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SEMEN ANALYSIS OF COVID-19 SURVIVORS AND UNINFECTED MEN: EXAMINING THE MOTILITY, CONCENTRATION, VITALITY, AND MORPHOLOGY PARAMETERS OF SPERMATOZOA

Sri Musta'ina[1], Eko Budi Siswidiyanto[2], Pety Narulita[3], Agustinus[1], Aucky Hinting[1], Atika[4], Zakiyatul Faizah[1*]

[1]Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[2]Andrology Specialist Study Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[3]Andrology Outpatient Clinic, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[4]Department of Public Health and Preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Semen quality in COVID-19 patients shows inconsistencies and variations. This research was conducted considering that health is the main capital for humans in Indonesia's development, as outlined in Sustainable Development Goal 3. The purpose of this study was to compare the semen quality of COVID-19 survivors with non-COVID-19 men. This study was an analytical observational study with a cross-sectional design. Subjects were selected through consecutive sampling of up to 26 men of childbearing age who met the predetermined criteria. Semen quality assessment using the WHO Semen Analysis Guide 6th edition. Quantitative data were analyzed using SPSS. The data normality test was carried out using the Saphiro-Wilk test. Then, the data were tested by t-test from two unpaired samples and by the Mann-Whitney test. Data from semen analysis based on COVID-19 severity were tested using variant analysis (One-way ANOVA) and the Kruskal Wallis test. The normal morphology of spermatozoa in COVID-19 survivors was significantly lower (p=0.011) compared to uninfected men. Other semen quality parameters did not differ significantly, although they were lower in COVID-19 survivors. The results of the analysis also showed no significant difference in semen parameters related to COVID-19 severity (p=0.488 for progressive motility; p=0.372 for non-progressive motility; p=0.325 for total motility; p=0.707 for immotility; p=0.412 for vitality; p=0.324 for concentration; and p=0.334 for normal morphology). The study provides evidence that COVID-19 survivors have a lower normal spermatozoa morphology compared to uninfected men. However, the motility, vitality, and concentration of spermatozoa did not differ significantly between the two groups.

Keywords: Coronavirus disease 2019 (COVID-19) survivors; spermatogenesis; ejaculate quality; COVID-19 severity; human and health

***Correspondence:** Zakiyatul Faizah, Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia. Email: zakiyatul-f@fk.unair.ac.id

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Highlights:
1. Spermatozoa can be affected by coronavirus disease 2019 (COVID-19) due to a disruption in spermatogenesis, leading to a decline in semen quality.
2. This study compared the semen quality of COVID-19 survivors and those who had not been infected with COVID-19, specifically on the first spermatogenesis cycle following the confirmation of COVID-19 infection.
3. This study is distinctive since no previous research in Indonesia has examined the semen quality parameters, such as the concentration, morphology, motility, and vitality of spermatozoa, in men who had a COVID-19 infection.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is caused by a new type of coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that has spread across numerous countries. Since its appearance in Wuhan, China, at the end of December 2019 until the beginning of August 2021, it has resulted in 197,788,117 confirmed cases and 4,219,578 deaths worldwide (World Health Organization 2021a). Indonesia has recorded 3,532,567 positive cases and 100,636 deaths as of August 4, 2021. The SARS-CoV-2 virus enters human cells through the angiotensin-converting enzyme 2 (ACE2) receptor. This binding causes a reduction in ACE2 expression and an increase in angiotensin II (AngII) levels. Consequently, there will be dysregulation and overactivation of the renin-angiotensin-aldosterone system (RAAS). The RAAS is a hormonal system that controls blood pressure and the volume of blood circulating in the body (Rysz et al. 2021). ACE2 is a type 1 integral membrane glycoprotein that is expressed and active in almost all body tissues. The expression of ACE2 is frequently observed in the kidney, endothelium, heart, and lungs. ACE2 has a catalytic effect similar to that of angiotensin-converting enzyme (ACE), even though ACE2 primarily functions as a carboxypeptidase rather than a dipeptidase. This difference in catalytic function causes an inability of conventional ACE inhibitors to inhibit ACE2 (Turner 2015). After binding to the ACE2 receptor and before entering the cell, the spike protein portion of the virus is recognized (priming) by a cellular protease, the transmembrane protease serine 2 (TMPRSS-2). The transcription of TMPRSS2 is regulated by androgen receptors. COVID-19 infection can cause endothelial dysfunction, as both ACE2 receptors and the protease TMPRSS-2 are expressed in endothelial cells (Younis et al. 2020, Kresch et al. 2021).

