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Research Article

Assessment of Thyroid Function and Cortisol Levels in Iraqi Patients with Vitiligo

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Abstract

Background: The loss of functioning melanocytes in the skin causes vitiligo, an acquired autoimmune condition that manifests as big, white, unsightly patches on the skin. Melanocyte loss is caused by several reasons, including oxidative stress, inflammation, autoimmune, and metabolic problems, while the exact etiopathology of the condition remains unknown. There is a relationship between vitiligo, thyroid hormones, and cortisol levels.

Objective: The study aims to measure cortisol hormone levels in the serum of vitiligo patients and examine the thyroid hormones (T3, T4, and TSH).

Cases and methods: In this case-control study, 80 vitiligo patients diagnosed between November 2023 and February 2024 by dermatologists at the Dermatology and Venereology Center in Medical City, Baghdad, were included. The control group consisted of 40 healthy people. Everyone had a venous blood sample. Cortisol levels and thyroid hormones were assessed using the electrochemiluminescence immunoassay method.

Results: The control group's mean age was 29.5 ± 13.28, whereas the patient group was 28.9 ± 14.15. There were no statistically significant differences in age between study groups. Age and gender differences were not considered between the two groups. The patient group had significantly higher mean T3, TSH, and cortisol levels than the control group. The two groups did not differ significantly regarding T4 ($P>0.05$).

Conclusion: A comparison of T3, TSH, and Cortisol levels revealed a difference between the two groups, but no difference in T4 levels was observed. More extensive research with larger sample sizes is required to clarify these findings.

Keywords: Autoimmune; Cortisol; Thyroid hormones; Stress; Vitiligo.

Introduction:

Vitiligo is an unsightly skin depigmentation illness that is clinically distinguished by the formation of disfiguring, depigmented, confined skin macules and patches. It is believed that the disease is predominantly caused by the destruction of melanocytes. Vitiligo's etiopathogenesis involves metabolic, genetic, environmental, and autoimmune mechanisms (1). Vitiligo prevalence varies geographically and is unrelated to gender or age. However, vitiligo most typically affects adults between the ages of 10 and 30 years (2).

Autoimmunity is the most widely recognized theory explaining the pathophysiology of vitiligo. This is supported by the fact that vitiligo is linked to a variety of other autoimmune disorders, including Hashimoto thyroiditis and Graves' disease (3). However, vitiligo is now understood to be more than just a skin condition; research has linked it to a number of systemic or organ-specific conditions, such as autoimmune illnesses, metabolic syndrome, psychological disorders, and ocular or otologic diseases (4,5).

The thyroid is defined as an endocrine gland that secretes the thyroid hormones thyroxine (T4) and triiodothyronine (T3). These influence normal growth, tissue differentiation, and metabolism. The pituitary gland secretes thyroid-stimulating hormone (TSH), which regulates thyroid hormone production (6). The term "hyperthyroidism" describes an overactive thyroid gland that causes an excess of thyroid hormone synthesis and a rapid metabolism in peripheral tissues (7). The medical condition known as hypothyroidism is typified by normal or reduced thyroid hormone levels and elevated thyroid stimulating hormone levels (8). Autoimmune thyroid diseases (AITDs) are chronic autoimmune disorders that induce poor immunoregulation, resulting in particular immune responses to thyroid antigens (9). Graves' disease (GD)

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and Hashimoto's disease have been identified as the most frequent thyroid function disorders (10).

The oxidative stress theory has received a lot of attention lately because numerous studies have shown that reactive oxygen species (ROS)-induced oxidative stress causes molecules and organelles to malfunction, sets off a subsequent immune response, and ultimately results in the death of epidermal melanocytes (11). Cortisol, a vital steroid hormone produced by the adrenal glands, influences a wide range of physiological functions, including metabolism, immunological function, and stress management. Cortisol disruption can lead to Cushing's syndrome and Addison's disease (12).

This study aims to evaluate triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH), and assess serum levels of cortisol hormone in patients with vitiligo.

Cases and Methods

The study was carried out between November 2023 and February 2024 at the Dermatology and Venereology Center of Medical City in Baghdad, Iraq. This cross-sectional study comprised 80 participants with Vitiligo. As controls, the study comprised 40 healthy volunteers of similar age and gender. The clinical evaluation of vitiligo includes demographic information, medically significant habits such as smoking, and a history of chronic illness. The medical history of vitiligo comprised the onset, course, duration, and site of affection.

