Evaluation of FSH and inhibin B in male after covid 19

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Abstract

Background: Coronavirus 2019 (COVID-19) is a novel viral respiratory disease caused by severe acute respiratory syndrome coronavirus 2, it affects all systems in human body even reproductive system. Aim of the study: The aim of this study was to evaluate hormonal dysfunction in male after Covid-19 recovery by estimation of luteinizing hormone, testosterone and inhibin-B. Material and Methods: A cross-sectional study was carried out in Salah Al-Din Governorate from of December 2021 to the end of April 2022, included 60 patient who have +ve PCR of previously hospitalized and with oxygen ventilation and have moderate to severe covid-19 after 6 months of recovery, the second group 30 patient that apparently be healthy as control group and evaluation of total testosterone, luteinizing hormone , Inhibin-B by enzyme linked immunosorbent assay technique. Results: The study showed no significant difference between Covid-19 patients (6 months after recovery) and health control group, the mean age of patients was 33.11 year. The study showed that the lowest mean of testosterone was recorded among Covid-19 patients (2.78 ng/ml) as compared with healthy control individuals (7.43 ng/ml) at P. value <0.001. The study showed that the mean of inhibin-B was highly reduced in recover Covid-19 patients (41.13 pg/ml) comparing with control group (76.84 pg/ml) at P. value <0.001. The study showed that the mean of luteinizing hormone was elevated significantly in recover Covid-19 patients (5.80 IU/L) comparing with control group (2.39 IU/L) at P. value <0.05. The study showed significant negative correlation between CRP and each of testosterone and inhibin-B among recovered Covid-19 patients and significant positive correlation with luteinizing hormone There was a significant negative correlation between luteinizing hormone and testosterone. Conclusions: There was a significant relation between male dysfunction and Covid-19 infection and low levels of inhibin-B and testosterone were recorded among recover Covid-19 patients comparing with healthy individuals.

Introduction

Coronavirus 2019 (COVID-19) is a novel viral respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in Wuhan China in December 2019. Since then, COVID-19 has spread globally and has infected more than 166 million people and caused more than 3.5 million deaths around the world [(1)]. The World Health Organization (WHO) declared the coronavirus outbreak a public health emergency of international concern on January 30, 2020, according to the WHO. Previously known as the 2019-novel Coronavirus (2019-nCoV), the virus was officially designated as SARS-CoV-2 by the International Committee on Taxonomy of Viruses on March 2, 2020. On February 11, 2020, the World Health Organization named the disease or COVID-19 [(13)]. The disease spread quickly throughout Southeast Asia, Europe, and North America, prompting the World Health Organization to declare COVID-19 a pandemic on March 11, 2020. Globally, till 1 July 2022, there have been 545,226,550 confirmed cases of COVID-19, including 6,334,728 deaths, and in Iraq, from 3 January 2020 1 July 2022, there have been 2,345,893 confirmed cases of COVID-19 with 25,239 deaths as reported to WHO reported to WHO. COVID-19 can present in a variety of forms ranging from mild to severe, and in some cases fatal, with an increase in severity associated with age and preexisting medical conditions [(1-7)].

Inhibins are glycoprotein hormones that belong to the Transforming growth factor beta (TGFβ) superfamily. Inhibins are composed of two subunits, an α-subunit and a β-subunit, linked by a disulfide bridge. There are two main isoforms of the β-subunit, βA and βB, resulting in two isoforms of the mature 32-kDa inhibin protein, inhibin A and inhibin B . The closely related activins are dimers of two β-subunits. It is produced primarily by growing antral follicles that are responsive to FSH. As the follicle continues to grow and become dominant, inhibin B secretion declines [(7-9)].

Results

The study included 60 patients recovered from moderate to severe covid-19 and 30 individuals that apparently be healthy as control group.

Table 1 show that the mean of age of Covid-19 patients was 33.11 year and the mean of age of the control group was 35.53 year with no significant difference between patients and health control group. The mean of testosterone Covid-19 patients (2.78 ng/ml) and in the control individuals was (7.43 ng/ml) (P. value <0.001). The mean of inhibin-B was (41.13 pg/ml) in Covid-19 patients and in the control, individuals was (76.84 pg/ml) (P. value <0.001). The mean of FSH was

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(7.58 IU/L) in Covid-19 patients and in the control, individuals was (3.88 IU/L) (P. value <0.01). The mean of LH was (5.80 IU/L) in recover Covid-19 patients (and in the control individuals was (2.39 IU/L) at P. value <0.05. The mean of CRP was (22.92 mg/dl) in Covid-19 patients which was elevated more than the normal range of CRP (normal rang: less than 6 mg/dl).

