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ORIGINAL

Endocrine Disorders Associated with Obesity: Cushing's syndrome and Hypothyroidism

Trastornos endocrinos asociados con la obesidad: síndrome de Cushing e hipotiroidismo

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ABSTRACT

Obesity has been related to a wide range of endocrine disorders, from common ones including ovarian syndrome and hypothyroidism to unusual ones like Cushing's syndrome (CS), hypothyroidism, and hypothalamic abnormalities. Obesity can arise via a variety of endocrine disorders using several mechanisms. Multiple tissues accumulate hyaluronic acid, which causes greater fluid retention as a result of reduced thermogenesis and lower cardiac output, both of which are signs of hypothyroidism. The pathophysiology of obesity in polycystic ovarian syndrome is the unclear since it's possible that obesity both contributes to and harms polycystic ovarian syndrome. Net androgen excess seems to have a significant impact on the development of central adiposity. The interaction between thyroid and growth hormones, together with increased adipocyte differentiation and adiposity, is important in Cushing's illness. Additional peculiar situations are also examined in the research, such as hypothalamic obesity brought on by a concomitant hormonal deficiency and central hypothyroidism.

Keywords: Polycystic Ovary Syndrome (PCOS); Hypothyroidism; Hypothalamic Obesity; Adrenocorticotrophic Hormone (ACTH); Thyroid-Stimulating Hormone (TSH); Thyroid Peroxides (TPO); Cortisol.

RESUMEN

La obesidad se ha relacionado con una amplia gama de trastornos endocrinos, desde los más comunes, como el síndrome ovárico y el hipotiroidismo, hasta los menos comunes, como el síndrome de Cushing (SC), el hipotiroidismo y las anomalías hipotalámicas. La obesidad puede surgir a través de diversos trastornos endocrinos mediante diversos mecanismos. Múltiples tejidos acumulan ácido hialurónico, lo que provoca una mayor retención de líquidos como resultado de una menor termogénesis y un menor gasto cardíaco, ambos signos de hipotiroidismo. La fisiopatología de la obesidad en el síndrome de ovario poliquístico no está clara, ya que es posible que la obesidad contribuya al síndrome de ovario poliquístico y lo perjudique. El exceso neto de andrógenos parece tener un impacto significativo en el desarrollo de la adiposidad central. La interacción entre la tiroides y las hormonas del crecimiento, junto con el aumento de la diferenciación de los adipocitos y la adiposidad, es importante en la enfermedad de Cushing. En la investigación también

se examinan otras situaciones peculiares, como la obesidad hipotalámica provocada por una deficiencia hormonal concomitante y el hipotiroidismo central.

Palabras clave: Síndrome de Ovario Poliquístico (SOP); Hipotiroidismo; Obesidad Hipotalámica; Hormona Adrenocorticotrópica (ACTH); Hormona Estimulante de la Tiroides (TSH); Peróxidos Tiroideos (TPO); Cortisol.

INTRODUCTION

The endocrine system is impacted by both CS and hypothyroidism, two distinct medical diseases. In contrast to CS which is characterized by the body producing too many cortical hormones, hypothyroidism is a disorder that arises when the thyroid gland does not generate enough thyroid hormones.[1] Skin thinning, stretch marks, high blood pressure, and mood swings are all prominent symptoms of CS, which is often caused by extended exposure to excess glucocorticoids. Additional symptoms can include central obesity, muscular weakness, glucose intolerance, and poor wound healing. Recent research has looked into pharmacological options that target glucocorticoid receptors to manage CS.[2] Although hypothyroidism and CS are separate illnesses, both can have a substantial impact on the body's metabolism and energy balance. In some circumstances, iatrogenic CS could result from exogenous glucocorticoid exposure rather than natural hormonal abnormalities.[3] The pituitary gland enlargement or the use of corticosteroid medicines are the two most frequent causes of CS. Treatment for CS typically involves addressing the underlying cause, which can involve surgery, radiation therapy, or medication.[4] Endogenous CS results from continuous exposure to high cortisol levels in the bloodstream. Cushing's disease (CD), which occurs when a pituitary corticotrope tumor secretes an excessive amount of adrenocorticotropic hormone (ACTH), accounts for around 70 % of CS cases. The remaining 30 % of instances are caused by nonpituitary tumors secreting ectopic ACTH or adrenal lesions producing their own cortisol, such as adenomas or hyperplasia.[5] Obesity affects about one-third of the global population, posing a significant public health concern as it is classified as an epidemic. It is distinguished by an excessive buildup of body fat, which is usually indicated by a body mass index (BMI) of 30 or above. This syndrome occurs when there is an imbalance between caloric intake and energy expenditure, which is frequently influenced by lifestyle factors, genetic predisposition, and metabolic diseases.[6] When a person has too much body fat, it's called obesity. The medical condition can cause a number of different health issues. One of the biggest risk factors for type 2 diabetes is obesity.[7] Obesity significantly increases the risk of cardiovascular disorders such as heart disease and stroke. Obesity is frequently central in Cushing's disease patients and is linked to metabolic problems such as hypertension, dyslipidemia, and insulin resistance, all of which increase cardiovascular risk.[8] Obesity-related excess weight can place additional strain on the joints, causing osteoarthritis and joint discomfort. Additionally, detrimental to mental health, obesity can cause sadness, anxiety, and poor self-esteem.[9] Obesity can result in the buildup of fat in the liver, which can induce non-alcoholic fatty liver disease and more serious liver damage. A number of different health issues can result from obesity, a complicated medical disease. The balanced diet and regular exercise can maintain a healthy weight, which can lower risk of developing these diseases.[10]

