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Synovial fluid evaluation in COVID-19 patients

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ABSTRACT

Background: COVID-19 can provide symptoms outside the respiratory tract and musculoskeletal symptoms. Some viruses can indeed cause arthritis, and the genetic material of these viruses can be found in a joint fluid using PCR assays. With this study, we will conduct an examination using PCR on the joint fluid of COVID-19 patients who have musculoskeletal symptoms, especially arthralgia, during the infection.

Methods: This cross-sectional study with a descriptive explanation of synovial fluid in COVID-19 patients was performed from April 1st to July 30th, 2021, with patient data collection conducted centrally at Wahidin Sudirohusodo Hospital Makassar Synovial fluid was taken from the knee using the sterile procedure in a patient that met the inclusion criteria, such as hospitalized patients who had positive PCR swab results in the nasopharynx for less than 2 weeks and had arthralgia symptoms on April – July 2021. Other musculoskeletal symptoms (e.g., myalgia and fatigue) were noted. About 2 ml sample of synovial fluid was tested using a PCR kit (M BioCov) in the laboratory. The sample shows a positive result when there is an amplification of RDNP with a CT value below 40.

Results: 189 patients with 21 participated, 14 subjects were male, and 7 subjects were female. Age range 18 - 72 years with arthralgia, myalgia, and fatigue symptoms. Only 2 patients had arthralgia, 13 patients had myalgia and arthralgia, 1 patient had fatigue and arthralgia, and 5 patients had all of the symptoms (arthralgia, myalgia, and fatigue). Only 1 patient had direct contact with the COVID-19 patient. PCR test for synovial fluid in all patients showed negative for COVID-19.

Conclusion: COVID-19 infection can be manifest in the musculoskeletal system. Detection of COVID-19 virus using a specimen from knee synovial fluid in a patient with musculoskeletal symptoms (arthralgia, myalgia, fatigue) was negative.

Keywords: COVID-19, musculoskeletal symptoms, synovial fluid.
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INTRODUCTION

In December 2019, a cluster of pneumonia cases of unknown cause appeared in Wuhan, China. The National Health Commission (NHC) of the People's Republic of China later announced that a novel coronavirus was responsible for the outbreak. On January 12th, 2020, the World Health Organization temporarily named the new virus the 2019 novel coronavirus (2019-nCoV), or known as COVID-19.[1,2] Examination of the presence of the virus can be done by Polymerase Chain Reaction (PCR) using samples taken from the respiratory tract.[3-9] Moreover, the examination material can also be obtained from the patient's blood and feces as a confirmatory examination to get better results.[9]

Beside respiratory symptoms, COVID-19 can provide symptoms outside the respiratory tract, such as visual disturbance, diarrhea, nausea and vomiting, and musculoskeletal symptoms.[3-6] The most frequently reported musculoskeletal symptoms were myalgia and arthralgia.[1,4,6-8] From previous studies, arthralgia was found in about 11-15% of patients suffering from COVID-19 infection.[6,8] However, it has never been reported the presence of viral genetic material in joint fluid in patients with arthralgia.

Some viruses can indeed cause arthritis, and the genetic material of these viruses can be found in a joint fluid using PCR assays. These viruses include alphavirus, parvovirus, hepatitis virus, and HIV.[10,11] With this study, we will conduct an examination using PCR on the joint fluid of COVID-19 patients who have musculoskeletal symptoms, especially arthralgia. The results of the Examination can be positive or negative values.

METHODS

This cross-sectional study with a descriptive explanation of synovial fluid in COVID-19 patients that conducted centrally at Wahidin Sudirohusodo Hospital Makassar. Total sampling was done prospectively by collecting the data from April 2021 to July 2021 with inclusion criteria, including the COVID-19 patients who confirmed throat swab by PCR results and were hospitalized and had symptoms of joint pain. Exclusion criteria were COVID-19 patients with positive throat swab PCR results more than 2 weeks after the first Examination.

The joint fluid examination was carried out using the PCR technique in the laboratory of the teaching hospital

of UNHAS Medical Faculty (HUM-RC). The number of COVID-19 patients hospitalized in 189 patients.

21 of 189 patients participated in this study. These patients noted other musculoskeletal symptoms such as myalgia and fatigue were recorded. The point of sampling joint fluid is through a soft spot in the knee area. The procedure is performed under local anesthesia, then a large (14G) needle is inserted to collect approximately 2 ml of fluid in the joint cavity. The liquid was put into a tube and stored in a refrigerator to be brought to the microbiology laboratory of the teaching hospital of UNHAS Medical Faculty. And examined using rt-PCR. This PCR examination has a CT value cut-off of 40 (M BioCoV).

The sample examined will give a positive value if there is an image of the RDRP curve with a CT value of below 40 and a control curve. While the negative results only show the control curve.

From the size of the sample examined, they had previously been treated because it had been confirmed with a positive throat swab PCR result. This Examination is the first throat swab PCR examination in less than 2 weeks after the Examination.

Of the 30 patients who showed symptoms of arthralgia, there were 21 people who participated in having their knee fluid taken with a written statement signed by the patient (informed consent). The statistical analysis of this study was presented descriptively and analyzed using IBM SPS version 25 for Windows and Microsoft Excel.

RESULT

The total population was 189 patients, with 30 people showing symptoms of arthralgia. Meanwhile, there were only 21 people who participated in this study. 14 subjects were male, and 7 subjects were female. Age range 12-25 years as many as 3 people, 26-45 years as many as 2 people, 46-65 years as many as 12 people, and over 66 years as many as 4 people.