Venous blood samples of 3 ml were collected from all participants and put in a gel tube, then allowed to clot for 5 minutes; after that, serum was separated by centrifugation at 3000 rpm for 15 minutes. The serum has been collected in an Eppendorf tube and then stored at -20 °C to be used for measuring triiodothyronine (T3), thyroxine (T4), thyroid-stimulating hormone (TSH), and cortisol levels.

The study included 120 participants, of whom 80 were patients with vitiligo, and 40 were healthy volunteer individuals, matched with the cases for age and sex, as a control group. The patients with vitiligo were classified into three distinct subtypes: generalized, localized, and universal.

Patients were excluded from the study if they met any of the following criteria: (1) Individuals with vitiligo undergoing treatment, (2) Those with infectious, inflammatory, malignant, or autoimmune conditions affecting the skin or other systems, (3) Individuals with immunosuppression or receiving immunosuppressive therapy, and (4) Women who were pregnant or breastfeeding.

Electrochemiluminescence immunoassay was used to evaluate serum levels of TSH, T3, T4, and cortisol (Cobas e411 immunoassay analyzer, Roche Diagnostics, Mannheim, Germany). TSH reference levels ranged from 0.27 to 4.2 µIU/ml, (0.8-2.0) ng/ml for T3, (4.5-12) ug/dl for T4, and (6.2-19.4) ug/dl for Cortisol following the provided instructions.

Statistical analysis: The SPSS software program, version 23.0 was used for data analysis in the study. The t-test statistical method, mean (±), standard deviation (SD), and P-values were applied to explain the different values after comparing between groups according to previously measured parameters. A value of $P \geq 0.05$ was considered statistically significant.

Results

The study involved 120 participants (80 with vitiligo and 40 healthy volunteers). The average age of vitiligo patients and controls was 28.9 ± 14.15 and 29.5 ± 13.28 years, respectively. The patients ranged in age from 8 to 60 years, whereas the healthy control group ranged from 9 to 57 years. The age differences between patients and controls were not statistically significant (p-value = 0.83).

According to the current study's findings, 42 out of 80 instances (52.5%) of vitiligo patients were found to be between the ages of 16 and 30, however, fewer cases were found among patients under the age of 16. The statistical differences were not significant when compared to the control groups' age groups (P-value = 0.99). (Figure-1).

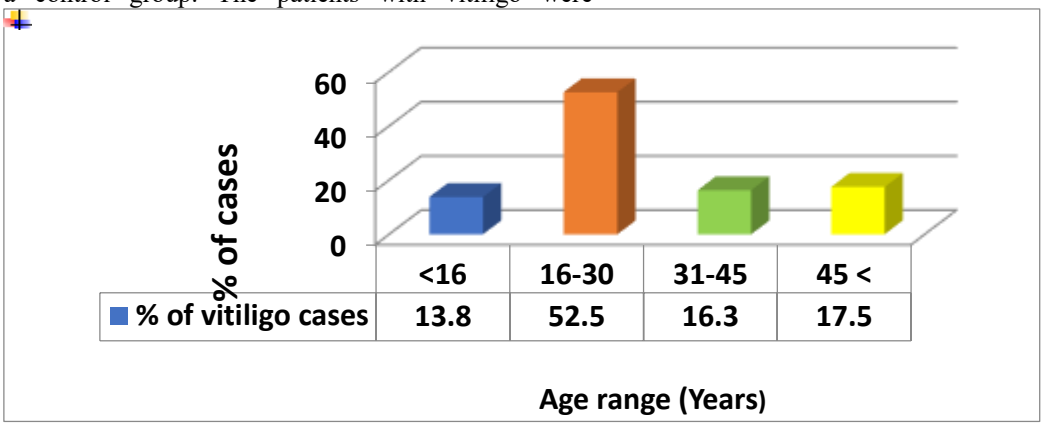

Figure 1: Distribution of studied groups according to age groups

The results of this study observed the vitiligo cases were recorded mostly among male groups than female groups with 48/80 (60 %), 32 (40.0%) respectively as arranged in Figure 2.

