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Research Article

Assessment of Thyroid Dysfunction and Cortisol Levels in Patients with Alopecia Areata

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Abstract

Background: Alopecia areata (AA) is a complex, multifactorial autoimmune disease in which a person's genetic predisposition plays a significant role. Alopecia areata has been linked to various autoimmune conditions. There is a significant likelihood that autoimmune thyroid disorders will coexist with these conditions.

Objectives: To determine the association between alopecia areata and subclinical thyroid dysfunction, and to assess serum cortisol levels and their relationship with AA.

Methods: The case-control study, conducted at the Dermatology Center of Baghdad Teaching Hospital from October 2023 to February 2024, involved 80 AA patients and 40 healthy controls. Thyroid hormones and cortisol levels were measured using electrochemiluminescence immunoassay.

Results: The mean age of AA patients was (29.4±10.49) years compared to (30.1±8.77) years in controls, with no statistically significant difference (p=0.75). Serum T3 levels were significantly higher in AA patients (1.5 ± 0.04 ng/ml) compared to controls (1.4 ± 0.03 ng/ml, p=0.03), though all values remained within the normal range. In contrast, no significant differences were observed in T4 levels (8.4 ± 0.21 vs. 8.7 ± 0.16 µg/dl, p=0.25) or TSH levels (1.7 ± 0.11 vs. 1.6 ± 0.08 µIU/ml, p=0.31) for the AA and controls, respectively. Serum cortisol levels were significantly higher in AA patients (11.1 ± 0.52 ng/dl) compared to controls (8.6 ± 0.23 ng/dl, p<0.0001). However, all measured cortisol levels in both groups remained within the normal reference range.

Conclusion: Significant differences in T3 and cortisol levels exist between alopecia patients and controls, suggesting hormonal involvement in AA. No significant differences were found in T4 and TSH levels, requiring further investigation.

Keywords: Alopecia areata; Autoimmune disease; Cortisol; Thyroid function test; TSH.

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Introduction

Alopecia areata (AA) is an intricate, multifaceted autoimmune illness where genetic predisposition plays a significant role. Thus, the two main factors influencing the initiation and progression of this disease are 'immunology' and 'heredity' (1). AA is clinically characterized by non-scarring hair loss, which appears as small bald spots on the scalp or other body parts. In more extreme situations, it may progress to total hair loss on the body (alopecia universalis) or complete hair loss on the scalp (alopecia totalis) (2). Although the exact aetiology of AA is unknown, contributing variables such as autoimmune processes, genetic predisposition, and perhaps stress is thought to be involved (3). Various theories suggest that the key factors in this disease are characterized by lymphocytic infiltration of the hair follicle and hair cycle disruption, which are driven by elements, such as the activities of cytotoxic T-cells, the release of cytokines as well as apoptosis (4). Regulatory T cells impact the progression of both AA and thyroid disease. Additionally, human leukocyte antigen (HLA) is another common link between AA and autoimmune thyroid disease (5).

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According to certain evidence, hypothyroidism characterized by decreased thyroid hormone levels (6), and induced by autoantibodies, is also associated with AA, specifically through a genetic link to HLA-DQB1*03 (7). In individuals with AA, autoimmune diseases such as lupus erythematosus, vitiligo, celiac disease, diabetes mellitus, psoriasis, and Hashimoto's thyroiditis have all been noted as concomitant conditions. However, the largest correlation has been seen between vitiligo and hypothyroidism (8). Thyroid autoimmune pathogenesis involves cellular and humoral immunity as well as genetic predisposition (9). According to a comprehensive meta-analysis conducted by Lee et al., those with AA had higher rates of autoimmune thyroid disease (ATD), such as Graves's disease and Hashimoto's chronic thyroiditis, than did the control group. Thyroid dysfunction (prevalence: 12.5%) was more common in patients with AA, especially subclinical hypothyroidism (prevalence: 10.4%) and hyperthyroidism (characterized by increased thyroid hormone levels) (10) (prevalence: 5.7%) (11). Evidence has indicated that AA may be more severe if thyroid problems are proven, such as subclinical malfunction or positive antithyroid antibodies with