In COVID-19 patients who experienced musculoskeletal symptoms, all subjects were found to have symptoms of arthralgia. In addition, there were other accompanying musculoskeletal symptoms, such as myalgia in 13 subjects and fatigue in 1 subject. There were 5 patients who experienced all musculoskeletal symptoms (arthralgia, myalgia, and fatigue) and 2 people who only had arthralgia symptoms. The results of the joint fluid examination using rt-PCR (Figure 1), none of them gave positive results.

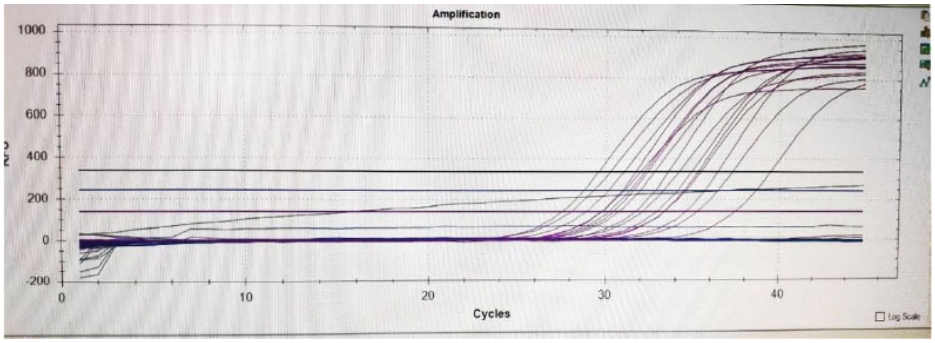

Figure 1. The curve of joint fluid rt-PCR examination results for COVID-19.

There were several patients who had to have symptoms of their musculoskeletal system before being infected. In the distribution of symptoms felt before being infected, as many as 13 cases had never felt symptoms in the musculoskeletal system, and 8 cases had symptoms before being infected.

DISCUSSION

In addition to respiratory symptoms, COVID-19 can provide non-respiratory symptoms such as visual disturbances, diarrhea, nausea and vomiting, and musculoskeletal symptoms.[3-10] The most commonly reported musculoskeletal symptoms were myalgia and arthralgia.[11-15] From previous studies, arthralgia symptoms were obtained in about 11-15% of patients suffering from COVID-19 infection.[6,8,16-21]

There were 21 people who were willing to take samples. All subjects had arthralgia, and some subjects had other accompanying musculoskeletal symptoms, such as myalgia in 13 people and fatigue in 1 person. There were 5 patients who suffered from all musculoskeletal symptoms (arthralgia, myalgia, and fatigue) and 2 people who only experienced arthralgia.

The manifestation of musculoskeletal symptoms from COVID-19 infection can be caused indirectly by an increase in inflammatory mediators, such as CRP and cytokines that can cause muscle weakness and myalgia. Furthermore, an increase in interleukin can induce osteoclasts and decrease osteoblasts, thereby reducing bone density; besides that, it can also give symptoms of arthralgia to arthritis in some patients.[22-27]

Proving the presence of the virus can be done by means of Polymerase Chain Reaction (PCR) using samples taken from the respiratory tract.[3-5] In addition, examination materials can also be obtained from the patient's blood and feces as a confirmatory examination to get better results.[28-33]

All PCR examinations of the patient's knee joint fluid showed negative results. This can be seen from the tool that shows only the control curve without any RDRP amplification. PCR examination of joint fluid has also been reported by several authors with negative results.[32-34]

This negative result may be related to the viral receptor, ACE2, which is found on alveolar type II (AT2) cells, upper esophagus, absorptive enterocytes from the ileum and colon, cholangiocytes, myocardial cells, endothelial cells, proximal renal tubular cells, and urinary tract cells. Although this receptor is present in the joint fluid, the presence of this virus was not found by PCR examination.[14,15,22,34,35]

From this study, negative results were obtained on all PCR examinations of joint fluid of patients with confirmed COVID-19 infection. It can be concluded that there was no 'trace' of viral genetic material in their joint fluid even though the throat swab PCR examination gave a positive result.[35,36]

Examination of samples examined by PCR in COVID-19 patients should be carried out simultaneously to minimize

bias in examination results from samples other than the nasopharynx. If the nasopharyngeal Examination is at different times, it is likely that the Examination of other materials (feces, blood, joint fluid) can give negative results.[37]

Possible musculoskeletal symptoms in COVID-19 are not related to the presence or direct infection of the COVID-19 virus. These symptoms tend to be caused by systemic processes, such as endothelial damage and increased inflammatory mediators (cytokine storm).

It can also be concluded that surgery on the joint area in patients infected with COVID-19 is relatively safe from the risk of direct transmission from the operating area. The limitation of this study is the small number of samples and single institution, so it cannot be applied in general. For further research, it may be possible to perform an examination to correlate CT values with the presence of viral genetic material in joint fluid or with the condition of patients experiencing cytokine storms.

CONCLUSION

Clinical manifestations of COVID-19 infection are not always related to respiratory problems but can also affect other organ systems. Therefore, to identify the early symptoms of this viral infection, symptoms outside the respiratory system must also be considered. The absence of virus in synovial fluid can prevent the surgeon from direct infection during the operation in the joint area, respectively, but other sources of infection (e.g., blood and respiratory droplet) still become a consideration.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

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ETHICAL STATEMENT

The ethical committee Faculty of Medicine Universitas Hasanuddin approved this study, with ethical clearance references number UH20090540.

AUTHOR CONTRIBUTION

Conceptualization and methodology, SM, AJ, NYA; data collection, SM, AJ, NYA; analysis and writing, SM, NYA, MM, AM, HY; review, SM, AJ, NYA, MM, AM, HY. All authors have read and agreed to publish the manuscript.

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