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

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ABSTRACT

Introduction: Melasma is a common acquired hyperpigmentary disorder primarily affecting sun-exposed areas, predominantly in women of reproductive age. Thyroid dysfunction has been proposed as a potential endocrine trigger; however, data from Nepalese populations remain limited.

Objectives: This study aimed to determine the prevalence of thyroid dysfunction in melasma patients compared to matched controls, and to assess its association with clinical parameters of melasma.

Methods: A 1:1 frequency-matched case-control study was conducted at Nepalgunj Medical College and Teaching Hospital, Kohalpur, Nepal (65 melasma cases, 65 controls). Serum TSH was measured by ECLIA. Analyses included Fisher's exact test, Mann-Whitney U test, Kruskal-Wallis test, and Spearman's rank correlation.

Results: The groups were comparable in age (median 30 years; p = 0.883) and sex (p = 1.000). Thyroid dysfunction was detected in 17/65 cases (26.2%) versus 4/65 controls (6.2%); OR 5.40 (95% CI 1.71–17.11; p = 0.003). Hypothyroidism accounted for 94.1% of cases with thyroid dysfunction. Median serum TSH was 2.97 mIU/L in cases versus 2.59 mIU/L in controls (p = 0.095). Centrofacial and malar distributions each comprised 44.6% of cases. Thyroid dysfunction was exclusive to female cases (17/56, 30.4%; p = 0.098). No significant correlation was identified between serum TSH and melasma duration (r = −0.077, p = 0.543).

Conclusions: Thyroid dysfunction was significantly more prevalent in melasma patients versus controls (OR 5.40; 95% CI 1.71–17.11; p = 0.003), with hypothyroidism predominating (94.1%). These findings highlight thyroid dysfunction as a relevant systemic co-morbidity in melasma, warranting further multicentre studies.

Keywords: *Case-control study, Melasma, Nepal, Thyroid dysfunction, Thyroid-stimulating hormone*

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INTRODUCTION

Melasma is a chronic, acquired facial hyperpigmentation disorder predominantly affecting women of reproductive age with Fitzpatrick skin phototypes III to V. [1,2] In Nepal, it accounts for 43% of facial pigmentary disorders presenting to dermatology outpatient departments, with a notable female predominance. [3]

Thyroid dysfunction is prevalent in Nepal (17–25%), predominantly as hypothyroidism, disproportionately affecting women of reproductive age. [4,5] A meta-analysis of seven studies (473 cases, 379 controls) confirmed significantly elevated serum TSH, anti-thyroid peroxidase antibody, and antithyroglobulin in melasma patients versus controls. [6] TSH promotes melanin synthesis through melanocyte stimulation. [7] Despite the concurrent burden of both conditions in Nepal, data from Nepalese clinical settings remain limited.

This study aimed to investigate the association between melasma and thyroid dysfunction as measured by serum TSH, and to describe the clinical profile of melasma in a hospital-based case-control study.

METHODS

The present study utilized a hospital-based case-control design and was conducted within the Department of Dermatology and Venereology at Nepalgunj, Medical College and Teaching Hospital (NGMC-TH), Kohalpur, Nepal, spanning from 15th August 2025 to 15th May 2026. Ethical approval was obtained from the Institutional Review Committee of NGMC-TH (IRC Ref: 78/082-083) on 14th August 2025, and written informed consent was secured from all participants. The study adhered to the principles outlined in the Declaration of Helsinki.

The sample size was determined utilizing the Kelsey formula for a 1:1 frequency-matched case-control study. Given an anticipated prevalence of thyroid dysfunction of 25% among cases and 5% among controls, with a two-tailed significance level of $\alpha = 0.05$ and a statistical power of 90%, the minimum required sample size was calculated to be 65 cases and 65 controls

(total n = 130), with an expected Odds Ratio of 6.33.

Participants comprised consecutive patients aged 18 to 60 years presenting to the Dermatology OPD with a clinical diagnosis of melasma confirmed by a dermatologist and corroborated by Wood's lamp examination. Exclusion criteria included known thyroid disease or current thyroid medications, other facial hyperpigmentation causes, pregnancy or lactation, use of oral contraceptive pills or photosensitizing drugs, or significant systemic illness. Controls were apparently healthy individuals frequency-matched 1:1 by age (±5 years) and sex, with no history or clinical evidence of melasma or thyroid dysfunction.

