How to Cite:
Sisca, E. M., Rezano, A., Pakpahan, C., Supardi, S., Agustinus, A., Darsini, N., Wen, M. D., Kirana, T., & Margiana, R. (2022). Preliminary report of profile FSH and LH of the COVID-19 survivors in Surabaya, Indonesia. *International Journal of Health Sciences*, *6*(S3), 2433–2451. https://doi.org/10.53730/ijhs.v6nS3.6054

Preliminary report of profile FSH and LH of the COVID-19 survivors in Surabaya, Indonesia

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***Abstract*---**Endocrine dysfunction in COVID-19 plays a role in clinical issues related to different disorders, including, hypogonadism,

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 18 Nov 2021, Manuscript revised: 09 Feb 2022, Accepted for publication: 27 March 2022

anxiety, stress and depression. Hypogonadism as an essential determinant for COVID-19-related pathogenesis which regulates the link between the brain and testes. In Indonesia, there is no studying about FSH and LH in COVID-19 survivors. Research design was cross sectional. We conducted this study at the Department of Biomedical Science Faculty of Medicine,, Universitas Airlangga Surabaya, Indonesia. A total of 34 male participants that recovery from COVID-19 enrolled, only 18 participants meet the criteria included. We conducted anamnesis, physical examination including height, weight, waist circumference and we analyzed hormone by using immunoflouroscene analyzer VIDAS and the ELFA method. Normal levels of FSH and LH were 1-8 IU / L and LH 2–10 IU / L, respectively. The mean age of COVID-19 survivors was 36.56 ± 5.69 while the mean marriage duration was 9.56 ± 6.17. The majority of participants had comorbid obesity class I of 6/18 (28.57%) with a mean waist circumference was 91.00 ± 11.68. Mild type COVID-19 was the most frequent 9/18 (50.0%). There were 3/18 (16.7%) pneumonia confirmed COVID-19, but only 2/3 pneumonia confirmed COVID-19 that had elevated FSH and LH levels. The mean of FSH level was 4.89 ± 2.88 mIU/mL, while LH level was 3.68 ± 1.57 mIU/mL. The mean of recovery duration was 2.75 ± 1.46 monts. Almost of participants had quarantine 11/18 (61.11%). The Man-Whitney test showed a significant difference in FSH and LH values between the pneumonia confirmed COVID-19 group and non-pneumonia group (p = 0.020). There is a significant difference in FSH and LH value between pneumonia confirmed group and non-pneumonia group. Changing of this hormone are an acute inflammatory response and reversible.

***Keywords*---**gonadotropins, pneumonia confirmed COVID-19, initial research, Surabaya Indonesia.

Introduction

Severe acute respiratory syndrome coronavirus (SARS-CoV) 2 ranks third in fatal coronavirus diseases in the twenty-first century, after SARS-CoV and middle east respiratory syndrome coronavirus (MERS-CoV)(Siddique et al, 2021). Since the pandemic declaration by the World Health Organization (WHO, 2022), SARS-CoV2 has been infected more than 486.7 million people, and contributed to the death of more than 6.1 million individuals around the world.WHO, 2021Amid today's life-changing uncertainty, the entire world has been negatively impacted by the outbreak of the SARS-CoV2 pandemic(Li et al, 2020).Coronavirus disease 2019 (COVID-19) presents with a broad clinical spectrum, including asymptomatic, mild upper respiratory tract illness to a severe pneumonia with respiratory failure and death(Zhou et al., 2020).

The surface spike (S) viral protein of SARS-CoV2 and transmembrane serine protease 2 (TMPRSS2) were known for the viral entry through angiotensin-converting enzyme 2 (ACE2) receptor and S protein priming at the surface of host cells(Hoffmann et al., 2020; Jackson et al., 2021; Wulandari et al., 2021). The

susceptibility of SARS-CoV2 infection is higher in any cells expressing ACE2, such as the small intestine, testis, kidneys, heart, thyroid and adipose tissue.(Li MY et al., 2020)ACE2 receptor is expressed in endothelial cells throughout our body therefore, endothelial dysfunction appears to be consistent with systemic manifestations observed in COVID-19 patients, such as hypertension, thrombosis, kidney injury, and diabetes(Sardu et al, 2020). Moreover, the inflammatory response plays a critical role in increasing the severity of COVID-19(Liu F et al., 2020). During COVID-19 progression, several inflammatory cytokine storms increase, such as interferon (IFN)-gamma, tumor necrosis factor (TNF), interleukin (IL) -10, IL-6, monocyte chemoattractant protein-1 (MCP-1) (Ramasamy and Subbian, 2021; Channappanavar and Perlman, 2017; Darmadi et al., 21021; Zanza et al., 2022).

