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Sars-Cov-2 Infection, Leukospermia occurrence and treatment efforts

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Abstract

Limited knowledge regarding the association between SARS-CoV-2 and male fertility highlights the needs for research to look further into its potential effects. This study investigates the correlation between SARS-CoV-2 infection and leukospermia, focusing on potential implications for sperm quality. A cross-sectional study was conducted at Telkomedika Clinic, involving 20 men with history of SARS-CoV-2-positive. Data collection comprised primary sources via observations and closed interviews, supplemented by secondary data from patient record. Analysis revealed a significant association between SARS-CoV-2 infection and leukospermia ($p < 0,05$), suggesting a potential decline in sperm quality. Changes in sperm parameters, including concentration, motility, and morphology, were observed. Our study highlights the importance of monitoring sperm quality in COVID-19 patients and highlights the virus's potential impact on male fertility. It emphasizes the necessity of integrating reproductive health considerations into COVID-19 management.

Keywords: COVID-19, Leukospermia, Male Fertility.

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1. Introduction

The global spread of the Covid-19 pandemic has resulted in over 620 million cases and more than 15 million deaths worldwide [1-3]. The dissemination of the virus has not only impacted economic paralysis but also affected public health [4]. In 2020, the recorded cases of coronavirus in Southeast Asia amounted to 14.1 thousand cases, with Malaysia reporting 3.8 thousand cases, the Philippines 3.7 thousand cases, Thailand 2.2 thousand cases, and Singapore 1.4 thousand cases. Indonesia ranked third with 2.5 thousand cases. Other countries such as Vietnam, Brunei Darussalam, Cambodia, Myanmar, Laos, and Timor Leste reported relatively low cases [5-6]. These figures illustrate the rapid spread of the coronavirus in Southeast Asia and its contribution to the human immune system. Infection leads to increased pro-inflammatory cytokines and cytokine storm development, which can lead to COVID-19 infection and exacerbation. Additionally, SARS-CoV-2 infection also causes abnormalities in granulocytes and monocytes, lymphopenia, lymphocyte activation and dysfunction, increased cytokine production, and increased antibodies [7]. Apart from respiratory diseases, it has been identified that the coronavirus also affects the male reproductive system due to the SARS-CoV-2 virus [5,8-9]. Li et al., (2020) concluded that SARS-CoV-2 enters the testicular interstitium through circulation during peak viremia, with Leydig cells, cells found in the male reproductive organs, potentially being one of the initial targets [10]. The spread of SARS-CoV-2 occurs through droplets and then migrates to the nose, mouth, and eyes, and subsequently to the reproductive system. SARS-CoV-2 is expressed at various levels in human tissue systems, demonstrating complex interactions between the virus and the host. Cases of COVID-19 in Indonesia show a significant upward trend. In 2020, the reported number amounted to 543,975 cases, and in 2021, it rose to 751,270 cases, marking an increase of 38.1%. In 2023, there were 6,811,780 cases, representing a decrease of 99.1%. As of January 23, 2024, there were 2459 active cases. These indications provide an overview of the rapid spread of the SARS-CoV-2 virus and its impact on male reproductive health [11]. The spread of SARS-CoV-2 is due to contact with infected individuals and exposure through coughing, sneezing, respiratory droplets, or aerosols [12]. Symptoms and tissue tropism of coronavirus infections vary greatly among host species. The spread of the coronavirus in Makassar City is characterized by increased socioeconomic activity and weakened immune systems in the community. The number of confirmed COVID-19 cases in 2020 was 4,995, with 164 deaths [13]. In 2021, there were 48,635 confirmed cases, an increase of 89.7%. The total number of confirmed cases due to COVID-19 during the period of 2020-2021 was 53,630, with 47,764 recoveries. These figures indicate that the spread of the coronavirus is likely to increase if not properly addressed. Furthermore, in addition to the impact on immune suppression, the spread of the coronavirus also leads to the emergence of various diseases, such as pneumonia, acute respiratory distress syndrome (ARDS).

The highest mortality occurring in elderly patients with comorbidities such as cardiovascular diseases, hypertension, diabetes mellitus, and Parkinson's disease, which have serious complications such as arrhythmias, shock, acute kidney injury, patients with these symptoms will experience respiratory failure. Studies supporting this research include:

1. Research conducted by Holtmann et al. (2020), confirming that SARS-CoV-2 causes a decrease in total sperm count and sperm motility in COVID-19 patients and damage to sperm and the male reproductive system [14].
2. A study by Li et al., (2020) found that SARS-CoV-2 infection can affect male reproductive health through testicular and prostatic tissues and sperm function [10].
3. A study by He et al. (2021) states that the testes contain ACE2 receptors, which are the entry points for the SARS-CoV-2 virus [15].