normal hormone readings (12). The well-known hypothalamic-pituitary-adrenal (HPA) axis, one of the four primary neuroendocrine systems through which the pituitary gland and hypothalamus control neuroendocrine activity, produces the steroid hormone cortisol (13). The body's cortisol concentration is a useful biomarker for several diseases and is indicative of several vital organismic processes that are essential for maintaining homeostasis (14). More precisely, a number of stress-related illnesses have been linked to or studied in relation to cortisol levels (15), even as Cushing's syndrome (neoplastic hypercortisolism) is thought to be diagnosed with them as a hallmark (16).

The present study aimed to evaluate the relationship between subclinical thyroid dysfunction and alopecia areata, as well as the link between serum cortisol levels and AA.

Patients, Materials, and Methods

A case-control study was carried out. Patients' and controls' blood samples were collected and tested at the Dermatology Center of Baghdad Teaching Hospital, Medical City, Iraq, between October 2023, and February 2024. Ethical approval No. 40256 on 23-10-2023 was obtained from the Center of Training & Human Development Department at Medical City Directorate in Baghdad, Iraq.

The study included 120 participants, of whom 80 were patients with alopecia areata, and 40 were healthy volunteer individuals, matched with the cases for age and sex, as a control group. The patients with AA were classified into three distinct subtypes: patchy alopecia areata (characterized by localized hair loss in patches), alopecia totalis (complete loss of hair on the scalp), and alopecia universalis (total absence of hair on both the scalp and body).

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

Serum Thyroid stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and Cortisol were measured using electrochemiluminescence immunoassay (Cobas e411 immunoassay analyzer, Roche Diagnostics, Mannheim, Germany), a method which is widely recognized for its high sensitivity and specificity, ensuring precise and reliable quantification of hormone levels in clinical and research settings.

The reference values were (0.27-4.2) µIU/ml for TSH, (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. To account for the diurnal variations in hormonal levels, blood samples were consistently collected at the same time of day for all participants.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 23 was used for statistical analysis. Descriptive statistics, including means, standard deviations, and ranges, were used to summarize the data. Frequencies and percentages were utilized for categorical variables, and comparisons were made using the chi-square test or Fisher's exact test when expected frequencies were below five. Continuous variables were analyzed using the independent t-test under the assumption of normal data distribution and equal variances. A statistically significant p-value was defined as less than 0.05.

Results

The current study found no statistically significant difference (P = 0.75) between the mean age of the patients and the control group, which were (29.4 ± 10.49) and (30.1 ± 8.77) years, respectively. The patients with AA were found to be mostly between the ages of 16 and 32 (36 out of 80 cases, or 45%), while fewer patients in the age groups over 45 years. This distribution was not statistically significant (*P*-value = 0.87), Figure 1.