Although the lungs have been identified as the primary pathogenic targets of SARS-CoV2, an increasing amount of evidence reported comorbid clinical symptoms and multi-organ defects involving the pathology of testes and brain in COVID-19 (Zanza C et al. 2022; Arbour et al., 2000; Abobaker et al., 2021).CoV invasion in concert with host immune mechanisms may persist existence of the virus that, leads to nervous system damage(Wu Y et al., 2020).Dysregulation of the blood-brain barrier caused by SARS-CoV2 leads to neuroinflammation and neuropathogenesis in the brain including the hypothalamus, affecting physiological functions like thermoregulators and hormonal balance(Wu Y et al., 2020; Hamming et al., 2004; Pascual-Goñi E et al., 2020; Baig et al., 2020).Endocrine dysfunction plays a role in clinical issues related to different disorders, including hypothyroidism, hypogonadism, anxiety, stress and depression that show in COVID-19 patients (Tribowo et al., 2021; Kandasamy et al 2019; Ranabir et al., 2011; Yu J, 2014). The hypothalamic-pituitary-gonadal (HPG) axis regulates the link between the brain and testes by gonadotropins and testosterone (Kandasamy et al., 2019; Oyola et al., 2017). Hypogonadism has been identified as an essential determinant of COVID-19-related pathogenesis. Transcriptome evidence confirmed prominent expression of the ACE2 receptor and TMPRSS2 in spermatogonia, spermatids, Leydig cells, and Sertoli cells (Stanley et al., 2020; Wang et al., 2020). In addition, the expression of TMPRSS2 was upregulated by androgens in men(Clinckemalie L et al., 2013; Lucas et al., 2014).

A reduced level of testosterone reflects a steroidogenesis defect in the testes. Among healthy individuals, the hypothalamus senses the low level of circulating testosterone and stimulates the pituitary gland to secrete FSH and LH through the HPG feedback loop (Oyola et al., 2017; Kandasamy et al., 2019). The circulating FSH and LH were increased in the severity of COVID-19 (Ma L et al., 2021; ayan S et al., 2020). It indicates the transient activation of the gonadotropin-producing cells caused by early inflammatory responses (Selvaraj et al., 2021).Therefore, understanding the pathological impact of SARS-CoV2 pathogenesis in the dysregulation of the HPG axis regarding abnormal gonadotropin hormone levels is crucial for survivors to develop reproductive and sexual disorders issues.
This is the preliminary study in Indonesia to examine the level of FSH and LH in COVID-19 survivors (in Discussion).

Materials and Methods

Design studies and participants.

This research is a cross-sectional study. We conducted this study between November 2020 and March 2021 in the Department of Biomedical Science, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia. A total of 34 male participants with a history of COVID-19 will meet as a subject subject, and 18 male participants will meet the criteria included. Inclusion criteria are males older than 18 years old, who have been married and had a child and have been confirmed COVID-19 by nasopharyngeal PCR test, and are already in recovery phase. The exclusion criteria were experienced varicolectomy, received psychiatric drugs such as SSRi in the last 3 months, received exogenous testosterone therapy in the last 6 months, cancer patients who are currently undergoing chemotherapy and have experienced testicular trauma. All participants gave written informed consent. This research evaluated by Ethical Exemption No. 274 / EC / KEPK / FKUA / 2020, Faculty of Medicine, Universitas Airlangga.

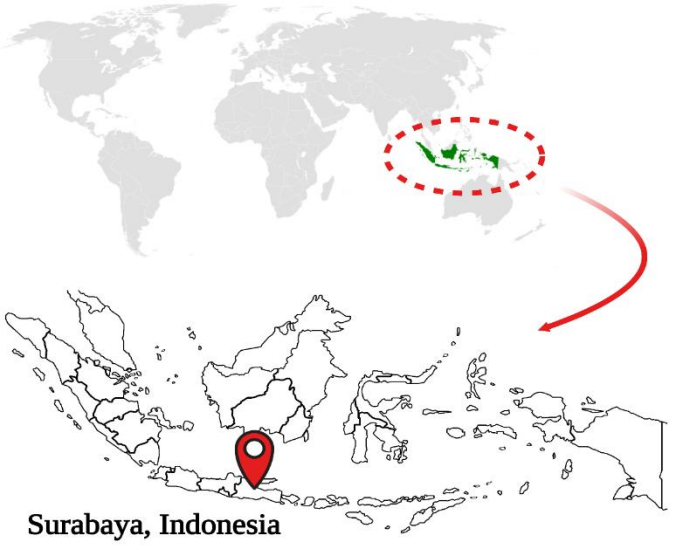

Figure 1. Location of the Study. This study was conducted in the Department of Biomedical Science, Faculty of Medicine, Universitas Airlangga, Surabaya Indonesia

