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Research Article

The Association Between Melasma and Thyroid Dysfunction: A Case-Control Study

Noor-Aldeen Jamal Hasan Al-Ansare*, Tin Htay Khine
Faculty of Medicine, Lincoln University College, Selangor, Malaysia

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Abstract

Background: Melasma is a common pigmentary disorder predominantly affecting women. Thyroid hormones influence skin homeostasis and melanocyte activity, suggesting a possible link with melasma. ***Objective***: To investigate the relationship between thyroid hormone levels and melasma in women. ***Methods***: A case-control study was conducted with 100 women aged 18–45 years, including 50 patients with melasma and 50 healthy controls. Free triiodothyronine (T3), free thyroxine (T4), and thyroid-stimulating hormone (TSH) levels in the blood were evaluated in both the clinic and the lab. ***Results***: Women with melasma were significantly older than controls (p=0.001). Compared to controls, melasma patients had lower median free T3 [3.0 (2.6–3.6) *vs*. 3.3 (3.2–3.5); p=0.02] and free T4 [1.3 (1.1–1.5) *vs*. 1.4 (1.3–1.4); p=0.001] and higher TSH levels [3.7 (2.8–4.2) *vs*. 2.2 (1.9–2.5); p=0.001]. These differences remained significant after adjusting for age. Overt thyroid dysfunction was uncommon and not significantly different between groups (p=0.35). ***Conclusions***: Subclinical alterations in thyroid hormones may be associated with melasma in women, independent of age, although causation cannot be established.

Keywords: Endocrine dysfunction; Free T4; Melasma; Pigmentation; Thyroid hormones; TSH.

العلاقة بين الكلف وخلل الغدة الدرقية: دراسة حالة وشاهد

الخلاصة

الخلفية: الكلف هو اضطراب صبغي شائع يصيب النساء بشكل رئيسي. تؤثر هرمونات الغدة الدرقية على توازن الجلد ونشاط الخلايا الصبغية، مما يشير إلى وجود ارتباط محتمل بالكلف. **الهدف**: دراسة العلاقة بين مستويات هرمون الغدة الدرقية والميلاسم لدى النساء. **الطرائق**: أجريت دراسة حالة وشاهد على 100 امرأة تتراوح أعمارهن بين 18 و45 عاما، بما في ذلك 50 مريضا مصابين بالكلف و50 ضابطا صحيا. تم تقييم مستويات الثلاثي يودوثيرونين الحر (T3)، والثيروكسين الحر (T4)، والهرمون المحفز للغدة الدرقية (TSH) في الدم في كل من العيادة والمختبر. **النتائج**: كانت النساء المصابات بالكلف أكبر سنا بشكل ملحوظ من عدد الضوابط (p=0.001). مقارنة بالمجموعات الضابطة، كان لدى مرضى الكلفا متوسط T3 حر أقل [3.0 (2.6-3.6) مقابل 3.3 (3.2-3.5)؛ p=0.02] وT4 الحر [1.3 (1.1-1.5) مقابل 1.4 (1.3-1.4)؛ p=0.001] ومستويات أعلى من TSH [3.7 (2.8-4.2) مقابل 2.2 (1.9-2.5); p=0.001]. ظلت هذه الفروقات ذات دلالة كبيرة بعد تعديل العمر. كان خلل الغدة الدرقية الظاهر غير شائع ولم يكن مختلفا بشكل ملحوظ بين المجموعات (p=0.35). ***الاستنتاجات***: قد ترتبط التغيرات تحت السريرية في هرمونات الغدة الدرقية بالكلف لدى النساء، بغض النظر عن العمر، رغم أنه لا يمكن إثبات السببية.

* ***Corresponding author***: Noor-Aldeen J. H. Al-Ansare. Faculty of Medicine, Lincoln University College, Selangor, Malaysia; Email: alansarenoor@gmail.com

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INTRODUCTION

Melasma is a common acquired chronic skin disorder characterized by symmetric hyperpigmented macules and patches, primarily affecting the face. It occurs predominantly in women and is exacerbated by several factors such as ultraviolet (UV) radiation, hormonal changes, and genetic predisposition [1]. Although melasma is traditionally considered a cosmetic condition, the growing evidence suggests that melasma may also reflect underlying systemic health conditions, including endocrine and autoimmune disorders [2]. Thyroid dysfunctions, including hypothyroidism, hyperthyroidism, and autoimmune thyroid disorders, significantly affect various physiological systems, including the skin [3]. The thyroid gland hormones regulate numerous metabolic and dermatological processes. Abnormal thyroid function has been linked to dermatological manifestations such as alopecia, vitiligo, and hyperpigmentation. Notably, more melanocyte activity is seen in people with hypothyroidism, which may lead to pigmentation disorders. This means that thyroid dysfunction could play a role in the development of melasma [4]. Several studies have attempted to prove the association between melasma and thyroid dysfunction. For instance, they found that hypothyroidism may be more prevalent in individuals with melasma than in the general population. Furthermore, oxidative stress and chronic inflammation common to both melasma and thyroid dysfunction suggest shared pathophysiological pathways. Reactive oxygen species (ROS), for example, hurt melanocytes and mess up skin homeostasis, which could mean that thyroid problems are connected to the cause of melasma [5–7]. In clinical practice, the possibility of an association between melasma and thyroid dysfunction could have significant implications for early diagnosis and treatment. Identifying thyroid abnormalities early in melasma patients may provide opportunities for more