Research examined the clinical and histological manifestations of acanthosis nigricans, as well as their relationships to dermoscopic manifestations and potential therapeutic implications. For histological analysis, a clinical examination, dermoscopy, and skin biopsy were performed.[11] Investigators undertook a comprehensive assessment of the literature to determine the global prevalence of various endocrine disorders, with a particular emphasis on CS. It emphasized the disease's considerable health burden and personal expenses, highlighting its epidemiological, clinical, and financial implications.[12] The investigation emphasizes the importance of future research into the underlying mechanisms that contribute to the occurrence of sleep apnea, which are currently unknown. Furthermore, the research concentrated on the prevalence of Obstructive Sleep Apnea (OSA) rather than a thorough assessment of sleep apnea, which encompasses both OSA and Central Sleep Apnea (CSA).[13] The research explains that metabolic disturbances are bidirectional correlated with thyroid dysfunction, whether excessive body weight causes men to develop hypogonadism, the way that menopause promotes the development of type 2 diabetes, abdominal obesity, and carbohydrate intolerance; moreover, it explains the emergence of insulin resistance, a crucial link between obesity and a number of related disorders.[14] The PCOS individuals had pelvis ultrasonography (USG) and had their demographic, anthropometric, clinical, hormonal hormonal parameters assessed. The proportion of subclinical hypothyroid patients in each category of lean people and overweight people was estimated. Comparing the clinico-biochemical characteristics of the two groups.[15] Creating a treatment strategy for overweight people begins with a thorough examination. A medical history needs to assess the aetiology and natural history of the emergence of obesity. The assessment should be furthered to rule out potential endocrine reasons by the physical examination and laboratory tests. The outcomes of those then serve as a reference for picking the best treatment strategy.

Hypothyroidism

Hypothyroidism is a common endocrine condition that affects roughly 2 % of adult females and 0,2 % of adult males. It is distinguished by the slow emergence of symptoms such as weight gain, exhaustion, and metabolic disruptions. Individuals with overt hypothyroidism report much more weight gain (54 %) than controls (13,8 %). The fundamental process is diminished thyroid hormone activity, which causes a slower baseline metabolic rate and altered lipid metabolism. New research emphasizes the link between thyroid function and polycystic ovarian syndrome (PCOS).[16] A blood TSH test would be used to assess patients with an inadequate threshold for hypothyroidism the early symptoms are erratic and vague

Symptoms of Overt Hypothyroidism

Since it can be impossible to connect the symptoms of hypothyroidism to the condition, it often goes undiagnosed. Clinical signs and symptoms are often not present for months or years after the path physiological alterations have occurred. Moreover, even common symptoms of hypothyroidism can go omitted or go untreated because of the gradually it starts to manifest. Despite the fact that most hypothyroid individuals can have some disease-related signs and symptoms, it could be challenging identify a "classic" clinical since symptoms can be nebulous hence mistaken for medical illnesses. Because of the complexity of the relationship between symptoms and physiological illness, doctors often use biochemical indicators of thyroid dysfunction to make a diagnosis.[17] Assessment of persons who are more likely to develop hypothyroidism is encouraged by several academic. Preventive Services Task Force do not screen in high-risk populations, including elderly women. When modest or general thyroid dysfunction symptoms appear in such persons, it does act as a caution for physicians to preserve a low entry for thyroid function examination. Using information from the research on symptoms and signs that arise, as a result, did not place much emphasis on them. There isn't enough data to say which symptom, if any, is more probable to indicate biochemical hypothyroidism. Patients with hypothyroidism are more inclined to report greater symptoms and more recent onset of symptoms. Therefore, serum thyroid function tests should be performed on individuals who complain of more symptoms, especially more recent symptoms.[18] The researchers demonstrated that change in symptoms is more effective than present symptoms in predicting the condition, and the more substantial the variety of symptoms reported (both current and altered), the higher the chance of predicting hypothyroidism. It's remarkable that the issue of excess weight isn't even included in the number of typical symptoms. Evident hypothyroidism is a prevalent illness that could be challenging to analyze on the basis of clinical finding. Biochemical testing for thyroid hormone and serum TSH levels is necessary for confirmation. The use of blood tests to detect a problem that is readily treated has produced a range of outcomes that are mentioned below table 1. It is commonly recognized that untreated hypothyroidism causes hypercholesterolemia, which can become better or return to normal with statin therapy.[19] Although it has never been scientifically proven, cardiovascular illness can have the potential to be lethal in hypothyroidism.

Table 1. Laboratory tests for individuals with hypothyroidism suspicion

TSH	Free T4 index	Thyroid peroxides' antibodies	Diagnosis
4,0-0,4 mU/l	low	2	Hypothyroidism in central
<10mU/l and>4	Low/ normal	-/+	hypothyroidism throughout the entire body, early primary aggressive hypothyroidism, and subclinical thyroid dysfunction
<10mU/l and >4	Low/ normal	-/+	The three types of hypothyroidism are subclinical, central, and early primary autoimmune.
>10mU/l	low-normal/ low	-	Iodine deficit, concurrent illnesses, external radiation caused by medications
<0,4 mU/l	low-normal/ low	-/+	hyperthyroidism that has already occurred
>10nM	elevated/normal	-/+	medications, thyroid hormone resistance, and test-related errors

The Action of Thyroid Hormones

Numerous crucial biological functions, including growth, neurological operation, thermal production, energy consumption, and other the processes of metabolism, are regulated by thyroid hormones. The thyroid gland produces the active hormone 3, 5, 3'-L-triiodothyronine (T3) as well as the prohormone thyroxine (T4). The iodothyronine biogases proteins D1 and D2 are responsible for catalyzing the conversion of T4 to T3 by 5 monodeiodination, which is how the body produces most of the circulating T3. While 5, deionization of T4 and T3 is inactivated by the D3 enzyme.[20] The relative activity of these three deiodinases affects how much T3 is

presenting intracellular. The thyroid hormones (T3 and T4) are controlled by body using a complex feedback loop. Figure 1 shows how the adrenal glands, in reaction to thyroid-releasing hormone (TRH), produce TSH, which promotes the release of T3 and T4 from the thyroid. It in body produces TSH.