A structured proforma documented demographic information, melasma duration (months), site of distribution (centrofacial, malar, or mandibular), and Wood's lamp findings (epidermal, Dermal or mixed). A venous blood sample (3 mL) was collected in a plain vacutainer. Serum TSH was quantified by third-generation ECLIA on a fully automated analyzer. The normal reference range was 0.4–4.5 mIU/L. Values >4.5 mIU/L were categorized as increased (hypothyroidism) and values <0.4 mIU/L as decreased (hyperthyroidism).

Data were entered and analyzed using SPSS version 25. Normality was assessed by the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages; non-normally distributed continuous variables as medians with interquartile ranges (IQR). Fisher's exact test or Chi-square test compared proportions. The Mann-Whitney U test compared serum TSH between groups. The Kruskal-Wallis test compared TSH across melasma distribution patterns. Odds Ratio (OR) with 95% CI assessed the strength of association. Spearman's rank correlation examined the relationship between serum TSH and melasma duration. Bonferroni correction was applied for multiple comparisons. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 130 participants were enrolled, comprising 65 melasma cases and 65 frequency-matched controls (Table I). The median age was 30 years (IQR 26–35) in cases and 30 years (IQR 26–36) in controls, with no statistically significant difference (Mann-Whitney U = 2080.5, p = 0.883). Female participants predominated in both groups (cases 86.2%, controls 84.6%), and gender distribution was comparable (Fisher's exact test, p = 1.000).

Table I: Demographic comparison of cases and controls

Variable	n (%)	Details
Duration-Median (IQR) months	24 (12–36)	Range 2–96 months
Site-Centrofacial	29 (44.6%)	Forehead, nose, upper lip, chin
Site- Malar	29 (44.6%)	Cheeks and nose
Site-Mandibular	7 (10.8%)	Ramus of mandible
Wood's lamp-Epidermal	63 (96.9%)	Enhanced contrast
Wood's lamp-Mixed	2 (3.1%)	Partial enhancement

IQR = interquartile range; p > 0.05 = not significant

Table II shows the clinical characteristics of melasma cases. The median duration of melasma was 24 months (IQR 12–36; range 2–96 months). The centrofacial and malar patterns were equally prevalent, each constituting 44.6% (n = 29) of cases, while the mandibular pattern was observed in 10.8% (n = 7). Wood's lamp examination identified an epidermal pigmentation pattern in 63/65 cases (96.9%), with a mixed pattern in only2 cases (3.1%).

Table II: Clinical characteristics of melasma cases (n = 65)

Variable	Cases (n=65)	Controls (n=65)	Test Statistic	p-value
Age-Median (IQR) years	30 (26–35)	30 (26–36)	Mann-Whitney U = 2080.5	0.883
Female-n (%)	56 (86.2%)	55 (84.6%)	Fisher's exact	1.000
Male-n (%)	9 (13.8%)	10 (15.4%)		

IQR = interquartile range

A comparison of serum TSH values is presented in Table III. The median serum TSH was higher in cases (2.97 mIU/L; IQR 1.90–4.32) compared to controls (2.59 mIU/L; IQR 1.86–3.33); however, this difference did not achieve statistical significance (Mann-Whitney U = 2471.5, p = 0.095).

Table III: Comparison of serum TSH values between cases and controls.

TSH Parameter	Cases (n=65)	Controls (n=65)	Test Statistic	p-value
Median (IQR) (mIU/L)	2.97 (1.90–4.32)	2.59 (1.86–3.33)	Mann-Whitney U = 2471.5	0.095
Range (mIU/L)	0.30–18.62	0.97–7.36		

Non-normally distributed (Shapiro-Wilk p < 0.001); IQR = interquartile range

Table IV presents the prevalence of thyroid dysfunction. Thyroid dysfunction was identified in 17/65 cases (26.2%) versus 4/65 controls (6.2%), a statistically significant difference (Fisher's exact test, p = 0.003). The OR was 5.40 (95% CI: 1.71–17.11), indicating melasma patients were 5.4 times more likely to exhibit thyroid dysfunction (Figure 1). Of the 17 cases, 16 (24.6%) had elevated TSH (hypothyroidism) and 1 (1.5%) had decreased TSH (hyperthyroidism). All 4 controls with abnormal TSH had elevated values.