Data collection

History taking and general physical examination were performed. We measured height, weight and waist circumference. There are several units available for use in FSH and LH in the laboratory, which are distanced, using the Immunofluorescence analyzer brand VIDAS and the method used by ELFA (enzyme-linked fluorescence assay). Before take cubital blood, we informed the participants not to take vitamin Biotin (B7) at least 72 hours before the FSH and LH examination. *2*.3 *Definitions*: Elevated FSH > 8 IU/L (normal 1-8 IU/L) (Barbonetti et al, 2018) and 2–10 IU/L (Von Eckardstein et al, 1999).

Statistical analysis

The data from the anamnesis, physical examination and interpretation of the FSH, LH assay that had been collected were analyzed bySPSS Statistics version 25.0 statistical software package (IBM SPSS Inc., Chicago, IL). Differences in distributions of patient characteristics by outcome subgroups are reported using differences with 95% CIs. Categorical data were compared using the the Mann-Whitney test.

Result

A total research subject was 18 that selected according to the criteria inclusion and exclusion.. The sample of this research subject was evaluated based on several variables. The sample characters can be seen in Table 1 below:

Table 1
Characteristics demographic of participants

Variable		Value
Total participants		18
Mean age (years)		36.56±5.69
Mean marriage duration (year)		9.56±6.17
BMI (kg/m2)		26.61 ± 3.42
Waist Circumference (cm)		91.00 ± 11.68
Degree of Severity	Asymptomatic	5 (27.8%)
	Mild	9 (50.0%)
	Moderate	1 (5.6%)
	severe	3 (16.7%)
Pneumonia	Yes	3 (16.7%)
	No	15 (83.3%)
FSH (mIU/mL)		4.89 ± 2.88
LH (mIU/mL)		3.68±1.57
Interpretation of FSH, LH assay	increased	2 (11.1%)
	Normal	16 (88.9%)
Time duration between infected SARS coV-2 and hormonal assay (month)		2.75±1.46
Type of care	Self-isolation	11 (61.11%)
	Hospitalized	7 (38.89%)

In our study, the mean age of male COVID-19 survivors was 36.56 ± 5 years, duration of marriage 9.56 ± 6.17 years. The mean of BMI is 26.61 ± 3.42 kg/m2, waist circumference was 91.00 ± 11.68 cm. According to the disease severity, we found that mild degree was the most frequent of the COVID-19 survivors 9 (50.0%) and others degree of disease severity were asymptomatic 5 (27.8%), severe 3 (16.6%), moderate 1 (5.6%). Mean of FSH 4.89 ± 2.88 mIU/mL, LH 3.68 ± 1.57 mIU/mL. Time duration between infected SARS coV-2 and hormonal assay 2.75 ± 1.46 months. Majority of survivors were quarantine 11 (61.11%) and only 3 survivors got pneumonia 16% (Table 1)

Table 3
Distribution of symptoms of the COVID-19 survivors

Symptoms	Total n = 18
Asymptomatic	5 (15.63%)
Click	
Anosmia	4 (12.5%)
Ageusia	0 (0%)
Influenza like illness	
fever	5 (15.63%)
Cough	3 (9.38)
Afternoon troat	2 (6.25%)
Rainy nose	2 (6.25%)
Malaise	3 (9.4%)
Short of breath	4 (12.5%)
Testicle pain	1 (3.13%)
Chest X-ray	
GGO bilateral pneumonia	3 (9.38%)

Based on Table 3, one participant has more than one complaint. The most complaints were asymptomatic and fever having the same percentage 5 (15.63%), short of breath and anosmia 4 (12.5%) respectively (table 3.) There were 3 participants (9.38%) had pneumonia confirmed COVID-19, they had ground glass opacity (GGO) bilateral pneumonia and one patient severe type had history of testicular pain and pneumonia confirmed COVID-19. We did not perform scrotal ultrasound to confirm the testicle pain, because by anamnesis and physical examination there is no swelling and pain leading to orchitis.

