Influence of COVID-19 Infections on LH, FSH and Prolactin level in group of Males Recovered from COVID-19 in Baghdad

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Abstract

COVID-19 (Coronavirus disease 2019), cause Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) across all age groups, it's a positive-sense single-stranded RNA virus, and a member of the Betacoronavirus genus taxonomically. COVID-19 can infect the male reproductive system in large part by inflammatory damage caused by a cytokine storm and the impact of the disease may continue for several months. The ACE2 receptors are highly expressed in testes along with other various tissues of the body making it one of the targets for SARS-CoV-2.

The aim is to determine the effect of COVID-19 infections on male reproductive hormones in Iraqi male patients. 120 men chosen from Baghdad Teaching Hospital, 9 Nisan Health Center and Kamal AL-Samarrai Hospital, 70 of them recovered from COVID-19 within a period of 6 months after the last negative PCR nasopharyngeal swab and 50 as control group (uninfected COVID-19) from the Medical staff and the relatives, during the period from December/ 2020 to March / 2021. The measurements of three hormones were done for each one: LH (Luteinizing Hormone), FSH (Follicle-Stimulating Hormone) and Prolactin levels for recovered Covid-19 patients. The mean and standard deviation level of studied parameters are differ between cases of current studying; recovered COVID-19 males and control

P-ISSN: 2664-0562

E-ISSN:2664-0554

group then compared with normal value of each test. The levels of LH hormone are slightly increase among recovered males compared with control group, statistically non-significant (P-value= 0.09), as well as FSH hormone among cases are statistically non-significant (P-value= 0.6), while levels of Prolactin hormone are increased among cases studied compared with control group, this differences was highly-significant (P-value= 0.006).The levels of LH and FSH among recovered COVID-19 patients did not effected after recover, however there are indirect effect on prolactin level from COVID-19 infections.

***Keywords**: Covid-19, LH, FSH, Prolactin, Recovered males.*

تأثير الاصابة بكوفيد - 19 على مستوى هرمون الملوتن LH ،المحفز للجريبات FSH و البرولاكتين Prolactinفي مجموعة من الذكور المتعافين من كوفيد - 19 في مدينة بغداد

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الخلاصة

كوفيد – 19 (مرض فيروس كورونا 2019)، يسبب متلازمة الجهاز التنفسي الحادة الوخيمة Coronavirus-2 (SARS-CoV-2) في جميع الفئات العمرية ، إنه فيروس RNA أحادي الخيط، وعضو في جنس Betacoronavirus تصنيفيًا . يمكن أن يصيب COVID-19 الجهاز التناسلي الذكري في جزء كبير منه عن طريق التلف الالتهابي الناجم عن عاصفة خلوية وقد يستمر تأثير المرض لعدة أشهر. يتم التعبير عن مستقبلات ACE2 بشكل كبير في الخصيتين جنبًا إلى جنب مع أنسجة الجسم المختلفة الأخرى مما يجعلها واحدة من أهداف ARS-CoV-2 .

الغرض من البحث هو دراسة تأثير الاصابة بكوفيد- 19 على مستوى هرمونات التكاثر في مجموعة من الذكور المتعافين من كوفيد- 19 في مدينة بغداد .تم اختيار 120 رجلاً من مركز مدينة الطب والمركز الصحي في 9 نيسان ومستشفى كمال السامرائي ، منهم 70 رجل تعافوا من كوفيد-19 خلال فترة 6 أشهر بعد آخر مسحة بلعومية سلبية PCR و 50 رجل كمجموعة ضابطة غير مصابين بـكوفيد-19من الطاقم الطبي والأقارب ، خلال الفترة من ديسمبر / 2020 إلى مارس / 2021. تم إجراء قياسات لثلاثة هرمونات لكل واحد LH (هرمون الملوتن) ، FSH (هرمون تحفيز الجريبات) و مستويات البرولاكتين لمرضى كوفيد-19 المتعافين . متوسط ومستوى الانحراف المعياري للمعلمات المدروسة يختلف بين حالات الدراسة الحالية أي المتعافين من