These three study results confirm that COVID-19 virus will impact on decreased immune system and disruption of male reproductive system. Furthermore, this study is focused on examining the relationship between SARS-CoV-2 infection and the occurrence of leukospermia associated with the male reproductive system and its management. The male reproductive system consists of several organs, namely the testes, epididymis, vas deferens, prostate gland, and bulbourethral gland. The testes are the main organ in the male reproductive system, responsible for producing sperm and testosterone hormones. Additionally, a study by Gacci et al, (2021) found that inflammatory markers and indications of decreased sperm quality in patients previously infected with COVID-19 will experience leukospermia and systemic inflammation [16]. Therefore, this study differs from previous study results. Referring to previous research results and based on the constructed study focus and characteristics of patients detected with SARS-CoV-2 having direct relevance to the occurrence of leukospermia in male patients in Makassar City. The urgency of this study is contextualized in three main aspects, namely (i) the direct impact of COVID-19 infection on male reproductive organs, (ii) the impact of symptoms caused by COVID-19 infection on decreased sperm quality, and (iii) the clinical implications of leukospermia occurrences in artificial insemination and IVF practices. Thus, the research questions to be answered in this study are: (i) Risk factors and effects caused by SARS-CoV-2 on the occurrence of leukospermia and decreased sperm quality; (ii) Is there a significant relationship between COVID-19 infection and the occurrence of leukospermia?

2. Materials and methods

This study employed a quantitative experimental approach with a cross-sectional design to investigate the relationship between SARS-CoV-2 infection and leukospermia occurrence in men.

2.1. Sample Selection

Purposive random sampling was used to select 20 male participants who were infected with SARS-CoV-2 and experiencing disruptions in their reproductive systems. The study was conducted at the Telkomedika Clinic in Makassar.

2.2. Data Collection

2.2.1. Primary Data

Observations and closed interviews were conducted with the participants to gather information on COVID-19 infection and reproductive health disturbances.

2.2.2. Secondary Data

Patient registration records were reviewed to obtain additional data on individuals with SARS-CoV-2 infection and reproductive system issues.

2.3. Data Measurement

- COVID-19 Infection: Measured using RT-PCR or Antigen SARS-CoV-2 testing.
- Leukospermia Occurrence: Assessed through leukocyte examination in semen samples.
- Sperm Quality Parameters: Evaluated based on sperm concentration, motility, and morphology.

2.4. Data Analysis

Descriptive Quantitative Analysis: Used to describe the observed variables and data obtained from the study participants. Chi-Square Test: Employed to analyze the relationship between SARS-CoV-2 infection and leukospermia occurrence. The test provided a statistical measure to determine the significance of the association between the variables Data Processing: Included editing, coding, and tabulation of raw data to facilitate analysis and interpretation of the results.

3. Results and Discussions

The characteristics of the study subjects are summarized in Table 1. This table shows the age, SARS-CoV-2 infection status, leukocyte values, and various sperm parameters of the participants. Out of the 20 participants, 13 were SARS-CoV-2 positive and 7 were negative. Leukocyte values, sperm motility, concentration, and morphology varied among the subjects.

The results from Table 2 indicate a significant association between SARS-CoV-2 infection and the occurrence of leukospermia, with a value of $0.005 < 0.05$. Furthermore, leukospermia is a condition characterized by the presence of >1.106 granulocytes/ml of semen and is often accompanied by an increase in cytokine levels as markers of inflammation [17]. The quantitative analysis revealed a significant association between SARS-CoV-2 infection and the occurrence of leukospermia in men, suggesting a potential link between the virus and changes in sperm quality parameters. Among the COVID-19 patients examined, 60.9% exhibited an elevated leukocyte count in semen, surpassing the normal threshold recommended by the WHO for leucocytospermia [10]. The immune response triggered by SARS-CoV-2 infection can induce uncontrolled inflammation, leading to decreased lymphocyte levels and inefficient initiation of adaptive immune responses [10]. The increased concentration of seminal leukocytes in COVID-19 patients may contribute to sperm abnormalities by activating reactive oxygen species [18]. Moreover, cytokines released by leukocytes can impede Sertoli cell functions and disrupt spermatogenesis [19]. The higher concentrations of proinflammatory cytokines and chemokines observed in the study corroborate the immune response findings in the testis and epididymis of COVID-19 patients. This immune

response, triggered by SARS-CoV-2 infection, can induce uncontrolled inflammation, resulting in reduced lymphocytes and inefficient initiation of adaptive immune responses [10]. The results from Table 3 demonstrate the association between SARS-CoV-2 infection and the decline in sperm quality.