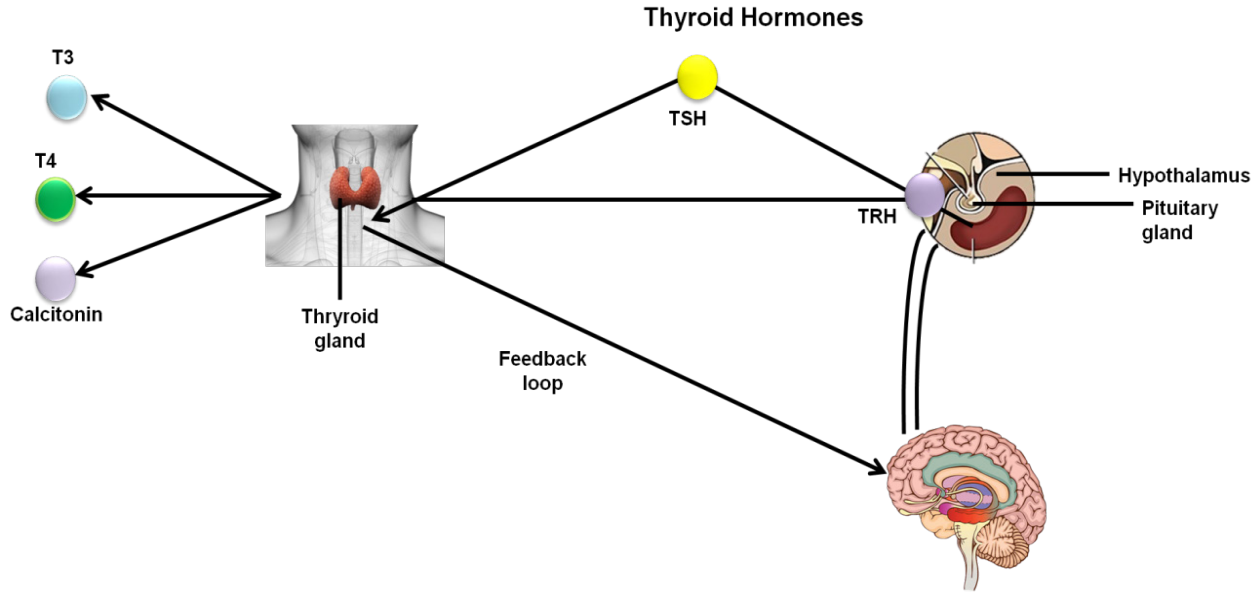

Figure 1. Thyroid Hormones

Typical T3 Effects, both genomic and non-genomic

Thyroid gland receptors recognize certain hypothyroidism response components in the promoter of T3-objective, depending on the quantity of thyroid hormone around, either promote or hinder translation. The impact of T3's genomic activity can change over the course of hours or even days.[21] T3 has a few short-lived effects that are unaffected by transcription and protein synthesis inhibitors. The term "non-genomic behaviors" applies to them.

Hypothyroidism's Pathophysiology of Weight Gain

Weight gain in hypothyroidism is influenced by a number of variables, including:

- Hypothyroidism causes hyaluronic acid to accumulate in the dermal tissues and in those of other organs. This substance creates mucinous oedema, which is what causes the thicker structures and puffy look since it is hygroscopic.
- Patients consistently report constipation that can end in faecal impaction, myxoedema, megacolon, and myxoedema ileus due to slowed intestinal peristalsis and glycoprotein accumulation in the intestine barrier.
- Thyroid hormones actions have also been linked to the myocardial and vascular system. Within three minutes, T3 improves systemic vascular resistance and boosts cardiac output in healthy adult men.[22] Even though pericardial and pleural effusions are more frequent, patients with severe hypothyroidism could develop ascites. The exudates include a lot of protein and glycosaminoglycans. Additionally, there is a decrease in tubular reabsorption, secretion, glomerular filtration rate, and renal blood flow. To decreased urine output, this causes decreased water clearance. Because the hydrophylic deposits in the tissues are retaining more water, the total amount of water in the body has increased overall.

Connection Other Hormones

Growth Hormone

IGF-I is produced less when thyroid hormones are absent because less growth hormone is secreted.

Leptin

Energy expenditure can be increased by leptin and thyroid hormones. Leptin levels have been reported to be higher in hypothyroidism. In addition, therapy with thyroxine decreased leptin release without regard to adiposity or noradrenaline levels. It seems that a negative feedback system tightly controls the levels of thyroxine and leptin. Depending on the animals' energy state, leptin has been found to modify 5-deiodinases in various tissues as well as to activate the hypothalamopituitary-thyroid axis. Leptin can function in the hypothalamus to activate the TRH, TSH axis because it caused in serum TSH.[23] The characteristic of hypothyroidism in organisms

is decreased tolerance to insulin, which is mostly brought on by an accelerated carbohydrates-fatty acids cycling that is only partially improved by intracerebroventricular leptin infusion.

Catecholamines

Since Cyclic Adenosine Monophosphate (cAMP) no longer responds as well to adrenaline in the hypothyroid condition, there is a reduction in adrenergic activity. This could be connected to how thyroid hormones influence cAMP production. Within 30 minutes, thyroxine affects catecholamine lipolytic activity and thermo genesis in vivo. The expression of mitochondrial genes and oxidative phosphorylation, however, seem to be directly impacted by thyroid hormone, according to the available research. The accumulation of thyroid hormones in mitochondria and their importance in controlling mitochondrial biogenesis, which affects cell growth, differentiation, and maturation, are regulated by thyroid hormones. The combined proceedings of catecholamine and thyroid hormone result in brown adipose tissue having three times more mitochondrial UCP1 than white adipose tissue. In contrast to other tissues, where T3 inhibits D2, T3 only potentiates D2 induction in brown adipose hankie.[24] Along with equilibrium mitochondria mRNA objectives, thyroid hormones also control the expression of the mitochondrial gene, which has an impact on respiration, enzyme function, and protein synthesis.

