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ORIGINAL ARTICLE

Assessment of metabolic syndrome in patients diagnosed with melasma in a dermatology service

Avaliação de síndrome metabólica em pacientes diagnosticados com melasma em um serviço de dermatologia

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Abstract

Objectives: The aim of this study was to evaluate the prevalence of metabolic syndrome (MetS) criteria in patients diagnosed with melasma. Few studies have evaluated metabolic parameters in patients with melasma, a chronic inflammatory skin condition. MetS is a complex disease represented by a set of factors related to central fat deposition and insulin resistance. There is an increased cardiovascular risk in individuals with this syndrome, and several studies seek to establish correlations between MetS and other inflammatory diseases such as psoriasis, hidradenitis suppurativa, lichen planus, vitiligo, and atopic dermatitis. **Methods:** Cross-sectional prevalence study assessing MetS in participants diagnosed with melasma between July and October 2024. **Results**: Fifty-eight women were included in the study, with a mean age of 46.7 years and a mean melasma duration of 10.5 years. 29.3% of the participants met three or more criteria for MetS. **Conclusion:** There was a considerable prevalence of MetS among the study participants. Although this association does not prove causality, it suggests the importance of considering metabolic factors in the clinical management of melasma and in the prevention of complications related to MetS.

Keywords: Melasma. Metabolic syndrome. Obesity.

Resumo

Objetivos: O objetivo deste estudo foi avaliar a prevalência dos critérios da síndrome metabólica (SM) em pacientes diagnosticados com melasma. Poucos estudos avaliaram parâmetros metabólicos em pacientes com melasma, uma condição inflamatória e crônica da pele. A SM é uma doença complexa representada por um conjunto de fatores relacionados à deposição central de gordura e resistência à insulina. Há um risco cardiovascular aumentado em indivíduos com essa síndrome, e vários estudos buscam estabelecer correlações entre a SM e outras doenças inflamatórias como psoríase, hidradenite supurativa, líquen plano, vitiligo e dermatite atópica. **Métodos:** Estudo transversal de prevalência avaliando síndrome metabólica em participantes diagnosticados com melasma entre julho e outubro de 2024. **Resultados:** 58 mulheres foram incluídas no estudo com idade média de 46,7 anos e tempo de evolução do melasma de 10,5 anos. 29,3% dos participantes apresentaram três ou mais critérios para síndrome metabólica. **Conclusão:** Houve considerável prevalência de SM entre as participantes do estudo, embora esta associação não comprove causalidade, sugere a importância de considerar os fatores metabólicos no manejo clínico do melasma e para a prevenção de complicações relacionadas à síndrome metabólica.

Palavras-chave: Melasma. Síndrome metabólica. Obesidade.

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Introduction

Melasma is a chronic, acquired pigmentation condition that predominantly affects women, accounting for 90% of cases. All ethnicities are affected, especially those with skin Types IV and V[1]. Although various factors are implicated in its pathogenesis, melasma has recently been considered a chronic inflammatory disease. The skin affected by the lesions, when compared to unaffected skin, shows significant inflammatory infiltration, epidermal atrophy, degeneration of the basal layer, solar elastosis, and disorganization of collagen fibers[1-3].

Metabolic syndrome (MetS) is a complex disorder represented by a combination of factors related to central fat deposition and insulin resistance. Individuals with this syndrome have an increased cardiovascular risk compared to the general population. Due to its growing prevalence, several studies have sought to establish correlations between MetS and other inflammatory diseases or immune-related conditions. In dermatological disorders, the presence of acanthosis nigricans, as well as diseases such as psoriasis, hidradenitis suppurativa, lichen planus, vitiligo, and atopic dermatitis, have been shown to be associated with MetS[4].

Despite the lack of an obvious correlation so far, MetS shares common pathological pathways with melasma, which is why this study aimed to assess the presence of MetS in patients with melasma.

Methods

Study design and patient selection

A cross-sectional prevalence study was conducted at the dermatology department of the University of Mogi das Cruzes between July 2024 and October 2024. A total of 58 female participants, aged over 18 years with a clinical diagnosis of melasma, were included in the study. The exclusion criteria were: (1) pregnant or postpartum women; (2) participants with edema of any nature, due to interference with body evaluation; (3) individuals with severe dermatological conditions (autoimmune, hereditary, or acquired) that could interfere with the clinical assessment of melasma. The study was approved by the Ethics Committee of the University of Mogi das Cruzes, and all patients signed the informed consent form.

