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Estimation of Total Thyroxine, Prolactin and Testosterone Hormones in Sera of Iraqi Schizophrenic Patients

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ABSTRACT

Schizophrenia is one of a highly common mental disorder around the world. However the real causes of this disease are still unclear somewhat. Recent studies have sought to identify potential role of hormones in the pathophysiology of schizophrenia. Accordingly this study is focused to monitor potential changes in the levels of total thyroxine (total T_4), prolactin and testosterone hormones in schizophrenic patients in Iraq. Sixty patients with schizophrenia (40 males and 20 females) and sixty healthy control group were included in this study. The ELISA technique was used to estimate the concentrations of these hormones in two study groups. The results obtained showed a significant decrease in serum level of total T_4 ($p<0.05$), highly significant increase in prolactin level ($p<0.001$) and highly significant decrease in testosterone level ($p<0.001$) in patients compared with the healthy control group. According to these findings there was significant difference in hormones levels between healthy subjects and schizophrenic patients, which suggest that the hormones may have prognostic significance in complex disorders including schizophrenia. However, further comprehensive studies are needed to clearly define the relationship between hormones and their role in schizophrenia.

KEYWORDS: schizophrenia; hormones; thyroxine; prolactin; testosterone.

INTRODUCTION

Schizophrenia is a condition that is generally misunderstood, in part because the word schizophrenia is incorrectly used in a wide range of contexts. Unlike popular mythology, schizophrenia has nothing to do with the personality of division. Schizophrenia is define as a chronic and severe mental disorder that affects the thinking, feeling and behavour of person. In fact, it seem like the patients with schizophrenia have lost their touch with reality [1, 2]. Studies have been shown that people with schizophrenic are more likely to be victims of violent crime, not that they are the perpetrators. Basically, scientists can not yet diagnose the cause of schizophrenia, but the belief is a disease accompanied by environmental conditions that qualify for the presence of a particular person, a genetic factor plays an important role in it [3,4].

The symptoms of schizophrenia are divided into three sections. Positive Symptoms of schizophrenia such as (Delusion, Hallucination, Thought disorders and Movement disorders), Negative Symptoms of schizophrenia and Cognitive Symptoms of schizophrenia[5,6] .

Statistics have indicated that 24 millions people around the world are infected with this disease, and the prevailing belief is that men were more affected than women, but the reality is that the disease affects both men and women in the same proportions [1]. It has been found that this disease is happen in different age groups, and may lead to an unusual person who becomes socially isolated in his own world and the mysterious hallucination of the mind.

Human body parts can communicate with each other in two ways: the first through the nervous system and the second through the hormones. Hormone is a chemical molecule that acts as a messenger transmitting a signal from one cell to another. Prolactin is a polypeptide hormone that is produced and secreted from specialized cells of the anterior pituitary gland which sits at the bottom of the brain [7]. Prolactin production is controlled by the endocrine system located in the hypothalamus (under the cradle) [8]. Normally, small amounts of prolactin is found in the blood of both men and women, and its levels are controlled by prolactin inhibiting factors (PIFs), such as dopamine [9].

Thyroxine (3,5,3',5'-tetraiodothyronine or T_4) is one of the thyroid hormones (TH), in addition to triiodothyronine (T_3), produced by the thyroid gland that are primarily responsible for regulation of metabolism processes [10]. T_4 is made up partly of iodine; therefore any deficiency in iodine will lead to decreased production

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of T_4, enlarges the thyroid tissue and will cause the disease known as simple goitre. In fact, T_4 is represent the major form of thyroid hormones in the blood that has a longer half-life than T_3. It is found that the ratio of T_4 to T_3 released into the blood is between 14:1 and 20:1. Also it is found that T_4 is converted to the active T_3 within cells by deiodinases (5'-iodinase) [11].

Testosterone is the primary male sex hormone and an anabolic steroid. In men, testosterone plays a key role in the development of male reproductive tissues such as the testis and prostate, as well as promoting secondary sexual characteristics such as increased muscle and bone mass, and the growth of body hair. In addition, testosterone is involved in health and well-being, and the prevention of osteoporosis [12-14].