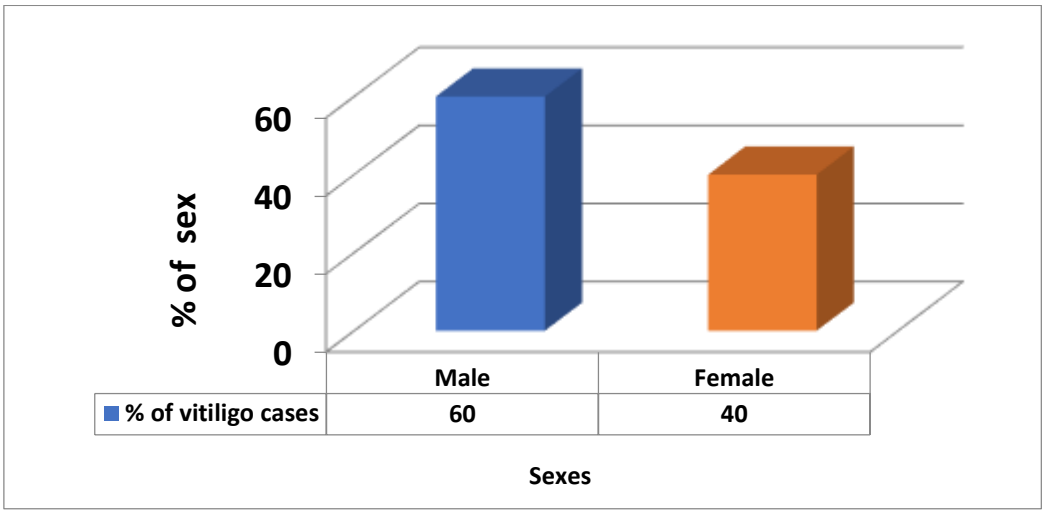

Figure 2: Distribution of the vitiligo group according to gender

Regarding the hormone levels between cases and control groups, the levels of T3 were higher among the Vitiligo patients than in the control group (P value=0.03), while there were no significant differences in the levels of T4 between Vitiligo patients than control groups (P-value=0.14). The results of the current study showed the levels of TSH were significantly different between cases and controls (P-value=0.001), as arranged in Table 1.

Table 1: Mean ± SD of T3, T4, and TSH concentrations by study groups

Hormones	Means ± S.D.		T-test	P-value
	Vitiligo	Control		
T3 (ng/ml)	1.5±0.03	1.4±0.03	2.53	0.03*
T4(µg/dl)	8.3±0.19	8.7±0.16	1.46	0.14 N.S.
TSH(µIU/mL)	2.2±0.16	1.6±0.08	3.25	0.001*

*Significant difference at P ≤ 0.05.
N.S.: non-significant difference at the 0.05 level by t-test.
TSH= Thyroid Stimulating Hormone; T4= Thyroxin T3= Triiodothyronine.

The results of this study observed the levels of cortisol were higher among patients than control groups with mean±SD (11.1±0.51, 8.6±0.23) respectively, with highly significant differences (P-value=0.0001).

Table 2: Mean ± S.D. levels of Cortisol in patients and controls

Hormone	Means ± S.D)		T-test	P-value
	Cases	Controls		
Cortisol(ug/dl)	11.1±0.51	8.6±0.23	4.49	0.0001*

*Highly significant differences under (P ≤ 0.01)

The receiver operating characteristic curve (ROC) analysis was done to assess the diagnostic value of cortisol among vitiligo patients. The results of the ROC analysis of cortisol as shown in Table 3 and Figure 3). A fair prediction of the AUC value result was seen for cortisol with (P = value .0001) at 0.691. The sensitivity was 50 ,% and the Specificity was 90 at the optimal cutoff value of more than 10.8, which differentiated patients from the control group.

Table 3: ROC analysis for the cortisol between Vitiligo patients and controls

Variable	Sensitivity	Specificity	AUC	Accuracy		Cutoff value
				L.B.	U.B.	
Cortisol	50	90	0.691	0.538	0.731	10.8

AUC : Area Under the Curve, L.B. : Lower Bound, U.B. : Upper Bound.