The classification of COVID-19 cases is divided into suspected, probable, and confirmed cases. The classification is carried out according to the assessment of clinical, epidemiological, and supporting examination criteria (Ministry of Health of the Republic of Indonesia 2021). Suspected cases include individuals who exhibit certain clinical symptoms, such as acute fever and cough. Suspected cases can also be identified by the presence of at least three of the following symptoms: fever, cough, weakness, headache, muscle aches, sore throat, runny nose/nasal congestion, shortness of breath, anorexia/nausea/vomiting, diarrhea, or loss of consciousness. Individuals who are suspected to have COVID-19 typically experience severe acute respiratory tract infections (ARI) and require hospitalization, with a history of fever (> 38°C) and cough in the last ten days. Alternatively, they may experience acute anosmia (loss of smell) or acute ageusia (loss of taste) without any other identifiable cause. Individuals who have a history of contact with a probable or confirmed case, or COVID-19 cluster and meet the aforementioned clinical criteria are also classified as suspected cases. Additionally, suspected cases include individuals who have tested positive for the rapid diagnostic antigen test (RDT-Ag) in areas A and B, despite being asymptomatic and without known contact with any confirmed or probable cases. The use of RDT-Ag should comply with relevant regulations. Probable cases refer to instances of suspected death that indicate COVID-19 based on a convincing clinical picture and specific criteria. In probable cases, no laboratory examination has been performed on the nucleic acid amplification test (NAAT) or RDT-Ag. Alternatively, the results of the NAAT/RDT-Ag do not meet the criteria for confirmed or negative cases. On the other hand, confirmed cases are defined as individuals who satisfy any of the following criteria: having a positive NAAT result, meeting the criteria for suspected cases or having close contact with a confirmed case, testing positive for RDT-Ag in areas B and C, or testing positive for RDT-Ag in area C (Ministry of Health of the Republic of Indonesia 2021).

The Ministry of Health of the Republic of Indonesia (2021) has established certain criteria for declaring complete isolation and recovery for confirmed COVID-19 cases, with symptoms being the primary indicator. Confirmed cases without any symptoms require isolation for at least ten days, starting from the date when the diagnostic specimen is collected. As for symptomatic confirmed cases, isolation is carried out for ten days, starting from the onset of symptoms and continuing for a minimum of three days after the patient no longer exhibits fever and respiratory disorders. Thus, cases accompanied by noticeable symptoms lasting for ten days or fewer must undergo isolation for a total of thirteen days.

The decree issued by the Ministry of Health of the Republic of Indonesia (2021) specified that COVID-19 severity can be divided into five classifications: asymptomatic, mild, moderate, severe, and critical. Asymptomatic COVID-19 cases are characterized by the absence of symptoms and clinical complaints. Mild COVID-19 cases are accompanied by clinical symptoms such as fever, cough, runny nose, fatigue, anorexia, shortness of breath, myalgia, headache, diarrhea, nausea, vomiting, anosmia, and ageusia without evidence of pneumonia. In addition, patients with mild COVID-19 generally exhibit oxygen saturation (SpO2) above 95% on room air. Moderate COVID-19 cases show clinical signs of pneumonia, such as fever, cough, shortness of breath, and rapid breathing, albeit not severe. The patients typically have a SpO2 range of 93–95% on room air. Severe cases are indicated by clinical signs of pneumonia (e.g., fever, cough, shortness of breath, and rapid breathing) and accompanied by a respiratory rate exceeding 30 breaths per minute, severe respiratory distress, or SpO2 below 93% on room air. Critical cases are distinguished by the presence of acute respiratory distress syndrome (ARDS), sepsis, and septic shock (Ministry of Health of the Republic of Indonesia 2021).

