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Assessment of some Hormone Concentration in Men with Schizophrenia in Thi-Qar Province/Iraq

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Abstract

Schizophrenia is a complex disease with a heterogeneous array of symptoms, including positive symptoms such as delusions and hallucinations, negative symptoms such as social withdrawal, and cognitive symptoms such as dysfunction in cognitive processes and functions.. A study was conducted on a patient group of 100 people and a control group of 10 healthy people to investigate the relationship between schizophrenia and its effects on certain hormones from the anterior pituitary lobe, thyroid hormones, and sex hormones. The working methods were followed according to the number (kits) used in measuring hormones. The results showed a significant decrease in the concentrations of both luteinizing hormone (LH) and prolactin hormone, while there was no significant difference in the concentration of follicle-stimulating hormone (FSH). There was also a significant increase in the concentrations of triiodothyronine (T3) and thyroxine (T4), and a significant decrease in the concentration of thyroid-stimulating hormone (TSH). Furthermore, there was a significant increase in the concentration of testosterone and a significant decrease in the concentrations of both estrogen and progesterone in patients with schizophrenia when compared to the control group (healthy men) at a probability level of $P \leq 0.05$. The study showed a negative effect of schizophrenia on the hormonal parameters studied.

Keywords: Schizophrenia, thyroid gland, sex hormones, anterior pituitary gland.

تقدير تراكيز بعض الهرمونات في مرضى فصام الشخصية من الرجال في محافظة ذي قار/العراق

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الخلاصة

يُعد الفصام مرض معقد يشتمل على مجموعة من الأعراض غير المتجانسة والتي تشمل الأعراض الإيجابية مثل الأوهام والهلاوس والأعراض السلبية مثل الانسحاب الاجتماعي بالإضافة الى الاعراض الادراكية مثل الخلل في العمليات والوظائف الادراكية . يصيب المرض 1٪ من الرجال والنساء حول العالم بنسب متساوية تقريباً. ادريت الدراسة على 100 من الرجال المصابين بمرض فصام الشخصية و 10 من الرجال الاصحاء لبحث العلاقة بين مرض فصام الشخصية وتأثيره على بعض هرمونات الفص الامامي للغدة النخامية وهرمونات الغدة الدرقية وهرمونات الغدد الجنسية وتم اتباع طرائق العمل حسب العدد (الكتات) المستعملة في قياس الهرمونات. أظهرت النتائج انخفاضا معنويا في تركيز كل من الهرمون اللوتيني LH وهرمون البرولاكتين في حين لم نجد فرقا معنوي في تركيز الهرمون المحفز للجريبات FSH , كما وجدنا ارتفاعا معنويا في تركيز هرمون ثلاثي يوديد الثيرونين T3وهرمون الثيروكسين T4وانخفاضا معنويا في تركيز الهرمون المحفز للغدة الدرقية بالإضافة الى ذلك وجدنا ارتفاع معنوي تركيز هرمون التستوستيرون وانخفاض معنوي في تركيز كل من هرمون الاستروجين والبروجيستيرون لدى مرضى فصام الشخصية عند مقارنتهم كع مجموعة السيطرة عند مستوى احتمال $P \leq 0.05$. اظهرت الدراسة وجود تأثير سلبي لمرض فصام الشخصية على المعايير الهرمونية التي تم دراستها.

1.Introduction

Schizophrenia is a complex disease with a heterogeneous array of symptoms, including positive symptoms such as delusions and hallucinations, negative symptoms such as social withdrawal, and cognitive symptoms such as dysfunction in cognitive processes and functions [1]. The disease affects approximately 1% of men and women worldwide, with equal prevalence, but it appears often later in women than in men [2]. Despite the complexity of this disease, the specific mechanism of action of its pharmacological treatments is the same. All antipsychotics used to treat psychosis work by blocking dopamine D2 receptors. These antipsychotics reduce psychotic symptoms in many patients with schizophrenia, but they are not without undesirable effects and do not address the negative symptoms [3].

