Original Research

The complex relationship between endocrine and psychiatric disorders: an epidemiological study of risk estimates

Zsófia Orbán[1], Adriana Mihai[2], Réka Bodea[3]

1) Department of Family Medicine, Mureș County Emergency Hospital, Târgu Mureș, Romania

2) Department of Psychiatry, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureș, Romania

3) Department of Epidemiology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureș, Romania

Abstract

Backgrounds and aims. Psychiatric comorbidities are frequently observed in patients with endocrine disorders, yet in Romania the extent and nature of this association remains underexplored in clinical settings. This study aims to evaluate the prevalence and characteristics of endocrine disorders, like Cushing's syndrome, Addison's disease, hypo- and hyperthyroidism, in patients diagnosed with depressive, anxious, and manic disorders.

Methods. We conducted a retrospective cross-sectional study using records from the Hipocrate/H3 electronic medical system between January 1, 2020, and September 1, 2024. Patients with ICD-10-coded endocrine diagnoses were identified, and the presence of documented psychiatric diagnoses was assessed. Odds ratios with 95% confidence intervals and chi-square tests were used to compare the odds of psychiatric comorbidity across endocrine diagnostic groups.

Results. The statistical analysis revealed that patients with Addison's disease, Cushing's syndrome and hypothyroidism were associated with significantly higher odds of psychiatric comorbidity ($p < 0.0001$). In contrast, in the case of patients with hyperthyroidism, we observed significantly lower odds of psychiatric disorders ($p < 0.0001$).

Conclusion. The study demonstrates that psychiatric comorbidities are common among patients with endocrine disorders, underscoring a meaningful relationship between endocrine dysfunction and mental health. Because the study was cross-sectional and based on clinical records, causal interpretation is not possible. The findings support the need for integrated endocrine and psychiatric assessment in patients with selected endocrine disorders.

Keywords: Cushing's Syndrome, Addison's Disease, hypothyroidism, hyperthyroidism, neuroendocrine system, cross-sectional studies, Romania

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Address for correspondence:
Zsófia Orbán
zsofia.orban@yahoo.com

Introduction

The intersection between endocrine and psychiatric disorders has gained increasing attention in recent years, as multiple observational and clinical studies over the past decade have shown consistent accumulating evidence suggesting a strong relationship between these two systems [1]. This association is highly significant clinically, because it has an impact on diagnosis, treatment, but also on symptom severity and clinical outcome, as well as on the quality of life of the affected patients.

Hormonal imbalances, whether stemming from the adrenal or from the thyroid gland, can significantly influence cognitive function, mood regulation, and behavior [2]. Chronic psychiatric stress and emotional trauma may also impact the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) axis, further complicating the clinical picture [3]. When these endocrine disorders are treated, most brain function alterations usually improve. Still, some of the more

subtle cognitive issues may persist even after the hormone levels return to normal [1].

Endocrine disorders might provoke a range of biological responses, so any hormonal change can activate multiple corrective pathways, as the body attempts to regain its homeostasis [4].

The consequence of hormonal imbalance may be inflammation and direct affectation of different brain regions involved in mood and thinking, leading to psychiatric problems such as depression, anxiety, mania, eating disorders. Sadly, sometimes these conditions can manifest even more dramatically: psychosis or suicidal thoughts may appear [1]. If this occurs in the limbic system, which in turn affects memory, emotions, and human behavior, the functions it regulates become impaired [5]. Cortical atrophy may develop [6], accompanied by secondary ventricular enlargement, neuronal demyelination, and loss of gray matter and hippocampal volume, structures that play a significant role in the development and progression of the disease [7,8]. Chronic endocrine illnesses that require constant self-management, such as diabetes and thyroid dysfunctions often can contribute themselves to psychological distress [1].

Among endocrine disorders, conditions such as Cushing's syndrome, Addison's disease, hypothyroidism and hyperthyroidism are known to alter neuroendocrine homeostasis, frequently resulting in psychiatric manifestations [9]. Differentiating between a primary psychiatric condition and one secondary to endocrine dysfunction is essential, as treatment approaches are different and the prognoses can vary considerably.