The COVID-19 pandemic has sparked increased scientific interest in understanding its effects on male reproductive health, particularly semen quality. Semen health plays a crucial role in human reproduction, making this area of research exceptionally important. Evidence indicates that the COVID-19 virus may negatively impact semen quality, although the specific mechanisms behind this relationship are complex and not yet fully understood (Cheval et al. 2020). COVID-19 patients have exhibited a decline in sperm count, motility, and morphology compared to uninfected individuals. However, the overall outcomes obtained from COVID-19 patients are inconsistent. Significant changes in semen quality parameters are observed in certain COVID-19 survivors but not in other individuals. Biological variations in semen quality parameters over time highlight the need for repeated examinations to draw definitive conclusions. Unfortunately, the availability of data is still limited, which hinders our capacity to ascertain the definitive interpretations regarding the spread of COVID-19 and its effects on semen (Hinting et al. 2020). This study aimed to evaluate the semen quality of COVID-19 survivors during their first spermatogenesis cycle following a positive diagnosis and to compare the results with those of uninfected individuals. It further sought to assess the impact of disease severity on semen quality. The findings of this study are anticipated to pave the way for further research on the influence of COVID-19 on semen quality parameters and male reproductive organs function. Ultimately, this research may provide valuable recommendations for clinicians to better manage men affected by COVID-19.

MATERIALS AND METHODS

This was observational and analytical study with a cross-sectional design. The research population consisted of male volunteer COVID-19 survivors and non-COVID-19 who came to the Medical Biology Section, Faculty of Medicine, Universitas Airlangga, and met the predetermined inclusion and exclusion criteria. The study subjects were selected through consecutive sampling until the required sample size was reached. Research data were obtained from two study subjects: uninfected male subjects and male COVID-19 survivors on the first spermatogenesis cycle (74 days) since testing positive for reverse transcription polymerase chain reaction (RT-PCR) swabs. The sample size was calculated using the average formula of two unpaired groups according to the reference values from previous studies (Lwanga et al. 1991, Ma et al. 2021). Each group must have at least 13 subjects, as per the formula.

The research procedure commenced by initially explaining the research objectives to potential subjects, followed by obtaining their signed informed consent. This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, under registration No. 232/EC/KEPK/FK UA/2021 dated 4/11/2021. The semen samples were obtained by masturbation after the subjects had undergone sexual abstinence for 2–7 days. The analysis of semen was carried out by the sixth edition of the World Health Organization laboratory manual for semen analysis after thawing the samples for 15–30 minutes at room temperature (Boitrelle et al. 2021). The parameters of routine semen analysis consisted of macroscopic and microscopic examinations. The macroscopic examination involved measuring the volume of semen using a digital scale, with the assumption that 1 mL of semen was equivalent to 1 g of ejaculate. Additionally, the macroscopic examination analyzed the color, viscosity, potential of hydrogen (pH) or acidity level, and the smell characteristics of sperm.

The microscopic examination of semen aimed to evaluate the motility, vitality, concentration, and normal morphology of spermatozoa. The procedure for preparing fixative solutions (diluents) used in the evaluation of concentration and morphology of spermatozoa was modified based on the guidelines from the Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, and Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (Agustinus et al. 2018). The assessment of ejaculate quality for this examination was also carried out according to the sixth edition of the World Health Organization laboratory manual for semen analysis.

Semen parameter data from all research subjects were analyzed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, N.Y., USA). The normality test of all data was carried out using the Shapiro-Wilk test. Data with a normality value $p > 0.05$ indicated a normal distribution. Data analysis that resulted in a normality value below 0.05 showed an abnormal distribution. The next analysis was an unpaired t-test to compare the data with normal distributions, while the Mann-Whitney test was used for data with abnormal distributions. The results of semen analysis based on the severity of COVID-19 were tested using variant analysis (One-way ANOVA) for data with normal distribution. Data with abnormal distribution were tested using the Kruskal-Wallis test. The test results with $p < 0.05$ showed statistical significance (Kishore & Jaswal 2022).