Mitochondrial Direct Effects of Thyroid Hormone

Although it has been hypothesized that the hormone 3, 3-diiodothyronine (T2) truly causes these rapid actions, T3 can quickly stimulate the process of oxidative phosphorylation in isolated rat liver mitochondrial. T3 also rapidly stimulates this form of TR. The fast thermogenesis brought on by T3 can be caused by these occurrences. Consequently, T3 and T2 both encourage incredibly express mitochondrial response.[25] A number of genes that are either encoded by the nuclear genome, such as mitochondrial transcription factor, Adenosine Triphosphate (ATP) subunit 6', Nicotinamide Adenine Dinucleotide (NADH)' dehydrogenase subunit 3, and parts cytochrome oxidase, has been demonstrated to be directly increased by thyroid hormone. The research has revealed T3 promotes the tub gene, in leads to fatness struggle when it is altered. T3/T4 therapy was demonstrated to restore normal tub expression in parts of the brain where hypothyroidism in rats was linked to altered tub mRNA and protein. Figure 2 illustrates the normal range at-home thyroid tests for free T4, free T3, and TPO, TSH, antibodies are generally the same as the standard laboratory reference ranges. Here are the general healthy ranges for these tests:

- TSH: typically, the normal healthy range is between 63 and 45 per percentage.
- Free T3: typically, the normal healthy range is between 28 and 35 per percentage.
- Free T4: typically, the normal healthy range is between 79 and 85 per parentage.
- TPO antibodies: typically, the normal healthy range is between 83 and 75 per percentage.

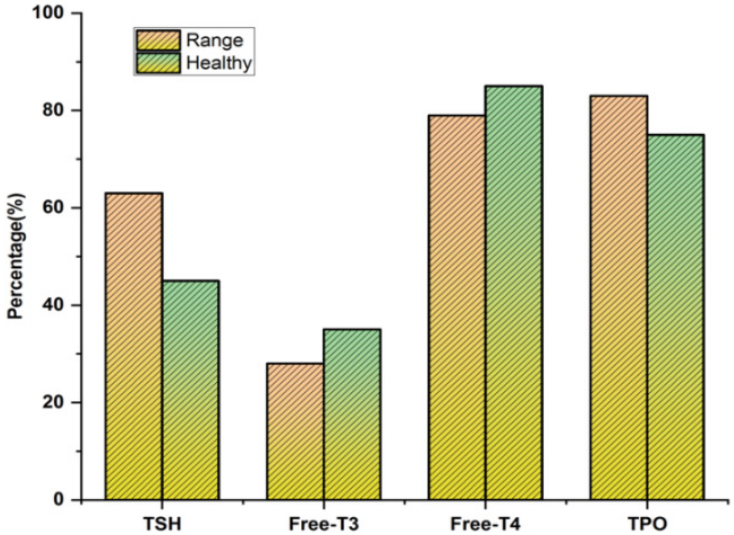

Figure 2. Normal healthy range for TSH, free T3, freeT4, and TPO antibodies

Polycystic ovarian syndrome

Up to 10 % of premenopausal women have PCOS, which is relatively general endocrine provision. This endocrine condition related to fat is by far the most complicated. Considered to have a complex origin, PCOS is a diverse condition. The existence of PCO morphology was not necessary according to criterion for PCOS,

which recognized that hyperandrogenism were the only diagnostic markers of the condition that needed be present.[26] In 2003, it determined PCOS must be considering an ovarian dysfunction disorder that includes hyper androgenic symptoms and PCO morphology, 13 years after the Rotterdam Consensus was formed. The criteria were deemed to be required for the analysis to disease' variability. The guidelines perfectly express a condition's essential characteristics. It complements relatively than replace the criterion for PCOS analysis. According to updated criterion, PCOS can become more common among all females. The "Rotterdam consensus" criteria state that novel PCOS features must comprise PCO and hyperandrogenism in females are normal menstrual cycles, particularly in those who present with PCO without androgen burden. Adulatory dysfunction in past, including amenorrhea or oligomenorrhea that started in adolescence, is the most obvious symptom of PCOS. Figure 3 depicts a healthy ovary on the left and an ovary with polycystic ovarian syndrome on the right. Later-life weight increase can also result in clinical signs of PCOS and acquired insulin resistance: Studies show that between 38 and 88 percent of women with PCOS are overweight.

