ORIGINAL ARTICLE

Clinical patterns and epidemiological characteristics of facial melasma in Brazilian women

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Abstract

Background Melasma is a common acquired chronic hypermelanosis of sun-exposed areas which significantly impacts quality of life. There are few epidemiological studies in medical literature concerning these patients.

Objective Characterize clinical and epidemiological data on Brazilian female patients with melasma.

Methods A semi-structured questionnaire was administered to melasma patients treated at a dermatology clinic between 2005 and 2010. Association between variables was performed by multivariate regression models.

Results We assessed 302 patients; intermediate skin phototypes III (34.4%) and IV (38.4%) were prevalent. Mean disease onset age was 27.5 ± 7.8 years and familiar occurrence of melasma was identified in 56.3%. The most commonly reported trigger factors were pregnancy (36.4%), contraceptive pills (16.2%) and intense sun exposure (27.2%). Preferred facial topographies were zygomatic (83.8%), labial superior (51.3%) and frontal (49.7%). Pregnancy induced melasma has been associated to early disease (OR = 0.86) and number of pregnancies (OR = 1.39). Childbearing was correlated to melasma extension. Older disease onset age was associated to darker skin phototypes. Co-occurrence of facial topographies supported clinical classification as centrofacial and peripheral melasma.

Conclusion This population was characterized by: a high prevalence in adult females, intermediate skin phototypes, disease precipitation by hormonal stimulus and familiar genetic influence.

Received: 29 August 2011; Accepted: 9 December 2011

Conflict of interest

None declared.

Introduction

Melasma is a common chronic acquired hypermelanosis that causes important aesthetic involvement and decreases quality of life. It mainly affects adult women of childbearing age from all ethnic groups and is characterized by brown symmetrical, homogeneous, irregular macules in sun-exposed areas, mostly on the face.[1–5]

The epidermis of melasma reveals local melanocytic hyperactivity without melanocyte hyperplasia. The number of melanosomes and their degree of maturity are increased causing hyperpigmentation in all epidermal layers. Dermal elastosis and slight lymphocytic infiltrate are also observed. However, most of the physiopathology is still not fully understood.[6–10]

Several factors have been implicated in melasma development, but none are individually responsible. Pregnancy, hormonal therapies, oral contraceptive pills, cosmetics, photosensitizing medications, endocrinopathies, emotional stress and anticonvulsants have been reported, along with a genetic predisposition and exposure to sunlight, as the main factors for melasma development.[11–14]

The American Academy of Dermatology estimates that melasma affects 5–6 million women in the United States.[15] Pigmentation disorders were the third largest group of diseases (8.8%) detected in dermatological consultations in the last Brazilian dermatological census, and the second largest dermatology office complaint in women (11.6%).[16]

Population-based studies in pregnant women have revealed a varying melasma prevalence of 10–70%, suggesting that other factors, such as ethnicity and sun exposure, are involved in its development.[17–20]

Family history of melasma occurs in about 50% of patients, particularly in those with darker skin types.[15]

There are several clinical classifications regarding the topographical locations of these lesions. Centrofacial, malar and mandibular are the most common, although some authors prefer

more objective classifications such as: central, peripheral, mixed (facial) and extrafacial.[3,21]

There are few epidemiological studies on the clinical issues of melasma or analytical studies that explore the relationship between its demographic and clinical variables. This work evaluates the main clinical patterns and epidemiological aspects of facial melasma in Brazilian women.

Materials and methods

An observational and analytical epidemiological study was performed by interviewing adult women with melasma attending the dermatology clinic from 2005 until 2010 at Botucatu School of Medicine-UNESP, São Paulo, Brazil. There were no restrictions regarding ethnicity, Fitzpatrick's skin phototype classification (I–VI),[22] diagnosis status (old and newly diagnosed), or treatment.

All volunteers answered a semi-structured questionnaire on clinical and demographic information specially developed for this study. Interviews were performed by dermatologists and supervised by the principal authors (A.A.T. and L.D.B.M.) during routine dermatologic consultation.