patient care, addressing both dermatological and endocrinological systemic aspects of their health [8]. However, the evidence supporting this connection is limited, as many studies have been small-scale or lacked comprehensive analysis of thyroid function markers. So, this study seeks to fill this knowledge gap by investigating the correlation between melasma and thyroid dysfunction through detailed evaluation of thyroid hormone levels and by comparing these markers in women with and without melasma. Although some studies have explored the relationship between melasma and thyroid function, the results remain inconsistent, largely due to the lack of appropriate control groups, as many reports investigated melasma patients alone without comparison to healthy controls. Therefore, this study aimed to evaluate the association between melasma and thyroid hormone levels in a case–control setting. This study adds to existing literature by addressing previous limitations through the inclusion of an appropriate control group and by distinguishing between biochemical thyroid hormone alterations and clinically diagnosed thyroid dysfunction.

METHODS

Study design and settings and ethics

This was an observational case-control study that included 100 female patients who attended a private outpatient clinic of dermatology, venereology, and sexually transmitted diseases in Wasit governorate of Iraq in the period from November 2024 to May 2025. The study adhered to the ethical principles outlined in the Helsinki Declaration, with ethical approval obtained from the Lincoln University College Ethical Committee as the authors affiliated academic institution in November 2024. Administrative permission (gatekeeper approval) letter to conduct the study and access medical records was obtained from the supervising dermatologist at the recruitment site in Wasit. This was a case control study, and the blood tests were performed as non-interventional diagnostic investigations for study purposes, which means the routine blood tests were requested by the treating physician to study the current outpatient general condition before starting the treatment plan and documented within the patients' medical records; the results were subsequently used for statistical analysis in the present study without requesting any additional laboratory tests. The study population was divided into two groups: 50 women clinically diagnosed with melasma and 50 women serving as controls. All participants provided written informed consent, and no therapeutic intervention was involved in our study.

Inclusion criteria

The inclusion criteria were: 1) Female patients aged 18–45 years; 2) diagnosed with melasma based on clinical evaluation and confirmed by dermatological examination; 3) patients willing to participate and provide informed consent; 4) Controls (non-melasma group) were matched to cases for sex and systemic health conditions and were selected to approximate the age distribution; 5) patients with no history of thyroid-related medical treatment in the past year (for both groups).

Exclusion criteria

The exclusion criteria were: 1) male patients; 2) patients with a history of other pigmentation disorders such as vitiligo or post-inflammatory hyperpigmentation; 3) pregnant women; 4) women who had taken medications influencing thyroid hormone levels within the previous six months. 5) Patients who have any type of cancer.

Data collection

Detailed history was obtained from all participants and included various demographic and lifestyle factors. These comprised age, marital status, and occupation. A thorough inquiry was made into any family history of melasma or thyroid dysfunction. The extent of sun exposure was also assessed, alongside the use of facial cosmetics, as both are known contributing factors in melasma development. A general clinical examination was performed for all participants to assess their overall health status and to exclude any systemic illness that might affect the study parameters.

Melasma assessment

The mMASI scoring was used to assess the area and degree of pigmentation of melasma lesions. The area parameter and the degree of pigmentation parameter were assessed at four face locations: on the forehead, left and right (malar) cheeks, and chin. The measurement of Melasma of the face was calculated in the following way:

mMASI Scoring Criteria: Area Scoring: 0 = No involvement, 1 = Less than 10%, 2 = 10% - 29%, 3 = 30% - 49%, 4 = 50% - 69%, 5 = 70% - 89%, 6 = 90% - 100%.

Darkness Scoring: 0 = Absent, 1 = Slight (light brown), 2 = Mild (dark brown), 3 = Marked (grey or blue), 4 = Severe (black).

Total mMASI score calculation

The total score was calculated by adding the results of the area and darkness scores for each of the four facial areas (forehead, right cheek, left cheek, chin). For the mMASI score calculation, the scores for each area were calculated as follows: Forehead score: Area score × Darkness score × 0.3. Right Cheek score: Area score × Darkness score × 0.3. Left Cheek score: Area score × Darkness score × 0.3. Chin score: Area score × Darkness score × 0.1. The total mMASI score was the sum of the scores from all four areas, and this number was used to measure and decide the intensity of melasma based on modified MASI criteria (0-8 mild, 9-16 moderate, and 17-24 severe) [9,10].