Correlation between Cushing's syndrome and anxiety and depressive disorders

Several theories have been proposed to explain how elevated cortisol levels contribute to psychiatric disorders, particularly depression. For example, chronic high cortisol reduces tryptophan levels, the precursor of serotonin, leading to decreased serotonin availability and lower serotonin receptor expression [10], which in turn impairs both neurotransmitter levels and receptor responsiveness to stimuli [8].

Elevated cortisol is not observed only in depression but also in schizophrenia and other psychoses. One study continuously monitored cortisol levels in women at high risk of developing psychosis. Compared with the control group, a significant majority of these high-risk women exhibited persistently elevated cortisol levels [8].

Relationship between Addison's disease and anxiety disorders

Although both glucocorticoid and mineralocorticoid levels are reduced in Addison's disease, circulating glucocorticoid levels are particularly important when considering psychiatric comorbidities. Literature reports many cases in which normalization of cortisol levels is associated with significant improvement in mental health. Consequently, cortisol may serve as a useful biological marker to help predict the likelihood of psychiatric disorders, symptom severity, and imminent onset [8].

When cortisol levels are extremely low, patients may experience symptoms resembling severe anxiety or even panic attacks, including extreme fatigue, abdominal pain, nausea, dizziness, rapid heart rate, and confusion, making it difficult to differentiate between adrenal crisis and anxiety attacks [11].

Moreover, studies in older adults with anxiety disorders have shown that cortisol levels upon awakening, measured in saliva, are significantly lower than in individuals without anxiety. Several population-based studies show that chronic anxiety may lead to reduced HPA axis activity, which in turn lowers cortisol levels [12].

Hyperthyroidism and hypothyroidism: two sides of the same coin

Neurotransmitters such as somatostatin and serotonin influence the HPT axis, highlighting the connection between thyroid function and mood. Elevated thyroid-stimulating hormone, thyroglobulin antibody and thyroid-peroxidase antibody levels have been associated with increased risk of depressive episodes and suicide attempts [9]. Hormone replacement therapy for hypothyroidism often leads to significant improvements in mood disturbances, including depression [9].

Both hypothyroidism and hyperthyroidism can cause mood disorders, including depression and anxiety. Several mechanisms have been proposed, including metabolic disturbances associated with hormonal imbalances that impair neuronal communication and cognitive function [13]. Dysfunction in thyroid feedback is evident, for example, in elevated thyrotropin-releasing hormone levels in the cerebrospinal fluid of depressed patients [14]. The "brain hypothyroidism" hypothesis suggests that even when peripheral hormone levels are normal, the brain may experience a localized hypothyroid state with associated functional consequences [15]. Routine thyroid testing has been recommended in depression diagnosis, and thyroid therapy may be considered in treatment-resistant cases [16,17].

Hyperthyroidism, in contrast, is more frequently associated with psychosis, emotional lability, agitation, anxiety, and apathy [18]. Sleep disturbances, memory deficits, and concentration problems can sometimes signal the onset of manic episodes. Interestingly, hyperthyroidism, like hypothyroidism, may also induce depressive symptoms [19].

Despite growing awareness, multiple studies in the last decade, data from Romania remains limited. Most existing studies are small, outdated, or focused on single disorders without examining the broader spectrum of psychiatric manifestations across endocrine diseases.

This study was guided by the hypothesis that patients with documented coexisting endocrine and

psychiatric diagnoses show different patterns of psychiatric comorbidity, depending on the type of endocrine disorder, specifically Cushing's syndrome, Addison's disease, hypothyroidism, or hyperthyroidism. We expected the distribution of depressive, anxiety and manic/bipolar disorders to vary among patients with Cushing's syndrome, Addison's disease, hypothyroidism, and hyperthyroidism.

Our specific objective was to identify statistically significant correlations and offer insight into the neuropsychiatric burden of endocrine diseases.