Table IV: Thyroid dysfunction among cases and controls.

TSH Status	Cases n (%)	Controls n (%)	OR (95% CI)	p-value
Thyroid dysfunction	**17 (26.2%)**	**4 (6.2%)**	**5.40 (1.71–17.11)**	**0.003†**
Increased TSH (>4.5 mIU/L)	**16 (24.6%)**	**4 (6.2%)**		
Decreased TSH (<0.4 mIU/L)	**1 (1.5%)**	**0 (0.0%)**		
Normal TSH (0.4–4.5 mIU/L)	**48 (73.8%)**	**61 (93.8%)**	**Reference**	-

† Fisher's exact test, p < 0.01; OR = Odds Ratio; CI = Confidence Interval; TSH reference: 0.4–4.5 mIU/L; bold row = primary outcome

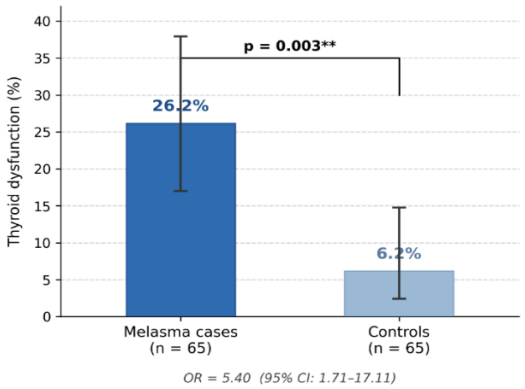

Figure 1: Prevalence of thyroid dysfunction among melasma cases and controls.

Error bars represent Wilson 95% CI. OR = 5.40 (95% CI 1.71–17.11); p = 0.003 (Fisher's exact test).

Table V presents subgroup analysis by distribution pattern. The mandibular pattern exhibited the highest proportion of thyroid dysfunction (4/7, 57.1%), followed by centrofacial (8/29, 27.6%), and malar (5/29, 17.2%). The median TSH was highest in the mandibular group (4.76 mIU/L; IQR 4.11–5.95). However, no significant difference was observed across groups (Kruskal-Wallis H = 3.952, df = 2, p = 0.139), likely due to the small mandibular subgroup (n = 7).

Table V: Thyroid dysfunction and serum TSH by site of melasma distribution (n = 65)

Site	n	Normal n (%)	Abnormal n (%)	Median TSH (IQR) mIU/L	p-value
Centro facial	29	21 (72.4%)	8 (27.6%)	2.97 (1.98–4.32)	0.139
Malar	29	24 (82.8%)	5 (17.2%)	2.65 (1.64–3.96)	
Mandibular	7	3 (42.9%)	4 (57.1%)	4.76 (4.11–5.95)	

‡ Kruskal-Wallis test; IQR = interquartile range

With regard to sex, thyroid dysfunction was exclusively observed among female participants, with 17 of 56 female patients (30.4%) exhibiting abnormal TSH values (Table IV). In contrast, none of the 9 male participants demonstrated thyroid dysfunction (Fisher's exact test, p = 0.098). Although this difference did not reach statistical significance, possibly attributable to the limited number of male participants, the finding is clinically noteworthy.

Wood's lamp examination revealed an epidermal pigmentation pattern in 63 cases (96.9%) and a mixed pattern in only 2 cases (3.1%). Formal statistical comparison between Wood's lamp

subgroups was not performed given the small number of mixed pattern cases.

Spearman's rank correlation revealed no significant correlation between serum TSH and duration of melasma ($r = -0.077$, $p = 0.543$), suggesting that melasma duration does not significantly influence serum TSH levels.