RESULTS

This study involved 26 subjects who were selected based on the established criteria. The research subjects were divided into two groups, namely COVID-19 survivors and uninfected men, with each group consisting of 13 male individuals. Table 1 summarizes the general characteristics of the research subjects.

Table 1. Characteristics of the COVID-19 survivors and uninfected men.

Characteristics	COVID-19 survivors (n=13)	Uninfected men (n=13)
Age (y.o.)	32.85±3.18	35.00±6.00
Number of children	1.77±0.59	1.85±0.80
Youngest child's age (y.o.)	2.54±1.50	4.23±3.60
BMI	26.63±3.74	24.53±2.45
Comorbidity (n, %)		
None	9 (62.9)	11 (84.6)
Mild asthma	1 (7.7)	0 (0)
Grade I hypertension	3 (23.1)	1 (7.7)
Grade II hypertension	0 (0)	1 (7.7)
COVID-19 vaccination status (n, %)		
Not yet vaccinated	0 (0)	1 (7.7)
Incomplete	0 (0)	1 (7.7)
Complete	13 (100)	11 (84.6)
Duration between COVID-19 diagnosis and recruiting (days)	19.77 (11–36)	-
COVID-19 severity (n, %)		-
Asymptomatic	2 (15.4)	-
Mild	9 (69.2)	-
Moderate	2 (15.4)	-

Legends: y.o.=years old; BMI=body mass index.

Table 2 shows the results of the semen analysis conducted using the unpaired t-test and the Mann-Whitney test in terms of average motility, vitality, concentration, and normal morphology of spermatozoa. The analysis yielded different results between the COVID-19 survivors and uninfected men. Statistically significant differences were only observed in the normal morphology of spermatozoa of COVID-19 survivors when compared to the uninfected men (p=0.011). There were no significant differences observed from the analysis of the other ejaculate parameters between the two groups, even though the COVID-19 survivors exhibited lower values.

Table 2. Overview of the semen analysis results.

Parameters	COVID-19 survivors (n=13)	Uninfected men (n=13)	p
Motility (%)			
Progressive	71(17–83)	68(42–83)	0.719
Non-progressive	8.2±2.3	9.2±3.1	0.497
Total motility	80 (22-88)	78 (53–90)	0.719
Immotility	19 (12-78)	22 (11–47)	0.426
Vitality (%)	86 (61–91)	85 (72–91)	0.572
Concentration (million/mL)	53±41	71±32	0.270
Normal morphology (%)	3 (2–9)	6 (2–9)	0.011*

Legends: An asterisk (*) signifies any statistical significance (p<0.050).

Table 3 displays the results of semen quality analysis between COVID-19 survivors and uninfected men using the one-way ANOVA test and the Kruskal Wallis test. The parameters of ejaculation quality are compared according to the severity of the disease, including asymptomatic, mild, and moderate. The results showed that there was no statistically significant difference in semen quality parameters between COVID-19 survivors and uninfected men.

Table 3. Comparison of semen quality parameters of COVID-19 survivors and uninfected men based on the disease severity.

Parameters	Asymptomatic	Mild	Moderate	p
Motility (%)				
Progressive	75 (71–79)	67±20	57.5 (44–71)	0.488
Non-progressive	8 (6–10)	7.7±2.1	10.5 (8–13)	0.372
Total motility	83 (81–85)	80 (22–88)	68 (57–79)	0.325
Immotility	17 (15–19)	19 (12–78)	30 (16–44)	0.707
Vitality (%)	84.5 (83–86)	89 (64–91)	74 (61–87)	0.412
Concentration (million/mL)	73.4 (52.3–94.5)	57.9±43.9	13.6 (8.6–18.7)	0.324
Normal morphology (%)	5.5 (2–9)	3 (2–6)	2 (2–2)	0.334

However, there is a tendency that the more severe COVID-19 is, the lower the ejaculation parameters and the clearer the parameters of concentration, total motility, and normal morphology. After examining the morphology of spermatozoa in COVID-19 survivors, the highest average percentage of abnormalities was found in the spermatozoa head (89.5%), neck and middle (38.5%), and tail (17.5%). Nevertheless, no abnormalities were detected in the form of excess cytoplasmic residue (ERC).

