THE EFFECTS OF COVİD-19 ON SEXUAL HORMONES İN IRAQİ ADULTS MEN PATİENTS.

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Abstract

In December 2019, the coronavirus infection 2019 (COVID19) linked with the severe acute respiratory syndrome coronavirus 2 (SARSCoV2) epidemic expanded quickly and became a worldwide pandemic. Although SARSCoV2 primarily affects the respiratory system, it has been detected in numerous organs. Concerns have been raised concerning COVID19's potential impact on male reproductive functioning. In this study, we compared the sex-related hormone levels between 60 reproductive-aged men with SARS-CoV-2 infection and 30 age-matched control men. Higher serum prolactin (PRL) and a lower serum of testosterone (T) were observed in the COVID-19 group. The serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were the same as in the control groups. In our opinion, male sex-related hormones are influenced by a wide range of circumstances, including environmental and psychological factors, COVID-19 infection can be a stressful situation. As a result, we should not only do follow-up physical health checks for patients who have recovered from COVID-19, but we should also pay attention to their psychological conditions. Should be pay more attention to gonadal function evaluation among patients who recovered from SARS-CoV-2 infection, especially the reproductive-aged men.

Keywords: Coronavirus, COVID-19, Sexual Hormones, Iraqi patients, reproductive system.
INTRODUCTION

Since the initial report in December 2019 in Wuhan, a new coronavirus-induced pneumonia (dubbed COVID-19 by the World Health Organization) has spread fast, triggering a worldwide pandemic outbreak (Li et al 2020). COVID-19 is caused by a previously undiscovered beta-coronavirus identified as SARS-CoV-2 because of its strong sequence similarity (80%) to SARS-CoV (Gralinski et al 2020). Exclude of respiratory symptoms such as cough, fever, and even acute respiratory failure, evidence of SARS-CoV-2 infection has been documented in numerous organs such as the digestive, circulatory, and urinary systems (Chai et al 2020).

Angiotensin-converting enzyme 2 (ACE2) is thought to be the receptor for SARS-CoV-2 binding and entry into host cells. Any cells that express ACE2 may theoretically be infected with SARS-CoV-2(Hoffmann et al 2020). ACE2 (angiotensin-converting enzyme 2) is strongly expressed by numerous cell types in the testes, including Leydig cells, Sertoli cells, and the germ line, and is known to be targeted by the spike protein that gives the COVID-19 virus its corona. As a result of these factors, COVID-19 infection increases the risk of testicular injury and infertility. However, after male germ cells leave the testes, either in the epididymis or after ejaculation, the virus may get access to them (Wang et al., 2020)( Verma et al., 2020).

In condition of infection, because the blood-testes barrier is not perfect enough to fully isolate virus, it may seed into the male reproductive tract (Li et al 2012). As shown in HIV or mumps-induced orchitis, virus-induced testes damage can impede gonadal hormone production and spermatogenesis (Liu et al 2018). SARS-CoV has been linked to orchitis in previous studies (Xu et al 2006). However, there is currently no clinical evidence that SARS-CoV-2 infection can impair male gonadal function. The expression of ACE2 in the testes has been linked to age. Patients aged 30 and older than 20 had the greatest levels of expression, while those aged 60 have the lowest amounts. This might.
indicate that COVID-19-induced testicular damage is more common in young male patients than in older patients. This also implies that multiple hormonal milieus have a significant pathophysiological role in SARS-CoV-2 infection in men (Shen et al 2020).

We examined sex-related hormones in reproductive-aged males with SARS-CoV-2 infection to age-matched healthy men in this study.

**Methods**

**Study design and patients**

We performed study in AL anbar city from 20 May to 28 July for patients recording from COVID-19. All cases were laboratory-confirmed as SARS-CoV-2 positive using quantitative PCR on nasal and pharyngeal swab specimens. We depended on the samples taken from COVID-19 patients after recovery and other samples were taken from healthy people as the control group.

The number of patients under study reached 60 patients recovered from COVID-19. The ages of the patients ranged from 20-50 years (with a median of 34 yrs). During the interview with the patients, information was taken on their medical history of several chronic disease (smoked or alcoholic), age and other used drugs.

