

Research Article

Frequency of Thyroid Nodules and Autoimmune Thyroid Disease in Patients with Adrenal Incidentaloma

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Abstract

Objectives: To evaluate the clinical, laboratory, and radiological characteristics of patients with adrenal incidentaloma and to investigate the relationship between adrenal incidentaloma and autoimmune thyroid disease.

Methods: This retrospective study included 66 patients diagnosed with adrenal incidentaloma between December 2018 and February 2019. Demographic characteristics, hormonal status, radiological findings, metabolic comorbidities, and thyroid ultrasonography findings were evaluated. Autoimmune thyroid disease was assessed according to thyroid autoantibody positivity and thyroid parenchymal heterogeneity.

Results: The mean age was 56.2 ± 7.9 years, and 77.3% of the patients were female. Overall, 83.3% of the patients were overweight or obese. Hypertension (29.5%), diabetes mellitus (21.4%), and hyperlipidemia (13.4%) were the most common comorbidities. Nonfunctioning adrenal adenoma was detected in 83.3% of patients. Thyroid nodules were significantly more frequent in patients with functioning adrenal adenoma than in those with nonfunctioning adenoma (90.9% vs. 56.4%, $p=0.04$). No significant association was found between hormonal activity and thyroid autoantibody positivity or thyroid parenchymal heterogeneity.

Conclusion: Functioning adrenal adenoma may be associated with increased thyroid nodule frequency; however, no relationship was demonstrated between adrenal hormonal activity and autoimmune thyroid disease.

Keywords: Adrenal incidentaloma, autoimmune thyroid disease, thyroid nodule

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Adrenal incidentaloma (AI) is defined as an adrenal mass incidentally detected during imaging studies performed without suspicion of adrenal disease. In recent years, the frequency of adrenal incidentaloma has increased significantly due to the widespread use of computed tomography (CT) and magnetic resonance imaging (MRI).^[1] The prevalence of adrenal incidentaloma in autopsy series has been reported to range between 1.4% and 8.7%.^[2] Adrenal incidentalomas are

more frequently observed in the elderly population, and most cases are diagnosed between the sixth and eighth decades of life.^[3]

The majority of adrenal incidentalomas are benign and nonfunctioning adrenal adenomas. However, clinically significant pathologies such as pheochromocytoma, primary hyperaldosteronism, subclinical hypercortisolism, adrenocortical carcinoma, and metastatic lesions may also be included in the etiology of adrenal incidentaloma.^[4] Therefore,

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evaluation of the hormonal activity and malignant potential of the adrenal mass is of great importance.

A detailed clinical evaluation, hormonal investigations, and radiological imaging methods are used together in the assessment of patients with adrenal incidentaloma. Current guidelines recommend the 1-mg dexamethasone suppression test in all patients to exclude autonomous cortisol secretion.^[5] In addition, plasma or urinary metanephrine levels are evaluated for pheochromocytoma,^[6] and primary hyperaldosteronism is investigated in the presence of hypertension or hypokalemia. In radiological evaluation, the size, density, and imaging characteristics of the adrenal mass provide important clues regarding malignancy.

Autoimmune thyroid diseases (AITD) are chronic autoimmune disorders that develop as a result of the interaction between genetic susceptibility and environmental factors. Hashimoto's thyroiditis and Graves' disease are the most common clinical forms of autoimmune thyroid diseases, and the prevalence in the general population is reported to be approximately 5%.^[7] HLA-associated genetic factors, immune regulatory genes, female sex, age, iodine intake, and environmental triggers are known to play a role in the development of autoimmune thyroid diseases.

In recent years, there has been increasing interest in the relationship between adrenal incidentaloma and various endocrine and autoimmune diseases. However, there are limited data in the literature regarding the frequency of autoimmune thyroid disease and associated clinical characteristics in patients with adrenal incidentaloma. Therefore, the present study aimed to investigate the frequency of autoimmune thyroid disease in patients with adrenal incidentaloma and to evaluate the accompanying clinical, hormonal, and radiological characteristics.

Methods

In this retrospective study, the clinical, laboratory, and radiological data of patients diagnosed with adrenal incidentaloma (AI) were evaluated.