Testosterone is biosynthesized in several steps from cholesterol and is converted in the liver to inactive metabolites [15], and on average a man's body produces about 7 milligrams of testosterone per day (but not all of the testosterone is produced by the body). Insufficient levels of testosterone in men may lead to abnormalities including frailty and bone loss. Testosterone is secreted primarily by the testicles of males and to a lesser extent the ovaries of females. Small amounts are also secreted by the adrenal glands. On average, in adult males, levels of testosterone are about 7–8 times as great as in adult females [16]. The purpose of this study was to determine the levels of total T_4, prolactin and testosterone hormones in patients with schizophrenia, taking into account the gender difference factor.

MATERIALS AND METHODS

Patients and Controls:

This study was conducted in College of Health and Medical Technology, Dept. of Medical Laboratory Science Technology, Baghdad, Iraq between October, 2016 and April, 2017. The study includes 60 patients with Schizophrenia, 40 males and 20 females, with age ranging from 40 – 60 years; the mean age 63.4 years. Sixty volunteers of control group, 40 males and 20 females, with age ranging from 40 – 60 years; the mean age 41.4 years. Patient samples were collected from Al-Rashad Psychiatric Hospital / Ministry of Health, Baghdad, Iraq.

Sample Collection:

Blood samples were collected from each individual of patients with schizophrenia and volunteers control, 5 ml of blood were drawn by vein puncture using disposable syringes. The blood sample was placed in gel tube, then left to stand at room temperature for 20-30 min. Sera were separated from clotted blood by centrifugation at 5000 rpm for 10 minutes, and the obtained serum transferred immediately to another test tube.

Determination of prolactin, total thyroxine and testosterone:

The quantitative determination of prolactin, total thyroxine (total T_4) and testosterone hormones concentration in human serum by an automated ELISA microplate reader analyzer, model IRE 96-SFRI – Medical Expo (SPAIN), was carried out following the protocol of the commercially available *Acuu Bind* Elisa kits supplied by Monobind Inc. (USA).

The results were analyzed statistically using SPSS (Statistical Process of Social Sciences) program version 22.0 for windows (IBM Corporation, New York, United States). Independent student t-test was used for assessment of mean differences between two groups (patients and control groups). The statistical tests were considered to be significant at the $p<0.05$ with 95% Confidence Interval. The upper and lower limits were recorded for each element in this study, and the values were expressed as mean ± standard deviation (SD).

Results and Discussion:

The serum mean values ± SD of total T_4, prolactin and testosterone hormones for the study groups (patients and control groups) were calculated statistically, and the collective results are presented in Table 1, where the data obtained were assigned for p values <0.05 with 95% Confidence Interval.

The data obtained of total T_4 showed a significant decrease in serum concentration of patients compared with the healthy control group ($p<0.05$). The concentrations of total T_4 in the control and schizophrenic patients were (9.65 ± 3.08 ng/ml) and (7.69 ± 4.31 ng/ml) respectively, as shown in Table 1.

Unlike total T_4, the results obtained for prolactin showed an increase in serum concentration of patients compared with the healthy control. The concentrations of prolactin in the control and schizophrenic patients were (8.20 ± 4.17 ng/ml) and (22.13 ± 12.84 ng/ml) respectively, as shown in Table 1. These results indicated the presence of a highly significant increase in prolactin concentration of schizophrenic patients as compared with control group ($p<0.001$). The data may highlight, to some extent, a positive impact of this hormone on the risk of schizophrenia.

Similarly to total T_4, the results obtained for testosterone hormone showed a clear decrease in the serum concentration that measured for schizophrenic patients when compared with those of control group. The recorded mean values ± SD of testosterone for control and patients were (4.83 ± 2.78 ng/ml) and (1.77 ± 1.05 ng/ml) respectively, as shown in Table 1. These results indicated the presence of highly significant decreased of testosterone hormone level in patients compared with those of control (p<0.001).