Methods

Study design and sampling method

This research was conducted as a retrospective cross-sectional study, descriptive and analytical in nature. Purposive, convenience sampling method was used and clinical data were collected over a period of 56 months, from January 1, 2020, to September 1, 2024. Sampling was determined by the availability of complete and validated clinical records rather than random selection, to ensure that the dataset reflected real-world clinical practice.

Sampling size

A total number of 7,797 psychiatric patients formed the primary group assessed for eligibility; 642 patients of this group had an endocrine disorder, of which 566 hypothyroidism and 76 hyperthyroidism. The study included all patients who met the inclusion criteria during the study period, no prior sample size calculation was needed. Therefore, the sample represents all available eligible patients.

Study population

The study was carried out at the Mureș County Clinical Hospital, Târgu Mureș, Romania. Clinical data were extracted from the Hipocrate (H3) Medical Information System, a national digital platform used for storing and managing electronic health records, with prior approval from the hospital's Ethics Committee (Approval No. 11046/09.09.2024). Data were collected from two departments: the Acute Psychiatry Clinic I and the Endocrinology Department of the Mureș County Clinical Hospital, Târgu Mureș, Romania. Both departments contribute data to the H3 system, allowing for cross-referencing and comprehensive analysis of patients with dual psychiatric and endocrine diagnoses. Patients diagnosed with endocrine conditions not included among the examined ones were assigned to the control group. All included cases were identified based on final, validated diagnoses recorded by specialist physicians, and duplicate entries across departments were removed by matching unique patient identification codes (CNP).

Inclusion criteria

Patients were eligible for inclusion if they they had a final, specialist-confirmed diagnosis of one or more of the following endocrine disorders: Cushing's syndrome, Addison's disease, hypothyroidism, or hyperthyroidism and a confirmed psychiatric diagnosis according to international diagnostic standards (ICD), including: major depressive disorder, generalized anxiety disorder, mixed anxiety-depressive disorder, manic episode, bipolar affective disorder, or schizoaffective disorder.

Exclusion criteria

Patients were excluded if the endocrine diagnosis was suspected but not confirmed, if the endocrine or psychiatric conditions did not match the target pathologies of the study, if essential demographic or diagnostic data were missing, or if duplicate records could not be resolved.

Data collection and processing

Data extraction was performed using both ICD-10 codes and keyword-based searches within the H3 database, to ensure inclusion of all relevant subtypes of the target conditions. The diagnosis codes were recorded based on specialist physician entries.

To simplify the analysis, most disease subtypes, based on clinical and laboratory assessments, are not discussed separately. "Cushing's syndrome" (ICD-E24) is used to refer collectively to pituitary-dependent Cushing's disease, drug-induced Cushing's, ectopic ACTH syndrome, and unspecified Cushing's.

"Addison's disease" (ICD-E27.1) refers to primary adrenal insufficiency, Addisonian crisis, drug-induced primary adrenal insufficiency, and unspecified adrenal insufficiency.

"Hyperthyroidism" (ICD-E05) encompasses diffuse toxic goiter, toxic single or multinodular goiter, ectopic thyroid tissue, factitious thyrotoxicosis, thyroid storm, and other thyrotoxic states.

"Hypothyroidism" (ICD-E03) covers subclinical iodine-deficiency hypothyroidism, congenital hypothyroidism, diffuse or absent goiter, drug- or exogenous-induced hypothyroidism, post-infectious hypothyroidism, acquired thyroid atrophy, and unspecified forms.

Eligible patients were compiled into a database created using Microsoft Excel 365, capturing variables such as age, sex, endocrine diagnosis psychiatric diagnosis, clinical symptoms, and temporal relationship between the disorders. For each variable, standardized sources and definitions were applied. Clinical symptoms were extracted from specialist notes within the electronic records.

Patients were explicitly grouped by sex during data collection and analysis and the symptoms were not systematically scored, but manually extracted.

Patients were stratified by sex and age groups (<19, 20–29, 30–39, 40–49, 50–59, 60–69, ≥70 years). Age categories were defined to ensure balanced subgroup comparisons. This type of segmentation was applied to reflect clinically relevant life stages associated with distinct endocrine and psychiatric risk profiles.

