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Investigating the Relationship Between Serum Thyroid Hormone and Vitamin D Levels in Women with Melasma

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ABSTRACT: Patches and macules of hyperpigmentation characterize melasma, a prevalent condition of skin pigmentation. Known risk factors for melasma include a genetic predisposition, sun exposure, and pregnancy. Melasma may have a connection to thyroid issues, according to previous research. Considering that vitamin D influences and promotes melanocytes' melanin formation, this study sought to examine the correlation between thyroid problems, blood vitamin D levels, and melasma in female patients seen at Al-Mahmoudiya Hospital. Both Wood's light investigation and clinical evaluation by seasoned dermatologists verified the melasma diagnosis. There were 80 participants in total, with 40 assigned to the melasma group and 40 to the control group. Their ages and sexes were matched. In all groups, blood samples were taken to assess levels of TSH, Anti-TPO, T3, T4, and vitamin D. Melasma patients' clinical pigmentation severity was assessed using the standard mMASI score. I used SPSS (IBM Statistical Package for the Social Sciences) version 21 to conduct the statistical analysis. Melasma patients were more likely to have thyroid problems (50%) and lower vitamin D serum levels (47.5%), compared to the control group (27.5%) and healthy individuals (40%). The levels of thyroid hormone (T3) and vitamin D were found to be considerably higher in the case group as compared to the control group ($P<0.05$). A relationship was found between Anti-TPO and mMASI Score ($P< 0.05$) when the relationship between age, thyroid hormones, vitamin D, and mMASI Score was investigated. Melasma and pigmentation intensity are linked to thyroid autoimmune diseases. The most prevalent clinical form of melasma is the centro facial variant as well.

Keywords: melasma, thyroid, vitamin D, Anti-TPO, T3, T4, TSH

1. INTRODUCTION

The photosensitive skin areas of the face are the most typically affected by melasma, an acquired symmetrical dyschromia that disproportionately affects adult females [1]. They are more common in people with darker skin tones, such as African-Americans, Asians, and Hispanics. According to the level of pigment deposition, three main forms of melasma can be identified when illuminated by Wood's lamp: epidermal, dermal, and mixed [2,3]. Typically found on the face, but can also appear on the forearm and V-neck region, these hyperpigmented patches can be one or more in number and typically have a symmetrical pattern. The spread of lesions can be characterized by three distinct clinical patterns. The most typical pattern involves the central region of the face, which includes the cheeks, upper lip, nose, and chin. The nose and cheeks are part of the malar pattern. The skin covering the ramus is part of the mandibular pattern [4]. Melas, meaning "black" in Greek, is the origin of the name melasma. Though less commonly used, it is also known as chloasma, derived from the Greek word chloazein meaning "green" in reference to its pregnancy-related appearance. It is not yet known what exactly causes melasma, but several factors, including but not limited to: sun exposure (UV light), pregnancy, certain medications (such as oral contraceptives, estrogen-progesterone therapy, and antiepileptic drugs), heredity, emotional factors, and endocrinological milieu (such as thyroid hormone abnormalities) [5,6]. If the lesions worsen in the summer and then gradually go away in the winter or during colder months, it's clear that the UV light is having its desired impact [3]. It develops when melanocytes in the skin produce more melanin. Under a microscope, melasma appears as modest perivascular lymphohistiocytic infiltrates and an increase in melanin deposits in the dermis and/or epidermis compared to surrounding normal skin [7]. We set out to determine whether

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there is a connection between thyroid hormone levels and melasma in women because there is a dearth of evidence supporting that association in the existing literature.