Blood samples

As part of routine clinical care, the treating physician requested the collection of blood samples under sterile conditions. Plain tubes were used for serum collection to measure TSH, FT3, and FT4. Serum levels of TSH, FT3, and FT4 were measured using a Mindray CL-6000i automated chemiluminescence immunoassay analyzer (Mindray Bio-Medical Electronics, Shenzhen, China) with manufacturer-provided reagent kits at a certified local laboratory. Thyroid function parameters were reported in standard units: free T3 (pg/mL), free T4 (ng/dL), and thyroid-stimulating hormone (TSH, µIU/mL). According to the laboratory reference ranges, normal values were defined as follows: Free T3: 2.0–4.4 pg/mL, Free T4: 0.8–1.8 ng/dL, and TSH: 0.35–5.0 µIU/mL. Subclinical hypothyroidism was defined as elevated TSH with normal FT4 levels, while overt hypothyroidism was defined as elevated TSH with reduced FT4 levels, in accordance with laboratory reference standards. According to standard operating protocols, the laboratory routinely applied internal quality control procedures.

Primary outcome measures

The primary outcome measures included assessment of thyroid function through serum levels of free T3, free T4, and TSH. Melasma severity was quantitatively assessed using the mMASI score. A key outcome of the study was the analysis of potential correlations between thyroid function parameters and melasma severity. The study aimed to determine whether abnormalities in thyroid hormones were significantly associated with more severe forms of melasma.

Secondary outcome measures

Secondary outcomes involved analyzing demographic and lifestyle-related factors. This included age, family history of melasma, degree of sun exposure, and usage of facial cosmetics. A comparison was made between cases and controls to identify any statistically significant differences that might influence melasma risk or severity.

Statistical analysis

Statistical analysis was conducted using SPSS software, version 26 (IBM, Chicago, IL, USA). Data normality was assessed via the Kolmogorov-Smirnov test. Categorical variables were expressed as frequencies and percentages and analyzed using the Chi-square or Fisher's exact test. Continuous variables were reported as mean ± standard deviation for normally distributed data and median (interquartile range) for non-normally distributed data. Comparisons were made using the independent t-test or Mann-Whitney U test. A p-value < 0.05 was considered statistically significant. Because age differed between the groups, we took this into account when interpreting the correlations to avoid misleading results and to minimize its potential confounding effect.

RESULTS

The median (IQR) age of the studied participants was 36 (29 – 41) years, with a range of 19 – 45, which was significantly higher in cases [39 (33.5 – 43)] than in controls [31.5 (25.7 – 39)] (p= 0.001). Most of the cases (42%) were in the age category of 31–40 years; however, most of the control (40%) were in the age category of 20–30 years (p= 0.07) (Table 1).

Table 1: Demographic data of the participants

Variables	Total (n=100)	Cases (n=50)	Control (n=50)	*p*-value
Age (year)				
Median (IQR)	36(29-41)	39(33.5-43)	31.5(25.7-39)	0.001*[a]
Range	19-45	19-45	19-45	
Age category				
<20	2(2)	1(2)	1(2)	
20 – 30	29(29)	9(18)	20(40)	0.07[b]
31 – 40	40(40)	21(42)	19(38)	
41 – 50	29(29)	19(38)	10(20)	
Gender				
Females	100(100)	50(100)	50(100)	-
Males	0(0)	0(0)	0(0)	

Values are presented as frequency, percentage, and range. [a] Mann-Whitney U test, [b] Chi-square test.

Table 2: Clinical data of the participants

Variables	Total (n=100)	Cases (n=50)	Control (n=50)	*p*-value
Family history of melasma				
Yes	11(11)	10(20)	1(2)	0.001*[a]
No	89(89)	40(80)	49(98)	
Fascial Cosmetics				
Yes	76(76)	50(100)	26(52)	0.001*[a]
No	24(24)	0(0)	24(48)	
Sun protection				
Yes	0(0)	0(0)	0(0)	-
No	100(100)	50(100)	50(100)	

Values are expressed as frequency and percentage. [a] Fisher exact test.

As regards the family history of melasma, we reported 11% of the cases with a positive family history of melasma [10 cases (20%) and 1 control (2%)] (p= 0.001). According to the usage of facial cosmetics, all cases had used the facial cosmetics versus 26 (52%) from the control (p= 0.001) (Table 2). In terms of the site of melasma, it was distributed all over the face (Centro-fascial, malar, and mandibular) in 100% of the cases. As regards the thyroid profile of the studied participants, the median (IQR) of the free T3 in the cases was 3 (2.6–3.6), which was significantly lower than that of the control, 3.3 (3.2–3.5) (p= 0.02). The median free T4 was also significantly lower in the cases than in the control [1.3 (1.1–1.5) *vs.* 1.4 (1.3–1.4), respectively] (p= 0.001). However, the TSH was higher in cases than in controls [3.7 (2.8–4.2) *vs* 2.2 (1.9–2.5), respectively] (p= 0.001) (Table 3).