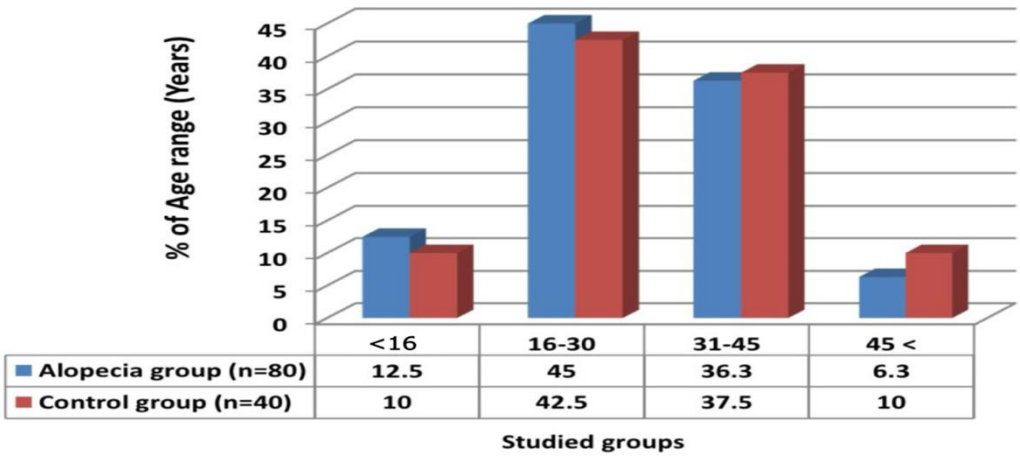

Figure 1: Distribution of the study groups according to age

Significant differences were found (*p*-value = 0.03) in the levels of T3 between AA cases and controls, with means of (3.2 ± 1.04) and (1.4 ± 0.03) ng/ml, respectively. No significant differences (P-values = 0.25 and 0.31) were found in the levels of both T4 and TSH between the AA cases and controls, with mean values of (8.4 ± 0.21) and (8.7 ± 0.16) ug/dl for T4, and (1.7 ± 0.11) and (1.6 ± 0.08) µIU/ml for TSH, respectively, Table 1. Only 8 out of 80 patients were found to have abnormal T3 levels, representing 8.8% of the study population. These findings suggest that while T3 levels differ significantly, the relationship between AA and thyroid dysfunction may be more complex and not solely dependent on T4 or TSH levels.

Table 1: Mean±SD values for T3, T4, and TSH concentrations in the study groups

Thyroid Function Tests	Mean±SD		T-test	*P*-value
	Alopecia group	Control group		
T3 (ng/mL)	1.5±0.04	1.4±0.03	2.11	0.03 (S)
T4 (µg/dl)	8.4±0.21	8.7±0.16	1.13	0.25 (N.S)
TSH (µIU/mL)	1.7±0.11	1.6±0.08	1.00	0.31 (N.S)

TSH= Thyroid Stimulating Hormone; T4= Thyroxin; T3= Triiodothyronine.

When the cortisol serum concentrations in the two groups were compared, as indicated in Table 2, it was found that the AA group values were substantially higher than those of the controls (11.1 ± 0.52)versus (8.6 ± 0.23) ng/dl, $P \leq 0.0001$.

Table 2: Mean±SD values for Cortisol in the study groups

Hormone	Means±SD		T-test	*P*-value
	Alopecia group	Control group		
Cortisol (ug/dl)	11.1±0.52	8.6±0.23	4.44	0.0001 (HS)

The Receiver Operating Characteristic curve (ROC) analysis was done to assess the diagnostic value of Cortisol in the AA patients and controls. The results of ROC analysis of AA are shown in Table (3) and Figure (2). Poor prediction of AUC value result was seen in AA with (*P*-value = 0.017) at 0.635. The senitivity was 38% and Specificity was 97% at the optimal cutoff value of 11.2 which differentiates patients from controls.

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

Variable	Sensitivity	Specicifity	AUC	Aaccuracy		Cutoff value
				L.B.	U.B.	
Cortisol	38%	97%	0.635	0.538	0.731	11.2