A total of 66 patients with radiologically detected "adrenal adenoma," "adrenal lesion," or "adrenal mass" identified during imaging studies performed for any reason between December 2018 and February 2019 were included in the study. Patient data were retrospectively obtained from hospital automation records and patient files.

Demographic characteristics, presenting complaints, accompanying diseases, medications, smoking status, and alcohol consumption history of the patients were recorded. Clinical findings suggestive of pheochromocytoma, Cushing syndrome, hyperaldosteronism, and malignancy were also evaluated. Anthropometric measurements including

height, body weight, and body mass index (BMI) were calculated. Systolic and diastolic blood pressure values were recorded. Physical examination findings including central obesity, moon face, dorsocervical fat accumulation, supraclavicular fullness, purple striae, and proximal muscle weakness were assessed.

The clinical indications leading to the diagnosis of adrenal incidentaloma and the imaging modalities used [ultrasonography (USG), computed tomography (CT), and/or magnetic resonance imaging (MRI)] were evaluated. Radiological assessment included the localization, size, density, and other imaging characteristics of the adrenal masses.

Hormonal evaluation included serum sodium and potassium levels, plasma aldosterone, plasma renin activity, basal ACTH, serum cortisol, dehydroepiandrosterone sulfate (DHEA-S), 24-hour urinary free cortisol levels, results of the 1-mg or 2-mg dexamethasone suppression tests, and 24-hour urinary catecholamine and metabolite levels. In addition, fasting blood glucose, HbA1c, liver and kidney function tests, and lipid parameters were recorded.

According to the hormonal evaluation results, patients were classified as having nonfunctioning adrenal adenoma, subclinical Cushing syndrome, Cushing syndrome, pheochromocytoma, or hyperaldosteronism. Patients with incomplete hormonal evaluations were assessed separately. Whether biopsy was performed, biopsy indications, and histopathological results were also recorded.

The relationship between adrenal adenoma and autoimmune thyroid disease was evaluated using thyroid ultrasonographic parenchymal heterogeneity and thyroid auto-antibody levels.

Statistical analyses were performed using IBM SPSS Statistics for Windows Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation or median (minimum–maximum), while categorical variables were expressed as numbers and percentages. Pearson's chi-square test was used for comparisons of categorical variables. Fisher's exact test was used when the expected cell count was less than 5. A p-value of <0.05 was considered statistically significant.

Ethics committee approval for the study was obtained from the local ethics committee (Approval No: 2019/373, Date: 25.12.2019). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

A total of 66 patients diagnosed with adrenal incidentaloma were included in the study. The mean age of the patients was 56.2±7.9 years (range: 40–71 years). Of the patients, 51

(77.3%) were female and 15 (22.7%) were male. According to body mass index (BMI) classification, 11 patients (16.7%) had normal weight, 26 (39.4%) were overweight, and 29 (43.9%) were obese.

Regarding the localization of adrenal masses, 26 patients (39.4%) had right adrenal involvement, 30 patients (45.5%) had left adrenal involvement, and 10 patients (15.1%) had bilateral adrenal masses.

The relationship between BMI and sex was evaluated using Pearson's chi-square test, and BMI was found to be significantly higher in female patients compared to male patients ($p=0.012$) (Table 1).

Pearson's chi-square test, $p=0.012$

When accompanying comorbidities were evaluated, the most common conditions were hypertension (29.5%), diabetes mellitus (21.4%), hyperlipidemia (13.4%), and hypothyroidism (8.9%). A history of malignancy was present in 11 patients (Table 2).

Regarding thyroid diseases, 5 patients (7.6%) had a history of thyroidectomy, and 14 patients (21.2%) had a history of levothyroxine use. Thyroid nodules were detected in 41 patients (62.1%), while thyroid parenchymal heterogeneity was observed in 35 patients (53%). Thyroid autoantibody positivity was present in 10 patients (15.2%).