Table 4
Distribution FSH, LH result according to pneumonia and non-pneumonia

	FSH	Total	LH	Total
Pneumonia (n = 3)	Increase	2 (66.7%)	increase	2 (66.7%)
	normal	1 (33.33%)	Normal	1 (3.33%)
Non-pneumonia (n = 15)	Normal	15 (100.0%)	Normal	15 (100.0%)

We found 3 patients with pneumonia confirmed COVID-19, 2/3 (66.7%) that increasing FSH, LH and interestingly that 1/3 (33.33%) with pneumonia had normal FSH and LH levels.

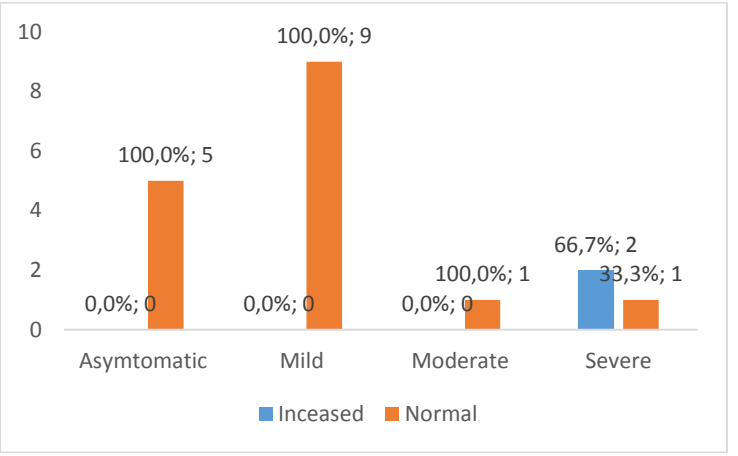

Figure 2. Distribution of FSH, LH levels according to disease severity.

According to figure 2, distribution of FSH, LH based on disease severity, there is elevated FSH and LH only in severe COVID-19 group amount 2/3 (66.7%) and does not occur in the asymptomatic, mild, and moderate groups.

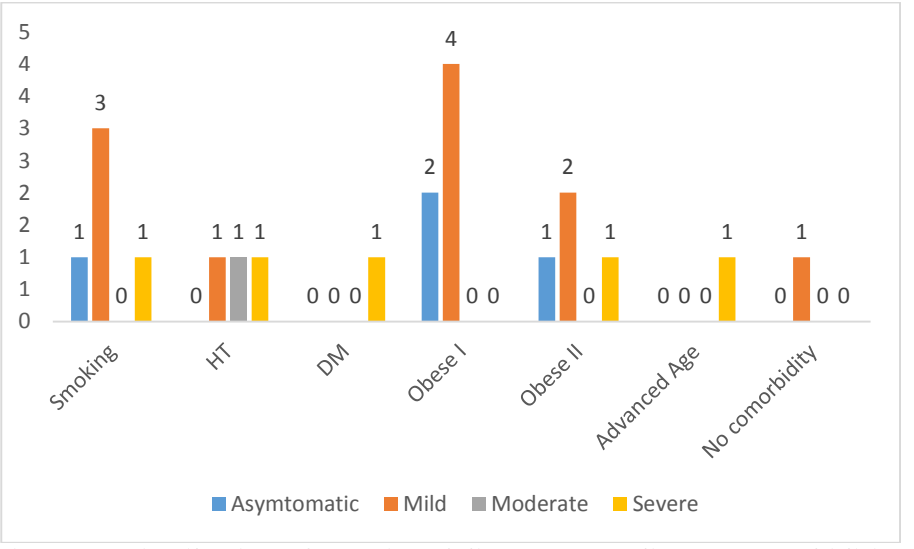

Figure 3. Distribution of severity of disease according to comorbidities

From Figure 2, it was found that the moderate group had the fewest comorbidities compared to other groups, namely hypertension. The asymptomatic group had fewer comorbidities than the mild and severe groups (3 vs. 5 comorbidities). According to block diagram above, we found that obese class I was the majority survivors in this research 6 (28.57%). This classification is based on the International Association for the Study of Obesity BMI Categories for Asia-Pacific (WHO, 2000). The latest market share is smoking 5 (23.81%) and obese class II. Hypertension and diabetes mellitus need attention as dangerous comorbidities in COVID-19 patients.