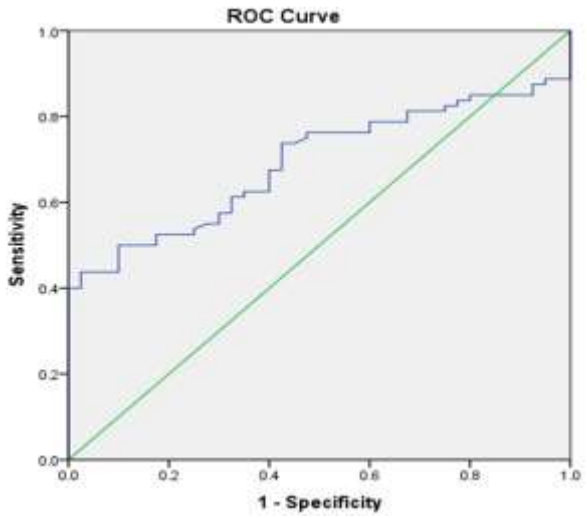

Figure 3: ROC Curve of Cortisol.

Discussion

In this study, patients with vitiligo had a mean age of 28.9. This finding was comparable with that of Tariq and Hussein (13), who discovered that the average age of patients with vitiligo was 28.55 years. In contrast with this study, Ahmed et al. (14) found that the average age of Iraqi patients with vitiligo was 21.53 years.

Previous research was inconclusive about whether male and female patients developed vitiligo at equal rates. The results showed that there were more male patients (48) than female patients (32). That finding was consistent with the Sarac et al. (15) study, which found that males with vitiligo (51) were more common than females (28), but it differed from the findings of Tariq and Hussein (13) and Ahmed et al. (14), who found that females outnumbered males.

Thyroid hormones regulate the majority of the body's metabolic processes: T3 and T4 from the thyroid gland, and TSH from the pituitary gland. Any abnormality in these hormones can have substantial clinical consequences on many body organs (16).

Numerous investigations have shown that vitiligo is associated with autoimmune thyroid disorders (17,18). Bashrahil et al., 2022 found a link between age and thyroid biomarkers (T3 (triiodothyronine), T4 (thyroxine), TSH, thyroglobulin antibody (TGAb), and thyroid peroxidase antibody (TPOAb) in vitiligo patients compared with controls (18).

In the current investigation, blood TSH levels in individuals with vitiligo were considerably greater than in healthy controls. Other investigations revealed similar findings [3, 19, 20]. In contrast with our findings, Ashawesh et al. found no significant difference in TSH levels between vitiligo sufferers and healthy persons. The literature appears to have inconsistent findings regarding TSH levels in vitiligo patients (21).

In the current investigation, serum T3 levels were significantly higher in vitiligo patients than in healthy controls, but there were no significant variations in T4 levels between the two groups. In a study of 100 individuals with NSV vitiligo, blood levels of T3 and T4 were significantly higher in the subgroup of generalized vitiligo patients than in the healthy controls (3). Previous research found no significant changes in T3 and T4 levels between vitiligo patients and controls (19, 20).

In a study by (22) they found that 18.8% of vitiligo patients had total thyroid dysfunction. Comparing the patients with the control group revealed no statistically significant differences, but 31% of patients had overt hypothyroidism and 69% had subclinical hypothyroidism.

Thyroid dysfunction, particularly the spectrum of autoimmune thyroid diseases, is associated with various skin abnormalities that may serve as indicators of more complex systemic disorders (23). Although vitiligo has a complex etiopathogenesis, the main cause is thought to be autoimmune or, less frequently, autoinflammatory. According to Chen et al., vitiligo and autoimmune thyroid disorders are positively causally related (24).

Furthermore, there are several theories that try to explain the pathophysiology of vitiligo, but the most frequently recognized one is that oxidative stress triggers immunological responses that lead to melanocyte death (25). Significantly, thyroid hormones are essential for controlling blood pressure, metabolism, and the elevated generation of reactive oxygen species (ROS), which results in oxidative stress. However, oxidative stress, which raises the body's levels of reactive oxygen species (ROS), can also directly lead to organelle and molecular malfunction, which can trigger an immunological response and ultimately result in melanocyte death (26).

The current study found that serum cortisol levels in vitiligo patients were considerably higher than in healthy controls. According to estimates, around 75% of vitiligo patients suffer from a psychological disorder. Depression, worry, and stress are all common psychological illnesses in vitiligo sufferers (27). Vitiligo patients experience emotional and behavioral impairment, sleep difficulty, stigmatization, depressive disorders, and a lower quality of life (28). Furthermore, according to a meta-analysis, individuals with vitiligo are just as likely to experience anxiety as those with eczema, psoriasis, and acne (29).