Special mention was given to those patients whose psychiatric condition developed within 6 years following

the primary diagnosis. This interval represents a midpoint among the time frames used in various studies conducting similar assessments. Prior to the study we observed onset,i.e. when a psychiatric disorder develops, which most commonly occurs within the first 6 years [20].

Statistical analysis

Descriptive statistics were used to assess prevalence and distribution. Inferential analysis was conducted using Pearson's chi-square (χ^2) tests to determine the strength of association between endocrine and psychiatric disorders. The significance level was set at $p<0.05$. Additionally, odds ratios (ORs) with 95% confidence intervals (CI) were calculated to estimate the relative risk of psychiatric comorbidity across endocrine conditions. Statistical analysis was performed using Microsoft Excel 365, including the Analysis ToolPak add-in.

These choices ensured methodological transparency and reproducibility within the constraints of a retrospective hospital-based dataset: Microsoft Excel was selected due to its compatibility with the H3 export format and its simplicity in managing medium-sized clinical datasets, χ^2 tests were chosen because they were appropriate for evaluating associations between diagnostic groups. The use of ORs with CI provides clinically interpretable effect estimates. ORs were calculated as crude, unadjusted effect estimates, without control for potential confounders such as age or sex.

Handling missing data

Missing data were addressed by excluding records with incomplete or inconsistent information for key variables (age, sex, endocrine and psychiatric diagnoses, and diagnostic timelines). Only fully documented, specialist-confirmed cases were included to ensure data reliability. The potential impact of excluding incomplete records is discussed in the Limitations section.

To minimize potential sources of bias, strict inclusion and exclusion criteria were applied, allowing only patients with clearly documented and verified endocrine and psychiatric diagnoses in the H3 system to be included. Moreover, duplicate records were removed using the unique patient codes (CNP), and cases with incomplete or ambiguous diagnostic information were excluded to reduce information bias related to misclassification or missing data. We tried to minimize coding inconsistencies by standardizing diagnostic categories according to ICD-10 terminology. Although detection bias cannot be fully eliminated in retrospective hospital-based datasets, the uniform data extraction process and reliance on specialist-confirmed diagnoses aimed to mitigate its impact.

Selection bias due to the exclusive use of hospital-based patients and information bias related to possible coding inaccuracies in the electronic medical records could not be eliminated. Remaining sources of bias that could not be controlled for were acknowledged and addressed in the Limitations section. No sensitivity analyses were performed; future studies should test robustness by varying diagnostic and age categorization criteria.

Results

The follow-up process and the flow of patients through the study are summarized in figure 1.

Demographic description

In total, 735 (100%) patients diagnosed with endocrine disorders and at least one psychiatric comorbidity were included in the study. The highest frequency of psychiatric comorbidity was observed in older adults, particularly in the 60–69 and 70+ age groups. The mean age was 56 years (SD ± 23,15). The population was overwhelmingly female (N = 598, 81.5%) (Figure 2).