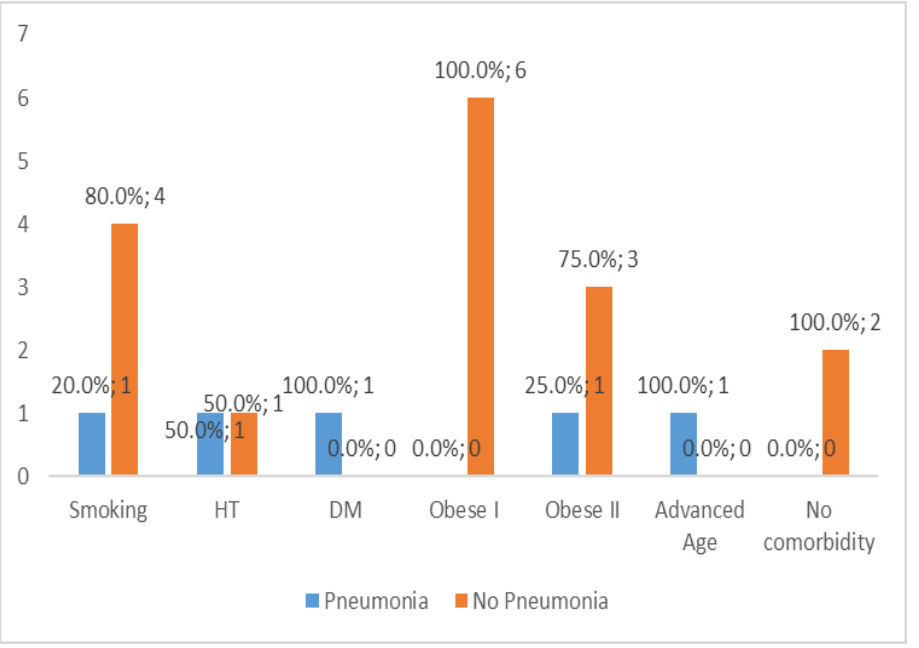

Figure 3. Distribution of pneumonia and non-pneumonia according to comorbidities

According to figure 3, We found that obese class I as the most comorbid of the overall study subjects. The pneumonia group had comorbids, namely hypertension, diabetes mellitus, smoking and advanced age, while the non-pneumonia group had 5 main comorbids, starting from the largest to the lowest, namely obese class I, smoking, obese class II, without comorbid and hypertensive.

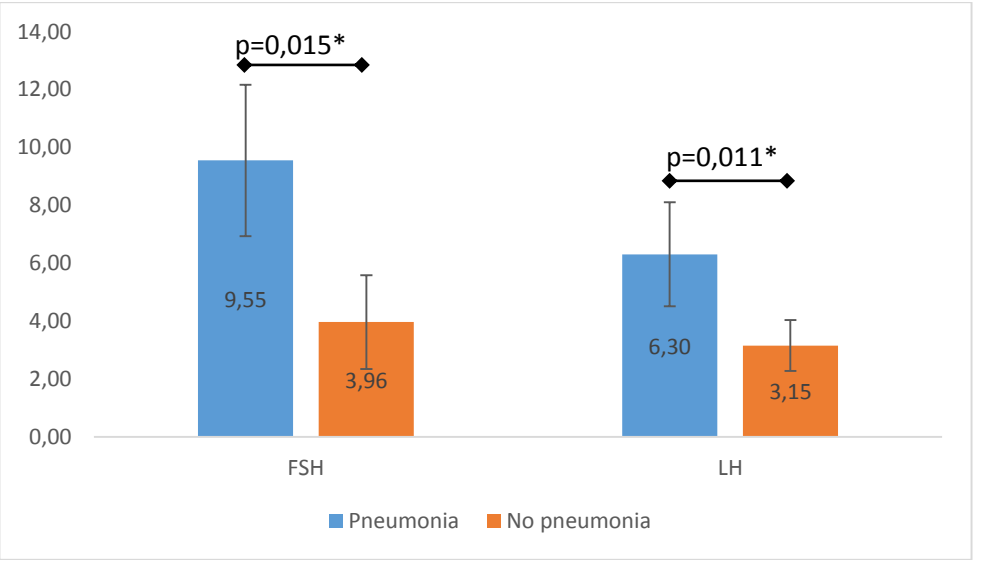

Figure 5. Comparative analysis of two independent samples not normally distributed using the Man Whitney Test

Mann Whitney's comparative analysis found that there was an increase in FSH p= 0.015 ($p < 0.05$) and LH p = 0.011 ($p < 0.05$), so there is a significant difference in FSH and LH value between the pneumonia and non-pneumonia group.