DISCUSSION

The SARS-CoV-2 virus as the causative agent of COVID-19 can disrupt various organs in the human body through the angiotensin-converting enzyme 2 (ACE2) receptor and the transmembrane protease, serine 2 (TMPRSS2) protein. The male reproductive organs are one of the targets of COVID-19 damage due to the presence of ACE2 and TMPRSS2 receptors in the testes. Damage to the testes can cause a decrease in reproductive hormone levels and disturbances in spermatogenesis, as indicated by changes in ejaculate analysis parameters (Holtmann et al. 2020, Ma et al. 2021b).

In this study, the semen parameters of COVID-19 survivors were observed within the first 74 days after their positive diagnosis and compared to those of uninfected subjects. The general characteristics of the two groups did not differ significantly, particularly regarding the number of children, the age of the youngest child, and comorbidities. All the COVID-19 survivors had received complete vaccination. Meanwhile, among the uninfected subjects, there was one individual who had not been vaccinated at all and one individual who had not received a complete vaccination. Nevertheless, the COVID-19 vaccination has been proven not to have any negative impact on ejaculate parameters, whether it is a messenger ribonucleic acid (mRNA) vaccine or other types (Gonzalez et al. 2021, Reschini et al. 2022).

This study used the sixth edition of the World Health Organization laboratory manual for semen analysis to assess semen obtained from the research subjects. According to the manual, the ejaculate parameters are determined as normal if they fall within the fifth percentile. The established values for fertile men are as follows: progressive motility at 30%, non-progressive motility at 1%, total motility at 42%, immotility at 20%, vitality at 54%, concentration at 16 million/mL, and normal morphology at 4% (World Health Organization 2021b). The ejaculate parameters of the uninfected subjects revealed a mean non-progressive motility of 9% and a mean immotility of 23%. These figures do not conform to the analysis manual due to their elevated values. This might be because the individual data for the immotility parameter exhibited varying values. Two men among the uninfected subjects had quite high spermatozoa immotility. The first subject had an immotile sperm count of 47%. He had been an active smoker for 15 years and was categorized as having class I obesity. Meanwhile, the second subject had an immotile sperm count of 43% and was categorized as having class II obesity. Previous studies have demonstrated that a high body mass index and active smoking activity for a long duration (more than five years) play a role in reducing the quality of ejaculate parameters (Pullanna et al. 2015, Salas-Huetos et al. 2021).

The subjects who had recovered from COVID-19 were deemed fertile. However, they exhibited the following mean values for ejaculate parameters: non-progressive motility of 8%, immotility of 24%, and normal morphology of 3.5%. These ejaculate parameters were not in accordance with the sixth edition of the World Health Organization laboratory manual for semen analysis (World Health Organization 2021b). The individual data for the immotile parameter demonstrated variations in the obtained values. Two subjects among the COVID-19 survivors had a fairly high immotility of spermatozoa. The first individual of the two subjects had an immotile sperm count of 44%. Meanwhile, the second subject exhibited an even higher immotile sperm count of 78%. Both subjects were categorized as having class I obesity according to their body mass index. The COVID-19 survivors' data for the normal morphology parameter showed varying values, ranging from 2% to 9%. Of the eight subjects with a low count of normal morphology, at least one individual was overweight, obese, smoker, hypertensive, or working with anesthetic drugs (ketamine). High body mass index, active smoking activity for a long duration (more than five years), and exposure to anesthetic ketamine are some conditions that have a role in reducing the quality of ejaculate parameters (Absalan et al. 2014, Pullanna et al. 2015, Salas-Huetos et al. 2021).