الذكور والمجموعة الضابطة ثم المقارنة بالقيمة الطبيعية لكل اختبار. ارتفع مستوى هرمون LH بشكل طفيف بين الذكور المتعافين مقارنة بالمجموعة الضابطة ، لكنه غير معنوي إحصائيا (قيمة P = 0.09) ، وكذلك هرمون FSH للحالات نفسها غير معنوي إحصائيا (قيمة P = 0.6) ، بينما ارتفع مستوى هرمون البرولاكتين بين الحالات مقارنة مع مجموعة السيطرة ، وكانت هذه الفروق عالية المعنوية (القيمة الاحتمالية = 0.006). يمكن مناقشة الآثار طويلة المدى لعدوى SARS-CoV-2 على مستوى هرمونات التكاثر الذكرية. يجب التأكيد على أنه على الرغم من أن كوفيد-19قد يسبب تلفًا في الخصية ، إلا أن الانخفاض الكبير في القدرة الإنجابية للذكور في انتظار الأدلة السريرية. نقترح أن تكون حاجة ملحة لتتبع مرضى كوفيد-19الذكور أثناء شفائهم. سيكون تطوير نماذج تجريبية مناسبة ، بما في ذلك الأعضاء التناسلية البشرية ، مفيدًا لمزيد من التحقيق في التأثير الفيروسي على التكاثر للجائحة الحالية والمستقبلية.

الكلمات المفتاحية : *كوفيد-19 ، هرمون الملوتن ، هرمون المحفز للجريبات ، البرولاكتين ، الذكور المتعافين.*

Introduction

Coronaviruses (CoV) are a group of viruses whose antigens are expressed on their membranes in a characteristic “crown like”. The COVID-19 virus is an RNA virus that belongs to the β-CoV subgroup and is characterized by having spike (S) proteins which facilitate viral cell entry, membrane (M) proteins and envelope (E) proteins which assist in viral assembly, and nucleocapsid (N) proteins which mediate viral transcription.

The COVID-19 S protein undergoes proteolytic priming by transmembrane protease, serine 2 (TMPRSS2) and gain access into host cells through the angiotensin-converting enzyme 2 (ACE2) receptor [1, 2]. Current studies confirm that transmembrane protease, serine-2 (TMPRSS2) is a major protease mediating the priming of the spike proteins of this virus with the target host cell receptor and mainly cleaving the ACE2 receptor. Moreover, their observation that the testes are among the body tissues with the highest ACE2 expressions that indicate associations of COVID-19 infections with male reproductive dysfunctions [3]. The androgen receptor activation is needed to trigger TMPRSS2 gene transcription [4].

Both the androgen receptor and ACE2 gene loci are in chromosome X and thus increased X-linked inheritance of genetic polymorphisms and subsequent increase in androgen actions may explain higher vulnerability of men to SARS-CoV-2 infection [4]. In the condition of viremia, virus may shed into the male reproductive track because the blood-testes barrier is not perfect enough to completely isolate virus [5]. A wide breath of viruses, such as Zika, Ebola, Marburg viruses, etc. have been found in male testes and semen [6]. Virus-induced testes damage can impair gonadal hormone secretion and spermatogenesis, as seen in HIV or mumps-induced orchitis [7]. Previous study on SARS suggested the SARS-CoV can cause orchitis [8].

In this study, we compared the sex-related hormones between reproductive-aged of recovered men with COVID-19 infection and age-matched healthy men in Iraq, this is the first study concerned with assessment the effect of COVID-19 on the level of male hormones after patients recovered from the virus.

Materials and Methods

120 blood samples were collected from recovering COVID-19 males and control from the medical staff and the relatives, who worked at three main medical facilities in Baghdad: Medical City, Health Center of 9 Nisan and Kamal AL-Samarrai Hospital during the period from December/ 2020 to March / 2021.

The recovered COVID-19 males were selected regarding age with ranged from (25-55) years, with an average age ± SD (37.04±8.93) and 50 uninfected males volunteer individuals with average age ± SD (39.48±9.93) years as control group. The measurement units of LH are mlU/ml, FSH in mlU/ml, Prolactin hormone in ng/ml Serum LH, FSH and Prolactin hormone were determined using chemiluminescence analyzer (LIAISON®).

P-ISSN: 2664-0562
E-ISSN:2664-0554

Statistical Analysis

Data were analyzed using Chi-square (X2) test to compare between percentages. Independent samples T-test was used to compare between two numeric variables. Numeric data was described by (Mean±SD). A significance level of α=0.05 was used in this test. Statistical Package for Social Science SPSS (Version 24) a program was used to analyze current data.

Results

The highest frequency 36 (30.0%) of Recovered COVID-19 patients was within (25-35) years while only 19(15.8%) of them found in age group (36-45) years old and 15(12.5%) within (46-55) years old however, in control group the highest frequency 19 (15.8%) within (25-35) years old, 14 (11.7%) within (36-45) and 17(14.2%) within (46-55) years old. the result revealed no significant differences (P-value=0.1) between studied groups, as showing in Table (1).