Table 5
Distribution of age, marriage duration, body mass index (kg/m2), waist

Code	age (years)	marriage duration (years)	Body Mass Index (kg/m2)	Interpretation of BMI	Waist Circumference (cm)	Time duration between infected SARS CoV-2 and FSH, LH assay (months)	Type of Care
S1	49	23	25	Obese class I	91	5	Hospitalized
S2	37	12	30	Obese class II	85	3	Hospitalized
S3	46	14	31	Obese class II	87	5	Hospitalized
S4	41	9	24.8	Risk to obese	80	1	Hospitalized
S5	42	20	31.1	Obese Class II	108	4	Hospitalized
S6	35	9	25.1	Obese Class I	91	1	Hospitalized
S7	35	6	31.2	Obese class II	109	3	Quarantine
S8	34	1	31.1	Obese class II	109	4	Quarantine
S29	39	16	22.1	Risk to obese	86	1	Hospitalized
S10	31	3.5	23.5	Risk to obese	85	2	Quarantine)
S11	29	2	25.7	Obese class I	90	4	Quarantine
S12	33	6.5	20	Normal	90	3	Quarantine
S13	32	6	27	Obese class I	80	4	Quarantine
S14	36	3	30.5	Obese class I	115	4	Quarantine
S16	31	7	23.4	Risk to obese	80	1.5	Quarantine

circumference, recovery duration and type of care

S17	29	7	24.8	Risk to obese	73	2	Quarantine
S18	42	14	24.8	Risk to obese	90	1	Hospitalized

Table 6
Comorbidities profile, degree of disease severity, pneumonia / non-pneumonia and interpretation of FSH and LH

No	Comorbidities	Degree of disease severity	Pneumonia / non-pneumonia	Interpretation of FSH, LH assay
S1	Elderly	severe	Pneumonia confirmed COVID-19	Normal
S2	Smoking, obese class II	Mild	Non-pneumonia	Normal
S3	Obese class II	Mild	Non-pneumonia	Normal
S4	Smoking	Mild	Non-pneumonia	Normal
S5	Obese class II	severe	Pneumonia confirmed COVID-19	Elevated FSH, LH
S6	Obese class I	Mild	Non-pneumonia	Normal
S7	Obese class II	Asymptomatic	Non-pneumonia	Normal
S8	Obese class I	Asymptomatic	Non-pneumonia	Normal
S9	Hypertension	Moderate	Non-pneumonia	Normal
S10	Hypertension	Mild	Non-pneumonia	Normal
S11	Obese I	Mild	Non-pneumonia	Normal
S12	No comorbidity	Asymptomatic	Non-pneumonia	Normal
S13	Smoking, obese class I	Mild	Non-pneumonia	Normal
S14	Obese class I	Asymptomatic	Non-pneumonia	Normal
S15	Obese class I	Mild	Non-pneumonia	Normal
S16	Smoking	Asymptomatic	Non-pneumonia	Normal
S17	No comorbidity	Mild	Non-pneumonia	Normal
S18	Smoking, diabetes mellitus	severe	Pneumonia confirmed COVID-19	Elevated FSH, LH

Discussion

In this study, there were 5 participants aged > 40 years and 15 participants aged 29-39 years. Similar to the Temiz's study, where the mean age was 37.21 ± 8.59 years (Temiz et al., 2021). Three of our study participants aged > 40 years (oldest age was 49 years) were diagnosed with confirmed COVID-19 pneumonia and hospitalized due to worsening condition. Consistent with several previous studies, the older the age, the more the risk of disease severity increases (Chaoqun Ma et al, 2020). Several comorbidities owned by our study subjects. The body mass index (BMI) of obese class I was most of the comorbidities of the entire sample of this study. It is slightly different from previous studies which stated that severe obesity (BMI > 40) worsened the condition of COVID-19 patients (Michalakis, & Ilias . 2020). Diabetes mellitus (DM), cardiovascular disease (CVD), hypertension, chronic kidney disease and immunosuppression are populations that are susceptible to SARS CoV-2 infection (Petrakis et al., 2022). The more

comorbidities, the more vulnerable. Baadani reported that two comorbidities (smoking and uncontrolled type 2 diabetes mellitus) had an odds ratio of 4.12 for death compared to having one comorbidity in viral pneumonia caused by H1N1 and MERS CoV (Al Baadani et al, 2019) As happened during the previous SARS and MERS outbreaks, people with diabetes are very susceptible to respiratory tract infections (Lundholm et al., 2020). There are at least three main mechanisms that cause diabetes mellitus susceptibility to infection, namely: excessive inflammatory reaction and imbalanced immune response; metabolic disorders can interfere with the function of macrophages and lymphocytes, thereby lowering the body's immunity; expression and activity of angiotensin-converting enzyme (ACE) 2 and vascular dysfunction and thrombotic complications. Thereby lowering the body's immunity; expression and activity of angiotensin-converting enzyme (ACE) 2 and vascular dysfunction and thrombotic complications. Thereby lowering the body's immunity.