Sometimes a condition called Treatment-resistant schizophrenia (TRS) occurs and can be defined as failure to respond to two doses of antipsychotics at the appropriate dose and duration. Treatment-resistant schizophrenia may be primary (early), which is present from the beginning of treatment, or secondary (late), which occurs after a period of response to treatment [4].

The precise causes and pathophysiology of schizophrenia remain unknown, as schizophrenia is a syndrome with complex symptoms. There is a belief that more than one factor causes this disease, and this belief is the most acceptable. The brain may be damaged as a result of genetic factors, while environmental factors play an important role in causing schizophrenia, as they lead to brain dysfunction early in a person's life, making the person predisposed to developing schizophrenia when faced with stressful environmental influences, leading to the development of this disease [5].

There is a reciprocal relationship between the nervous and endocrine systems, as hormones affect mental health. Disorders of the pituitary gland, such as Cushing's disease, Sheen syndrome, and acromegaly, are associated with a wide range of psychological symptoms. Psychotic symptoms may also be caused by taking high doses of steroids, and disorders of the adrenal and thyroid glands may lead to the emergence of psychotic symptoms [6].

The effect of sex hormones on the risk of developing schizophrenia begins during embryonic life, as many stressful factors during pregnancy interfere with the normal effect of hormones on brain development, and this may lead to the occurrence of schizophrenia in the future [7]. So the study designed to investigate of some hormones concentration in schizophrenia patients.

2. Methods and materials

2.1 Study design

The study was designed to investigate the changes of some hormones concentration (LH, FSH, prolactin, T3, T4, TSH, testosterone, estrogen, and progesterone). This study was conducted two groups. The first group included 100 men with schizophrenia attending Imam Hussein Teaching Hospital in Thi-Qar province during the period from August 1st,

2024 to January 3ed, 2025. They were diagnosed with schizophrenia by specialists based on the standard diagnostic criteria found in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [8]. The second group included 10 healthy men who did not suffer from any disease.Five mill of venous blood where collected from each subjects (patients and control) and placed in gel tubes, the serum was separated and stored at -20°C until used.

2.2 Hormone Measurement

Hormones (LH, FSH, prolactin, T3, T4, TSH, testosterone, estrogen, and progesterone) were measured using ELISA technology using HS Huma Readers from the German company (Human) and an ELISA kit from the American company (Elabscience).

3.2 Statistical Analysis

The statistical analysis was conducted using SPSS version 27 .All statistical analysis was performed using computer software SPSS 27, the results were analyzed and presented as mean standard error (Mean±SE).

3. Results and discussion

1.3 The relationship between schizophrenia and some anterior pituitary hormones (FSH, LH, and prolactin)

The results of the current study revealed a significant decrease in the concentration of luteinizing hormone (LH) and prolactin, while there was no significant difference in the concentration of follicle-stimulating hormone (FSH) in men with schizophrenia when compared to the control group at a probability level of P≤0.05, as shown in Table (1).

Table 1- The effect of schizophrenia on some hormones of the anterior lobe of the pituitary gland

Hormone	Group	N	Mean	Standard Deviation
LH μIU/mL	Infected	10	1.11350 b	0.481287
	Control	10	1.84120 a	0.382445
FSH mIU\mL	Infected	10	27.58230 a	0.672975
	Control	10	27.51300 a	3.227833
Prolactin ng/mL	Infected	10	8.37960 b	1.057575
	Control	10	19.46680 a	5.627387

The difference in letters indicates significant differences.

Luteinizing hormone (LH) is a hormone produced by the anterior pituitary gland that nourishes the gonads. It plays a major role in men, particularly in controlling testosterone secretion from Leydig cells. The hypothalamic-pituitary-gonadal axis controls the secretion of this hormone. The results of the current study indicated a significant decrease in its concentration, which may explain the occurrence of a defect in the mechanism of regulating the components of the above axis as a result of schizophrenia. [9] indicated that the hormones of the anterior pituitary gland play a pivotal role in many of the basic physiological pathological processes that are assumed to be changed in patients with schizophrenia.