DISCUSSION

The present study identified a statistically significant association between melasma and thyroid dysfunction. Thyroid dysfunction was observed in 26.2% of cases versus 6.2% of controls (OR 5.40; 95% CI 1.71–17.11; $p = 0.003$), indicating melasma patients were 5.4 times more likely to exhibit thyroid dysfunction. This is consistent with Rostami Mogaddam et al. (2015), who reported thyroid dysfunction in 18.5% versus 4.3% of controls ($p = 0.008$). [8] Abdulsada and Neama (2024) similarly demonstrated elevated TSH in melasma patients. [9] A meta-analysis by Kheradmand et al. (2019) pooling 473 cases and 379 controls confirmed higher serum TSH, anti-TPO, and antithyroglobulin in melasma patients. [6] Patel et al. (2023) and Yadav and Dutta (2022) similarly reported higher thyroid dysfunction in melasma patients. [10,11]

Although median serum TSH was higher in cases (2.97 mIU/L; IQR 1.90–4.32) than controls (2.59 mIU/L; IQR 1.86–3.33), this did not achieve statistical significance (Mann-Whitney $U = 2471.5$, $p = 0.095$). Among the 17 cases, 16 (94.1%) had elevated TSH indicative of hypothyroidism. This predominance aligns with published literature, [6,8] including Mehmood et al. (2021) who reported hypothyroidism predominating in 76% of melasma cases. [12] Hypothyroidism is the most prevalent thyroid dysfunction in Nepal, disproportionately affecting women of reproductive age, [4,5] and may contribute to hyperpigmentation through hypothalamic-pituitary-thyroid axis stimulation of melanocyte activity. [7]

Centrofacial and malar patterns were equally prevalent (44.6% each), with the mandibular pattern in 10.8%. Patel et al. (2023) reported malar distribution as most common (55%).

[10,13] Although the proportion of thyroid dysfunction was highest among mandibular melasma patients (4/7, 57.1%), this did not reach statistical significance (Kruskal-Wallis $p = 0.139$), likely due to the small subgroup ($n = 7$). Wood's lamp examination revealed an epidermal pattern in 96.9%, consistent with the predominance of epidermal melasma in South Asian phototypes. [14]

Thyroid dysfunction was exclusive to female cases, with 17 of 56 female patients (30.4%) demonstrating abnormal TSH, while none of the nine male cases had thyroid dysfunction ($p = 0.098$). This aligns with the established female predominance of thyroid dysfunction [4,5] and with the Kheradmand et al. finding of more pronounced differences among women. [6] The role of oestrogen in both thyroid autoimmunity and melanogenesis may partly explain this observation. [15]

Spearman's correlation revealed no significant association between serum TSH and melasma duration ($r = -0.077$, $p = 0.543$), [10] implying thyroid dysfunction may represent a concurrent systemic condition rather than a consequence of extended melasma.

The present study has several limitations. Firstly, as a retrospective case-control study, causality cannot be established. Secondly, thyroid assessment was limited to serum TSH without fT3, fT4, anti-TPO antibody, or antithyroglobulin measurement, precluding comprehensive thyroid autoimmunity evaluation. Thirdly, thyroid dysfunction was classified by TSH alone, without distinguishing subclinical from overt hypothyroidism. Fourthly, while the overall sample provided 90% statistical power for the primary outcome, subgroup analyses were constrained by small cell sizes, particularly for male cases ($n = 9$) and the mandibular subgroup ($n = 7$). Fifthly, as a single-center study, findings may not be fully generalizable. Sixthly, melasma duration was self-reported, introducing recall bias. Seventhly, disease severity was not objectively quantified using the Melasma Area and Severity Index (MASI) score.

The present study provides evidence of a significant association between melasma and

thyroid dysfunction in the Nepalese population, with a 5.4-fold increased odd of thyroid dysfunction in melasma patients compared to controls (OR 5.40; 95% CI 1.71–17.11; p = 0.003). Hypothyroidism was the predominant pattern, accounting for 94.1% of affected cases, consistent with the known prevalence of hypothyroidism in Nepal. [4,5] Tekou and Labbene (2023) proposed that melasma may serve as a cutaneous marker of underlying thyroid dysfunction. [16] Future prospective multicentre studies with comprehensive thyroid autoantibody profiling, free hormone measurement, and objective melasma severity scoring (MASI) are warranted to further characterise this association.

CONFLICT OF INTEREST

None

SOURCES OF FUNDING

None

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