Table 3: Thyroid profile of the studied participants

Variables	Total (n=100)	Cases (n=50)	Control (n=50)	p-value[a]
Free T3 pg/ml				
Median (IQR)	3.3(3-3.5)	3(2.6-3.6)	3.3 (3.2-3.5)	0.02
Range	0.5-4.1	0.5-4.1	2.2-3.9	
Free T4 ng/dl				
Median (IQR)	1.4(1.2-1.4)	1.3(1.1-1.5)	1.4(1.3-1.4)	0.001
Range	0.1-1.6	0.1-1.6	0.9-1.5	
TSH uIU/ml				
Median (IQR)	2.6(2.1-3.7)	3.7(2.8-4.2)	2.2(1.9-2.5)	0.001
Range	1.1-71.5	1.1-71.5	1.1-5.4	

[a] Mann-Whitney U test.

Thyroid dysfunction was comparable between the cases and control (p= 0.35), in which 3 cases (6%) and one control (2%) were diagnosed as subclinical hypothyroidism, and only one case (2%) was diagnosed as hypothyroidism. No cases of hyperthyroidism were reported in our study. Even though the individuals with melasma are showing 4 times more likely to have thyroid dysfunction than those without melasma OR= 4, 95% CI [0.45 - 39.5]), on the other hand, we cannot claim patients are 4 times more likely when the lower bound is 0.45 (meaning they could be less likely), so this is considered a non-significant finding. Although the odds ratio was numerically elevated (OR=4), at the same time, on the other hand, we have the wide 95% CI (0.45–39.5) crossing 1.0, indicating that this association is not statistically significant, and no statistically significant difference in the diagnosis of thyroid dysfunction was observed between melasma cases and controls (p= 0.35), indicating the absence of a significant association at the categorical diagnostic level, most probably due to our small sample size of patients (Table 4).

Table 4: Prevalence of thyroid dysfunction between melasma and control

Variables	Total (n=100)	Cases (n=50)	Control (n=50)	p-value[a]
Normal	95 (95)	46 (92)	49 (98)	0.35
Subclinical Hypo	4 (4)	3 (6)	1 (2)	
Hypothyroidism	1 (1)	1 (2)	0 (0)	
Hyperthyroidism	0 (0)	0 (0)	0 (0)	

Values are expressed as frequency and percentage. [a] Chi-square test.

The melasma severity was evaluated by the mMASI. The median (IQR) mMASI was 13.5 (13–14.2), with a range of 9–15.3. All cases were categorized as moderate melasma. The correlation between the mMASI and free T4 (r= -0.2, p= 0.02). A statistically significant positive correlation was found between mMASI and the following: TSH (r=0.6, p= 0.001), and age (r=0.3, p= 0.001) (Table 5).

Table 5: Spearman's correlation analysis between the mMASI and the thyroid parameters and age

Variables	mMASI	
	r	p-value
Free T3 pg/ml	-0.14	0.16
Free T4 ng/dl	-0.2	0.02
TSH uIU/ml	0.6	0.001
Age	0.3	0.001

All melasma cases were categorized as moderate melasma (mMASI > 9), with no statistically significant correlation between thyroid dysfunction and the mMASI (p= 0.6). However, a statistically significant correlation was found between the mMASI and the age category. By comparing the age categories in terms of the mMASI, we found that the median (IQR) mMASI was higher in the age category of 41–50 and the age category of 31–40 than the other two age categories (p= 0.001 for all participants and 0.05 for cases) (Tables 6 and 7, respectively). Table 6 includes both melasma cases and healthy controls (n= 100); therefore, mMASI values of 0 reflect the absence of melasma among control participants.

Table 6: Correlation between the mMASI and the participant's age (n=100)

Variables	<20	20-30	31-40	41-50	p-value[a]
Median	5.4	0	12.4	13.3	0.01
(IQR)	(0)	(0-12.4)	(0-13.4)	(0-14.2)	
Range	0-10.8	0-14.3	0-14.2	0-15.3	

[a] Kruskal Wallis test.

Regarding age binning in Tables 1, 6, and 7, age categories were presented in 10-year intervals; the 41–50 category includes participants aged 41–45 years only, in accordance with the study inclusion criteria (≤ 45 years).

Table 7: Correlation between the mMASI and the patient's age

Variables	<20	20-30	31-40	41-50	*p*-value[a]
Median	-	13.2	13.4	14.2	0.05
(IQR)		(12.4-14.1)	(13-14)	(13.3-14.3)	
Range	-	12-14	12.3-14.2	9-15.3	

[a] Kruskal Wallis test.