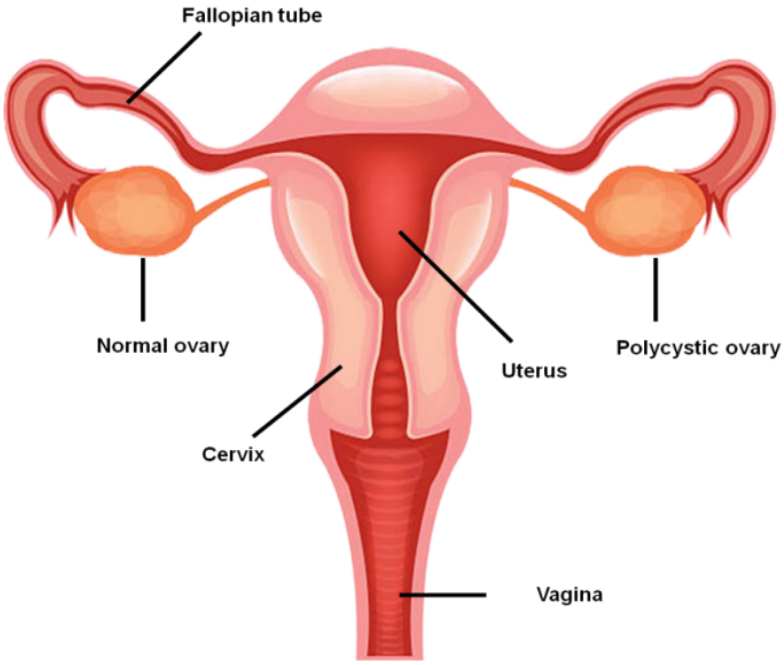

Figure 3. Lustration showing a normal ovary and a polycystic ovarian syndrome

The traditional definition of PCOS by Stein and Eventual included an increase in body weight as one of the diagnostic criteria. It would indicate that excess body fat is a significant factor in both the maintenance of PCOS and, most likely, its onset. It is supported by the fact that PCOS women who lose weight often experience a significant improvement in menstruation regularity, which lends credence to the idea that obesity plays a major part in the illness.[27] This is case for the majority of the women who are affected by the ailment. On the reasons why PCOS patients tend to be overweight are not entirely understood. Data from association studies explain that PCOS has a major inherent foundation; nevertheless, the genes that predispose a person to develop PCOS have not yet been properly determined. PCOS genes probably include genes that influence body mass index and obesity in addition to those controlling ovarian steroid genesis. The effect of an inherited susceptibility to fat in an environment is the most logical explanation for the processes behind the development of obesity in females with PCOS. Obese PCOS patients can amplify and possibly increase the visibility of the metabolic and clinical irregularities that are unique to this disorder. Compared to control women who are age- and BMI-matched, a considerable proportion of PCOS-affected women exhibit glucose Resistance, With The Difference Being More Noticeable in Higher BMI-Affiliated Women.

Distribution of Body Fat inPCOS

Obesity (BMI) and a centrally distributed fat tissue make up the bulk of PCOS instances that are being seen. Given that this kind of overweight is particularly associated with a higher possibility of heart attacks and type 2 diabetes, obesity is often defined in categories which recommend an assessment of the metabolic disorder as having a waist measurement that is more than 80 cm for women. The waist-to-hip ratio was shown to be linked with PCOS in a major case series research that was conducted. Insulin resistance is a feature of PCOS. When the two categories are compared for a large abdomen as opposed to BMI, the difference in glucose resistance from PCOS women and unaffected women is significantly less noticeable. This demonstrates how the existence

of belly fat affects the hormone sensitivity seen in PCOS. Excessive testosterone concentrations during early development can be the likely cause of central fat accumulation.[28] It's probable that androgen fat deposition alone causes hyperandrogenemia in PCOS patients to its negative effects on insulin subsequent gonadotrophic effects of hyperinsulinemia on the ovaries. Hyperandrogenemia can be both a cause and a consequence of android fat in women with PCOS. According to some theories, women with PCOS are more likely to put on weight because of a vicious cycle where android fat spawns android fat, exacerbating the issue. The cycle can be broken by altering one's diet and/or using drugs that make insulin more sensitive. Obesity that isn't PCOS-related and simple obesity is both linked to increased androgen because these factors are produced:

- 17-hydroxysteroid dehydrogenase is used to produce testosterone from androstendione.
- Synthesis of dihydrotestosterone from testosterone via 5 reductase.
- Reduced aromatas from 16-hydroxylated dehydroepiandrosterone result in lower levels of oestradiol, oestrone, and oestriol.

PCOS-Related Appetite-Regulating Hormones

It is debatable whether leptin plays a part in PCOS, despite its critical function in the control of women's appetite, body weight, metabolism, and reproductive capability. It has been suggested that certain women with PCOS can have ovarian malfunction (resulting in anovulation and infertility) linked to unusually high blood concentrations of leptin. The reduced sensitivity dominant ovarian follicles to IGF- caused by hyperleptinaemia has been demonstrated to contribute to anovulation and decreased control of the growth of human ovarian follicles. Serum leptin levels are related to the percentage of body fat in both PCOS patients and healthy people. Serum leptin concentrations are connected with obesity rather than PCOS. Ghrelin circulation normally rises while fasting and falls after eating.[29] Insulin resistance and ghrelin are adversely associated in PCOS. Contrary to insulin-sensitive PCOS women, who have levels that are similar to controls, insulin-resistant PCOS women have noticeably low ghrelin concentrations that are comparable to those of gastric stay away from patients. The circulation of ghrelin often increases during fasting and decreases after meals. Glucose-resistant PCOS women revealed substantially low hormone values comparable to those of gastric banding patients, in contrast to women with PCOS and normal insulin resistance, whose dosages are identical to controls.

Cushing's syndrome (cs)

Obese people can provide a chance for an early Cushing's disease diagnosis. Since the patient could not show all the normal symptoms or indications, this calls for a high degree of clinical suspicion. Obesity, hirsutism, and amenorrhea were among a group of symptoms and linked to an adrenal hyperplasia-related main pituitary dysfunction. CS which is brought on by ectopic ACTH, was not recognized until 1962, despite later accounts of adrenal tumours that produced the same condition. Patients with CS often exhibit a gradual weight increase with central fat accumulation. Patients also have "buffalo hump" development from fat deposition across the thoracocervicalspine.[30] Typical fat depots across the cheekbones and temporal areas result in "moon shape facies." The most distinguishing CS symptoms and indicators include bruising, muscular weakness, thinning skin, excess, and truncal obesity. The concomitant conditions incorporate impaired glucose tolerance tests, hypertension, hirsutism, osteoporosis, and diabetes mellitus. The symptoms and indications of CS gradually appear as a result of excessive levels of free cortisol, whether endogenous or exogenous brought on by prednisolone, dexamethasone, or other topical and inhalation steroids. CS causes are listed in table 2.

Table 2. Causes of CS

Pseudo-CS
Depression
Alcoholism
ACTHdependent
Macronodular adrenal hyperplasia
Ectopic ACTH syndrome
CRH syndrome
Cushing's disease
ACTH 1–24 iatrogenic therapy
ACTHindependent
Aberrant receptor expression
Cuneo-Albright syndrome
Adrenal cancer and adenoma
Individualized Cushing's syndrome and primary pigmented adrenal nodular hyperplasia

The most frequent cause of ectopic CS is ACTH discharge, which associated to 0,5 % of bronchogenic carcinomas, followed by carcinoid tumors (lung, pancreas). The quantity, dose, and susceptibility of the patient

to glucocorticoids were all taken into consideration; people with iatrogenic CS have a range of symptoms and indicators. The less prone have testosterone excess-related symptoms or physical manifestations such hirsutism, oligomenorrhoea, or amenorrhea.