Table 1: Serum levels of hormones (total T_4, prolactin and testosterone) in patients with schizophrenia and healthy volunteer control groups.

Hormone	Control			Patients			*p* value
	Mean	SD	Upper & lower limit	Mean	SD	Upper & lower limit	
total T_4 (ng/ml)	9.65	3.08	10.44 8.86	7.69	4.31	9.10 7.29	0.004
Prolactin (ng/ml)	8.20	4.17	10.07 7.36	22.13	12.84	27.52 22.75	<0.001
Testosterone (ng/ml)	4.83	2.78	5.55 4.11	1.77	1.05	2.05 1.50	<0.001

Schizophrenia is one of the most severe mental disorders around the world. Although we cannot determine the physiology of schizophrenia, studies have indicated that the removal of hormones may play a role in the development of schizophrenia [17]. It should be mentioned here that thyroid hormones are necessary to develop and make the brain function normally [18]. Previous study has revealed the existence of a range of changes in the levels of thyroid hormones with different cases of mental illness [19]. It has been found that thyroid hormones have been stimulated to change in the case of schizophrenia, where a recent study showed an increase in levels of thyroid hormones and decreased TSH levels in patients with schizophrenia [20].

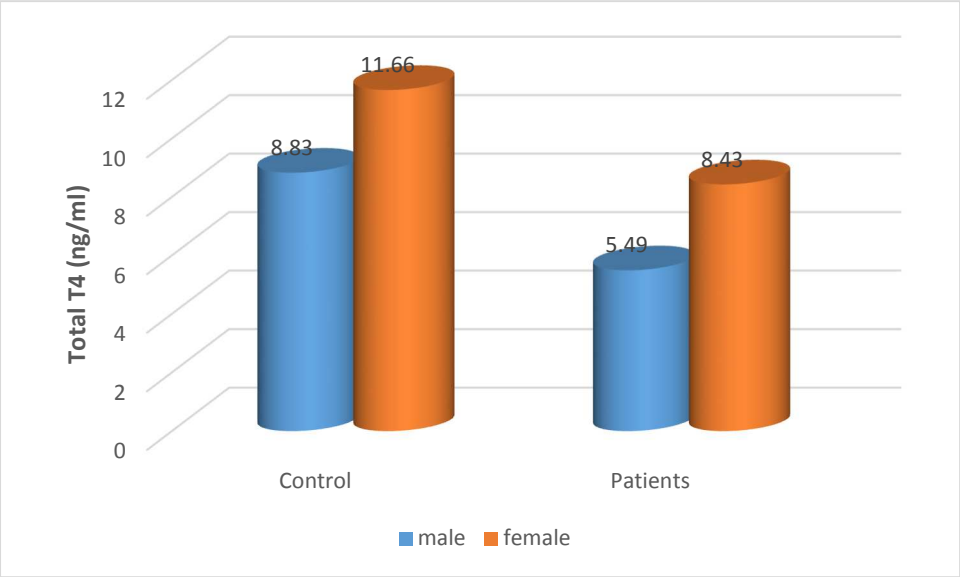

Figure 1: Diagram shows the means values of serum total T_4 (ng/ ml) in schizophrenic patients and control groups.

Previous study, on the relationship between thyroid hormone levels and schizophrenia, gave similar results with the findings of the present work [21]. These findings suggest that the decrease in thyroid hormone observed in

the schizophrenic patients may be associated with the treatment of neuroleptics. The results obtained in Table 2 and Figure 1 show that there was a decrease in the level of T_4 in men than those of women. These difference between men and women were observed in two study groups (schizophrenic patients and healthy subjects), which may be attribute to the gender physiology.

Table 2: Serum levels of hormones (total T_4, prolactin and testosterone) in patients with schizophrenia and healthy control groups according to gender (male and females}.