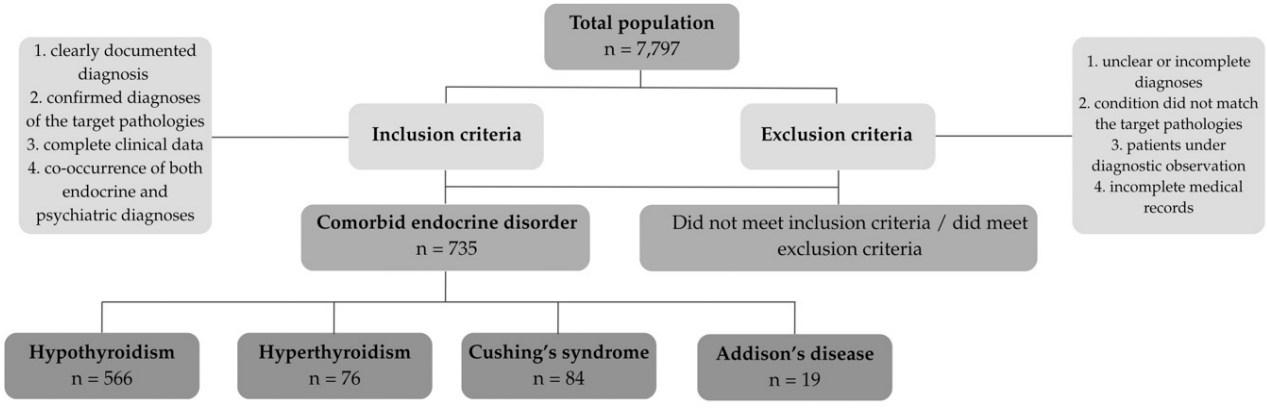

Figure 1. Statistical characteristics of the study.

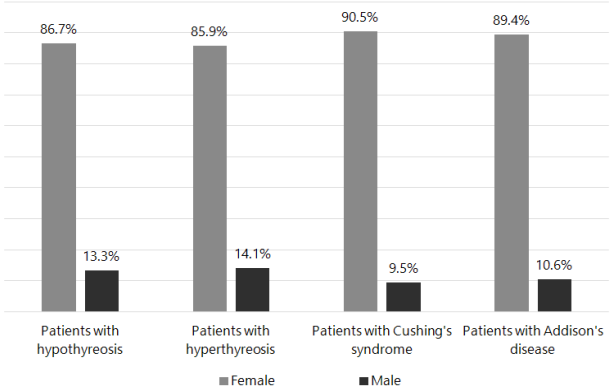

Figure 2. Gender predominance in thyroid and adrenal disorders.

A more detailed demographic distribution and statistical characteristics are also presented in table I.

Regarding psychiatric comorbidities, across the four endocrine groups, depressive disorder was most common in hypothyroidism (N = 406, 71.7%) and appeared in 35 (41.6%) of Cushing's and 6 (31.5%) of Addison's cases. Mixed anxiety–depressive disorder predominated in Addison's disease (N = 10, 52.6%) and hyperthyroidism (N = 43, 56.5%). Anxiety disorder appeared in 9 (10.7%) of Cushing's patients, 3 (15.7%) of Addison's patients, and 16 (21%) of those with hyperthyroidism. Bipolar and schizoaffective disorders were rare, occurring only in hypothyroidism. Psychiatric comorbidity onset within 6 years of the primary endocrine diagnosis occurred in 36 (42.8%) of patients with Cushing's syndrome, 9 (47.3%) with Addison's disease, 49 (8.6%) with hypothyroidism, and 38 (50%) with hyperthyroidism.

Statistical associations between endocrine conditions and psychiatric disorders

The inferential analysis (OR, χ^2 test) demonstrated significant associations between all four endocrine conditions and psychiatric outcomes (Table II). Patients with Cushing's syndrome had higher odds of psychiatric disorders, while those with Addison's disease and hypothyroidism also showed increased risk. The strongest association observed in Addison's disease. Hyperthyroidism showed lower recorded odds of psychiatric comorbidity compared with the other endocrine groups in this dataset. Odds ratios and corresponding chi-square statistics for all conditions are presented in table II.

Table I. Descriptive statistical characteristics of the study sample (N= 735, 100%).

Variable	Patients with Cushing's syndrome		Patients with Addison's disease		Patients with hypothyroidism		Patients with hyperthyroidism	
	N	Percent	N	Percent	N	Percent	N	Percent
Sex								
Female	75	89.3%	15	78.9%	444	78.4%	64	84.2%
Male	9	10.7%	4	21.2%	122	21.6%	12	15.8%
Age group								
Under 19 years	4	4.7%	1	5.2%	2	0.3%	1	1.3%
20–29 years	5	5.9%	1	5.2%	24	4.2%	4	5.2%
30–39 years	7	8.3%	4	21%	65	11.4%	5	6.5%
40–49 years	3	3.5%	2	10.5%	37	6.5%	9	11.8%
50–59 years	24	28.5%	4	21%	40	7%	14	18.4%
60–69 years	25	29.7%	5	26.3%	124	21.9%	20	26.3%
Over 70 years	16	19%	2	10.5%	274	48.4%	23	30.2%
Associated psychiatric disorders								
Depressive disorder	35	41.6%	6	31.5%	406	71.7%	17	22.3%
Anxiety disorder	9	10.7%	3	15.7%	0	0%	16	21%
Mixed anxiety-depressive disorder	28	33.3%	10	52.6%	138	24.3%	43	56.5%
Bipolar disorder	0	0%	0	0%	15	2.6%	0	0%
Schizoaffective disorder	0	0%	0	0%	7	1.2%	0	0%
Psychiatric onset within 6 years of primary diagnosis	36	42.8%	9	47.3%	49	8.6%	38	50%