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

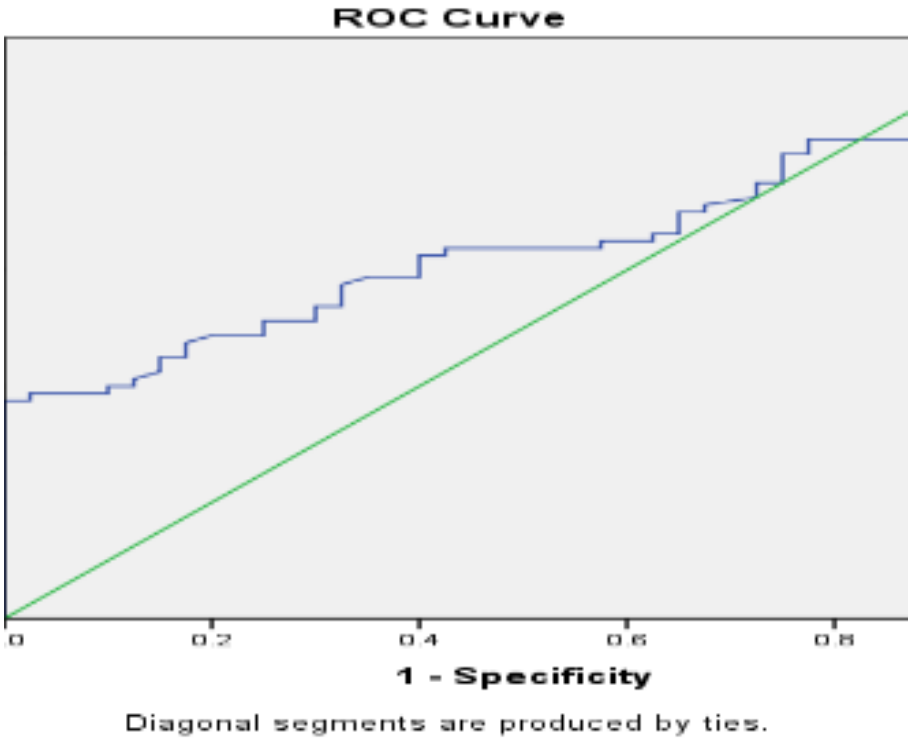

Figure 2: ROC curve for Cortisol

Discussion

Thyroid function in AA patients and healthy controls was assessed in the current study by measuring T3, T4, and TSH concentrations. There may not be any evident damage, as the study did not uncover statistically significant changes in the T4 and TSH concentrations between AA patients and healthy controls. However, variations in T3 concentrations suggest a potential association between thyroid function and AA patients.

The results of the current study are in line with the findings of Nayaf *et al,* (17), who observed that although there were no statistically significant differences in TSH or T4 concentrations between AA patients and healthy controls, there was a difference in T3 concentrations. However, the TSH and T4 hormone levels were significantly greater in AA patients than in the controls, according to the findings of Muhammed *et al* (18), although there was no discernible difference in T3 levels between AA cases and controls.

The current study also reveals that only 13% of AA patients exhibited abnormal thyroid function tests, with subclinical hypothyroidism being discovered in 5% of AA patients and subclinical hyperthyroidism in 8.8% of AA patients. Only 7.1% of AA patients in a Rai *et al* study., (19) had abnormal thyroid function testing. Similar findings were found by a study conducted in Al-Ramadi City, which found a statistically significant difference in thyroid function tests between AA patients and controls (20).

Although there is ongoing research, the relationship between AA and thyroid entities does not imply causation. It is not universally agreed upon that a certain subset of AA patients is predisposed to acquire thyroid-related endocrine abnormalities, such as positive antibodies and/or abnormal hormonal panels, and that these thyroid abnormalities actively contribute to the development of a more severe form of AA.

By working through stress hormones, research indicates that stress can cause hair loss (21). Among the primary stress hormones in humans, cortisol is one of the hormones that makes up the HPA axis (22). Cortisol, a vital glucocorticoid hormone secreted by the adrenal glands, plays a fundamental role in regulating numerous physiological functions (23). Glucocorticoids (GCs) are well-known for their potent anti-inflammatory properties, which have been widely utilized in clinical settings for decades (24).

limitations

A small sample size and a brief patient follow-up period are two of the study's shortcomings.

Conclusion

A significant relationship exists between elevated T3 and cortisol levels and alopecia areata, indicating the possible contribution of thyroid dysfunction to the occurrence of AA. The lack of significant differences in the T4 and TSH levels suggests a more intricate endocrine interaction beyond primary thyroid abnormalities. The cortisol levels alone may not be sufficient diagnostic markers for AA and should likely be used in conjunction with other diagnostic tools, to improve accuracy.

Authors' declaration

There are no conflicts of interest. We hereby attest that every Figure and Table in the manuscript is our own. Furthermore, authorization 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 (22/518, dated September 18, 2023) the project was accepted by the local ethics committee at the College of Science for Women, University of Baghdad.