Fictitious-CS

The clinical characteristics of CS not all of them, are present in this illness. It's possible that cortisol has been rising intermittently. Pseudo-CS is most often caused by chronic drinking, while the exact reason is unclear. The metabolism of cortisol is hampered in chronic liver illness, according to research. Additionally, it was shown that excessive alcohol in patients also stimulated the release of cortisol. The number of depressed CS patients is high.[31] Depression can exhibit some of the CS symptoms, which improve with therapy. Depression patients are more suppressible after dexamethasone and respond less strongly to the corticotropin-releasing hormone (CRH) examination with ACTH.

The Diagnosis of CS

Figures 4 and 5 discuss sensitivity and specificity for a potential corticosteroid overload diagnosis which can be difficult to diagnose and demands several evaluations. Because comparatively few diagnostics for the disorder have sensitivity and specificity, endocrine capability and medical occurrence are necessary in the analysis of CS.

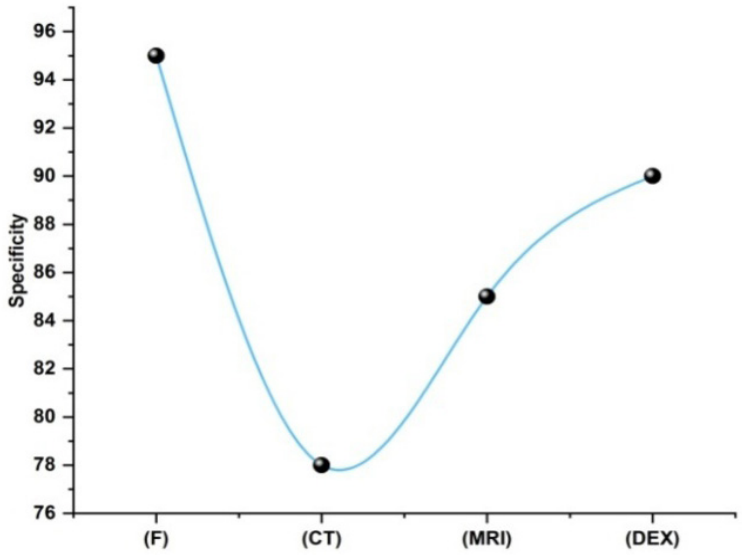

Figure 4. Comparison of specificity

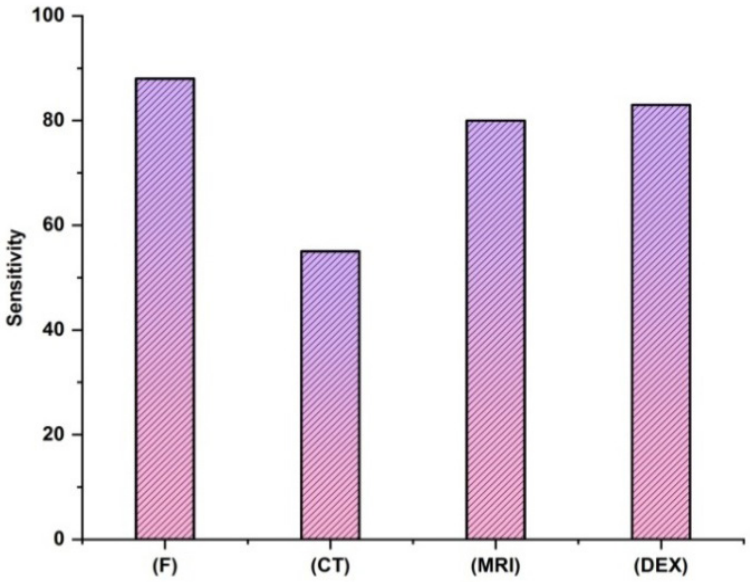

Figure 5. Comparison of sensitivity

Hypothalamic obesity

Hypothalamic/pituitary illness has to be investigated in cases with acquired obesity that wasn't present from infancy and that also included headaches, a growth problem, and other development abnormalities. Selective pituitary failure can occur as a consequence of further hypothalamic hormone deficiencies, including those of TRH and growth hormone-releasing hormone. Under the heading "Hypothyroidism," the cause of obesity linked to TRH deficiency has already been covered. This often happens as a consequence of craniopharyngiomas or later surgical procedures that harm the hypothalamus. 52 % of individuals eventually acquire morbid obesity. In the past, the process has been generally attributed to hypothalamic feeding dysregulation, which resulted in hyperphagia, obesity, and insulin resistance.[32] It has been proposed that since e patients' hypothalamus structures are unresponsive to endogenous leptin, the acquire hypothalamic obesity. Growth hormone replacement therapy can reduce the centrally distributed increased adiposity associated with growth hormone insufficiency. Long-term survival has increased as pediatric brain tumor therapy has grown more effective. When the tumor has just been surgically removed, endocrine problems are rare. Radiotherapy increases the chance of developing endocrine dysfunction, and some studies indicate that chemotherapy can have an extra negative impact. Radiotherapy to the spine and head can spread radiation that results in primary hypothyroidism. Obesity can be brought on by tumors directly affecting the hypothalamus or by radiation or surgery-related hypothalamic damage. Understanding the causes of the long-term morbidity associated with pediatric brain tumors can help shift the course of therapy and raise the survivors' standard of living. These problems are treatable, preventable, and early detected.