Basal cortisol and thyroid-stimulating hormone (TSH) were collected from patients in the morning and analyzed at the institutional laboratory by chemiluminescence and radioimmunoassay. TSH values outside 0.4–4.0 μg/dL and basal cortisol values outside 3.7–19.4 μU/mL were considered abnormal.

This study was approved by Botucatu School of Medicine Research Ethics Committee (293/2004), and all participants signed an informed consent form for clinical and laboratorial investigation.

Categorical variables were represented by their percentages and 95% confidence intervals were estimated (CI 95%). Quantitative data were represented by mean and standard deviation, or median and interquartile range if non-parametric. Normality was assessed by Shapiro-Wilk test.[23]

Subgroups were explored by multivariate analysis. Dependent variables were adjusted by other covariates using an unconditional multiple logistic regression model. Association between categorical variables was estimated by odds ratio (OR) and its respective CI 95%. Multivariate analysis of continuous dependent variables was performed by a generalized linear model. All multivariate models were built according to the selection of covariates which reached significance ($P < 0.3$) in a bivariate analysis.[24] All tests considered a two tailed P value of 0.05 as significant.

Topographical lesion patterns were evaluated by hierarchical cluster analysis (Ward's method).[25]

Data were tabulated in MS Excel 2007 and analyzed by SPSS 17.0 software.[26,27]

Results

Three hundred and two patients were included in the study; their main clinical and demographical information are presented in Tables 1 and 2.

Melasma onset occurred in adulthood (menacme) (Fig. 1), age (mean ± standard deviation) was 27.5 ± 7.8 years. Disease duration (median ± interquartile range) was 9 ± 11 years.

There were no Asians and no currently pregnant women in the sample.

Intermediate skin phototypes (Fitzpatrick) were prevalent (Table 1), a positive family history of melasma was also expressive, mainly (70.4%) in first-degree relatives, as was living by the sea or on a farm.

Pregnancy, birth control pills and intense sun exposure were the most common causative elements identified by patients (Table 1).

Hierarchical cluster co-occurrence analysis of facial topographies revealed two main patterns of lesion distribution in patients (Fig. 2).

Group 1 revealed a centrofacial pattern and Group 2 a peripheral topography. Table 2 presents both topography frequencies, and their clinical and cluster-related classifications.

Combined facial patterns were the most common presentation, followed by the centrally exclusive ones. The zygomatic, labial superior, frontal, nasal and parotid regions were the most affected. Extrafacial occurrence was observed in 7.9% of those with facial melasma. Six or more facial regions were involved in most patients.

Zygomatic occurrence was frequently associated to other lesions (90.5%), mainly centrofacial topographies.

Abnormal TSH hormonal profiles were found in 25.3% (24.1% high and 1.2% low) and cortisol in 9.6% (7.7% high and 1.9% low) of patients. These findings were consistent with prevalence levels in the adult female population ($P > 0.3$).[28] High TSH levels were associated to intense sun exposure induced melasma (OR = 2.15; CI 95% 1.00–4.69). High cortisol levels were associated to a lower number of pregnancies (OR = 0.02; CI 95%

Table 1 Main demographic patient data

		N	Percentage (%)	CI 95%
Skin phototype	I	2	0.7	0.0–1.6
	II	28	9.3	6.0–12.6
	III	104	34.4	29.1–39.8
	IV	116	38.4	32.9–43.9
	V	47	15.6	11.5–19.7
	VI	5	1.7	0.2–3.1
Family occurrence†		169	56.3	50.7–62.0
First-degree		119	47.6	41.4–53.8
Living at seacoast or farm		159	52.6	44.5–60.8
Sun exposed occupations		146	48.5	40.7–56.4
Ever smoking		73	31.2	25.2–37.2
Hormonal contraceptive‡		115	38.1	32.6–43.6
Regular sunscreen use‡		251	57.3	52.7–62.0

†First or second degree.
‡Current use.
CI, Confidence interval 95%.