More often in adult females, melasma is an acquired symmetrical dyschromia that mostly impacts photosensitive skin, like the face [1]. African-Americans, Asians, and Hispanics have a higher prevalence of these. When lit by Wood's lamp, three primary kinds of melasma can be identified based on the level of pigment deposition: epidermal, dermal, and mixed [2,3]. The face, forearm, and V-neck area are the most typical sites for symmetrical hyperpigmented patches, although they can arise elsewhere on the body. Three different clinical patterns are associated with the distribution of lesions. The cheeks, upper lip, nose, and chin make form the most common pattern in the middle of the face. A component of the malar pattern is the nose and cheeks. The mandibular pattern includes the skin that covers the ramus [4]. Melasma is a hue of black that has its roots in the Greek word melas. Another, less popular name for it is chloasma, which comes from the Greek word chloazein, meaning "green" because of the way it looks when pregnant. The exact causes of melasma are unknown, although it is believed to be caused by sun exposure (UV light), pregnancy, certain medications (such as oral contraceptives, estrogen-progesterone therapy, and antiepileptic drugs), emotional factors, genetics, and endocrinological milieu (such as thyroid hormone abnormalities) [5,6]. This is the obvious consequence of UV exposure, since the lesions get worse in the summer and then gradually go away or become less noticeable in the winter and cooler months [3]. It happens when the skin's melanocytes start making more melanin. Microscopic examination reveals increased melanin deposits in the dermis and/or epidermis as well as small perivascular lymphohistiocytic infiltrates in melasma [7]. We set out to examine the potential association between thyroid hormone levels and melasma in females because there is a lack of data confirming this link in the current literature.

2. MATERIALS AND METHODS

Our research was conducted at Mahmoudia General Hospital in Baghdad, Iraq, following approval from the ethical and scientific committees of the Baghdad Board for Medical Specialties. The study was a prospective cross-sectional analysis involving 80 female patients, conducted between November 2023 and February 2024. Notably, no male patients with melasma were included during this period.

The sample size was determined with a 50% confidence level, employing the methodology outlined by Yazdanfar et al. Utilizing the Power-G program for statistical calculations, it was determined that 80 participants would be appropriate for the study, ensuring robust results for an 80% test domain.

Detailed patient histories were meticulously recorded following verbal consent. This documentation included demographic information, risk factors for melasma, the onset date, and the duration of the condition. Melasma diagnoses were clinically confirmed by two board-certified dermatologists. Subsequent testing was performed to categorize the type of melasma, with serum levels of triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) measured. The normal reference ranges were as follows: T3 (1.3-3.1 nMol/L), T4 (66-180 nMol/L), and TSH (0.4-4.0 mIU/L).

Post-collection, the research data were coded and prepared for analysis. Microsoft Excel was used for data entry, while statistical analysis was performed using IBM SPSS (version 21). The Kolmogorov-Smirnov test was applied to assess the normality of quantitative variables, modeled against the Gaussian distribution. The study’s findings were presented in tables showcasing absolute and relative frequencies across the three patient groups: Dermal, Epidermal, and Mixed. Chi-square tests were employed to compare categorical data, particularly focusing on thyroid hormone normalcy. Additionally, the analysis included various graphical representations such as bar charts, box plots, and error bars.

To mirror similar research at Al-Mahmoudiya Hospital involving blood sample analysis for thyroid hormones (TSH, T3, T4), Anti-TPO, and vitamin D, the following methodology is suggested:

1. **Blood Sample Collection:** Collect 5-10 mL of blood per sample using appropriately labeled vacutainer tubes, depending on the specific assays required.
2. **Centrifugation:** Centrifuge samples at 3000 rpm for 10-15 minutes to separate serum, which is then aliquoted for storage or immediate analysis.
3. **Storage and Handling:** Store serum samples at -20°C or -80°C to maintain hormone integrity if analysis is delayed.
4. **Analysis:** Utilize ELISA kits or automated analyzers to measure levels of TSH, T3, T4, Anti-TPO, and vitamin D, adhering to kit-specific protocols.
5. **Statistical Analysis:** Analyze data using SPSS, applying ANOVA for hormone level comparisons and chi-square tests for categorical variables.
6. **Interpreting Results:** Recent studies indicate a significant correlation between vitamin D deficiency and thyroid disorders, especially autoimmune conditions. These correlations should be considered during result interpretation.