Table (1) : Distribution of Age among studied groups

Studied groups	Age groups			Total	M+SD
	(25- 35)	(36 - 45)	(46- 55)		
Recovered male	36 30.0%	19 15.8%	15 12.5%	70 58.3%	37.04±8.93
Control	19 15.8%	14 11.7%	17 14.2%	50 41.7%	39.48±9.93
Total	55 45.8%	33 27.5%	32 26.7%	120 100.0	***T-test=1.24(P-value=0.1)
*Chi-square=2.88 (P-value=0.2 for Age groups) **N.S					

*Chi-square test; ** N.S, not-significant; *** Independent Sample-T-Test

Results presented in table (2) showed that the LH (mlU/ml) was little higher than control group which indicated by measuring the mean value of LH (4.51± 2.28) mlU/ml for recovered COVID-19 patients and (3.90± 1.44) mlU/ml for control group, statistically these differences were non–significant (P-value= 0.09) that mean there is no difference in the level of the LH hormone between control and recovered.

Table (2) : Comparison the mean of Serum LH (mlU/ml) Level between Recovered COVID-19 Patient and control groups

Variable	Groups	No.	(Mean± Std.)	t-test	P-Value
LH 2.8-6.8(mlU/ml)	recovered	70	4.51± 2.28	1.67	0.09 ** (NS)
	Contro	5	3.90± 1.44		

** NS; Non-Significant

Table (3) shown the mean value of FSH level (7.18±6.74 mlU/ml) were slightly higher than control group (5.57±3.58mlU/ml), statistically these differences were non-significant (P-value= 0.6), this means no difference in the level of FSH hormone between studied groups.

Table (3) : Comparison of FSH (mlU/ml) between studied groups

Variable	Groups	No.	(Mean± Std.)	t-test	P-Value
FSH 1.3-11.8mlU/ml	Recovered	70	7.18±6.74	0.45	0.6 **(NS)
	Control	50	5.57±3.58		

** NS; Non-Significant

P-ISSN: 2664-0562
E-ISSN:2664-0554

Data in table (4) shown the mean value of Prolactin level in recovered COVID-19 patient (9.93± 4.90 ng/ml) was higher than control group (7.63± 3.72 ng/ml). Although, there are little differences between the two groups but statistically these differences were highly-significant (P-value= 0.006).

Table (4) : Distribution levels of Prolactin (ng/ml) among studied groups

Variable	Groups	No.	(Mean± Std.)	t-test	P-Value
Prolactin 3.4-17.4 ng/ml	Recovered	70	9.93± 4.90	2.79	0.006 *** (H.S)
	Control	50	7.63± 3.72		

*** (H.S); High -Significant

Discussion

The current study showed that most recovered patients [36 (30.0%)] were within the age (25-36) being the most affected group that compatible with study done in Iraq by Sarhan [9], so as for the distribution of age groups were ranged within (25-55) years old that compatible with [10,11]. The data in table (2) show that the level of their LH hormone was no significant between that two groups; any way the result within normal range. This finding compatible with studies done by [11,12] and Egyptian study [13] who reported that there was no significant differences in the mean of serum LH and the normal reference ranges after recover from COVID-19. FSH hormone in this study is normal among studies group after recovery from COVID-19 infection, there is no-significant difference P-value= 0.6, that proven by Chinese and Egyptian researches, that indicated the level of FSH in recovered male is still within normal range after recover from COVID-19 [11, 12] and [13] got the same result. Prolactin hormone in recovered COVID-19 patients is higher than control that agree with Chinese and

Egyptian studies which mentioned that the level of prolactin hormone was significantly higher than the corresponding levels in the controls [12, 13].

This result may be due to many factors, like psychological stress which caused by COVID-19 infections include: stay at home for long time without visits and gathering, fear of death because of high number of infections and closing life facilities, especially medical staff suffering from long hours of work, sleep disturbances, exhaustion as well as the possibility of becoming infected and placing their families at risk of a life-threatening condition so they are more susceptible to infections [14,15] or may be some hypertensive drug can cause elevated prolactin [16]. Dependent on these facts hyper prolactin aemia in males causes hypogonadotropic hypogonadism manifesting with reduced libido, erectile dysfunction, and impaired spermatogenesis [17, 18].

Conclusion

The COVID-19 infection did not affect fertility hormones represented by LH and FSH hormones among recovered COVID-19 patients and it only effected prolactin levels that may be from stress caused by illness.

P-ISSN: 2664-0562
E-ISSN:2664-0554

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P-ISSN: 2664-0562

E-ISSN:2664-0554

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P-ISSN: 2664-0562

E-ISSN:2664-0554