Table 2 Main clinical patient data

		N	Percentage (%)	CI 95%
Triggering factors	Anyone reported	274	90.7	87.4–94.0
	Pregnancy†	110	36.4	31.0–41.9
	Intense sun exposure	82	27.2	22.1–32.2
	Contraceptive pills	49	16.2	12.1–20.4
	Psychological stress	20	6.6	3.8–9.5
	Cosmetics	10	3.3	1.3–5.3
	Hormone replacement therapy	3	1.0	0.0–2.1
Affected facial site	Zygomatic (malar)	253	83.8	79.6–87.9
	Labial superior	155	51.3	45.7–57.0
	Frontal	150	49.7	44.0–55.3
	Nasal	122	40.4	34.8–46.0
	Parotid	90	29.8	24.6–35.0
	Mentonian	88	29.1	24.0–34.3
	Glabellar	76	25.2	20.3–30.1
	Temporal	73	24.2	19.3–29.0
	Mandible	54	17.9	13.5–22.2
	Upper chest	18	3.3	3.3–8.6
	Upper limbs	7	0.6	0.6–4.0
	Neck	7	0.6	0.6–4.0
Clinical classification‡	Central	156	51.7	46.0–57.3
	Peripheral	15	5.0	2.5–7.4
	Combined	131	43.4	37.8–49.0
Cluster classification	Centrofacial (Cluster 1)	209	69.2	64.0–74.4
	Peripheral (Cluster 2)	93	30.8	25.6–36.0

†Among who have got pregnant.
‡Facial types.
CI, confidence interval.

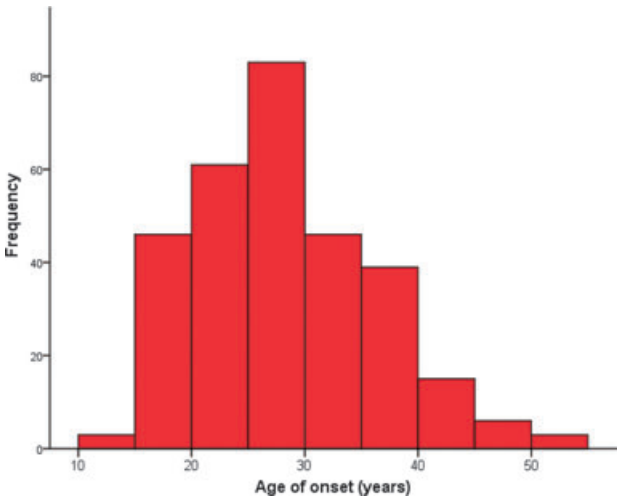

Figure 1 Histogram of facial melasma onset ages.

0.01–0.23) and disease induced by oral contraceptives (OR = 6.77; CI 95% 1.07–42.98), but not to any clinical variable.

A first-degree family report of melasma was associated to a higher chance of living on a farm or by the sea (OR = 1.76; CI 95% 1.07–2.88) and longer disease duration (OR = 1.03; CI 95% 1.00–1.07), but not to any clinical pattern or skin phototype.

Of those who reported pregnancy ($n = 244$), the median (± interquartile range) was 2 ± 2 pregnancies. Melasma triggered during gestation was associated to early disease onset (OR = 0.86; CI 95% 0.82–0.90) and directly to the number of pregnancies (OR = 1.45; CI 95% 1.14–1.84), but not to any clinical pattern.

Oral contraceptive pill induced melasmas were inversely associated to the number of pregnancies (OR = 0.71; CI 95% 0.55–0.92) and mentonian lesions (OR = 0.41; CI 95% 0.18–0.93).

Late melasma onset positively correlated to multiple pregnancies and peripheral clinical classification ($P < 0.05$). Nevertheless, lighter skin phototypes, melasma induced by pregnancy or contraceptive pills, and frontal and upper lip lesions correlated to early disease onset ($P < 0.05$).

