

# OBSERVATIONAL STUDY

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## Prevalence, epidemiology, and clinical characteristics of melasma in Philippine dermatology patients: a multicenter, cross sectional study

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**Background:** Melasma is an acquired hyperpigmentary disorder occurring on sun-exposed areas of the face and neck. There is little information on its prevalence, epidemiology and clinical characteristics in the Philippines.

**Objective:** To determine the prevalence, epidemiology and clinical characteristics of melasma in Philippine dermatology patients.

**Methods:** This was a multicenter, cross-sectional study conducted from July to December 2013. The investigators determined the prevalence of melasma in 12,068 dermatology patients from six government hospitals and private clinics in Metro Manila, Philippines. The melasma patients, aged 18 years and above, were given self-administered questionnaires with topics related to demographic information and medical history. They were also examined by the investigators (dermatologists) to determine the clinical profile of their melasma.

**Results:** Of the 12,068 dermatology patients who were seen at the selected hospitals and private clinics, 153 (1.26%) were clinically diagnosed with melasma. A majority of the melasma patients were Filipinos (73.20%), aged 41-50 years old (37.91%), with an average age of  $42.40 \pm 9.68$  years, and Fitzpatrick skin types III and IV (29.41% and 57.52%, respectively). Melasma was more prevalent in females (81.70%), most of whom had prior history of pregnancy (76.8%). Oral contraceptive use was also reported in 37.6% of the female patients from which 63.83% have used it for only 1 year or less. A majority had no coexisting thyroid disease (75.16%) and daily sun exposure was limited to 1 hour or less for most patients (43.14%). Their melasma was mostly malar in distribution (60.13%), epidermal (61.44%), and mild (51.63%) to moderate (27.45%) in severity. The average mMASI score was  $4.63 \pm 3.32$ .

**Conclusion:** The prevalence of melasma was low among Philippine dermatology patients sampled. A majority of the melasma patients were Filipinos, aged 41-50 years old, with Fitzpatrick skin type IV, limited sun exposure, and no coexisting thyroid disease. They were mostly females with a prior history of pregnancy. Their melasma was mostly malar in location, epiderma type, and mild in severity. These descriptive data can serve as baseline information for further studies on melasma in the Philippines.

*Keywords: melasma, Asian skin, pigmentary, Philippines*

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### INTRODUCTION

**M**elasma is an acquired hyperpigmentary skin disorder characterized by irregular light to dark brown macules occurring on sun-

exposed areas of the skin, mostly on the face and neck.<sup>1</sup>

The three clinical patterns of melasma are centrofacial, malar, and mandibular. The centrofacial pattern is the most common and consists of lesions on the forehead, cheeks, nose, upper lip, or chin. The malar pattern describes lesions located primarily on the cheeks and nose. The mandibular pattern consists of lesions on the ramus of the mandible.<sup>2</sup>

Its histologic subtypes are epidermal, dermal, and mixed. Wood's lamp evaluation is helpful in identifying these subtypes.<sup>3</sup>

Pigmentation disorders like melasma often comprise a considerable percentage of cases seeking dermatologic consult.<sup>4</sup> Because it often occurs in the face, such pigmentary dermatoses have a significant impact on the patient's quality of life, prompting a demand for dermatological care.<sup>1</sup> A study conducted in Southeast Asia reported that melasma accounted for 0.25 to 4% of patients seen in dermatology institutes: 4% of cases were reported in Malaysia while 0.98% were reported in Indonesia<sup>5</sup>. Despite being a common dermatologic complaint, the incidence of melasma in the population is not precisely known.<sup>1, 5, 6</sup>

Melasma is more common in females (90%) than in males (10%).<sup>5, 6</sup> It affects mainly women of childbearing age<sup>7</sup>, with peak incidence in patients aged 30 to 44 years, based on the previously mentioned 1995 study on melasma in Southeast Asia<sup>5</sup>. It also occurs more frequently in more pigmented phenotypes (Fitzpatrick skin types IV-VI) such as Hispanic, Asian, and African-American skin.<sup>8</sup>

There are many factors that contribute to the pathogenesis of melasma. The most important of these are genetic predisposition, ultraviolet (UV) radiation and hormonal dysfunction.<sup>6</sup>