Table 1. Comparison of body mass index distribution between female and male patients

Body mass index	Female n (%)	Male n (%)	Total n (%)
Normal (18.5–24.9 kg/m ²)	5 (45.5)	6 (54.5)	11 (16.7)
Overweight (25–29.9 kg/m ²)	20 (76.9)	6 (23.1)	26 (39.4)
Obese (≥ 30 kg/m ²)	26 (89.7)	3 (10.3)	29 (43.9)

Table 2. Distribution of accompanying comorbid diseases in patients

Comorbid disease	n (%)	Comorbid disease	n (%)
Hypertension	33 (29.5)	Rheumatoid arthritis	2 (1.8)
Diabetes mellitus	24 (21.4)	Multinodular goiter	2 (1.8)
Hyperlipidemia	15 (13.4)	Renal cell carcinoma	2 (1.8)
Hypothyroidism	10 (8.9)	Hyperparathyroidism	1 (0.9)
Asthma	7 (6.3)	Atrial fibrillation	1 (0.9)
Chronic kidney disease	3 (2.7)	Colon cancer	1 (0.9)
Thyroid cancer	3 (2.7)	Cervical cancer	1 (0.9)
Breast cancer	3 (2.7)	Endometrial cancer	1 (0.9)
Coronary artery disease	2 (1.8)	Ankylosing spondylitis	1 (0.9)

Table 3. Comparison of thyroid nodule frequency between patients with functioning and nonfunctioning adrenal adenoma

Thyroid nodule	Nonfunctioning adenoma n (%)	Functioning adenoma n (%)	Total n (%)
Present	31 (56.4)	10 (90.9)	41 (62.1)
Absent	24 (43.6)	1 (9.1)	25 (37.9)
Total	55 (100.0)	11 (100.0)	66 (100.0)
Pearson's chi-square test, $p=0.04$			

Among the study population, 55 patients were classified as having nonfunctioning adrenal adenoma, whereas 11 patients had functioning adrenal adenoma [subclinical Cushing syndrome, Cushing syndrome, primary hyperaldosteronism, and pheochromocytoma]. Thyroid nodules were detected in 31 patients (56.4%) with nonfunctioning adrenal adenoma and in 10 patients (90.9%) with functioning adrenal adenoma. The relationship between hormonal activity and the presence of thyroid nodules was found to be statistically significant according to Pearson's chi-square test ($p=0.04$) (Table 3).

The relationship between functioning and nonfunctioning adrenal adenomas and autoimmune thyroid disease was evaluated based on thyroid autoantibody positivity and thyroid parenchymal heterogeneity. No significant association was found between hormonal activity and thyroid autoantibody positivity ($p=0.66$) (Table 4). Similarly, no statistically significant relationship was observed between hormonal activity and thyroid parenchymal heterogeneity ($p=0.46$) (Table 5).

Discussion

The frequency of adrenal incidentalomas has increased significantly in recent years, mainly due to the widespread use of imaging modalities.^[1] In the present study, the mean age of patients diagnosed with adrenal incidentaloma was 56.2 ± 7.9 years, which is consistent with previously reported data in the literature.^[3] The higher prevalence of adrenal incidentalomas in elderly populations may be explained by the increased use of imaging techniques with advancing age and the age-related increase in nodular changes within the adrenal cortex.^[8]

Previous studies have reported that adrenal incidentalomas are more common in women. In a large series conducted by the Italian Association of Clinical Endocrinologists Study Group on Adrenal Tumors, the female-to-male ratio was reported as 1.39.^[9] Similarly, the majority of patients in our study were female (77.3%). This finding may be associated

Table 4. Distribution of thyroid autoantibody positivity among adrenal adenoma subgroups

Hormonal activity	Thyroid Autoantibody positive n (%)	Thyroid Autoantibody negative n (%)	Total n (%)
Nonfunctioning adenoma	8 (14.5)	47 (85.5)	55 (83.3)
Subclinical cushing syndrome	0 (0.0)	3 (100.0)	3 (4.5)
Cushing syndrome	0 (0.0)	2 (100.0)	2 (3.0)
Primary hyperaldosteronism	1 (25.0)	3 (75.0)	4 (6.1)
Pheochromocytoma	1 (50.0)	1 (50.0)	2 (3.0)
Total	10 (15.2)	56 (84.8)	66 (100.0)

Pearson's chi-square test, $p=0.66$.