Total number of melasma affected areas directly correlated to early disease onset and disease induced by pregnancy ($P < 0.05$).

Cases with longer follow-up were associated to darker skin phototypes, mandibular and parotid (peripheral) involvement and induction by pregnancy ($P < 0.05$). Upper lip occurrence was associated to more recent cases ($P < 0.05$).

Discussion

In this sample, facial melasma was common in middle-aged woman with intermediate skin phototypes. A high familiar disease frequency was reported, and topographical exploration of co-occurrences revealed two main facial clinical patterns: centrofacial and peripheral.

Despite the high frequency of melasma in dermatological patients, there are few epidemiological studies with representative samples. Also, disease characteristics in different populations can vary according to genetic and environmental aspects.[14] Far Eastern and Latin people, and pregnant women are the best studied groups, as melasma rarely affects patients with lower skin phototypes and frequently occurs or worsens during pregnancy.[8,18,29,30]

Several series of cases, in different ethnic groups have emphasized female involvement (9 : 1) during childbearing age.[4,8,31] Reports of rare melasma findings in Andean children strengthen the adult profile and add weight to photoexposure as a major risk factor.[29] In our study, the higher levels of disease onset between the second and fourth decades corroborate findings in literature and suggest a possible hormonal relationship in its pathophysiology.[32–35]

In studies on idiopathic melasma, Sacre *et al.* found normal thyroid hormonal levels, prolactinic and gonadotrophic stores in their patients. The abnormal TSH and cortisol levels in our study did not indicate they were major endocrinological factors, as the observed alterations were similar to subclinical disease frequencies in the adult female population.[28,36]

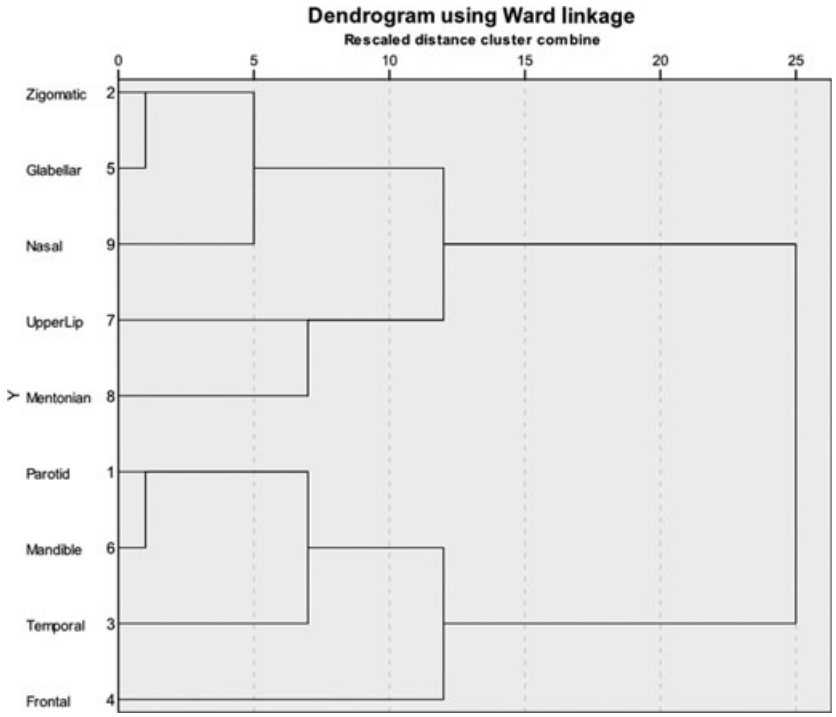

Figure 2 Dendrogram revealing two main co-occurrence patterns for melasma facial lesions.

Intense sun exposure induced melasma has been associated to abnormal TSH levels. Lutfi *et al.* found a higher prevalence of thyroid autoimmunity in melasma patients, but they did not stratify prevalence by melasma cause.[32] The role of anomalous TSH in sun exposure developed melasma should be investigated by further studies.