Indeed, vitiligo's origin and progression have been connected to stress and mental health issues. Thus, vitiligo may be significantly influenced by psychiatric disorders and stress (30). Due to the stressful circumstances of modern life, it is imperative that numerous physiological and psychological problems associated with stress be promptly prevented and treated (31).

Conclusion

T3, TSH, and cortisol levels seem to be considerably higher in vitiligo patients than controls, whereas T4 were not. Further research may provide a clearer picture on this issue.

Authors' declaration

We hereby attest that every Figure and Table in the manuscript is our own. Furthermore, authorisation has been granted for the re-publication of the Figures and images that are attached to the manuscript, which are not owned.

The authors sign the approval based on ethical considerations. Ethical Clearance: According to document number (40257 on 23-10-2023) the project was accepted by the local ethics committee at the College of Science for Women, University of Baghdad.

Conflicts of interest: None

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Authors' contribution

Study conception & design: (Talib A. Hussein). Literature search: (Fatima H. Mohsen). Data acquisition: (Fatima H. Mohsen). Data analysis & interpretation: (Fatima H. Mohsen, Talib A. Hussein and Ghassan H. Abdulqahar). Manuscript preparation: (Fatima H. Mohsen). Manuscript editing & review: (Talib A. Hussein and Ghassan H. Abdulqahar).

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تقييم هرمونات الغدة الدرقية(T3 ، T4، TSH) ومستويات الكورتيزول لدى المرضى العراقيين المصابين بالبهاق

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الخلاصة:
الخلفية: يتسبب فقدان الخلايا الصبغية الوظيفية في الجلد في الإصابة بالبهاق، وهو حالة مناعية مكتسبة تظهر على شكل بقع بيضاء كبيرة وغير مرغوبة على الجلد. يعود فقدان الخلايا الصبغية إلى عدة عوامل، بما في ذلك الإجهاد التأكسدي، والالتهاب، والمشاكل المناعية الذاتية، والاضطرابات الأيضية، في حين أن الأسباب المرضية الدقيقة لهذه الحالة لا تزال غير معروفة. هناك علاقة بين البهاق وهرمونات الغدة الدرقية وكذلك مستويات الكورتيزول.
الاهداف: تهدف الدراسة الى قياس مستويات هرمون الكورتيزول في مصل دم مرضى البهاق وفحص هرمونات الغدة الدرقيةT3). ، T4، وTSH)
المواد وطرق العمل: شملت هذه الدراسة المقطعية (الحالة - الشاهد) 80 مريضا بالبهاق تم تشخيصهم بين نوفمبر 2023 وفبراير 2024 من قبل أطباء الجلدية في مركز الأمراض الجلدية والتناسلية في مدينة الطب، بغداد. واشتملت مجموعة الضبط على 40 شخصا سليما. تم سحب عينة من دم وريدية من كل فرد، وتم تقييم مستويات الكورتيزول وهرمونات الغدة الدرقية باستخدام طريقة المناعة الكيميائية اللمعية الكهربائية.
النتائج: كان متوسط العمر في مجموعة الضبط 29.5 ± 13.28، بينما كان في مجموعة المرضى 28.9 ± 14.15، ولم تكن هناك فروق ذات دلالة إحصائية في العمر بين المجموعتين. لم تؤخذ الاختلافات في العمر والجنس بين المجموعتين في الاعتبار. أظهرت مجموعة المرضى مستويات أعلى بشكل ملحوظ في متوسط T3 ، وTSH، والكورتيزول مقارنة بمجموعة الضبط . ولم تظهر أي فروق ذات دلالة إحصائية بين المجموعتين فيما يتعلق ب T4.
الاستنتاج: أظهرت المقارنة بين مستويات T3 ، وTSH، والكورتيزول اختلافا بين المجموعتين، في حين لم يظهر أي اختلاف في مستوياتT4. هناك حاجة إلى دراسات أكثر شمولا مع عينات أكبر لتوضيح هذه النتائج.
الكلمات المفتاحية: مناعة ذاتية, الكورتيزول, هرمونات الغدة الدرقية, التوتر, البهاق.