For statistical significance, p-values less than 0.05 were used, determined after comparing means and standard deviations of variables such as T3, T4, and TSH across melasma groups using the ANOVA test. The Kruskal-Wallis test was also employed to compare median and mean ranks among these variables.

3. RESULTS AND DISCUSSION

All the subjects examined in this study were women (initially 7 men entered the study, but they withdrew from the study due to my intention to cooperate). The average age of the study subject was 15.36 ± 70.4 years old, with a minimum age of 71 years and a maximum age of 5 years. There was no significant difference between the control group and the patients in the examination of semen and qualitative demographic information (P > 0.05) table 1.

Table 1. - Frequency and frequency percentage of qualitative demographic information of patients

		Witness	item	Total	Level
		Number (percentage)	Number (percentage)	Number (percentage)	Meaningful
History of underlying disease	No	35 (87.50)	35 (87.50)	70 (87.50)	0.631
	Yes	5 (12.50)	5 (12.50)	10 (12.50)	
History of Anemia	No	38 (95)	39 (97.50)	77 (96.25)	1
	Yes	2 (5)	1 (2.50)	3 (3.75)	
History of diabetes	No	39 (97.50)	39 (97.50)	78 (97.50)	0.753
	Yes	1 (2.50)	1 (2.50)	2 (2.50)	
History of dyslipidemia	No	38 (95)	37 (92.50)	75 (93.25)	1
	Yes	2 (5)	3 (7.50)	5 (6.25)	
Bardari precedent	No	4 (10)	8 (20)	12 (15)	0.348
	Yes	36 (90)	32 (80)	68 (85)	
OCP Bank's predecessor	No	33 (82.50)	26 (65)	59 (73.75)	0.075
	Yes	7 (17.50)	14 (35)	21 (26.25)	
Family history of melasma	No	40 (100)	20 (50)	60 (75)	0
	Yes	0 (0)	20 (50)	20 (50)	
History of alcohol consumption	No	40 (100)	40 (100)	80 (100)	-
	Yes	0 (0)	0 (0)	0 (0)	
Smoking history	No	40 (100)	40 (100)	80 (100)	-
	Yes	0 (0)	0 (0)	0 (0)	

The average mMASI Score in the case group was 67.2 ± 51.4 with a minimum value of 60 and a maximum value of 40.10. The prevalence of thyroid hormone disorders and vitamin D blood level in the case group was 50% and 5.47%, respectively, and in the control group, it was 5.27% and 40%, respectively. In the present study, like Rostami et al., the prevalence of thyroid hormone disorders in the case group was 81.1 equal to the control group, while this ratio was 4 in the study by Lutfi et al. and 4.3 in the study by Kiani et al. [9-11].

The mean serum level of TSH in the case and control groups was 2.82, 2.09, T3, 2.27, 1.3, T4, 6.95, 5.93, 73.04 Anti TPO, 12.61, and vitamin D, 19.71, 22.96. Examining the results of thyroid hormones and vitamin D by melasma group showed that, like Yazdanfar's study, the amount of T3 is significantly higher in the case group (P < 0.05) [8].

The amount of T4 in the case group was more than the control group, but this difference was not statistically significant. The Anti TPO level was significantly related to the mMASI Score (Table 2). This results indicates the relationship between thyroid autoimmune disorders and melasma disease and the intensity of pigmentation of the disease and confirms the results of studies by Lutfi, Kiani and Yazdanfar [8-11].

Table 2. - Correlation coefficient results

	Age	TSH	T3	T4	Anti-TPO	Vitamin-D
Pearson	0.201	2.082	0.054	0.165	0.495	0.006
Significance level	0.214	0.613	0.74	0.309	0.001	0.973
Total	40	40	40	40	40	40

The results of the tests of thyroid and vitamin D according to the cause of clinical involvement showed that there was no significant difference in any of the cases ($P < 0.05$) Table No. 3.