The ejaculate examination in this study was only carried out once. This could potentially allow for bias in the parameter analysis of ejaculate. Individual biological variations might also contribute to bias in the analysis. The ideal ejaculate examination is carried out two or three times (World Health Organization 2021b). In addition, there were no data on ejaculate parameters of COVID-19 survivors whose normal morphology was below 4% before infection. This condition resulted in the determination that there was still a bias regarding the relationship between the normal morphology of spermatozoa of COVID-19 survivors before and after infection. This was evidenced by the presence of five COVID-19 survivors with a normal morphology of at least 4%.

Among the 13 COVID-19 survivors, two men were confirmed positive in November 2021. According to the official release from the Ministry of Health of the Republic of Indonesia, the first case of Omicron variant COVID-19 infection was detected on December 15, 2021. The confirmation was based on a swab test conducted on December 8, 2021. Meanwhile, the Delta variant has become the dominant variant in Indonesia from mid-2021 until the end of 2021 (Gunadi et al. 2021). Therefore, it was highly probable that the Delta variant of the coronavirus was the cause of infection in the two research subjects. The first subject demonstrated asymptomatic severity and normal semen parameters. On the other hand, the second subject exhibited moderate severity with low values in all semen parameters, including motility, vitality, concentration, and normal morphology. The Delta variant of SARS-CoV-2 was associated with a higher viral load compared to other variants (Gunadi et al. 2021).

The unpaired t-test and the Mann-Whitney test conducted in this study revealed that the normal morphology parameter was significantly different between the COVID-19 survivors and uninfected subjects. The other semen parameters also exhibited differences between the two groups, albeit not significant. Compared to the uninfected subjects, the semen quality of the COVID-19 survivors appeared to be lower. Temiz et al. (2021) used a cross-sectional design to examine 30 COVID-19 patients and compared them with uninfected subjects. Their study found a value of p=0.006 for the normal morphology parameter, indicating a significant difference between the groups. Similar to the findings of this study, their study did not discover any significant differences in the other semen parameters.

Another cross-sectional analysis was conducted by Ruan et al. (2021) on 55 COVID-19 survivors and 145 uninfected subjects. The study revealed that total motility and sperm concentration were significantly lower in COVID-19 survivors compared to the control subjects. There was a considerable time gap of 64-93 days between recovering from COVID-19 and conducting the semen examination. The subjects were divided into different groups according to the duration between their recovery and semen analysis, specifically less than or more than 90 days. The findings indicated a trend of decreasing semen quality and a longer duration. This is in contrast to other studies that have found improvements in semen parameters over time following the recovery. During the onset of the next spermatogenesis cycle, there is usually a differentiation of new spermatogonia germ cells into mature spermatozoa that are not affected by COVID-19 (Rahman et al. 2021, Falahieh et al. 2021, Donders et al. 2022). Therefore, examination repetition is required to analyze whether the semen quality parameters have improved or are still affected by COVID-19. This is important as various individual conditions, such as biological variations, can affect semen yield (World Health Organization 2021b).

In this study, semen quality was assessed and compared according to the severity of COVID-19. The results showed that there was a non-significant difference among the moderate, mild, and asymptomatic groups. Nevertheless, there was a tendency for semen quality to decline with increasing severity of the COVID-19 disease. These results are in line with a study conducted by Donders et al. (2022), who found no significant difference in semen parameters across different severity groups. The study included a wide range of duration between the recovery and the semen analysis, namely 1–181 days. Meanwhile, this study only focused on COVID-19 survivors with a duration of 11–36 days between their recovery and semen analysis. The longer duration could be potentially ambiguous as it involved subjects within multiple spermatogenesis cycles at the time of semen analysis. Other studies found significant differences in subjects with mild and moderate severity compared to control subjects with moderate severity (Holtmann et al. 2020, Gacci et al. 2021). The difference in results could be due to the unbalanced number of subjects across asymptomatic, mild, and moderate severity categories in this study. There were only two COVID-19 survivors with asymptomatic and moderate severity. In addition, it could be attributed to the differences in the characteristics of the research subjects.