Participants were assessed for age, skin phototype, duration of melasma, comorbidities, and laboratory test results, including fasting blood glucose levels, high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC), triglycerides (TG), glycated hemoglobin (HbA1C), and insulin levels. In addition, blood pressure, abdominal waist circumference, weight, height, and body mass index (BMI) were measured. MetS was defined according to the criteria established by the National Cholesterol Education Program = Adult Treatment Panel III[5], which includes the presence of three or more of the following components: elevated abdominal circumference (≥ 102 cm in men and ≥ 88 cm in women), elevated blood pressure (≥ 130/85 mmHg or on antihypertensive treatment), elevated TG (≥ 150 mg/dL or on treatment for hypertriglyceridemia), low HDL cholesterol levels (< 40 mg/dL in men and < 50 mg/dL in women), and elevated fasting glucose levels (≥ 100 mg/dL or on treatment for diabetes). The presence of three or more of these criteria was considered as fulfilling the criteria for MetS[5].

Statistical analysis

The exploratory data analysis included descriptive statistics, such as mean, standard deviation, median, minimum value, and maximum value for numerical variables, and frequency and proportion for categorical variables. For the analysis of continuous variables, descriptive statistics were considered, along with the Shapiro-Wilk test to assess the assumption of normality. The prevalence of MetS was analyzed using the Clopper-Pearson method (Altman, 2000), with the epiR package (Stevenson and Sergeant, 2024). Statistical analysis was performed using the R programming language (R Core Team, 2024).

Results

Clinical characteristics

The clinical characteristics of the participants are shown in table 1. The sample consisted of 58 women, with a mean age of 46.7 years and a mean melasma duration of 10.5 years. The mean levels of HDL, TG, fasting glucose, and TC were 54.9 mg/dL, 121 mg/dL, 91.8 mg/dL, and 193.2 mg/dL, respectively. The mean HbA1C was 5.4%, while the insulin levels and homeostasis model assessment of insulin resistance (HOMA-IR) were 10.9 μU/mL and 1.2, respectively. Regarding body composition, the mean BMI was 26.7, waist circumference was 87.6 cm, and the mean systolic blood pressure and diastolic blood pressure were 120.5 mmHg and 79.07 mmHg, respectively.

Table 1. Descriptive statistics of variables according to the presence or absence of metabolic syndrome

Variables	MetS negative (< 3 criteria for MetS) n = 41	MetS positive (≥ 3 criteria for MetS) n = 17
Age	45.4 ± 9.3	49.9 ± 10.0
WC	83.6 ± 10.0	97.1 ± 8.1
SBP	117.0 (95.0-130.0)	130.0 (120.0-160.0)
DPB	75.0 (63.0-100.0)	85.0 (80.0-104.0)
HDL	54.0 (44.0-109.0)	43.0 (31.0-91.0)
TG	93.0 (43.0-183.0)	196.0 (95.0-303.0)
Fasting glucose	89.0 (72.0-142.0)	100.0 (87.0-130.0)
LDL	106.0 (70.0-197.0)	118.0 (72.0-219.0)
TC	183.0 (136.0-288.0)	200.0 (142.0-307.0)
Weight	70.8 ± 10.7	78.9 ± 11.1
Height	1.63 ± 0.06	1.61 ± 0.08
BMI	26.1 ± 3.1	29.7 ± 2.7
HBA1C	5.4 (4.7-6.7)	5.7 (5.1-5.8)
Insulin	8.88 ± 4.85	18.87 ± 9.97
HOMA-IR	1.5 (0.6-4.8)	2.6 (2.3-9.3)
Evolution time of melasma	6.0 (1.0-28)	5.0 (2.0-30.0)
Skin phototype II	11 (27)	2 (12)
Skin phototype III	17 (41)	8 (47)
Skin phototype IV	12 (29)	7 (41)
Skin phototype V	1 (2)	0 (0)

WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; TG: triglycerides; LDL: low-density lipoprotein; TC: total cholesterol; BMI: body mass index; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance. Continuous variables are described as mean ± standard deviation or median (minimum-maximum); categorical variables are described as number (percentage).