Genetic predisposition is the most important risk factor for melasma while sun exposure is the most important triggering factor.<sup>1</sup> UV radiation directly induces the increase in melanogenic activity, resulting in epidermal pigmentation. In intertropical regions where the level of UV radiation is higher, the population incidence of melasma is increased.<sup>1</sup>

Hormonal changes involving sexual hormones (estrogen and progesterin) such as what happens in pregnancy, combined oral contraceptive (COC) use, and hormone replacement therapy also trigger the appearance of melasma.<sup>1</sup> This is attributed to elevations in the level of estrogen and progesterone which can lead to increased pigmentation.<sup>1</sup> In a 2010 prospective study involving 197 patients in Tunisia, sun exposure was reported as the main aggravating or

triggering factor by 84% of melasma patients, followed by COC use by 38%, and pregnancy by 50%.<sup>9</sup>

Melasma has also been associated with endocrinopathies and autoimmune thyroid diseases.<sup>10, 11</sup> Among the endocrinopathies, thyroid dysfunction has often been cited and investigated as one of the factors implicated in the etiopathogenesis of melasma.<sup>12</sup> However, some studies reported that the observed prevalence of thyroid diseases has not increased relative to the general population.<sup>11, 18</sup> This association needs further investigation.

This study aimed to determine the prevalence, epidemiology, and clinical characteristics of melasma in Philippine dermatology patients. With the increasing number of melasma cases seen in our clinical practice, we envisioned the need to investigate and gather more information on the prevalence and nature of this condition (epidemiological and clinical characteristics) in Philippine dermatology patients. This data will help us gain valuable insights into how we can more effectively manage melasma cases in the country.

## **MATERIALS AND METHODOLOGY**

### **Trial Design**

This was a multicenter, cross-sectional study on the prevalence, epidemiology, and clinical characteristics of melasma among dermatology patients from 6 selected government hospitals and private clinics in Metro Manila, Philippines. This study was approved by the Institutional Review Board prior to commencement.

### **Participants**

A total of 12,068 dermatology patients were seen at the dermatology sections of six selected government hospitals and private clinics in Metro Manila, namely, the Research Institute for Tropical Medicine (RITM), East Avenue Medical Center, Ospital ng Maynila, Asian Hospital Dermatology Department, Skin Care Solutions, and Casa Medica Health Clinic. Patients were initially screened for melasma by dermatology residents at the respective clinics. Identified melasma cases were referred to and assessed by the investigators (dermatologists) for eligibility to participate in the succeeding parts of the study. Patients aged 18 years and above who were newly diagnosed with melasma based on the assessment of the investigator (regardless of sex and concomitant diseases) were recruited. Informed consent was obtained from the eligible patients prior

to inclusion in the study. This study was conducted for a period of six months, from July to December 2013.

### **Interventions**

The study was divided into three parts. In part I, the number of patients diagnosed with melasma and the total number of dermatology patients seen at the selected hospitals and clinics within the six-month period were noted. From these data, the prevalence of melasma was calculated.

In part II, the patients answered a questionnaire on demographic information and medical history, which was provided by the investigators during routine dermatologic consultation. The questionnaire was specially developed for this study. It was initially tested among 10 people aged 18 years and above to check for validity and reliability.

Part III was a clinical assessment to determine the clinical profile of the melasma patients. The assessment and interview were conducted by the investigators, who were also dermatologists, during routine dermatologic consultation. Prior to the commencement of the study, the investigators were trained in filling out the Case Report Form (CRF) and given a Fitzpatrick skin color chart to define the skin type of the patient.

Completed questionnaires and CRFs were collected once a week. The total number of patients seen each week per clinic/institution was documented.

### **Outcomes**

The following study parameters were assessed by the investigators: a) prevalence of melasma, b) demographic information and medical history, and c) clinical profile of melasma patients.

Demographic information and medical history of patients included age, gender, race, presence of thyroid disease, history of pregnancy and oral contraceptive (OCP) use, duration of OCP use, and daily duration of sun exposure.

The clinical profile of patients consisted of the Fitzpatrick skin type, melasma classification, type of melasma (by Wood's Lamp examination), and melasma severity using the modified Melasma Area and Severity Index (mMASI). Permission was obtained from the University of Texas Southwestern Medical Center (Dallas, Texas, USA) to use this MASI Training Program created by Dr. Amit Pandya.