The decrease in the concentration of luteinizing hormone may also be due to an increase in the concentration of testosterone in the blood, which was demonstrated by the results of the current study. It is known that there is a negative feedback mechanism that controls the regulation of the relationship between the secretion of luteinizing hormone and testosterone. When testosterone levels in the blood increase, the secretion of gonadotropin-stimulating hormone (GnRH) from the hypothalamus, which is responsible for stimulating the secretion of luteinizing hormone from the anterior lobe of the pituitary gland, is inhibited, thus causing a decrease in the secretion of LH [10].

It is also possible that the decrease in LH concentrations may be a result of antipsychotic treatment. [11] indicated in his study on male white mice that this treatment causes a decrease in the concentration of luteinizing hormone (LH) and thyroid-stimulating hormone (TSH). The decrease in these hormones may be a result of weight gain in patients with schizophrenia and the resulting disturbances in the hypothalamus. [12] indicated that treatment with antipsychotics leads to weight gain over time. Weight gain resulting from antipsychotics is also associated with disruption of the hypothalamic-pituitary-gonadal axis, which affects hormone secretion. The results of the current study showed that most patients with schizophrenia experienced weight gain at a rate higher than the normal body mass index.

The results also indicated a significant decrease in the concentration of prolactin, and the reason for the decrease in the concentration of this hormone in patients with schizophrenia may be due to treatment with the drug aripiprazole, as [13] indicated that this drug works as a partial stimulator to stimulate dopamine D2 receptors, It does not completely stop the action of dopamine, but rather partially reduces its activity, so it is likely to reduce the secretion of the hormone prolactin. In the same topic, [14] indicated that the dopaminergic system regulates the secretion of prolactin from the pituitary gland, and the tonic activation by dopamine of dopamine D2 receptors , expressed in the lactotroph cells in the pituitary gland, may lead to inhibition of prolactin synthesis.

Low prolactin levels in schizophrenia patients may be due to the prevalence of smoking among them. The study of [15] indicated that smoking prevalence among schizophrenia patients exceeds 60%, and the results of the current study demonstrated the prevalence of smoking among male schizophrenia patients. In the same view, [16] and [17] indicated that nicotine inhibits prolactin secretion by activating nicotinic receptors in dopaminergic neurons and stimulating dopamine release as a prolactin inhibitor. The results of the current

study were consistent with those of [18], which demonstrated a decrease in prolactin concentrations in schizophrenia patients.

2.3 The relationship between schizophrenia and thyroid function

The results of the current study indicate a significant increase in the concentration of both triiodothyronine (T3) and thyroxine (T4) and a significant decrease in the concentration of thyroid-stimulating hormone (TSH) in the schizophrenia group compared to the control group at a probability level of $p<0.05$, as shown in Table (2).

Table 2- The effect of schizophrenia on thyroid function

Hormone	Group	N	Mean	Standard Deviation
T3 ng/mL	Infected	10	1.23800 a	0.107729
	Control	10	0.51940 b	0.056441
T4 ng/mL	Infected	10	24.13760 a	0.764875
	Control	10	13.57700 b	1.118621
TSH µIU/mL	Infected	10	4.99300 b	0.222104
	Control	10	8.34480 a	0.145566

The difference in letters indicates significant differences.

The results of the current study indicated the presence of differences in the concentrations of thyroid hormones and the stimulating hormone, which indicates the occurrence of disorders in the secretions of the thyroid gland and the stimulating hormone secreted from the anterior lobe of the pituitary gland, which may be due to the effect of schizophrenia on the hypothalamic-pituitary-thyroid axis, which completely controls the secretions of the thyroid gland, or vice versa. [19] indicated the association of differences in the concentrations of thyroid hormones with the risk of developing many psychological disorders, whether the difference is a deficiency or an excess in the secretion of these hormones.