Table II. Odds ratio in endocrine and psychiatric dysfunctions.

	Psychiatric comorbidity N (%)	Without psychiatric comorbidity N (%)	OR	χ^2	df	95% CI	p value
Cushing's syndrome	84 (13.5%)	536 (86.4%)	1.743	19.80	1	[1.3237-2.0304]	<0.0001
Addison's disease	19 (20%)	76 (80%)	2.6888	10.79	1	[1.5631-3.5365]	<0.0001
Hypothyroidism	566 (9.1%)	5506 (90.8%)	1.2554	7.60	1	[1.0679-1.4758]	<0.0059
Hyperthyroidism	76 (4.3%)	1659 (95.6%)	0.4505	50.89	1	[0.3574-0.5678]	<0.0059

Discussion

The present study identified a significant association between Cushing's syndrome, Addison's disease, hyperthyroidism, and hypothyroidism and well-defined psychiatric comorbidities. However, the direction of these associations varied across diagnostic groups. Our results should be viewed as a single piece of a much larger puzzle, in the sense that patients do not struggle only with these two categories of diseases, but with a multitude of pathologies that can trigger, amplify, or even suppress another illness.

The existing scientific literature shows that endocrine dysfunction frequently manifests with neuropsychiatric symptoms [1] due to the close interactions between hormonal regulation, metabolic homeostasis [20], and brain function [1].

Anxiety disorders tend to appear in conditions with a significant impact on body image, such as hyperthyroidism, where excessive hormone production fuels anxiety [21]. Mania, as we also observed in our database, is not a primary comorbidity in most endocrine disorders [22]. A large registry study showed that after a hyperthyroidism diagnosis there was higher risk of psychiatric hospitalization (HR 1.51, 95% CI 1.11–2.05) and increased initiation of psychotropic treatment (antidepressants HR 1.54; anxiolytics HR 1.47) [23].

Depressive disorder emerged as the most prevalent psychiatric diagnosis, followed by anxiety disorder, just as prior studies suggested: mood symptoms are among the earliest and most persistent clinical manifestations of hormonal imbalance [2]. Disorders such as hypothyroidism and Addison's disease, for instance, have long been associated with psychomotor slowing, low mood, anhedonia, and cognitive impairment, whereas hyperthyroidism typically produces restlessness, irritability, emotional lability, and heightened anxiety. Meanwhile, Cushing's disease is characterized by cortisol excess, which has well-documented effects on hippocampal function, stress regulation, and mood disturbance [8]. Systematic reviews and cohort studies report very high rates of depression in Cushing's (often >50%) and show that neurocognitive deficits, reduced quality of life, and structural brain changes may persist even after biochemical remission [24].

One aspect that stands out in our results is the high proportion of women among our patients. The literature shows that the incidence of these endocrine pathologies is much higher in women, and that they are more sensitive to the psychiatric conditions we examined [25–28].

Sex differences in adrenal diseases

Recent research focusing on differences between the adrenal glands of men and women has reached particularly important conclusions regarding sex-specific variations, whose consequences are visible in our results as well. Certain regions of the adrenal cortex develop differently in females, showing greater regenerative capacity [29], activity, weight, and thickness in the studied animal models [30]. There are also differences in the stress response between women and men [29], with the hypothalamic–pituitary–adrenal (HPA) axis being more strongly activated in women. Furthermore, estrogens inhibit the renin–angiotensin–aldosterone system while activating the HPA axis [29,31].