The mMASI by Pandya et al. is a modification of the MASI, eliminating homogeneity as criterion because it had the lowest interrater agreement.<sup>13</sup> It is computed by rating darkness and area of involvement of four areas of the face. The rating/score for each of the four areas are inserted into an equation, resulting in the final mMASI score.<sup>13</sup> Based on a retrospective study of 79 patients, mean mMASI scores of 3.8, 6.5 and 8.9 corresponded to mild, moderate and severe melasma, respectively.<sup>13</sup>

All data were entered in a database and were subjected to range and validation checks and statistical analysis.

### **Sample Size**

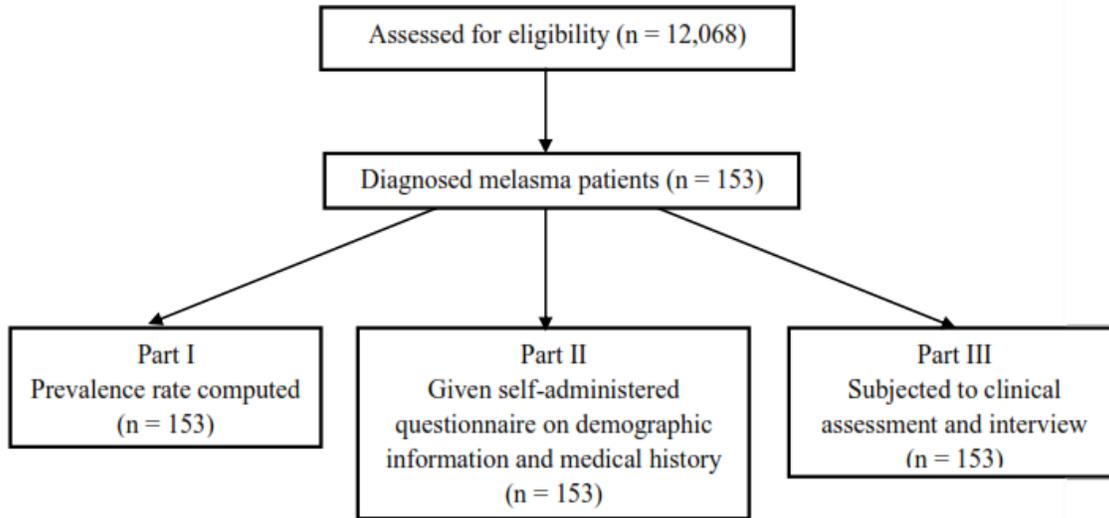
The prevalence of melasma among dermatology patients at RITM was 2.2%, 2.4% and 2.2% in 2010, 2011, and 2012, respectively. Using this data to estimate a prevalence rate of 3%, the minimum sample size required for this study was 4,477 patients. This was calculated using a confidence interval of 95% and a 1% desired width of the confidence interval. The total number of patients interviewed and examined in this study was 12,068.

### **Statistical Methods**

Frequency and percentages were used to summarize qualitative variables such as classification of Fitzpatrick skin types, melasma classification, and types of melasma. Means and standard deviations were computed for quantitative variables such as age and mMASI score. Missing values were not replaced nor estimated. Microsoft Excel 2016 was used for data processing and analysis.

## RESULTS

### Participant Flow



**Figure 1.** Flowchart showing the screening and assessment of patients in the study

### Numbers Analyzed

Out of 12,068 dermatology patients seen at the dermatology departments of the selected hospitals and clinics, only 153 were clinically diagnosed with melasma (all newly diagnosed) and were at least 18 years of age, making them eligible to participate in the current study. All 153 melasma patients were included in the computation for the prevalence rate, given the self-administered questionnaire, and clinically assessed by the investigators. However, since participation in the survey was completely voluntary, patients were free to skip items that they preferred not to answer or were not applicable to them. Hence, the reporting of unavailable data, referred to here as missing data, which is the reason the total number of responses per item does not always add up to 153. Questions pertaining to pregnancy and OCP use were only answered by female participants (n=125) and the question regarding the duration of OCP use was answered only by those who had used OCP (n=47). Melasma classification based on distribution, on the other hand, was not mutually exclusive. Some patients

had one, two, or all three types of melasma based on distribution (malar, forehead, and centrofacial).