Increased levels of thyroid hormone T4 may be associated with the use of antipsychotic drugs. [20]indicated that the concentration of this hormone increases in the acute phase of schizophrenia due to the effect of antipsychotic drugs on the metabolism of thyroid hormones. [21]indicated that typical antipsychotics, such as phenothiazines, reduce the response of TSH to Thyrotropin Releasing Hormone (TRH) by stabilizing alpha-adrenergic receptors. Antipsychotics affect these receptors, and this effect may lead to an increase in T4 through negative feedback.

While [22] pointed out that the increase in hydrogen peroxide H_2O_2 may be the cause of hyperthyroidism and thus an increase in its hormones, as hydrogen peroxide is considered an important factor in the formation of thyroid hormones, as it enhances the conversion of iodide to iodine and the association of monoiodotyrosine (MIT) and diiodotyrosine (Dit), and the synthesis of RT3 Reverse (RT3), which is an inactive form of T3, which leads to hyperthyroidism and thus an increase in the secretion of its hormones.

On the other hand, the study of [23]showed that schizophrenia causes a disruption in the antioxidant system, resulting in the production of high concentrations of reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2). In the same context, the study of [24] indicated that oxidative stress in patients with schizophrenia causes an increase in hydrogen peroxide concentrations due to a deficiency in antioxidant enzymes such as catalase and glutathione, which decompose H_2O_2 to prevent oxidative stress. The results of the current study were consistent with those of [25], which found increased concentrations of T3 and T4 in patients with schizophrenia. However, the results of the current study differed from those of [26], which showed decreased concentrations of thyroid hormones in patients with schizophrenia when compared to the control group.

Low thyroid-stimulating hormone (TSH) secretion may be due to high dopamine levels in schizophrenia patients. The study of [27] indicated that dopamine, noradrenaline, and serotonin play an important role in regulating the secretion of the anterior pituitary gland by interacting with regulatory hormones in the hypothalamus. Dopamine, in particular, is associated with inhibiting TSH secretion. The study of [28] also showed that high dopamine concentrations inhibit TSH secretion. On the other hand, the studies of [29], [30] and [31] have shown an increase in dopamine concentration in patients with schizophrenia. The results of the current study, regarding the presence of a decrease in TSH in schizophrenia patients, are consistent with the results of [32] and [33], who found a significant decrease in TSH concentrations.

3.3 The relationship between schizophrenia and the concentrations of some sex hormones in men

The current study found a significant increase in testosterone concentrations and a significant decrease in estrogen and progesterone concentrations in schizophrenia patients compared to the control group at a probability level of $p \leq 0.05$, as shown in Table (3).

Table 3- The effect of schizophrenia on the concentrations of sex hormones

Hormone	Group	N	Mean	Standard Deviation
Testosterone	Infected	10	4.63250 a	1.303668
ng/mL	Control	10	3.07700 b	0.544593
Estrogen	Infected	10	0.09950 b	0.013738
ng/mL	Control	10	0.13960 a	0.027468
Progesterone	Infected	10	7.43550 b	0.865184
ng/Ml	Control	10	8.39240 a	0.670884

The difference in letters indicates significant differences.

The secretion of sex hormones, like other hormones, is subject to the control system of the endocrine glands in terms of the presence of stimulating and inhibiting factors for secretion. Therefore, any change in this system, especially the hypothalamus-pituitary-gonadal axis, causes a clear change in the secretion of these hormones depending on environmental or health factors, whether internal or external. Therefore, an increase in the concentration of testosterone and a decrease in the concentration of estrogen and progesterone is the result of a defect in the axis (hypothalamus-pituitary-adrenal gland or the sex gonads).