After age was taken into account, multivariate binary logistic regression analysis was used to look at the independent link between thyroid hormone parameters and melasma. The analysis demonstrated that TSH was the only independent predictor of melasma, with higher TSH levels being significantly associated with increased odds of the disease (OR= 0.257, 95% CI: 0.135–0.488, $p< 0.001$). Age did not show a significant independent association with melasma ($p= 0.363$), indicating that the observed differences in thyroid function between cases and controls were not attributable to age alone. Similarly, free T3 and free T4 levels were not independently associated with melasma after adjustment, suggesting that their effects may be mediated through TSH regulation rather than direct hormonal influence (Table 8).

Table 8: Binary logistic regression analysis for predictors of melasma Dependent variable

Variable	β coefficient	SE	OR	95% CI	*p*-value
Age (year)	−0.033	0.037	0.967	0.900 – 1.039	0.363
Free T3 (pg/ml)	0.425	0.706	1.529	0.383 – 6.102	0.547
Free T4 (ng/dl)	1.957	1.826	7.076	0.197 – 253.790	0.284
TSH (µIU/ml)	−1.359	0.327	0.257	0.135 – 0.488	<0.001

DISCUSSION

A total number of 100 females were included in this case-control study. They were divided into 50 melasma cases and 50 non-melasma controls. Although controls were recruited within the same age range, perfect age matching was not achieved. Therefore, age was treated as a potential confounder and was adjusted for in multivariate analysis. Binary logistic regression analysis was performed to assess the independent association between thyroid hormone parameters and melasma after controlling for age. Understanding the correlation between melasma and thyroid dysfunction has significant clinical implications. For instance, recognizing thyroid dysfunction as a potential underlying factor in melasma may enhance the diagnostic process and treatment outcomes. Screening for thyroid abnormalities in melasma patients, especially those with treatment-resistant pigmentation or other symptoms of thyroid dysfunction, could lead to earlier diagnosis and management of thyroid conditions. Additionally, addressing thyroid imbalances may improve the efficacy of melasma treatments, such as topical agents, chemical peels, or laser therapy [7]. So, the aim of this study was to assess thyroid dysfunction and autoimmunity in melasma patients compared to controls. In this case-control study, involving 100 females divided into 50 melasma cases and 50 non-melasma controls, we observed several noteworthy findings that provide insights into the potential interplay between these two conditions. The median age of the studied participants was significantly higher in melasma cases than in controls, highlighting age as a potential risk factor for melasma. Most cases fell into the age group of 31–45 years, consistent with the literature that suggests melasma predominantly affects individuals in their reproductive years. The hormonal changes associated with this age group, including fluctuations in estrogen and progesterone levels, may contribute to the development of melasma. These hormonal changes can stimulate melanocytes, leading to increased melanin production and the development of melasma [11]. Another explanation for the prevalence of melasma in this age group is that by the age of 31–50, individuals have typically accumulated substantial sun exposure, which can trigger or exacerbate melasma in genetically predisposed individuals [12]. When age was taken into account as a possible confounding factor using multivariate binary logistic regression analysis, it was found that high TSH was the only factor that could independently predict melasma. Age, free T3, and free T4 did not have any statistical significance. This finding shows that the changes seen in melasma patients' thyroids aren't just caused by getting older; they also have a clear endocrine connection, with TSH being a better indicator of subclinical thyroid dysregulation than peripheral thyroid hormones. The fact that TSH is still a risk factor on its own supports the idea that a subtle imbalance in the thyroid axis, rather than overt thyroid disease, may play a role in melanocyte activation and the development of melasma. This finding helps explain why most of the people in this study who had melasma stayed clinically euthyroid despite having significant hormonal differences. It also shows how important it is to look at TSH elevations even when they are below the clinical threshold when evaluating melasma patients. Suman Babu and Sridevi Patil [13] had done a study similar to our study in sample size and aim. They found that the mean age of the melasma cases was 30.2 ± 3.4 years, which is consistent with our study findings. A significant proportion of melasma cases reported a positive family history compared to controls (20% of cases vs 2% of the control). This finding aligns with the existing literature that emphasizes genetic predisposition as a major contributor to melasma [14], including 312 melasma patients in their study, and found that 33.33% of the patients had a positive family history. A multinational survey involving 324 women found that 48% had a family history of melasma, with 97% of these cases occurring in first-degree relatives [15]. The universal use of facial cosmetics among melasma cases (100%) compared to controls (52%)