Hormone	Sex	Control			Patients			*p* value
		Mean	SD	Upper & lower limit	Mean	SD	Upper & lower limit	
total T_4 (ng/ml)	male	8.83	2.77	9.71 7.94	5.49	3.07	6.47 4.50	<0.05
	female	11.66	3.24	13.18 10.14	8.43	4.63	10.27 5.58	<0.001
Prolactin (ng/ml)	male	7.35	3.81	9.53 6.16	16.4	8.9	20.46 13.37	<0.001
	female	10.76	5.44	13.24 8.27	36.98	12.7	44.78 32.03	<0.001
Testosterone (ng/ml)	male	5.86	2.28	6.58 5.12	1.4	0.62	1.59 1.19	<0.001
	female	1.84	1.89	2.72 0.95	1.6	1.3	3.16 1.94	0.261

The results obtained in this study for prolactin hormone are in agreement with the data obtained of previous study by (Riecher-R¨ossler *et al.,* 2013), who reported that the concentration of prolactin in the serum of schizophrenia patients was higher than in the healthy control group [22]. On the other hand, they disagree with the data of another previous study by (Warner *et al.,* 2001), who reported that the serum prolactin level of schizophrenic patients was lower than those in the healthy control subjects [23]. As we previously knew, prolactin is a polypeptide hormone secreted by the pituitary gland, and there are different factors may affect prolactin secretion such as sex, sexual activity, birth, stress, smoking and also medication [24]. Of the most important reasons of high prolactin secretion in the blood can be physiological, as in pregnancy and lactation, and may be as satisfactory as prolactinoma [25]. Production of prolactin is reduced by releasing dopamine in the pituitary hypothalamus circuit and can be increased by blocking Type 2 dopamine receptors. Therefore, most antipsychotics drugs used for treatment can cause high prolactin secretion. As a result, this increase can causes a variety of negative effects including: lack of sexual desire and erectile dysfunction in male [26], delayed or menopause and galactura in female [27] Accelerated osteoporosis in female [28], weight gain and, possibly, increased risk of cancer, in particular breast cancer [29]. Although variety of studies suggested that the increase of prolactin concentration in the blood may be related to the treatment response in schizophrenic patients, a recent work also reported an increase prolactin secretion in patients with schizophrenia who do not receive medication [30]. In this study, it has been found that the prolactin level of female is higher than male, and also showed that the hormone level in female patients is highly affected than those of male, as shown in Table 2 and Figure 2. The table shows a significant increase in prolactin level of female and male patients with schizophrenia compared with control. These data is in agreement with the results of a previous study which reported that the level of prolactin in female patients higher than male [31]. In fact, this elevated in hormone level is expected and may be due to antipsychotics given to patients as sedatives.

It has been reported that any dysfunction in the gonadal sex hormones, including testosterone, may contribute to and play an important role in the pathophysiology of schizophrenia [32]. The results obtained in this study agree with the results of previous studies which concluded that a significant male patients with schizophrenia had hypotestosteronemia compared to healthy control male [33, 34].

Table 2 and figure 3 show the difference in the testosterone level between both sexes in patients with schizophrenia and healthy control, bearing in mind that testosterone hormone is also found in women but in small level compared to that in men. A comparison between studies groups that have made in this work showed no significant difference of testosterone level between women patients with schizophrenia and healthy control women, Table 2. In fact, we restrict the maximum age for study groups to 60 years because some studies have been proven that testosterone levels decrease with increased age [35, 36].