Exogenous sexual steroids have been implicated as melasma triggers, and for being specifically responsible for its later appearance, masculine cases and extrafacial topography.[5,37–41]

Oral contraceptive pills and pregnancy are classically reported triggers of the disease. Moreover, we found that higher cortisol levels were also associated to hormonal induced melasmas, strengthening the endocrine origin hypothesis.[42] Whilst persisting indefinitely in only one third of pregnant melasma patients,[15,43] when induced by oral contraceptive pills it does not tend to disappear after pill suspension.[29,44] Our study revealed that pregnancy induced melasma began earlier and was more common in those who have had multiple pregnancies, corroborating Ortonne *et al.*[15]

The effects of estrogen and progesterone in melanogenesis have been reported by many authors.[37,45,46] Pregnancy and oral contraceptives pills were disease triggering factors in more than 50% of cases in our study.[21,46,47]

First degree family history occurred in more than 45% of cases, supporting genetic factors as important in developing melasma.[13,29,48] In our analysis, more than half the patients reported some family member with melasma, although these data must be carefully interpreted considering memory bias and also the association between family linkage and having lived on a farm or by the sea. Patients who reported positive family history also had longer disease duration, suggesting a genetic predisposition to a disease sustaining factor.

Melasma prevalence was higher in intermediate skin phototypes (Fitzpatrick scale III, IV and V). The low incidence of melasma in extreme skin phototypes suggests some stability or homogeneity in ultraviolet (UV) reaction regarding their pigmentation system.[10]

Areas affected by melasma have intense melanogenesis, more efficient citocrinic activity (melanosome transference), and mature melanosome transportation with greater proportion of eumelanin, simulating a localized higher skin phototype. This argument is strengthened by increased melasma frequency in Latin and Asian phenotypes, as opposed to a lower frequency in Caucasian and African peoples.[8,15,31,49] Our data also showed that the highest phototypes have the oldest disease onset ages, substantiating melanin UV protection in melasma development.

Unprotected UV radiation exposure is supposed to be the most important environmental triggering factor in clinical issues of melasma.[4,44] This could also be seen in our sample due to the predominant centrofacial location of lesions and a study reporting more than 25% melasma onsets after intense sun exposure.[50] Another Brazilian study also found this centrofacial predominance.[51]

The clinical classification of melasma is a theme that must be better assessed with proper methodological designs. Although

evident by Woods lamp examination, the division between dermal and epidermal does not have histopathological support, besides being related to treatment resistance.[6,8,51,52] Categorization into facial and extra-facial types is simple, but reductionistic, and does not give value to the many clinical presentations on the face, or other associations. Their designation as centrofacial, malar and mandibular does not take into account the peripheral and combined forms.[3,4,34] Our study identified a predominance of central melasma, with a higher frequency in the centrofacial regions.

There was no evidence to support an exclusively mandibular classification, as suggested by some authors.[53] In fact, 64.8% of mandibular incidence co-occurred with parotid topography, and just two cases (3.7%) presented solely with mandibular lesions.

The main limitations of this study are related to the evaluation of patients under dermatological treatment and the possibility that treatment and length of time modify clinical patterns of the disease. Furthermore, the possibility of memory bias regarding familiar history and triggers should be considered. Finally, this study was a sample of women attending a public dermatology service and cannot therefore be representative of all Brazilian women.

Conclusions

We characterized a sample of Brazilian women with facial melasma. The main findings were disease onset at childbearing age, high reported frequency of familiar disease, intermediate skin phototypes and precipitation by hormonal stimuli. The co-occurrence of facial topographies supported a clinical classification of centrofacial and peripheral melasma.

Author contribution

Luciane, Hélio, Márcia and Mariângela contributed to project ideation; Andréia, Luciane, Hélio, Camila and Tatiana performed data collection/tabulation and text elaboration; Hélio, Camila and Tatiana analyzed the data; Andréia, Luciane, Hélio, Camila, Tatiana and Mariângela revised and approved the text.

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