Table 41: Descriptive Statistics of the studied groups					
Parameters	Patients		Control		P value
	Mean	SD	Mean	SD	
Age (years)	33.11	4.12	35.53	3.98	0.17
Inhibin B (pg/mL)	41.13	15.96	76.84	20.45	< 0.001
LH (IU/L)	5.80	2.11	2.39	1.43	< 0.05
CRP (mg/dl)	22.92	11.51			

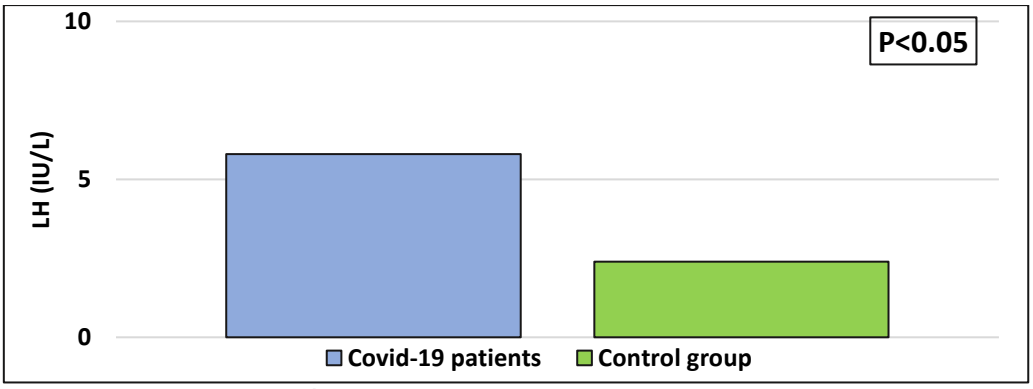

Figure 1: Mean of LH in recover Covid-19 patients and the control group

The study showed significant negative correlation between CRP and inhibin-B among recovered Covid-19 patients (r: -0.559 and P<0.001), Figure 2.

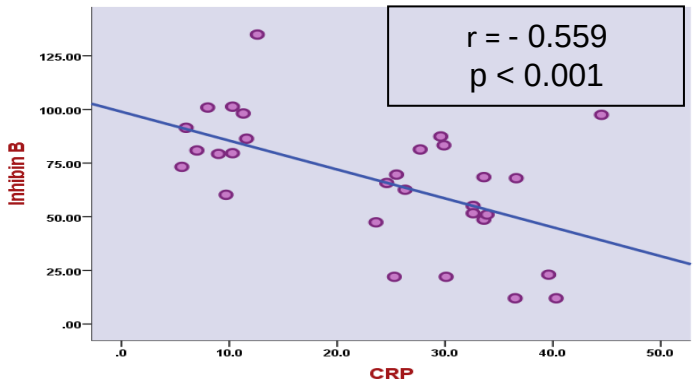

Figure2: Correlation between CRP and inhibin-B among recovered Covid-19 patients

The study showed significant positive correlation between CRP and LH among recovered Covid-19 patients (r: 0.607 and P<0.01), Figure 3.