Preexisting hypertension was more likely to develop into severe clinical conditions. However, pre-existing hypertension was not independently associated with a high risk of severe COVID-19 (Xiong et al., 2019). In individuals infected with COVID-19, hypertension has been identified as the most common cardiovascular comorbidity, which has been shown to increase the risk of hospitalization and death. Initial research suggested that inhibitors of the renin – angiotensin – aldosterone pathway could increase the likelihood of viral infection and worsen illness, generating concern given the significant global incidence of hypertension. Nonetheless, further research backed the use of antihypertensive medicines, stating that they do not worsen COVID-19 infection in hypertensive individuals, but rather may have a positive effect (Peng Mei et al., 2021).

Another important comorbidity is smoking. Smoking is bad for the lungs. This may be due to changes in the structure, lung function and host immunity (Arcavi & Benowitz, 2004). Diseases related to the respiratory system, such as viral infections, are more likely to attack a smoker than a non-smoker. Guan et al., concluded that smokers or a history of smoking had a 14,285 times risk of suffering from confirmed COVID-19 pneumonia compared to nonsmokers (OR = 14,285; 95% CI: 1,577– 25,000) (Guan et al., 2019). Our study showed that pneumonia group has more serious comorbidities than non-pneumonia such as diabetes mellitus, hypertension, class II obesity, smoking and advanced age.

A previous study in hospitalized patients with COVID-19 who had central obesity showed an odds ratio of 8.93 times for the risk of death (CI 3.26–24.5). Waist circumference is an independent risk factor for mortality (Khalangot, et al.,). A similar study that evaluated obesity as a risk factor for outcomes in patients with COVID-19 showed that there was an increased risk of death from COVID-19 in obese patients with an odds ratio of 1.34 (95% CI: 1.05-1.72); p = 0.019 (Morys F-fendo). Regarding waist circumference, our study found that the average waist circumference was 26.61 ± 3.42. Serum levels of LH, FSH, and leptin were significantly higher in overweight and obese infertile men than in normal weight infertile men and those with WC <102 cm. (Maghsoumi et al, 2020).

In one study at the Field Hospital (a specialized facility that treats COVID-19 patients, as evidenced by swab results and positive PCR (polymerase chain

reaction) tests infected with SARS-COV-2) Wahyuhadi et al., reported that the survival rates of asymptomatic, mild, moderate types of COVID-29 were 52.8%, 46%, 0.1% respectively (Wahyuhadi et al., 2021) while Ibrahim et. al., reported that 44% of samples received at the clinical microbiology laboratory at the Universitas Indonesia came from subjects with moderate or severe hospitalized cases (Ibrahim et al., 2020). From these two previous studies, it was concluded that the asymptomatic type of COVID-19 was the majority type of all disease severity groups, while in our study the mild type of COVID-19 is the most dominant of other disease severity groups.

Several variations of the main complaints of COVID-19 patients have been reported. Ibrahim et.al reported that since March - April 2020 the clinical microbiology laboratory of Universitas Indonesia in Jakarta had received 4617 specimens from subjects with 73% complaints of respiratory problem (with or without other symptoms), 32% complaints of respiratory problem with fever, 23% complaints of respiratory problem and other symptoms without fever, and only 4% complaints of headache, malaise, or gastrointestinal problems. A study based on the dataset of patients with COVID-19 on the website of the Indonesian COVID-19 Task Force, Ministry of Health of Indonesia (https://covid19.go.id/peta-sebaran) until June 3rd, 2020, reported that the 3 most common complaints were cough (76.2%), history of fever (50.4%), and current fever (47.1%), which were the most common symptoms among the patients with COVID-19 (Karyono, & Wicaksana, 2020). A retrospective analytical study at a tertiary referral hospital in Surabaya, reported the symptoms of shortness of breath were 54.4%, cough were 51.2%, and fever were 40.1% (Bintoro et al., 2021). The study that we conducted found 3 most common complaints, namely asymptomatic and anosmia with the same proportion were 5 (15.63%), while fever and short of breathing were 4 (12.5%). Non-pneumonia COVID-19 is more dominant than pneumonia COVID-19 (15 survivors vs. 3 survivors) namely asymptomatic and anosmia with the same proportion were 5 (15.63%), while fever and short of breathing were 4 (12.5%). Non-pneumonia COVID-19 is more dominant than pneumonia COVID -19 (15 survivors vs. 3 survivors) namely asymptomatic and anosmia with the same proportion were 5 (15.63%), while fever and short of breathing were 4 (12.5%). Non-pneumonia COVID-19 is more dominant than pneumonia COVID-19 (15 survivors vs. 3 survivors).