### Outcomes and Estimation

#### Prevalence of Melasma

Out of 12,068 dermatology patients seen at the six selected government hospitals and private clinics, 153 (1.26%) were diagnosed with melasma.

#### Demographic Information and Medical History

Melasma patients were mostly 41 to 50 years old (58/153, 37.91%) and the average age was  $42.40 \pm 9.68$  years. They were predominantly female (81.70%) and of Filipino descent (73.20%) (Table 1). The female to male ratio was 4.6:1.

From the 125 females diagnosed with melasma, a majority (96/125, 76.8%) had prior history of pregnancy but only 47/125 (37.6%) had used oral contraceptives. Most of them (70/153, 56%) did not use OCP. OCP use lasted only one year or less for 30/47 (63.83%) of the patients who had used it.

**Table 1.** Demographic characteristics of melasma patients from selected hospitals and clinics in Metro Manila, Philippines (n = 153)

	<b>Frequency (%); Mean <math>\pm</math> SD</b>
<b>Age</b>	42.40 $\pm$ 9.68
20 – 30	28 (18.30)
31 – 40	37 (24.18)
41 – 50	58 (37.91)
> 50	28 (18.30)
Missing data	2 (1.31)
<b>Sex</b>	
Male	27 (17.65)
Female	125 (81.70)
Missing data	1 (0.65)
<b>Race</b>	
Filipino	112 (73.20)
Chinese-Indonesian	1 (0.65)
Filipino-Chinese	1 (0.65)
Filipino-Spanish	1 (0.65)
Missing data	38 (24.84)

**Table 2.** Medical history of melasma patients from selected hospitals and clinics in Metro Manila, Philippines

	<b>Frequency (%); Mean <math>\pm</math> SD</b>
<b>Pregnancy (n=125)</b>	
Yes	96 (76.8)
No	28 (22.4)
Missing data	1 (0.8)
<b>Oral Contraceptive Use (n=125)</b>	
Yes	47 (37.60)
No	70 (56.00)
Missing data	8 (6.40)
<b>Duration of Oral Contraceptive Use in months (n=47)</b>	
$\leq$ 12	30 (63.83)
> 12	14 (29.79)
Missing data	3 (6.38)
<b>Thyroid Disease (n=153)</b>	
Yes	25 (16.34)
No	115 (75.16)
Missing data	13 (8.50)
<b>Daily Duration of Sun Exposure in minutes (n=153)</b>	
$\leq$ 30	66 (43.14)
31 - 60	51 (33.33)
> 60	25 (16.34)
Missing data	11 (7.19)

Thyroid disease was present in only 25/153 (16.33%) of patients, which means that a majority (75.16%) had no thyroid problems. Although there were 13 counts of missing data on thyroid condition, the number of patients without thyroid disease still comprised the majority. In terms of sun exposure, a majority (66/153, 43.14%) reported a daily sun exposure of 30 minutes or less.

### Clinical Profile of Melasma Patients

Based on Fitzpatrick skin type classification, the most common skin type was Type IV (88/153, 57.52%), followed by Type III (45/153, 29.41%) (Table 3). Melasma was more commonly the epidermal type by Wood's lamp examination (94/153, 61.44%) and malar based on distribution (92/153, 60.13%). In terms of severity, most patients presented with mild melasma (51.63%) followed by moderate severity (27.45%). The average mMASI score was  $4.63 \pm 3.32$ .

**Table 3.** Clinical profile of melasma patients (n = 153)

Profile of Melasma	Frequency (%); Mean $\pm$ SD
<b>Fitzpatrick Skin Type</b>	
Type I	0
Type II	12 (7.84)
Type III	45 (29.41)
Type IV	88 (57.52)
Type V	5 (3.27)
Type VI	0
Missing data	3 (1.96)
<b>Melasma Classification</b>	
Malar	92 (60.13)
Forehead	35 (22.88)
Centrofacial	47 (30.72)
<b>Type of Melasma (Wood's Lamp)</b>	
Epidermal	94 (61.44)
Dermal	13 (8.50)
Mixed	38 (24.84)
Missing data	8 (5.23)
<b>Melasma Severity</b>	
Clear	3 (1.96)
Mild	79 (51.63)
Moderate	42 (27.45)
Severe	23 (15.03)
Missing data	6 (3.92)
<b>mMASI Score</b>	
	4.63 $\pm$ 3.32
< 3	55 (35.95)
3 - 6	57 (37.25)
> 6	38 (24.84)
Missing data	3 (1.96)