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Authors' contributions

Study conception & design: (Talib A. Hussein). Literature search: (Baneen S. Qasim). Data acquisition: (Hadeel J. Hasan). Data analysis & interpretation: (Baneen S. Qasim). Manuscript preparation: (Baneen S. Qasim). Manuscript editing & review: (Baneen S. Qasim, Talib A. Hussein, and Hadeel J. Hasan).

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تقييم اضطراب الغدة الدرقية ومستويات الكورتيزول في مرضى الثعلبة البقعية

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الخلاصة
الخلفية: الثعلبة البقعية (AA) هي مرض مناعي ذاتي متعدد العوامل، يلعب الإستعداد الجيني دورًا رئيسيًا في حدوثه. تم ربط الثعلبة البقعية بالعديد من الحالات المناعية الذاتية، ومن المرجح أن تتزامن مع إضطرابات الغدة الدرقية المناعية الذاتية.
الهدف: تحديد ما إذا كان هناك إرتباط إحصائي بين الثعلبة البقعية وإضطراب الغدة الدرقية تحت السريري، وتقدير مستويات الكورتيزول في مرضى الثعلبة وإستكشاف علاقتها بالمرض.
المنهجية: أُجريت الدراسة الحالية في مركز الأمراض الجلدية في مستشفى بغداد التعليمي / مدينة الطب في بغداد من تشرين الأول 2023 إلى شباط 2024. شملت الدراسة 80 مريضًا بالثعلبة و40 شخصًا سليمًا كعينة ضابطة. تم قياس مستويات هرمونات الغدة الدرقية والكورتيزول باستخدام تقنية المناعة الكهروكيميائية.
النتائج: كان متوسط عمر مرضى الثعلبة البقعية (29.4 ± 10.49) عامًا مقارنة بـ (30.1 ± 8.77) عامًا في مجموعة الضابطة، ولم يكن هناك فرق ذو دلالة إحصائية بين المجموعتين ($p = 0.75$). كانت مستويات T3 في مصل الدم أعلى بشكل ملحوظ لدى مرضى الثعلبة (1.5 ± 0.04 نانوغرام/مل) مقارنة بالمجموعة الضابطة (1.4 ± 0.03 نانوغرام/مل، $p = 0.03$)، ومع ذلك، بقيت جميع القيم ضمن المعدل الطبيعي.في المقابل، لم تُلاحظ فروق ذات دلالة إحصائية في مستويات T4 (0.21 ± 8.4 مقابل 8.7 ± 0.16 ميكروغرام/ديسيلتر، $p = 0.25$) أو مستويات TSH (0.11 ± 1.7 مقابل 1.6 ± 0.08 ميكروووحدة دولية/مل، $p = 0.31$) بين مرضى الثعلبة ومجموعة الضابطة.أما مستويات الكورتيزول في مصل الدم، فكانت أعلى بشكل ملحوظ لدى مرضى الثعلبة (11.1 ± 0.52 نانوغرام/ديسيلتر) مقارنة بمجموعة الضبط (8.6 ± 0.23 نانوغرام/ديسيلتر، $p < 0.0001$)، ومع ذلك، بقيت جميع القيم المقاسة ضمن النطاق المرجعي الطبيعي في كلا المجموعتين
الإستنتاج: توجد علاقة مهمة بين ارتفاع مستويات الهرمون الدرقي الثالث والكورتيزول والثعلبة البقعية، مما يشير إلى المساهمة المحتملة لخلل الغدة الدرقية في حدوث الثعلبة البقعية. يشير عدم وجود فروق كبيرة في مستويات الهرمون الدرقي الرابع والهرمون المحفز للدرقية إلى تفاعل هرموني أكثر تعقيدًا. قد لا تكون مستويات الكورتيزول وحدها علامات تشخيصية كافية للثعلبة البقعية، ومن المرجح أن يتم استخدامها جنبًا إلى جنب مع أدوات تشخيصية أخرى لتحسين الدقة.
الكلمات المفتاحية: الثعلبة البقعية، الأمراض المناعية الذاتية، الكورتيزول، اختبار وظائف الغدة الدرقية، الهرمون المحفز للدرقية.