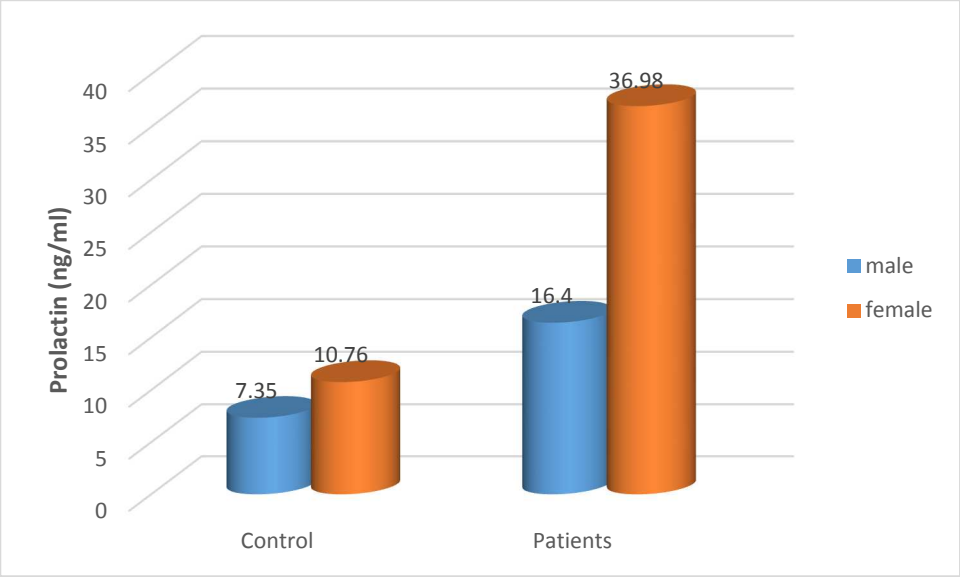

Figure 2: Diagram shows the means values of serum Prolactin (ng/ ml) in schizophrenic patients and control groups.

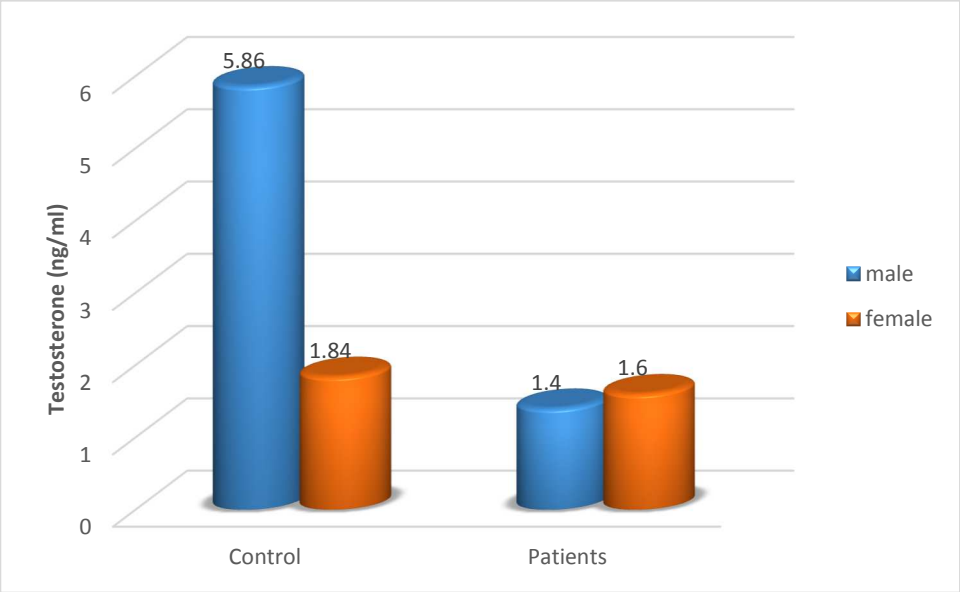

Figure 3: Diagram shows the means values of serum testosterone (ng/ ml) in schizophrenic patients and control groups.

Testosterone has been shown to have neurological effects in neurological diseases such as alzheimer's disease and parkinson's disease[37]. Moreover, in healthy older men, the addition of external testosterone has been shown to improve spatial and verbal memory [38]. Although schizophrenic patients can be difficult to treat, control the hormones level may be assist in treat this disease. Therefore, further investigation to the effectiveness of testosterone as a treatment assistant for emotional treatment and impotence treatment a reduction in schizophrenia will be required.

Conclusion:

Some hormones, especially sex hormones, thyroid hormones and prolactin, may play a role in the patho-physiology of schizophrenia. So that the levels of these hormones should be routinely measured in patients with schizophrenia. In this study, the variability in results between two study groups has been shown very clear. Therefore, further studies is greatly needed to establish if there is a potential therapeutic effects of these hormones (total T4, prolactin and testosterone) on treatment of schizophrenia.

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