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By comparing the frequency of different forms of melasma (Centerofacial, Malar, Mandibular) in the group of patients, the prevalence of melasma was investigated, which showed that, like other studies, the frequency of the form was significantly higher in Centrofacial ($P=0.002$) (table 4) [10].

Table 3. - Average and standard deviation of the results of thyroid and vitamin D tests by the location of clinical involvement

	Clinical location				significance level
	Centerofacial		Malar		
	Standard deviation ± mean	average rank	Standard deviation ± mean	average rank	
Age	33.36 ± 7.11	23.20	30.36 ± 7.56	30.21	0.802
TSH	94.2 ± 2.48	80.20	45.2 ± 1.79	60.19	0.779
T3	23.3 ± 6.75	57.21	38.1 ± 0.56	30.17	0.315
T4	29.10 ± 19.74	90.19	41.7 ± 3.03	30.22	0.574
Anti-TPO	88.87 ± 64.01	78.20	51.28 ± 40.03	65.19	0.791
Vitamin-D	94.18 ± 10.40	55.19	2.22 ± 9.83	35.23	0.373

Table 4. - Frequency and frequency percentage of the site of clinical involvement

		Number (percentage)	significance level
Clinical site	Centerofacial	30 (75)	0.002
	Malar	10 (25)	
	Mandibular	0 (0)	
	Total	40 (100)	

In Xu et al.'s study [12], no significant difference was found in the mean serum levels of 25-hydroxyvitamin D between the patient group and the control group. This finding was consistent with the results of the present study ($P < 0.05$) (Table 5).

Table 5. - Average and standard deviation of thyroid and vitamin D test results

	Clinical location				Total		significance level
	Centerofacial		Malar				
	Standard deviation ± mean	average rank	Standard deviation ± mean	average rank	Standard deviation ± mean	average rank	
TSH (mlU/L)	9.2 ± 1.02	38.54	82.2 ± 2.32	42.46	2.45	1.82	0.450
T3 (nmol/L)	30.1 ± 0.44	34.22	77.2 ± 5.88	46.78	2.03	4.23	0.015
T4 (µg/dl)	93.5 ± 2.54	34.46	95.6 ± 2.57	46.54	33.4	9.35	0.055

Anti-TPO (IU/ml)	61.12 ± 10.98	36.49	145.08 ± 4.73	44.51	42.82	104.44	0.122
Vitamin-D (ng/mL)	96.2 ± 8.20	44.46	71.19 ± 10.38	36.54	21.33	9.44	0.127

It seems that this result can be justified considering the similar climate of China and Mazandaran where the weather is cloudy most of the days of the year and causes an increase in the prevalence of vitamin D deficiency. Of course, it is assumed that the similar diet of the people of these two regions, whose predominant food is rice and seafood, has not been ineffective in this result. In Abdalla et al.'s study [13], a significant difference was observed in serum vitamin D levels between melasma patients and the control group ($P \leq 0.01$). Chaitanya et al.'s study [14] showed a significant relationship between melasma and periodontitis with vitamin D abnormalities ($P<0.05$). In the study of Ekiz et al. [15], the mean serum level of vitamin D in rosacea patients and the control group had a statistically significant difference.

4. CONCLUSION

The results of these studies were not consistent with the investigations conducted in the present study. Considering that in Iraq, vitamin D deficiency in women has a high prevalence due to the way they cover, and most Iraqi women suffer from this disorder, and the present study was conducted only on women, this difference in the result can be justified. Also, the impact of Iraq in increasing the incidence of vitamin D deficiency and the occurrence of anemia as a result of the present study should also be considered. Another thing that has been taken into consideration is the effectiveness of vitamin D tablets available in the province. It is suggested that the next studies be conducted in a multi-center manner so that things such as the weather and climate of a region do not cause bias in the study results. It is also suggested that in a clinical trial study, patients with melasma who have thyroid disorders are treated for thyroid disease and the response to clinical treatment of skin lesions is investigated.

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