The study included 30 healthy control group who haven’t any disease. The control group came from the population who previously received reproductive function evaluation and were classified as having normal fertility (healthy individuals) and the data of their sex-related hormones were collected.
Sex-related hormone assessment

In the study group, serum testosterone (T), prolactin (PRL), luteinizing hormone (LH), follicle stimulating hormone (FSH), were detected by MINI VIDAS machine according to the instructions from the manufacturer (Biomerieux-France).

Statistical Analysis

All statistical analysis was performed using SPSS 23.0 (Chicago, IL, USA). Continuous variables were expressed as means ± standard deviations (SD). Categorical variables were summarized as the counts and percentages (%) and tested by Chi square test. Differences between two groups were analyzed by t test. Correlation coefficient were found to estimate relationship between all variables. Statistical significance was defined as p values of < 0.05

Results

The total number of covid-19 patient was 60. The ages of the patients ranged from 20-50 years old, the average age was 34.10 (± 8.39) years old. 30 apparently healthy subjects were included in the study as a healthy control group, which had an average age of 31.81 (± 5.89) years old. Chi-square test showed that there were no significant differences in age of the groups (age: P= 0.34).

Table (1) shows the mean ±SD of testosterone was (3.02±1.22) ng/ml, and the age-matched group was (3.66±0.70) ng/ml. The showed significant differences compared with the levels in the non-COVID-19 controls (P< 0.03) and the mean ±SD of Prolactin was (18.20±6.23) ng/ml, and the age-matched group was (12.35±4.45 )ng/ml .The showed high significant differences compared with the levels in the non-COVID-19 controls (P< 0.0001).
Table (1): The mean and standard deviation of sex-related hormone for both covid-19 patient and age-matched group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean±SD</th>
<th>t-test</th>
<th>Sig.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Patient</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>Testosterone ng/ml</td>
<td>3.02 ± 1.22</td>
<td>3.66 ± 0.70</td>
<td>-2.247</td>
</tr>
<tr>
<td>Prolactin ng/ml</td>
<td>18.20 ± 6.23</td>
<td>12.35 ± 4.45</td>
<td>3.643</td>
</tr>
</tbody>
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*Significant at P≤0.05. NS Non-significant at P≤0.05.
Figure (1): Serum of Testosterone ng/mL in the study groups show lower levels as compared with controls.

Figure (2): Serum of prolactin ng/mL in the study groups show higher levels as compared with controls.

Table (2) shows the mean ±SD of LH was (4.09±1.56) mIU/ml, and the age-matched group was (4.13±1.27) mIU/ml. The showed non-significant differences compared with the levels in the non-COVID-19 controls (P< 0.920). And the mean ±SD of FSH was (4.31±1.80) mIU/ml, and the age-matched group was (4.82±0.89) mIU/ml. The showed non-significant differences compared with the levels in the non-COVID-19 controls (P< 0.205).

Table (2): The mean and standard deviation of sex-related hormone for both covid-19 patient and age-matched group.

<table>
<thead>
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</thead>
<tbody>
<tr>
<td></td>
<td>Patient</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>LH mIU/mL</td>
<td>4.09 ± 1.56</td>
<td>4.13 ± 1.27</td>
<td>-1.01</td>
</tr>
<tr>
<td>FSH mIU/mL</td>
<td>4.31 ± 1.80</td>
<td>4.82 ± 0.89</td>
<td>-1.287</td>
</tr>
</tbody>
</table>
Discussion

Many viruses, including the Zika virus, the mumps virus, and the human papillomavirus, have been shown to induce testicular damage and infertility. SARS-CoV appeared in 2003 and quickly spread around the world (Liu et al., 2018)( La Vignera et al., 2015). Orchitis can be a side effect of SARS, according to Xu et al. On autopsy, they discovered

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six SARS patients who had severe orchitis (marked by extensive germ cell death, few or no spermatozoa in the seminiferous tubules, and leukocyte infiltration). SARS-CoV-2 shares around 80% nucleotide similarity with SARS-CoV (Xu et al., 2006), and both coronaviruses employ ACE2 as the host cell receptor to infect humans (Ren et al., 2020). In testicular tissue, ACE2 is abundantly expressed. As a result, it's fair to believe that SARS-CoV-2 infection might induce testicular tissue damage, which can lead to reduced sexual function and fertility (Felsenstein et al., 2020) (Li et al., 2013).