highlights the role of external factors, particularly the potential for cosmetic products to induce or exacerbate pigmentation through irritant or allergic mechanisms. In addition to sun exposure, prolonged use of facial cosmetics has been suggested as a contributing factor to melasma, particularly when products contain photosensitizing or irritant components. In the present study, cosmetic use was significantly more frequent among melasma cases; however, the specific types and ingredients of cosmetic products were not analyzed, and therefore a causal relationship cannot be established (Table 2**)**. In agreement with our study [16], we found that 67 melasma patients were assessed for cosmetic usage. Commonly used products included cold creams and skin moisturizers, medicated soaps, fairness creams, hair colors, facial bleach, and sunscreens. UV radiation exposure is a key triggering factor in melasma development, as it increases melanogenic activity, leading to epidermal pigmentation [17,14,23]. Previous studies have identified intense sun exposure as a trigger in 27.2% of patients [18]. In our study, 100% of patients reported no usage of sunscreens. As none of the participants reported using sunscreen, the effect of sun-protection practices could not be evaluated in this study. So, the talk about sun exposure is based on its known role in the development of melasma, not on differences seen in the study population (Table 2). Our study revealed significant differences in thyroid hormone levels between melasma cases and controls. Specifically, melasma cases exhibited lower levels of free T3 and free T4 and higher TSH levels. These findings suggest a potential association between thyroid function and melasma, as hypothyroidism and subclinical hypothyroidism were more prevalent among cases. Elevated TSH levels, a hallmark of hypothyroidism, have been implicated in increased melanocyte activity and melanin production, possibly through thyroid hormone receptors in melanocytes. Human melanocytes have been shown to have functional TSH receptors. TSH can stimulate these cells by making cAMP and starting up the MAPK pathway. This suggests that elevated TSH levels may directly influence melanocyte function and contribute to hyperpigmentation [19]. The pathophysiological interpretation of these findings requires considering the classical negative-feedback loop between TSH and thyroid hormones. In subclinical hypothyroidism, which is suggested by the pattern of low-normal free T4 with elevated TSH, the pituitary increases TSH secretion to compensate for marginal reductions in circulating T4 [20]. Elevated TSH exerts a direct melanogenic effect because human melanocytes express functional TSH receptors capable of activating cAMP and MAPK pathways [21]. Therefore, the hyperpigmentation seen in melasma could theoretically arise from reduced inhibitory influence of low-normal free T4 on melanocyte metabolism, as thyroxine normally down-regulates melanogenic enzyme activity, so when its levels fall toward the lower end of the normal range, melanocytes become more responsive to stimulatory signals, resulting in increased melanogenesis and contributing to melasma severity, and direct stimulation of melanocytes by elevated TSH [22]. This dual mechanism may explain why TSH correlated positively with the mMASI score. Although T3 and T4 levels were lower and TSH levels were higher in melasma cases compared to controls, most participants in both groups were clinically euthyroid. Only one case of hypothyroidism and three cases of subclinical hypothyroidism were observed in the melasma group, compared to one case of subclinical hypothyroidism in the control group. This indicates no statistically significant association between melasma and thyroid disorders, which may be attributed to the small sample size of our study. In a study by [23], which included 82 melasma cases and 40 controls, they found that the cases and controls were comparable in terms of T3 and T4. However, the TSH was significantly higher in cases than in controls, indicating that the thyroid dysfunction incidence was 5 times greater than in controls, which agreed with our findings. Evaluated the relationship between melasma and thyroid function parameters [23]. They included 102 melasma patients and 55 controls. Their results were relatively similar to ours, and they found that the level of T3 and T4 was normal in most cases without any significant correlation to the melasma type. However, they reported abnormal elevation of TSH in the melasma cases and reported a statistically significant association between hypothyroidism and melasma. The difference between our study and Talaee *et al*. study can be explained by their larger sample size, in which the statistically and clinically significant associations between the TSH and melasma had appeared. Similar to our study findings [24], reported a 23% incidence of melasma in patients with thyroid diseases. Evaluated the TSH and FT4 levels to identify potential thyroid abnormalities in melasma patients [25]. They reported no overt thyroid abnormalities were detected. Another notable study on the thyroid-melasma association reported a higher frequency of thyroid abnormalities in melasma patients (58.9%) compared to the control group [26]. However, the limited number of thyroid abnormality cases in our study (8%) prevented a direct comparison with Lutfi et al.'s findings. The high percentage of thyroid dysfunction in Lutfi *et al*.'s study may be attributed to that, they investigated the correlation between thyroid disorders and melasma, actively including participants with known thyroid abnormalities, which likely increased the prevalence in their sample [27]. The severity of melasma, as assessed by the mMASI, showed significant correlations with thyroid function markers. Notably, mMASI was negatively correlated with free T4 levels and positively correlated with TSH. These correlations suggest that thyroid dysfunction may exacerbate melasma severity. However, the lack of a statistically significant correlation between thyroid dysfunction and mMASI underscores the complexity of this relationship and indicates that other factors, such as genetic and environmental influences, may modulate the severity of melasma. Assessed the melasma using the mMASI score and found that mild and severe idiopathic melasma is associated with TSH disturbance, which is in agreement with our study findings [24]. The findings of this study have important clinical implications. Screening for thyroid