Emotional, physical, or psychological stress and pain associated with infection can stimulate the hypothalamic-pituitary axis. Therefore, hypothalamic-pituitary disorders and resulting abnormalities in the rhythm of LH secretion can also be the cause (Ling Ma et al., 2020b). Our study found that the mean of FSH and LH values were in normal limit, but there were 2 survivors showed elevated FSH and LH. An increase in FSH and LH values occurred in two COVID-19 survivors with a history of confirmed COVID-19 pneumonia, while 1 survivor with pneumonia had normal FSH and LH values. There were differences in recovery duration (the time between being positive for SARS CoV-2 and the time of examining the sample) of the three survivors with pneumonia. The recovery duration for sample 1 (S1) was 5 months, for sample 5 (S5) 4 months, and for sample 18 (S18) 1 month. In sample 1, FSH and LH having returned to normal values was caused by the possibility of a longer recovery duration than the other two samples, which was 5

months. FSH and LH levels will recover after 3 months following the spermatogenesis cycle (Heller and Clermont, 1963). In our study, it is possible that there has been a recovery on the HPG axis because the average recovery duration was 2.75 ± 1.46 months.

SARS CoV-2 also causes pulmonary embolism and pneumonia. According to Harrison's textbook, the definition of pneumonia is a variety of pathogens infecting the pulmonary parenchyma, rather than a single illness. It is not recommended to use the terms lobar or bronchopneumonia. Community-acquired, nosocomial, and aspiration are the clinical classifications. The pathology of pneumonia is inflammatory alveolar infiltration and acute lung parenchyma inflammation (Levison et al., 1994). Pneumonia can develop androgen deficiency through the mechanism of arterial hypoxia and hypercapnia. It's unclear if hypoxia causes primary or secondary hypogonadism. Pneumonia confirmed COVID-19 devided into mild pneumonia, severe pneumonia, ARDS (acute respiratory distress syndrome), sepsis and septic shock (WHO, 2020). The most prevalent symptom at the start of the illness is fever, which might emerge 2–14 days after exposure. High fevers (over 38 ° C) might last anywhere from one to four days. Sperm parameters such as sperm production, motility, morphology, and DNA fragmentation are all affected by the febrile illness. Due to an increase in the number of these faults, a rise in testicular temperature, as well as a disruption in the thermoregulatory processes that control testicular heat. According to previous research, SARS-CoV-2 infection causes a reversible detrimental effect on sperm parameters for up to one cycle (74 days) of spermatogenesis. SARS-CoV-2 can have long-term negative effects on testicles via immunological or inflammatory reactions, even though the patient has fully recovered. All recovered male patients, especially the young ones.

Previous study in pneumonia confirmed COVID-19 group reported that LH values were statistically significantly higher than the non-pneumonia confirmed COVID-19 survivors group, even though statistically was not significant. Testosterone levels were found significantly lower in patients with COVID-19 pneumonia ($p < .001$). This examination of testicular hormones supports the hypothesis that acute testicular injury can be connected to COVID 19 infection. COVID-19 infection could also harm testicular tissues, according to this finding (Sezgin Okçelik, 2020). Similar with this study, our study found there is significant differences in FSH and LH value between pneumonia and non-pneumonia confirmed COVID-19.

The weaknesses in our research are that the testosterone assay was not performed and the majority of disease severity was mild type. The number of research subjects was only 18 patients. Increased FSH and LH levels do not exclude the possibility of overlapping due to systemic effects of the underlying disease or may also occur due to systemic effects of COVID-19. The elevated FSH and LH only occurred in the pneumonia confirmed COVID-19, although there was one survivor with pneumonia confirmed COVID-19 who had normal FSH and LH levels. The alteration of this hormones was probably not due to localized testicular damage.

Conclusions

There is a significant difference FSH, LH value between pneumonia COVID-19 and non-pneumonia confirmed COVID-19. Alteration of this hormones as an acute inflammation response and reversible.

Data availability

The data used to support in this study are available from the corresponding author on reasonable request.

Conflicts of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors would like to express gratitude to all staff of the Department of Biomedical Science Faculty of Medicine, Universitas Airlangga and Andrology Unit dr. Soetomo General Academic Hospital especially all participants, colleagues, and acquaintances involved in this study for their help to accomplish this project.

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