Since the major roles of testes are spermatogenesis and androgens secretion, sex-related steroids can be used to evaluate the status of male gonad. In order to learn the effect of SARS-CoV-2 infection on male reproductive function, we compared the sex hormone profiles between COVID-19 patients and age-matched healthy men with normal fertility. In this study, the serum T levels have statistically changed in the COVID-19 group compared to the age-matched group Where it decreased relative, and we believe that the reason is due to the psychological factor.

We agree with Temiz et al (2021) findings that the testosterone serum decreased and the reason is due to acute patient stress due to the COVID-19 and its uncertainties.

Ma et al (2020) findings showed that patients with COVID-19 had a normal T level. The author speculated that the testes might have been injured in a process linked to the inflammation indicator C-reactive protein. Our study is not consistent with the above research on T. The reason for the difference between the two studies may be that the former study involved patients in the infection period, while our study involved patients in the recovery period.

In another study Koç et al (2021) which we agree with, Following the diagnosis of COVID-19, the patients' T levels were found to be significantly lower. Despite the fact that only a small number of patients had their sex-related hormone levels examined, the results of this study are noteworthy because they show the dependent group analysis
results of a hormone like T, which has a broad range of variance throughout the population.

Our findings that the prolactin serum was significantly higher in the COVID-19 group compared to control groups. We attribute the reason to psychological factors and stress. In agreement with our findings, Ma et al (2020) indicated that the serum PRL level was also significantly elevated in COVID-19 patients. Since serum PRL may be impacted by a variety of factors, such as diet, stress, drugs, etc., the increase was not unexpected. But it should be mentioned that high PRL levels may lead to pituitary suppression and decreased gonadotropins.

The current study showed that the serum LH and FSH were not significantly different between the COVID-19 group and the control group. Xu et al (2021) did study identified several patients (designated ‘long-term positive’ patients) who had SARS-CoV-2 RNA-positive throat swabs for a sustained period but who had no respiratory symptoms. The results of the study showed no significant differences in T, FSH, LH, PRL the two duration groups, and T, LH, and FSH were both within the normal reference ranges. In addition, both duration groups had normal serum biochemical and inflammatory markers. This indicates that, even if ‘long-term positive' patients have a prolonged illness course, their tissues and organs (such as the liver, kidneys, and testes) can nevertheless retain or be restored to their normal physiological condition. It's possible that this is related to the virus's low virulence or restricted transmission in these people. It's also possible that the virus and the human body have achieved a point of equilibrium, in which the body's immunity, regulatory abilities, and compensating powers are sufficient to deal with the virus's long-term effects.

Another study was conducted by Kadihasanoglu et al (2021) the serum LH and prolactin levels were higher in patients with COVID-19 and non–COVID-19 respiratory tract
infections. Even though prolactin levels were unaffected by disease severity, patients with severe illness had the lowest LH levels compared to those with mild or moderate disease. Despite the fact that SARS-CoV-2 has a negative impact on LH, FSH levels in patients and controls were not different. This study found a link between a lower TT and a longer stay in the hospital, allowing for the prediction of illness progression in COVID-19 patients.

In conclusion, we must keep in mind that male sex-related hormones are influenced by a wide range of circumstances, including environmental and psychological factors. COVID-19 infection can be a stressful situation. As a result, we should not only do follow-up physical health checks for patients who have recovered from COVID-19, but we should also pay attention to their psychological condition and suggest counseling for patients who may benefit. The study concluded that men infected with the Coronavirus are more likely to have low levels of testosterone hormone and high prolactin hormone. Coronavirus has no effect on LH and FSH hormones.

REFERENCES


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