CONCLUSIONS

CS is a hormonal disorder that occurs when the body produces an excessive total of cortisol, a hormone produced by the adrenal glands. One can get the conclusion that endocrine-related obesity is not as widespread as patients and some doctors. However, because less prevalent underlying endocrine reasons can be effectively treated, therapeutic therapy of obese individuals should also involve proper screening for endocrine problems that can be treatable. Research has observed that individuals with systemic CS have a relatively high prevalence of primary thyroid diseases. Research confirming the hypothesis in those who are predisposed, the resolution of hypercortisolism triggers the beginning of autoimmune thyroid diseases. The discovered a much higher incidence of cystic thyroid disorders in people with CS as opposed to an organization of control systems, where the occurrence of thyroid nodules was comparable to that reported for everyone. It does not seem probable that an excess of glucocorticoids is responsible for the development of thyroid disorders given that the prevalence was a little higher than that seen in control individuals in our small sample of patients with adrenal tumours. The hyperactivity of the corticotrophic organism can be influenced by other factors, or growth factor that encourages both corticotrope and thyrocyte development. A bigger sample of people with adrenal tumours can be examined to distinguish between these possibilities. This research and clinical work on CS and hypothyroidism hold promise for improved understanding and management of these conditions in the future.

BIBLIOGRAPHIC REFERENCES

1. Paragliola RM, Corsello A, Papi G, Pontecorvi A, Corsello SM. Cushing's syndrome effects on the thyroid. International journal of molecular sciences. 2021 Mar 19;22(6):3131. https://doi.org/10.3390/ijms22063131

2. Pivonello R, Bancos I, Feelders RA, Kargi AY, Kerr JM, Gordon MB, Mariash CN, Terzolo M, Ellison N, Moraitis AG. Relacorilant, a selective glucocorticoid receptor modulator, induces clinical improvements in patients with Cushing syndrome: results from a prospective, open-label phase 2 study. Frontiers in endocrinology. 2021 Jul 14;12:662865. https://doi.org/10.3389/fendo.2021.662865

3. Matejek N, Hoos J, Holterhus PM, Bettendorf M, Choukair D. Topical glucocorticoid application causing iatrogenic Cushing's syndrome followed by secondary adrenal insufficiency in infants: two case reports. Journal of Medical Case Reports. 2022 Dec 8;16(1):455. https://doi.org/10.1186/s13256-022-03659-2

4. Jadoon N. Abstract# 1318176: Central Hypothyroidism Secondary to Cushing Syndrome From an ACTH-Producing Neuroendocrine Tumor. Endocrine Practice. 2022 Dec 1;28(12):S37. https://doi.org/10.1016/j.eprac.2022.10.074

5. Nieman LK. Molecular derangements and the diagnosis of ACTH-dependent Cushing's syndrome. Endocrine Reviews. 2022 Oct 1;43(5):852-77. https://doi.org/10.1210/endrev/bnab046

6. Jurek, A., Krzesiński, P., Uziębło-Życzkowska, B., Witek, P., Zieliński, G., Wierzbowski, R., Kazimierczak, A., Banak, M. and Gielerak, G., 2024. Obesity-Related Hemodynamic Alterations in Patients with Cushing's Disease. Journal of Clinical Medicine, 13(6), p.1658. https://doi.org/10.3390/jcm13061658

7. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. Metabolism. 2019 Mar 1;92:98-107. https://doi.org/10.1016/j.metabol.2018.10.011

8. Varlamov EV, Vila G, Fleseriu M. Perioperative management of a patient with Cushing disease. Journal of the Endocrine Society. 2022 Mar 1;6(3):bvac010. https://doi.org/10.1210/jendso/bvac010

9. Legaki AI, Moustakas II, Sikorska M, Papadopoulos G, Velliou RI, Chatzigeorgiou A. Hepatocyte mitochondrial dynamics and bioenergetics in obesity-related non-alcoholic fatty liver disease. Current obesity reports. 2022 Sep;11(3):126-43. https://doi.org/10.1007/s13679-022-00473-1

10. Pardeshi SS, Khemani UN, Kamath RR, Kura MM, Jafferany M. Therapeutic implications of dermoscopic findings in acanthosis nigricans: A clinical and histopathological study. Dermatologic Therapy. 2020 Nov;33(6):e14521. https://doi.org/10.1111/dth.14521

11. Crafa A, Calogero AE, Cannarella R, Mongioi' LM, Condorelli RA, Greco EA, Aversa A, La Vignera S. The burden of hormonal disorders: a worldwide overview with a particular look in Italy. Frontiers in Endocrinology. 2021 Jun 16;12:694325. https://doi.org/10.3389/fendo.2021.694325

12. Webb SM, Valassi E. Consequences of Cushing's syndrome: health versus personal costs. The Journal of Clinical Endocrinology & Metabolism. 2022 Sep 1;107(9):e3959-60. https://doi.org/10.1210/clinem/dgac269

13. Pasquali R, Casanueva F, Haluzik M, Van Hulsteijn L, Ledoux S, Monteiro MP, Salvador J, Santini F, Toplak H, Dekkers OM. European Society of Endocrinology Clinical Practice Guideline: endocrine work-up in obesity. European journal of endocrinology. 2020 Jan;182(1):G1-32. https://doi.org/10.1530/EJE-19-0893

14. Nayak PK, Mitra S, Sahoo J, Mahapatra E, Agrawal S, Lone Z. Relationship of subclinical hypothyroidism and obesity in polycystic ovarian syndrome patients. Journal of family medicine and primary care. 2020 Jan 1;9(1):147-50. https://doi.org/10.10.4103/jfmpc.jfmpc_654_19

15. Ali R, Fernandez-Lopez K, Maria Belalcazar L. PMON98 High-dose dexamethasone suppression test in ACTH-dependent Cushing's syndrome: Lessons learned on the lack of cortisol suppression. Journal of the Endocrine Society. 2022 Nov 1;6(Supplement_2):A572-3. https://doi.org/10.1210/jendso/bvac150.1187

16. Lee HJ, Jo HN, Noh HK, Kim SH, Joo JK. Is there association between thyroid stimulating hormone levels and the four phenotypes in polycystic ovary syndrome?. Ginekologia Polska. 2023;94(3):203-10. 10.5603/GP.a2021.0239

17. Gambineri A, Cecchetti C, Altieri P, Ribichini D, Preiato VL, Fanelli F, Pagotto U. Secondary PCOS: Well-defined causes, leading to the PCOS phenotype. InPolycystic Ovary Syndrome 2022 Jan 1 (pp. 15-22). Elsevier. https://doi.org/10.1016/B978-0-12-823045-9.00008-0

18. de Silva NL, Somasundaram N, Constantine R, Kularatna H. Apoplexy of Crooke cell tumour leading to the diagnosis of severe Cushing disease; a case report. BMC Endocrine Disorders. 2021 May 1;21(1):93.https://doi.org/10.1186/s12902-021-00761-2

19. Gao C. Clinical features of endocrine diseases complicated with rhabdomyolysis. Journal of Xi'an Jiaotong University (Medical Sciences). 2020:919-22.