The mechanism by which COVID-19 affects the male reproductive organs is not yet fully understood. While all male reproductive organs are potentially infected, infections of the testes and epididymis are more common. The effect on the testes and epididymis can be direct or indirect. The direct effect is caused by the attack of viral particles that reach the reproductive organs at the time of viremia. The indirect effect can occur due to high fever and the presence of inflammatory mediators (cytokines). The magnitude of the effects on the function of reproductive organs and semen parameters is mainly determined by the degree of viremia and the specific conditions of each person (Zafar et al. 2021). According to Li et al. (2020), COVID-19 leads to increased cell apoptosis and reduced Leydig cells in the seminiferous tubules. It has been demonstrated that histological changes, including orchitis and vascular changes, result in a reduction in Sertoli and Leydig cells. Additionally, the changes lead to the thickening of the basement membrane, a reduction in spermatogenesis, and an increase in lymphocyte inflammatory cells. These effects are particularly observed through a post-mortem analysis in severe COVID-19 cases (Moghimi et al. 2021, Duarte-Neto et al. 2022).

In many cases, impaired spermiogenesis during the process of spermatogenesis can cause decreased semen parameters, especially in terms of motility, normal morphology, and deoxyribonucleic acid (DNA) integrity. Spermiogenesis is a complex process characterized by morphological and biochemical changes in the haploid spermatid form. It also involves the formation of acrosomes and changes in the morphology of the cell nucleus. The assembly and structure of the flagellum are responsible for locomotion, chromatin condensation, and the elimination of cytoplasmic remnants. Reduced spermiogenesis can affect the spermatozoa morphology due to failure to change the shape of the spermatozoa. Semen exhibiting morphological defects indicate impaired spermiogenesis, affecting numerous parts such as the head, midpiece, tail, and cytoplasmic residues (Kleshchev et al. 2021). High fever causes changes in the morphology of the spermatozoa head. The presence of testicular inflammation and direct infection of SARS-CoV-2 in the testes might account for the reduction in the normal morphology of spermatozoa, resulting from disturbances in the process of spermiogenesis.

Strength and limitations

A limitation of this study is the disproportionate number of COVID-19 survivors across the asymptomatic, mild, moderate, severe, or critical severity categories. The low willingness of the COVID-19 survivors to participate made it challenging to adjust the number of research subjects across these categories. The comorbidities of the subjects had the potential to complicate the interpretation of semen parameters due to the negative effects of comorbidities on semen quality (Salas-huevos et al., 2020, Pullanna et al., 2015). Unstudied reproductive hormone profiles could also lead to confusion in interpreting the semen parameters, as male reproductive hormone imbalances can affect semen parameters (Zhao et al., 2020). Furthermore, the use of a cross-sectional design in this study limited the ability to assess the semen parameter data before and after infection (follow-up) from the COVID-19 survivors. Despite the limitations, this study contributed valuable information to the existing literature on the semen quality parameters of COVID-19 patients, which is currently lacking in Indonesia.

CONCLUSION

The normal morphology of spermatozoa in COVID-19 survivors, particularly within 74 days after the confirmation of a positive diagnosis, is significantly lower compared to uninfected men. The motility and concentration parameters in COVID-19 survivors were also lower, although the differences were not significant. In addition, there are no significant differences in semen quality parameters when accounting for the severity of COVID-19. However, COVID-19 survivors show a downward trend in their semen quality as the disease severity increases.

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Conflict of interest

None.

Ethical consideration

The ethical approval for this study was issued by the Health Research Ethics Committee, Faculty of Medicine and Health Sciences, Universitas Lambung Mangkurat, Banjarmasin, Indonesia, under protocol No. 061/KEPK-FK UNLAM/EC/II/ 2020 dated 25/02/2020.

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Author contribution

SM drafted the article, performed critical revision of the article for important intellectual content, and provided final approval of the article. EBS contributed to the conception and design, drafting of the article, provision of study materials or patients, provision of administrative, technical, or logistic support, and collection and assembly of data. ZF contributed to the conception and design, critical revision of the article for important intellectual content, and final approval of the article. PN contributed to the conception and design, analysis and interpretation of the data, and provision of study materials or patients. AG and AH carried out the critical revision of the article for important intellectual content. AT conducted the critical revision of the article for important intellectual content and provided statistical expertise.

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