquinone (HQ). This study compared five groups in which each group used 4% hydroquinone, and

the efficacy of adjunct drugs such as 10% GA and 0.01% hyaluronic acid was assessed. The efficacy of additional GA cream for HQ was not proven. Sarma and colleagues research concluded no evidence that recommends the use of GA cream in melasma.[22,23] The combination of the Kligman formula, 0.025% tretinoin, AHA 8%, and vitamin C was the fourth most widely used therapy in new melasma patients in this study.[23] Based on the Perdoski guidelines, the Kligman formula and 0.025% tretinoin were not described as a treatment option in melasma.[22] In comparison, AHA 8%, glycolic acid (GA) can be used as a topical therapy in melasma. Vitamin C or ascorbic acid is recommended as oral therapy in melasma when the pigmentation covers a wider area and extends to the dermis.

Chemical peels are a well-known modality of treatment and form the second-line of management in melasma and may be helpful in the improvement of its epidermal component. Chemical peeling agents used in the Cosmetic division for melasma are GA with concentrations of 20%, 35%, 50%, 70%, and Jessners solution, following the Perdoski guidelines.[22] GA is usually used at concentrations of 20–70%, its absorption into the skin influenced by pH, concentration, and duration of application to the skin. Chemical peeling is usually used in combination with topical treatment.

Laser and light therapy are generally used as a second or third-line treatment when there is a failure with topical treatments. Neither of these second and third-line treatments is curative, and relapse may occur after discontinued treatment. Laser and light therapy have a role in the treatment of melasma.[24] These devices should be used with caution, especially among Asians, as the risk of post-inflammatory hyperpigmentation after treatment is quite high. Melasma can sometimes darken after laser and light treatments. Patients should be counseled and advised about the risk of complications. Laser and light therapy may be offered to melasma patients who are recalcitrant to topical medications. Laser and light therapy can be therapeutic options that benefit patients.[24,25]

Response to treatment modalities is usually assessed based on a decrease in the MASI score. The MASI score was calculated by adding the number of degrees of darkness severity (d) and homogeneity (h), multiplied by the value of the area involved (a), for each of the 4 facial areas: the forehead (f), right malar (rm), left malar (lm), and the chin (c). MASI total score = 0.3A(f)[D(f)+H(f)] +0.3A(lm)[D(lm)+H(lm)] + 0.3A(rm) [D(rm)+H (rm)]+ 0.1A(c)[D(c)+H(c)].[25] In this study, it was not possible to analyze the success of therapy because of limited data regarding MASI scores in medical record data.

The limitation of this study is study participants are restricted to only those that presented to the Dermatology Clinic, which may not reflect the exact general population due to its retrospective, observational, hospital-based study. Complete MASI score is needed in medical records, so patients' progression of melasma can be known and treated accurately.

CONCLUSION

The conclusion is the number of new melasma patients in the Cosmetic Division of the Dermatology and Venereology Dr. Soetomo General Academic Hospital Surabaya in 2015-2018 was 739 patients, with the highest number of women being 734 patients (99.3%), and the least being men as many as 5 patients (0.7%). The most recent work of melasma patients was housewives as many as 366 patients (49.5%). The risk factors found in this study were sun exposure as the most common risk factor for melasma in 258 patients (34.9%), followed by sun exposure and contraception in 128 patients (17.3%), sun exposure and family history in 97 patients (13.1%), as well as sun exposure and cosmetics in 72 patients (9.7%). The success of therapy cannot be carried out because an incomplete MASI score is obtained in the medical record. Evaluation of repeat visits found in this study showed that most patients did not make repeat visits as many as 448 people (60.6%).

CONFLICT OF INTEREST

There is no conflict of interest regarding the manuscript.

ETHICS CONSIDERATION

This study was obtained ethical clearance and approved by Clinical Research Unit from the Ethics Committee of Dr. Soetomo General Academic Teaching Hospital Surabaya (1759/KEPK/2020).

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AUTHOR CONTRIBUTIONS

All authors contribute to the study from the conceptual framework, data acquisition, data analysis until reporting the study results through publication.

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