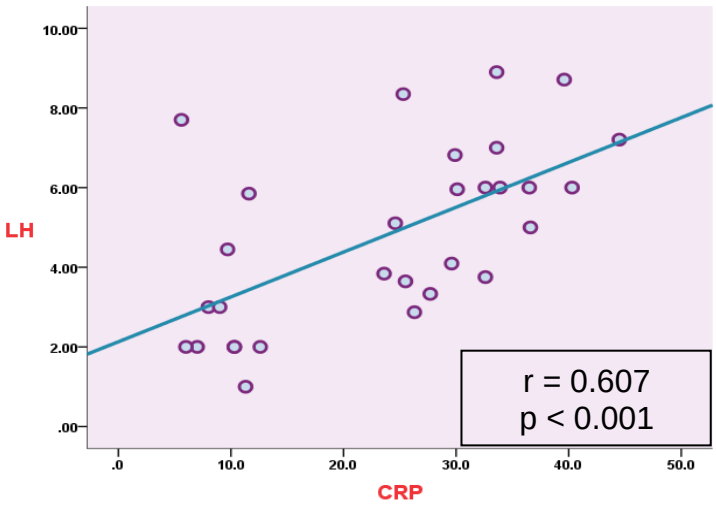

Figure 3: Correlation between CRP and LH among recovered Covid-19 patients

Discussion

In agreement with our finding, Aboelnaga *et al* [10] found that the late recovered COVID-19 pneumonia patients had significantly lower total testosterone. Several studies have highlighted a statistically significant decrease in testosterone levels with COVID-19 infection; however, the majority of these studies have been conducted in patients with active disease and long-term consequences are still not known and need exploration [11,12]. Low testosterone and high LH levels in recovered COVID-19 patients in comparison with age-matched healthy controls were reported also reported by several studies. Similarly, male patients with COVID-19 had lower testosterone levels even in comparison with non-COVID-19 respiratory tract infections and age-matched controls, this may point to a specific pathogenic impact on testicular functions [13-16].

On the other hand, our findings were in contrast with another recent Chinese study's findings on recovering COVID-19 patients which did not observe any significant change in comparison with healthy control participants [17]. This contrast may be explained by different patients' selection regarding ethnicity and disease severity. Few pathogenic mechanisms can explain testosterone deficiency in COVID-19 pneumonia. Acute stage hypogonadism in male COVID-19 patients like other critical infections may be explained via the mechanism of secondary immune reactions and oxidant sensitive-inflammatory pathways. The SARS CoV- 2 infection could induce secondary inflammation and oxidative stress is more likely to impair androgen synthesis [18]. Furthermore, direct damage of testicular tissue by the SARS-CoV-2 virus was hypothesized. High expression of ACE2 receptors in Leydig and Sertoli cells could suggest direct SARS-CoV-2 impact at the testicular level in active COVID-19 patients; however, the extent of this damage still needs to be verified. There are recent studies that reported injury to Sertoli cells and seminiferous tubules, Leydig cells loss in COVID-19 patients [19], and damage of seminal tubules in post mortem COVID-19 patients [20]. Another mechanism via the ACE2 pathway was postulated. The high expression of ACE2 receptors at Leydig cells and its decreased expression by SARS-CoV-2 leads to subsequently enhanced angiotensin II levels [21]. Angiotensin II could reduce stimulated testosterone synthesis by Leydig cells [17]. Our finding was in agreement with the findings of Moreno-Perez *et al* [94] who discover a reduced level of inhibin B among late recovered COVID-19 pneumonia patients. Additionally, Ahmed [22] indicated that the mean inhibin B levels in COVID-19 patients (54.29 ± 7.33) were lower than in healthy controls (64.14 ± 37.66). Additional studied were consistent with our results which revealed that, although testosterone and inhibin B levels were lower in COVID-19 patients than healthy controls and implying that low testosterone and inhibin B levels have an independent impact in causing poor outcomes in these patients [23-26]. Similarly, Guo *et al* [27] also found that inhibin B reduced among COVID-19 patients out of Covid-19 infection, several studies demonstrated that inhibin B concentration was higher in fertile men than in those with infertility and abnormal spermatogenesis (except in those with obstructive azoospermia or spermatogenic arrest at some stages. Men who underwent castration had undetectable inhibin B levels, confirming the fact that serum inhibin B reflect testicular function and, more precisely, Sertoli cell function[28-32].

A recent study reported that the effect of SARS-CoV-2 infection was evaluated on gonadal function and male sex hormones; based on the results of elevation in LH levels in serum of recovered patients compared to the healthy men. Rastrelli *et al* [33] reported that inflammatory cytokine storm in SARS-CoV-2 infection may be a potential risk factor for Leydig cells and would result in elevation of FSH serum levels, subsequently.

The study showed significant negative correlation between CRP and testosterone among recovered Covid-19 patients (r: -0.441 and P<0.01).In agreement with our results, Ma *et al* [36] found negative correlation between testosterone level and CRP. Thus, it is known that CRP contribute to low grade systemic inflamation inhibit Leydig cell function and decrease the sensitivity of Leydig cells to luteinizing hormone, which could result in a reduction in testicular output of testosterone [37,38].

Conclusions

There was a significant relation between male dysfunction and Covid-19 infection.Low levels of inhibin-B and testosterone recorded in recover Covid-19 patients comparing with healthy individuals Levels of FSH and CRP were was elevated significantly in recover Covid-19 patients.

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