## DISCUSSION

Results of this six-month study showed a melasma prevalence of 1.26% (153 out of 12,068 patients) among dermatology patients from the six selected government hospitals and private clinics in Metro Manila. Based on a recent article on melasma updates, the prevalence of melasma varies from 1.5% to 33.3%, depending on the population being studied.<sup>14</sup> Given this range of prevalence rates, we could say that the melasma prevalence calculated in this study is low. A study conducted in Southeast Asia in 1995 reported a melasma prevalence of 0.25 to 4% among patients seen in dermatology institutions.<sup>5</sup>

Melasma is more prevalent in females than in males.<sup>1,3,4,6,9,15</sup> Although the generally accepted ratio of female to male predominance is 9:1, other studies have shown varying ratios such as 39:1 in Brazil and 21:1 in Singapore.<sup>2</sup> In this study, the ratio is 4.6:1. This is very close to the 4:1 ratio reported in an Indian study of 312 patients.<sup>20</sup> However, since this data is limited to dermatology patients, this ratio may also reflect the greater tendency of women to be more psychologically distressed by cosmetic disfigurement than men and to seek dermatologic consult as a result.<sup>15,16</sup>

In particular, women of childbearing age are mostly affected by melasma<sup>17</sup>. Hence, female sex hormones have been suggested to play a role in the development of melasma.<sup>1, 8, 29</sup> In this study, most of the melasma patients were females (125/153, 81.70%) and most were aged 41 to 50 years old (58/153, 37.91%), with the average age of 42.4 ± 9.68 years. Similarly, in a 2006 multicenter study on Asian patients from Korea, Philippines, Singapore, Hong Kong and Taiwan, the majority of patients were also females (248/260, 95.4%) and the average age was 45 years.<sup>6</sup> However, since the age reported in our survey is the age when melasma was first diagnosed and not necessarily the age of onset of the disease, it cannot be concluded whether the patients developed the disease early or late in menarche. On one hand, the high average age of melasma patients in the study could simply mean that older people tend to seek more dermatologic consult. On the other hand, the diagnosis of melasma at a relatively late age could mean late onset of the disease, which is commonly seen in Asian countries such as India, with an average age of melasma development of 30 years old; Singapore, 34 years old, and other Southeast Asian countries, 30-44 years old.<sup>3,18,19</sup> This delay in development of melasma has been attributed to melanin, which seems to play a photoprotective role.<sup>9,20</sup> In this study, a majority of the melasma patients were Filipinos (73.2% or 112/153) and a majority had a more pigmented phototype with Fitzpatrick skin type IV (57.5% or 88/153).

Some of the factors implicated in the development of melasma like thyroid disease, sun exposure, pregnancy and oral contraceptive pill (OCP) use were investigated in this study.<sup>1, 13, 17</sup>

Endocrinological conditions like thyroid disease have previously been associated with melasma. However, some studies have also shown that the prevalence of thyroid diseases in melasma patients is not higher than the general population.<sup>22, 23, 29</sup> In this study, 75.16% (115/153) of the melasma patients reported no thyroid disease or any thyroid problem. Establishing an etiological correlation between thyroid disease and melasma still needs further investigation.

Another factor associated with melasma is exposure to UV radiation without protection. This is said to be the most important environmental triggering factor in melasma.<sup>9, 23</sup> However, it was noted in this study that 43.14% (66/153) of the patients had a self-reported daily sun exposure that lasted only 30 minutes or less. The minimal daily sun exposure of the majority of patients suggests that sun exposure may not be the triggering factor of melasma among these patients. However, since this data was self-reported, it is also possible that data may be subject to recall error and bias. In future studies, more objective measures of sun exposure such as polysulfone badges worn daily may be employed to derive more reliable information.