Table 5. Distribution of thyroid parenchymal characteristics among adrenal adenoma subgroups

Hormonal activity	Homogeneous parenchyma n (%)	Heterogeneous parenchyma n (%)	Total n (%)
Nonfunctioning adenoma	25 (45.5)	30 (54.5)	55 (83.3)
Subclinical Cushing syndrome	1 (33.3)	2 (66.7)	3 (4.5)
Cushing syndrome	1 (50.0)	1 (50.0)	2 (3.0)
Primary hyperaldosteronism	3 (75.0)	1 (25.0)	4 (6.1)
Pheochromocytoma	1 (50.0)	1 (50.0)	2 (3.0)
Total	31 (47.0)	35 (53.0)	66 (100.0)

Pearson's chi-square test, $p=0.46$.

with the more frequent use of imaging studies in female patients.

Metabolic disorders are known to occur more frequently in patients with adrenal incidentaloma.^[10] Previous studies have demonstrated associations between adrenal incidentaloma and obesity, hypertension, diabetes mellitus, and hyperlipidemia.^[11] In our study, 83.3% of the patients were overweight or obese. In addition, hypertension, diabetes mellitus, and hyperlipidemia were the most common accompanying comorbidities. These findings support the association between adrenal incidentaloma and metabolic disorders.

In the present study, adrenal masses were most frequently localized in the left adrenal gland (45.5%). In contrast, previous reports have indicated that adrenal masses are more commonly detected in the right adrenal gland, which has been attributed to the limited ability of ultrasonography (USG) to visualize the left adrenal gland.^[12] The difference observed in our study may be related to the predominant use of CT and MRI as imaging modalities.

Functional evaluation demonstrated that the majority of patients had nonfunctioning adrenal adenoma (83.3%), which is consistent with the rates reported in the literature.^[13,14] Among the functional lesions, primary hyperaldosteronism was the most common (6.1%), whereas the frequency of pheochromocytoma was 3%.

One of the most remarkable findings of our study was the significantly higher frequency of thyroid nodules in patients with functioning adrenal adenoma. Thyroid nodules were detected in 90.9% of patients with functioning adrenal adenoma compared to 56.4% of patients with nonfunctioning adrenal adenoma ($p=0.04$). Similarly, a previous study conducted in Türkiye reported a higher prevalence of thyroid nodules in patients with adrenal incidentaloma compared to the control group.^[15] This finding suggests that cortisol and other adrenal hormones may contribute to thyroid proliferation through growth factors and insulin resistance mechanisms.

However, no significant association was found between hormonal activity and autoimmune thyroid disease in our study. Evaluations based on thyroid autoantibody positivity and thyroid parenchymal heterogeneity demonstrated no significant differences between functioning and nonfunctioning adrenal adenoma groups. These findings suggest that adrenal hormonal activity may be associated with thyroid nodule formation but may not be directly related to autoimmune mechanisms.

Limitations of the Study

The retrospective and single-center design of the study, as well as the limited sample size, are important limitations. In addition, the absence of a control group prevented a

clear evaluation of whether the frequency of thyroid nodules was increased compared to the general population. In addition, the retrospective design may have introduced selection bias.

Conclusion

Adrenal incidentaloma has become an increasingly common condition in clinical practice due to the widespread use of imaging modalities. Comprehensive clinical, laboratory, and radiological evaluation of these patients is essential for the assessment of hormonal activity and malignancy risk.

In our study, obesity, hypertension, diabetes mellitus, and hyperlipidemia were frequently observed in patients with adrenal incidentaloma. In addition, the frequency of thyroid nodules was found to be significantly higher in patients with functioning adrenal adenoma. However, no significant association was demonstrated between autoimmune thyroid disease and adrenal hormonal activity.

These findings suggest that adrenal hormonal activity may be associated with the development of thyroid nodules. Therefore, more careful evaluation for the presence of thyroid nodules may be beneficial in patients with adrenal incidentaloma. Nevertheless, further prospective studies with larger patient populations are needed to better clarify the relationship between adrenal incidentaloma and autoimmune thyroid diseases.

Disclosures

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics committee approval was obtained from the Local Ethics Committee of Selçuk University Faculty of Medicine before the study (Approval No: 2019/373, Date: 25.12.2019).

Informed Consent: Informed consent was waived due to the retrospective design of the study.

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