The opposite is true for men, where testosterone may inhibit HPA axis function and activate the renin–angiotensin–aldosterone system (RAAS) [32,33]. From the analysis of our results and visualizations, it becomes clear that the prevalence of endocrine dysfunctions such as Cushing's syndrome and thyroid disorders is higher among peri- and postmenopausal women, while in men the prevalence appears more constant and evenly distributed.

It is well known that the same disease can manifest with completely different symptoms in the two sexes, whether related to adrenal cortex dysfunction [29,34,35] or thyroid issues [36–38]. In the case of Cushing's syndrome, this is evident despite the fact that symptoms are often vague, variable, and can overlap with other pathologies. The literature mentions that psychiatric symptoms and vision disturbances are more common in women, while nephrolithiasis is more frequent in men, but these parameters were beyond the scope of our study [39,40]. In several cases, insomnia and chronic headaches in women are observed, although the frequency of these symptoms in women is high in general as well [41,42].

Sex differences in thyroid disorders

The relationship between thyroid disorders and psychiatric comorbidities has long been documented in the literature. Both thyroid disorders can affect also

thinking and memory, which is why thyroid function testing is recommended in cognitive disorders [43], especially in elderly patients whose brains are more sensitive to hormonal changes [44]. The literature also shows that women are at significantly higher risk of developing autoimmune diseases, a situation largely attributed to estrogen fluctuations [45,46], which intensify immune responses [47], and also to the presence of two X chromosomes, which contain more immune-related genes that predispose women to greater autoimmune vulnerability [48]. Reviews of autoimmune thyroid disease report markedly higher female: male ratios and a much higher prevalence of Hashimoto's/Graves' in women [49]. In our study, we found that most of the patients diagnosed with Graves' disease were women.

Some of the results can be attributed to a detection bias, because psychiatric disorders that are identified, may influence prevalence estimates. We relied on documented psychiatric histories in medical records, but some psychiatric symptoms may be underreported, especially in men. This may exaggerate sex differences if women are more likely to report or receive a psychiatric diagnosis.

Psychiatric manifestations in adrenal disorders

Psychiatric comorbidities most frequently encountered in Cushing's syndrome include depression, as well as manic and anxiety disorders.

The mechanisms underlying these symptoms may be linked to the presence of glucocorticoid receptors in the central nervous system, where they are found in very large numbers. Damage to various brain regions can cause specific alterations depending on the area involved [50]. For example, impairment of the anterior cingulate cortex may result in memory disturbances, emotional regulation difficulties, and impaired decision-making [51, 52]. Other regions that may be affected include the hippocampus and amygdala, structures essential for regulating the stress response, emotions, and memory [53]. Another surprising consequence of hypercortisolism is the reduced glucose uptake by neuronal cells, which leads to their deterioration and to cerebral atrophy [54–55]. This process exacerbates symptoms caused by hippocampal and other brain region damage.

Psychiatrically, the most frequent condition was the depressive disorder, followed by mixed anxious-depressive disorder, and an anxiety disorder. In the remaining cases, a form of the previously mentioned disorders was present but did not constitute the primary diagnosis; instead, these conditions were comorbidities of other psychiatric disorders and were therefore not included in the main categories.

Unlike in Cushing's syndrome, studies regarding psychiatric complications in adrenal insufficiency are lacking. In our research, the symptom profile of Addison's disease closely followed the literature. From the psychiatric perspective, mixed anxious-depressive disorders appeared in most Addison patients, followed by major depressive disorder and anxiety disorder.