dysfunction in melasma patients, particularly those with treatment-resistant pigmentation, could facilitate early diagnosis and management of thyroid conditions. Addressing thyroid imbalances may improve the efficacy of melasma treatments, such as topical depigmenting agents, chemical peels, and laser therapy. Moreover, the association between melasma severity and thyroid dysfunction highlights the need for a multidisciplinary approach involving dermatologists and endocrinologists to optimize patient care. This study's strengths include its well-defined case-control design and comprehensive assessment of thyroid function and melasma severity. However, this study is limited by a relatively small sample size, which may limit the generalizability of the findings. Future longitudinal studies with larger cohorts are needed to elucidate the temporal relationship between melasma and thyroid dysfunction. The extreme TSH value observed (71.5 µIU/mL; Table 3) was reviewed in relation to the complete thyroid profile of the patient and was considered as a pathological finding consistent with overt hypothetical error, rather than an analytical error. Our findings do not demonstrate a statistically significant association between melasma and clinically diagnosed thyroid dysfunction (p= 0.35). Accordingly, causal language was avoided, and the results are interpreted as an association rather than a risk, consistent with the case–control study design. Controls (non-melasma group) were matched to cases for sex and systemic health conditions and were selected to approximate the age distribution. However, complete age matching could not be achieved, as reflected in the results section. Therefore, age was treated as a potential confounding factor and adjusted for in the multivariate binary logistic regression analysis. After adjustment, TSH remained the only independent predictor of melasma. The persistence of TSH as an independent predictor suggests that subtle dysregulation of the hypothalamic–pituitary–thyroid axis, rather than overt thyroid disease, may play a role in melasma pathogenesis. Only four participants had clinically diagnosed thyroid dysfunction, which limits categorical analyses based on diagnosis. With a larger sample size, a higher number of clinically diagnosed or subclinical thyroid dysfunction cases would be expected, allowing more robust categorical analyses; therefore, this represents a limitation of the study. Although all patients were classified as having moderate melasma, the numerical mMASI values showed sufficient within-category variability in severity (range: 9.0–15.3), and because the correlation analysis was performed using continuous mMASI scores, this variability was adequate to detect the observed associations.

Study Limitations

Nevertheless, incomplete age matching should be considered a limitation of the study. This study included only female participants to reduce biological heterogeneity related to sex hormones, as melasma predominantly affects women; however, this limits the generalizability of the findings to male patients and is also considered a limitation of our study.

Conclusion

Despite the differences in mean T3, T4, and TSH levels between cases and controls, thyroid dysfunction was rare, questioning its link to melasma. Although this study was not designed to recruit patients with thyroid disease and included a limited sample of melasma patients, incidental cases of thyroid disorders were observed in the melasma case group. Due to the small number of affected participants, the findings do not permit firm conclusions regarding a direct relationship.

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Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

REFERENCES

1. Basit H, Godse KV, Al Aboud AM. Melasma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459271/
2. Jo JY, Chae SJ, Ryu HJ. Update on melasma treatments. *Ann Dermatol*. 2024;36:125. doi: 10.5021/ad.23.133
3. Shahid MA, Ashraf MA, Sharma S. Physiology, thyroid hormone. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
4. Cohen B, Cadesky A, Jaggi S. Dermatologic manifestations of thyroid disease: a literature review. *Front Endocrinol (Lausanne)*. 2023;14:1167890. doi: 10.3389/fendo.2023.1167890.
5. Çakmak SK, Özcan N, Kılıç A, Koparal S, Artüz F, Çakmak A, Köse K. Etiopathogenetic factors, thyroid functions and thyroid autoimmunity in melasma patients. *Postepy Dermatol Alergol*. 2015;32(5):327-330. doi: 10.5114/pdia.2015.54742.
6. Rostami Mogaddam M, Iranparvar Alamdari M, Maleki N, Safavi Ardabili N, Abedkouhi S. Evaluation of autoimmune thyroid disease in melasma. *J Cosmet Dermatol*. 2015;14(2):167-171. doi: 10.1111/jocd.12138.
7. Kheradmand M, Afshari M, Damiani G, Abediankenari S, Moosazadeh M. Melasma and thyroid disorders: a systematic review and meta-analysis. *Int J Dermatol*. 2019;58(11):1231-1238. doi: 10.1111/ijd.14497.
8. Tekou A, Labbene I. Association of melasma with thyroid disorders. *Sch J Appl Med Sci*. 2023;11:1736–1742. doi: 10.36347/sjams.2023.v11i09.024.
9. Proietti I, Battilotti C, Svara F, Innocenzi C, Spagnoli A, Potenza C. Efficacy and tolerability of a microneedling device plus exosomes for treating melasma. *Appl Sci*. 2024;14(16):7252. doi: 10.3390/app14167252.
10. Al-Ansare NJH, Khine TH. The Relationship between melasma and thyroid dysfunction—analyzing anti-thyroid peroxidase antibody profiles: An immuno-dermatological perspective. Al-Rafidain J Med Sci. 2025;9(2):290- 295. doi: doi: 10.54133/ajms.v9i2.2558.
11. Espósito ACC, Cassiano DP, da Silva CN, Lima PB, Dias JAF, Hassun K, et al. Update on Melasma-Part I: Pathogenesis. *Dermatol Ther (Heidelb)*. 2022;12(9):1967-1988. doi: 10.1007/s13555-022-00779-x.