20. Fleseriu, M., Rosario Pivonello, M.D., AtanaskaElenkova, M.D., Salvatori, R., Richard Feelders, M.D., Geer, E., Greenman, Y., Przemyslaw Witek, M.D. and Biller, B. LEVOKETOCONAZOLE IN THE TREATMENT OF ENDOGENOUS CUSHING'S SYNDROME: IMPROVEMENTS IN CLINICAL SIGNS AND SYMPTOMS, PATIENT-REPORTED OUTCOMES, AND ASSOCIATED BIOCHEMICAL MARKERS IN THE PHASE 3 SONICS STUDY. Endocrine Practice. 2019; 25:245-246.

21. Maldar A, Kulkarni A, Chauhan P, Misra B, Shah N, Chadha M. Single-center experience with Bilateral Inferior Petrosal Sinus Sampling (BIPSS) in adrenocorticotropin-dependent Cushing's syndrome. Indian Journal of Endocrinology & Metabolism. 2022 Dec 2;26. https://doi.org/10.4103/2230-8210.363665

22. Vielkind M, Tommerdahl K, Hawkins S, Mohon RT. Multiple subspecialists involved in late diagnosis of rapid-onset obesity with hypothalamic dysregulation, hypoventilation, and autonomic dysregulation syndrome.

InC47. CASE REPORTS: PEDIATRIC CYSTIC FIBROSIS, LUNG INFECTION, AND SLEEP DISORDERED BREATHING 2019 May (pp. A4981-A4981). American Thoracic Society. https://doi.org/10.1164/ajrccm-conference.2019.199.1_MeetingAbstracts.A4981

23. Lesia Z, Larysa Z. PRETERM LABOR: THE INFLUENCE OF ENDOCRINE DISORDERS. InThe 6th International scientific and practical conference "Multidisciplinary scientific notes. Theory, history and practice"(November 01–04, 2022) Edmonton, Canada. International Science Group. 2022. 712 p. 2022 Nov 1 (p. 384).

24. Ahmed SF, Bapir R, Fattah FH, Mahmood AG, Salih RQ, Salih AM, Tahir SH, Kakamad FH. Simultaneous pituitary and adrenal adenomas in a patient with non ACTH dependent Cushing syndrome; a case report with literature review. International Journal of Surgery Case Reports. 2022 May 1;94:107038. https://doi.org/10.1016/j.ijscr.2022.107038

25. Parksook WW, Laichuthai N, Sunthornyothin S. Clinical Characteristics and Treatment Outcomes in Endogenous Cushing's Syndrome: A 15-Year Experience from Thailand. Case Reports in Endocrinology. 2020;2020(1):2946868. https://doi.org/10.1155/2020/2946868

26. Bostan H, Duger H, Akhanli P, Calapkulu M, Turkmenoglu TT, Erdol AK, Duru SA, Sencar ME, Kizilgul M, Ucan B, Ozbek M. Cushing's syndrome due to adrenocorticotropic hormone-secreting metastatic neuroendocrine tumor of unknown primary origin: a case report and literature review. Hormones. 2022 Mar:1-8. https://doi.org/10.1007/s42000-021-00316-z

27. Chong HP, Alazzani H, Boelaert K. Endocrine disorders in pregnancy. Obstetrics, Gynaecology& Reproductive Medicine. 2019 Nov 1;29(11):301-5. https://doi.org/10.1016/j.ogrm.2019.08.005

28. Paharia N. Evaluation of Dry Eyes in Hypothyroid patients in comparison to Euthyroid subjects. Indian Journal of Endocrinology & Metabolism. 2022 Dec 2;26. https://doi.org/10.4103/2230-8210.363703

29. Wijewickrama PS, Ratnasamy V, Somasundaram NP, Sumanatilleke M, Ambawatte SB. A challenging case of Cushing's disease complicated with multiple thrombotic phenomena following trans-sphenoidal surgery; a case report. BMC Endocrine Disorders. 2021 Dec;21:1-7. https://doi.org/10.1186/s12902-021-00701-0

30. Matarneh AS, Hamad AO, Hamad MK, Elouzi EB, Mahmood NS, Al-Sawalmeh K, Al-Bozom I, Hussein MS, Yassin MA. A rare initial presentation of a thymic neuroendocrine tumor as Cushing's syndrome. Clinical Case Reports. 2021 Jul;9(7):e04435. https://doi.org/10.1002/ccr3.4435

31. Gorlanov IA, Leina LM, Skorodok YL, Milyavskaya IR. Cutaneous manifestations of endocrine diseases in children. Pediatrician (St. Petersburg). 2021 Aug 11;12(2):53-64. https://doi.org/10.17816/PED12253-64

32. Limumpornpetch P, Morgan AW, Tiganescu A, Baxter PD, Nyawira Nyaga V, Pujades-Rodriguez M, Stewart PM. The effect of endogenous Cushing syndrome on all-cause and cause-specific mortality. The Journal of Clinical Endocrinology & Metabolism. 2022 Aug 1;107(8):2377-88. https://doi.org/10.1210/clinem/dgac265

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CONFLICT OF INTEREST

None.

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