Significantly, SARS-CoV-2 infection correlates with a value of 0.007 < 0.05 regarding progressive motility. Additionally, concerning sperm concentration, SARS-CoV-2 infection exhibits a significant association with a value of 0.015 < 0.05, indicating decreased sperm concentration. Moreover, there is statistical significance in sperm morphology changes, with a p-value of 0.012 < 0.05. These findings suggest that although COVID-19 affects sperm quality early after disease diagnosis compared to non-infected patients, it indicates a detrimental impact on sperm quality since the early stages of the disease, potentially compromising male fertility [20]. Furthermore, one of the causes of male infertility is impaired sperm motility. Imperfect motility leads to a decrease in sperm quality and a reduced probability of fertilization. Inflammation in the male reproductive tract is one of the causes of decreased motility [21]. Inflammation increases leukocyte recruitment in the male reproductive tract and enhances the production of reactive oxygen species (ROS), which are toxic to sperm, thus disrupting the process of sperm formation and maturation [22-23]. Men infected with SARS-CoV-2 demonstrated changes in sperm parameters, such as diminished sperm concentration, decreased motility, and anomalous morphology, implying a potential effect on male fertility [24-25]. Among the patients, 25.6% were oligo-crypto-azoospermic, indicating low sperm concentration [16]. A greater proportion of individuals recently recovered from either mild COVID-19 (87.4%) or severe COVID-19 (71.9%) exhibited abnormal sperm quality compared to control subjects (19.4%) [20].

Table 1: Subject Characteristics.

No	Age	Sars-Cov-2	Leukocyte value	Motility			Concentration	Morphology
				Progressive	Non-Progressive	Immotile		
1	26 years	Positive	1.1	35	45	50	45.1	3
2	36 years	Negative	1.1	15	45	50	8.6	1
3	27 years	Positive	1.1	30	40	30	32.3	2
4	29 years	Positive	1.2	30	35	35	43.1	2
5	30 years	Positive	2.2	30	35	35	20.3	2
6	33 years	Positive	1.1	35	35	35	60.1	2
7	30 years	Positive	3.1	10	15	20	9.2	1
8	29 years	Negative	0.77	15	20	15	6.7	1
9	31 years	Negative	1.2	30	50	20	17.5	2
10	45 years	Negative	2.2	15	20	20	15.1	1
11	31 years	Positive	1.5	35	40	40	15.2	2
12	36 years	Positive	1.1	35	40	35	41.2	2
13	31 years	Positive	1.1	45	35	40	15.3	2
14	35 years	Positive	1.5	35	35	35	29.2	2
15	31 years	Positive	1.7	40	45	35	40.5	1
16	36 years	Positive	1.2	35	45	35	30.5	2
17	40 years	Negative	1.1	30	30	30	32.1	2
18	46 years	Negative	0.87	10	25	65	20.2	1
19	28 years	Positive	3.4	30	40	40	15.1	2
20	30 years	Negative	1.1	15	20	30	6.9	1

Table 2: Relationship of SARS-Cov-2 to the incidence of leukospermia.

SARS-Cov-2	Leukospermia		Non-Leukospermia		Total		*P* Value
	n	%	n	%	n	%	
Covid	13	65,0	0	0	13	65,0	0,005
Non-Covid	5	71,4	2	28,6	7	35,0	

Table 3: Relationship of SARS-Cov-2 to Impaired Sperm Quality.

Sperm Parameters		Covid		Non-Covid		*P Value*
		n	%	n	%	
Motility	Progressive >32	3	33.3	6	66.7	0.007
	Progressive <32	10	90.9	1	85.7	
Concentration	>15 million	12	80	3	20	0.015
	<15 million	1	7.7	4	40	
Morphology	Normal >4	2	28.6	5	71.4	0.012
	Abnormal <4	11	84.6	2	28.6	

4. Conclusions

In conclusion, our study unveils a significant correlation between SARS-CoV-2 infection and the occurrence of leukospermia, suggesting a notable impact on male reproductive health. The observed alterations in sperm quality parameters among men with COVID-19, including decreased sperm concentration, reduced motility, and abnormal morphology, emphasize the necessity for vigilant monitoring of fertility in individuals recovering from the virus. Furthermore, these findings underscore the urgency of further research aimed at unraveling the underlying mechanisms of SARS-CoV-2's effects on male fertility and developing targeted interventions to mitigate potential reproductive complications associated with the infection. It is imperative for healthcare providers to grasp the implications of COVID-19 on male reproductive health, particularly concerning leukospermia, to implement effective strategies for managing and addressing potential fertility issues in affected individuals.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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