12. Handel AC, Miot LDB, Miot HA. Melasma: a clinical and epidemiological review. *Bras Dermatol*. 2014; 89:771–782. doi; 10.1590/abd1806-4841.20143063.
13. Suman Babu PS, Sridevi Patil C. Melasma and thyroid profile: a case-control study. *IP Indian J Clin Exp Dermatol*. 2020;6:76–78. doi: 10.18231/j.ijced.2020.017.
14. Achar A, Rathi SK. Melasma: A clinico-epidemiological study of 312 cases. *Indian J Dermatol*. 2011;56:380–382. doi: 10.4103/0019-5154.84722.
15. Liu W, Chen Q, Xia Y. New mechanistic insights of melasma. *Clin Cosmet Investig Dermatol*. 2023;16:429–442. doi: 10.2147/CCID.S396272.
16. Prabha N, Mahajan VK, Mehta KS, Chauhan PS, Gupta M. Cosmetic contact sensitivity in patients with melasma: results of a pilot study. *Dermatol Res Pract*. 2014;2014:316219. doi: 10.1155/2014/316219.
17. Hexsel D, Lacerda DA, Cavalcante AS, Machado Filho CA, Kalil CL, Ayres EL, et al. Epidemiology of melasma in Brazilian patients: a multicenter study. *Int J Dermatol*. 2014;53(4):440-444. doi: 10.1111/j.1365-4632.2012.05748.x.
18. Tamega Ade A, Miot LD, Bonfietti C, Gige TC, Marques ME, Miot HA. Clinical patterns and epidemiological characteristics of facial melasma in Brazilian women. *J Eur Acad Dermatol Venereol*. 2013;27(2):151-156. doi: 10.1111/j.1468-3083.2011.04430.x.
19. Ellerhorst JA, Sendi-Naderi A, Johnson MK, Cooke CP, Dang SM, Diwan AH. Human melanoma cells express functional receptors for thyroid-stimulating hormone. *Endocr Relat Cancer*. 2006;13(4):1269-1277. doi: 10.1677/erc.1.01239.
20. Cooper DS, Biondi B. Subclinical thyroid disease. *Lancet*. 2012;379(9821):1142–1154. doi: 10.1016/S0140-6736(11)60276-6.
21. Slominski A, Wortsman J, Tobin DJ. The cutaneous serotoninergic/melatoninergic system: securing a place under the sun. *FASEB J*. 2005;19(2):176–194. doi: 10.1096/fj.04-2079rev.
22. Costin GE, Hearing VJ. Human skin pigmentation: melanocytes modulate skin color in response to stress. *FASEB J*. 2007;21(4):976–994. doi: 10.1096/fj.06-6649rev.
23. Al-Shamma YMH, Al-Wakeel HHA, Al-Awadi IJM. The prevalence of thyroid disorders in patients with melasma. *Al-Qadisiyah Med J*. 2017;12:107–111. doi: 10.28922/qmj.2016.12.21.107-111.
24. Talaee R, Ghafarpasand I, Masror H. The relationship between melasma and disturbances in the serum level of thyroid hormones and indices. *Med J*. 2015;2:19–23.
25. Dogra A, Dua A, Singh P. Thyroid and skin. *Indian J Dermatol*. 2006;51:96. doi: 10.4103/0019-5154.26927.
26. Rahman Y, Krisanti RIA, Wisnu W, Sitohang IBS. The comparison between free thyroxine and thyroid-stimulating hormone levels on melasma severity: a cross-sectional study. *Maced J Med Sci*. 2021;9:426–431. doi: 10.3889/oamjms.2021.5952.
27. Lutfi RJ, Fridmanis M, Misiunas AL, Pafume O, Gonzalez EA, Villemur JA, et al. Association of melasma with thyroid autoimmunity and other thyroidal abnormalities and their relationship to the origin of the melasma. *J Clin Endocrinol Metab*. 1985;61(1):28-31. doi: 10.1210/jcem-61-1-28.