Psychiatric manifestations in thyroid dysfunctions

Patients with thyroid pathologies frequently experience psychiatric symptoms, which are closely linked to hormonal fluctuations resulting from endocrine dysfunction [47–50]. The reverse is also true: patients with psychiatric disorders more often exhibit thyroid dysfunction [56]. Thyroid hormones also play an essential role in regulating serotonin and norepinephrine neurotransmission, and disruptions in these processes further explain mood disorders [57]. Hypothyroidism may cause suboptimal cerebral blood flow, leading to hypoxia, which can worsen cognitive problems [58]. A meta-analysis found that hypothyroidism is associated with clinical depression (OR 1.30; 95% CI 1.08–1.57), overt hypothyroidism showing even a larger effect (OR 1.77) [59].

It should be also mentioned that pychiatric conditions often worsen or exacerbate physical symptoms (for example, generalized anxiety worsens insomnia [60]), thereby creating a vicious cycle.

In contrast with findings from the scientific literature, hyperthyroidism showed lower recorded odds of psychiatric comorbidity in this hospital dataset. This may reflect sample characteristics, underreporting of psychiatric conditions, or treatment effects, such as antithyroid medications reducing anxiety and mood disturbances. Selection and statistical biases may also have contributed, highlighting more the need for cautious interpretation.

Moreover, numerous studies and clinical evidence concerning Cushing's syndrome suggest that the adverse effects of the disease on the brain and the entire body do not fully resolve even after effective treatment and a return to eucortisolism [61]. Additionally, recent studies indicate that prolonged hypercortisolism correlates with structural brain abnormalities, reduced quality of life, depression, and an unfavorable cerebral metabolic profile [7,62].

The decision to include only individuals with definitive endocrine diagnoses and well-documented psychiatric histories ensured that the study captured clinically meaningful associations rather than incidental or transient symptoms. Moreover, the dataset spanning January 2020 to September 2024 allowed for the examination of symptom patterns over a period marked by increased healthcare utilization and heightened public health stressors, which may have amplified psychiatric vulnerability in hormonally dysregulated patients. While the cross-sectional design does not allow causal inference, the results support the notion that endocrine disorders may act as biological stressors that predispose individuals to psychiatric morbidity.

Limitations

It is important to highlight that our study presents several limitations, particularly regarding its representativeness at the level of the general population. The analyzed data originate from a single medical institution, and the retrospective nature of the study makes it challenging to establish relationships between endocrine and psychiatric disorders. This design may also introduce constraints related to data quality and completeness.

The use of a retrospective study design and a purposive, convenience sampling method does not allow for the identification of causal relationships, but only associations between variables. Therefore, all interpretations must be made with caution.

Retrospective data collection also imposes significant limitations and information bias, as it does not allow for clarification, expansion, or correction of missing or ambiguous information. This methodological constraint may result in information bias.

During the time period covered by our research, the COVID-19 pandemic occurred, which may have triggered or exacerbated pre-existing psychiatric disorders and influenced the number of patients diagnosed or hospitalized.

Additionally, we should mention the fact, that no sensitivity analyses were performed. However, future studies could assess the robustness of these associations by varying diagnostic criteria or analytical groupings.

The ORs were crude and unadjusted; therefore, the results may be confounded by age, sex, disease severity, treatment status, and healthcare utilization.

Potential sources of bias may affect the validity of the findings. The sample consists exclusively of hospital-based patients and may not fully represent the general population. Potential coding errors or inconsistencies in medical records may have affected data extraction and classification. Missing data could have influenced the accuracy of diagnostic categorization and variable coding.

Conclusions

Based on our retrospective study of patients with documented coexisting endocrine and psychiatric diagnoses, psychiatric comorbidities were frequently observed among patients with selected adrenal and thyroid disorders. Depressive disorders predominated among patients with hypothyroidism and Cushing's syndrome, while mixed anxiety-depressive disorder was common among patients with Addison's disease and hyperthyroidism. These findings should be interpreted cautiously because the study was cross-sectional and based only on routinely recorded clinical data. Casual or bidirectional relationships cannot be inferred, and the results should not be interpreted as prevalence estimates for the general population. Nevertheless, the results support the clinical value of psychiatric assessment in patients with endocrine disorders and endocrine evaluation in selected patients with psychiatric symptoms. Further prospective, multicenter studies are needed to clarify prevalence, temporal relationships, and long-term outcomes.

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