The study of [34] indicated that schizophrenia causes a disturbance in the axis regulating the secretion of sex hormones. [35] also explained that the disturbance in sex hormone levels is caused by a dysfunction in the hypothalamic-pituitary-gonadal axis, which contributes to the pathophysiology of schizophrenia. Recent studies indicate an important role for sex hormones in the pathophysiology of schizophrenia. In a related context, some studies have indicated that the role of testosterone in the development of schizophrenia is not fully understood [36]. The reason for the increased concentration of testosterone may be an increase in the rate of its production in the body. The study of [37] indicated that steroid hormones (testosterone and estrogen) cause an increase in the number of neurons containing the enzyme tyrosine hydroxylase, which is necessary for the synthesis of dopamine, thus increasing dopamine in the synapses, reducing its reabsorption, and also increasing the local production of testosterone in the brain, which causes its concentration in the blood to rise, even if the gonads are removed.

The reason for the high concentration of testosterone may be a reaction and a defense mechanism against some of the negative feelings that people with schizophrenia are exposed to. The study of [38] indicated that testosterone is linked to the feeling of strength and self-confidence, due to its effect on increasing muscle mass and its association with dominance, control and power behavior. Therefore, people with schizophrenia may tend to have delusional beliefs that represent their feeling of greatness and control, which increases the secretion of testosterone.

The reason for the increase in testosterone may be due to the nature of the period in which people with schizoid, which represents the third and fourth decades of life, as the study of [39] indicated that the increase in testosterone levels is related to age in patients with schizophrenia, The peak incidence of schizophrenia occurs in late adolescence for both sexes, a second peak may occur in women after menopause. In the same context, the study of [40] indicated that increasing the testosterone level is a characteristic sign of schizophrenia in men with this disease.

Increased testosterone levels in men with schizophrenia may be due to smoking. The studies of [41]and [42] have indicated that cotinine, a metabolite of nicotine, acts as an aromatase inhibitor, leading to increased androgens in males, including testosterone. The results of the current study demonstrated that a high percentage of men with schizophrenia were smokers, which explains the increased testosterone concentration. The results of the current study are consistent with the study by [43], which found increased testosterone concentrations in schizophrenia patients compared to the control (healthy) group. The results of the current study are inconsistent with the study by [44], which found a decrease

in testosterone concentrations in patients with schizophrenia compared to healthy people. The results also indicated a significant decrease in estrogen concentrations in men with schizophrenia. The reason for this decrease may be due to a feedback mechanism that controls the relationship between estrogen and testosterone concentrations and gonadal nutrients in the pituitary gland. Since a decrease in gonadal nutrients (luteinizing hormone) causes a loss of the primary stimulus for estrogen secretion, the results of the current study demonstrated a decrease in luteinizing hormone (LH) concentration. The decrease may be due to the high morning cortisol concentration in men with schizophrenia. The study of [45] showed that the high concentration of cortisol in the blood of affected individuals is the result of chronic stress or a dysfunction in the hormonal system resulting from dysfunction in the hypothalamic-pituitary-adrenal (HPA) axis. The study of [46] indicated that there is a reciprocal relationship between the (hypothalamic-pituitary-adrenal) axis and the (hypothalamic-pituitary-gonadal) axis. Therefore, frequent activation of the stress axis has an inhibitory effect on the secretion of estrogen and progesterone. This may explain the result of the decrease in the concentration of estrogen and progesterone in the results of the current study. The results of the current study, which found low estrogen levels in schizophrenia patients, are consistent with the study conducted by [47].

The results of the current study also showed a significant decrease in the concentration of progesterone in the group of schizophrenia patients when compared with the control group. Progesterone is known to be a neuroprotective factor in the central nervous system (CNS) by influencing the sheathing processes, regulating the plasticity of astrocytes, helping neurons survive and resist neurodegenerative diseases, and reducing the risk of cerebral edema and inflammation [48].

Low progesterone levels in patients with schizophrenia may be due to the side effects of antipsychotic medications that affect the dopaminergic pathway, which interferes with the hypothalamus's role in controlling hormone secretion through the hypothalamic-pituitary-adrenal axis [49]. The results of the current study are consistent with those of [50], which showed a significant decrease in progesterone levels in patients with schizophrenia.

4. Conclusions

Schizophrenia disease had adverse effects on concentration of studied hormones.

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