Pregnancy and OCP use have also been associated with melasma development. There is increased prevalence of melasma with pregnancy and OCP use possibly due to hormonal influences, as previously suggested.<sup>25,29</sup> High levels of the female hormones estrogen, progesterone, and melanocortin are said to be possible triggering factors of melasma during pregnancy.<sup>1, 8</sup> In a study involving 2,000 pregnant women in India, 50.8% had melasma.<sup>26,29</sup> In our study, 96 out of 125 (76.8%) women had been pregnant. OCP use was common, with 37.60% (47/125) of the female patients admitting to having used OCP, but the majority (70/125, 56%) did not use OCP and the rest (6.40%) did not confirm either way. More than half (30/47, 63.83%) of those who used OCP had used it for a duration of only 12 months or less. These data suggest that pregnancy but not OCP use may be the main triggering factor for melasma in this group of patients. However, this hypothesis warrants further investigation.

In terms of skin type, most patients had Fitzpatrick type IV (88/153, 57.52%), followed by type III (45/153, 29.41%). These findings are similar to one Brazilian study that shows that a majority of melasma cases occurred in these two skin types.<sup>21</sup> In a multicenter study on Asian patients, most patients had skin phototype IV (168/260, 64.6%) or III (71/260, 27.3%).<sup>6</sup> The

prevalence of melasma in more pigmented phototypes (Fitzpatrick scale III, IV and V) is known to be high.<sup>9</sup> Tamega et al. suggested that the low incidence of melasma in the darkest phototypes may be due to some stability or homogeneity in their ultraviolet (UV) reaction regarding their pigmentation system.<sup>9, 26</sup> It has also been argued that individuals with skin type I cannot produce additional pigmentation while those with skin type VI can produce pigment at maximum efficiency<sup>1</sup>.

In our study, the type of melasma was mostly epidermal (94/153, 61.44%) and the most common classification was malar (92/153, 60.13%). Another study conducted in the same institute (RITM) in 2009 also reported malar melasma to be the most common among their patients (49/56, 87.5%).<sup>27</sup> A 2006 study of Asian patients also reported the most common type of melasma to be epidermal (152/260, 58.5%) and malar as the most affected location.<sup>6</sup> Another study involving 85 women in southern Brazil also found the most common pattern of melasma to be malar (46.4%)<sup>28</sup>. In contrast, a 2013 study on facial melasma among Brazilian women and a study in Tunisia involving 188 female patients both showed the predominance of centrofacial melasma rather than malar.<sup>9, 10</sup> The predominant type of melasma observed apparently varies depending on the population being studied.

Furthermore, most patients presented with mild (51.63%) followed by moderate melasma (27.45%). The average mMASI score was  $4.63 \pm 3.32$ . This approximates the mean mMASI score of 3.8, which has also been classified as mild in a retrospective study involving 79 patients.<sup>13</sup> This is unlike most published studies where the means of MASI scores are about 10 to 13, which are classified as moderate melasma.<sup>29</sup>

The main limitation of this study is the possibility of recall error and bias. There are also missing data due to the inability of some patients to answer certain questions in the survey. Also, this study's sample of patients newly diagnosed with melasma were obtained only from six dermatology clinics in Metro Manila and therefore cannot be representative of the entire population of Metro Manila, much less the entire Philippine population. According to Ogbechie-Godec and Elbuluk, the prevalence and incidence rates calculated from dermatology clinics may be an underestimate of the number of affected

individuals in the population as some patients with milder disease may no longer seek consultation or clinical assessment.<sup>28</sup>

Despite these limitations, the results of this study give us an insight on the common profile of melasma patients in the Philippines. Knowledge of such profile will allow physicians to identify individuals who are strongly susceptible to developing the disease and to plan primary prevention strategies for them. This may also help researchers and physicians develop treatments or design a multimodal therapeutic approach that is more effective for Philippine melasma patients---one that takes into consideration the epidemiology and clinical characteristics of their melasma.

## CONCLUSION

The prevalence of melasma was low among the Philippine dermatology patients sampled. The majority of the melasma patients in this study were Filipinos, aged 41-50 years old, with Fitzpatrick skin type IV, limited sun exposure, and no thyroid disease. They were mostly females with a prior history of pregnancy. Their melasma was mostly malar in location, epidermal type and mild in severity. These descriptive data can serve as baseline information for further studies on melasma in the Philippines. These can also provide physicians with a better understanding of the nature of the disease among Philippine patients for improved management of individual melasma cases.

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