Components of metabolic syndrome

The estimated prevalence of MetS was 29.3%, with a standard error of 0.0598. The 95% confidence interval, ranged from 19.2% (lower limit) to 42.0% (upper limit).

Discussion

Few studies have assessed metabolic parameters in patients with melasma. In the study by Karaali[6], which compared 51 patients with melasma to 44 patients without the condition, MetS was more frequent in patients with melasma compared to the control group, although the author did not find statistical significance in his study. In our prevalence assessment, 29.3% of the participants had three or more criteria for MetS, however, 74% of the evaluated participants were overweight or obese, 53.4% had a waist circumference ≥ 88 cm, 18.9% presented altered fasting glucose and 25.8% alterations in HbA1c levels.

Ghassemi et al.[7] in a case-control study evaluating the lipid profile and fatty liver in patients with melasma, found significantly higher LDL levels (104.23 ± 25.00 mg/dL) in patients with melasma compared to the control group (89.85 ± 23.00 mg/dL, p = 0.020). In our assessment, the median fLDL was 106 mg/dL among patients without MetS and 118 mg/dL among patients with MetS. Regarding other lipid parameters, 39.6% of women had HDL levels < 50 mg/dL and 24.3% had TG > 150 mg/dL. A common pathway between MetS and melasma is the WNT signaling pathway, which plays a crucial role in various biological processes in the body. In MetS, studies have explored its relationship with body mass regulation, glucose metabolism, lipogenesis, and LDL clearance[8-10]. In melasma, the activation of the WNT receptor leads to the stabilization of β-catenin, which is translocated to the cell nucleus where it binds to transcription factors such as microphthalmia-associated transcription factor (MITF), stimulating the expression of genes involved in melanogenesis. Studies have also shown that the inhibitory factor of this pathway, known as Wnt-1 (WIF-1), is reduced in the skin affected by melasma. The negative regulation of WIF-1 promotes melanosome transfer, along with the expression of MITF and tyrosinase through the positive regulation of the WNT signaling pathway[10,11].

In obese patients, studies have observed higher rates of melanogenesis[12] and elevated levels of α-melanocyte-stimulating hormone, which binds to the melanocortin 1 receptor on human adipocytes and stimulates melanogenesis[13]. Moreover, adipose tissue is a key site for the peripheral production and metabolism of estrogens in women[14], and this hormone plays a role in the pathogenesis of melasma due to its effects on the skin through receptors, especially the ER2 receptor, which directly stimulates melanogenesis[3].

Regarding MetS, the most widely accepted theory of its pathophysiology is insulin resistance, in which an increase in adipose tissue plays an important role[4,15]. The accumulation of fat in MetS, along with the progressive development of insulin resistance, induces a cascade of hormonal changes. As such, when it comes to skin diseases, it is known that

conditions influenced by these changes, such as acne and androgenetic alopecia, may experience clinical worsening[4]. Although we did not find a significant difference, the group of participants with MetS had higher levels of insulin (18.87 ± 9.97) and HOMA-IR: 2.6 (2.3-9.3) compared to those who did not meet all the criteria for MetS. Regarding the evolution time of melasma in participants with MetS versus without MetS, the median melasma evolution time was 5 years (ranging from 2 to 30 years) and 6 years (ranging from 1 to 28 years), respectively, and there was no statistically significant difference between the two groups (p = 0.738). Similarly, the median age was 44 years (27-68 years) and 47 years (34-68 years) among patients without and with MetS (p = 0.139).

Thus, although there is no clear correlation between the two diseases, several common mechanisms are present in both conditions. Understanding these mechanisms and the potential associations of melasma with other conditions opens new perspectives for the development of more effective therapies for its treatment.

Conclusion

Despite the methodological limitations in a cross-sectional study with a limited sample size, the results demonstrate a considerable prevalence of MetS among the participants. This prevalence justifies the need for prospective studies with control groups to investigate causality and the mechanisms involved in this association. Although this association does not prove causality, it suggests the importance of considering metabolic factors in the clinical management of melasma and in the prevention of complications related to MetS.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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