

## ORIGINAL ARTICLE

# Phenomena of the most Frequent Cold Symptoms in COVID-19 Patients


## Fenomena Gejala Pilek paling Sering pada Pasien COVID-19

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### ABSTRACT

#### Background

COVID-19 is an infectious disease caused by SARS-CoV-2, a new coronavirus that has never been identified in humans that causes various symptoms. Symptoms of COVID-19 that are quite often found are cough, runny nose, fever. Antigen rapid test is an examination with high sensitivity and specificity, often used in COVID-19 detection. This study aims to determine the relationship between cough, cold, and fever symptoms with positive results of COVID-19 antigen rapid test.

#### Methods

This study used cross-sectional design using medical records. The variables assessed were cough, cold, fever, and the results of COVID-19 antigen rapid test. Data analysis was performed using chi-square test and logistic regression test with significance level of  $p < 0.05$ .

#### Results

Subject are mostly are 31-45 years old and female. Subjects had symptoms of cough (88.2%), fever (80%), and runny nose (60%). The results of the COVID-19 rapid test antigen were found to be more reactive (80%). The distribution of reactive results of the COVID-19 rapid antigen test was 86.7% in cough, 92.2% in colds, and 91.2% in fever. There was a significant relationship between cough ( $p=0.000$ ), runny nose ( $p=0.001$ ), and fever ( $p=0.000$ ) with reactive results of the COVID-19 rapid test antigen. Patients with cold symptoms have an 8.67 times greater risk of reactive COVID-19 antigen rapid tests.

#### Conclusions

There is a relationship between symptoms of cough, runny nose, and fever with reactive results in patients aged 17 years and over. Complaints of a cold have a higher risk of reactive results on the COVID-19 rapid test antigen examination compared to cough and fever. This means that patients with colds need to be more aware of being infected with COVID-19.

**Keywords:** cough; cold; fever; antigen rapid test; COVID-19

**ABSTRAK****Latar Belakang**

COVID-19 adalah penyakit menular yang diakibatkan oleh SARS-CoV-2 coronavirus baru yang belum pernah teridentifikasi pada manusia yang menimbulkan berbagai macam gejala. Gejala COVID-19 yang cukup sering ditemukan adalah batuk, pilek, demam. *Rapid Test* Antigen merupakan pemeriksaan dengan sensitivitas dan spesivitas yang cukup tinggi sehingga sering digunakan untuk deteksi COVID-19. Penelitian ini bertujuan untuk mengetahui hubungan gejala batuk, pilek, dan demam dengan hasil reaktif pada pemeriksaan *rapid test* antigen COVID-19.

**Metode**

Penelitian ini menggunakan *design cross-sectional* menggunakan data rekam medis. Variabel yang dinilai berupa batuk, pilek, demam, dan hasil pemeriksaan *rapid test* antigen COVID-19. Analisis data menggunakan uji statistik *chi-square* dan regresi logistik dengan tingkat kemaknaan  $p < 0.05$ .

**Hasil**

Karakteristik subjek dominan berusia 31-45 tahun dan berjenis kelamin perempuan. Subjek bergejala batuk (88.2%), demam (80%), dan pilek (60%). Hasil pemeriksaan *rapid test* antigen COVID-19 ditemukan lebih banyak yang reaktif (80%). Distribusi hasil reaktif *rapid test* antigen COVID-19 adalah 86.7% pada batuk, 92.2% pada pilek, dan 91.2% pada demam. Terdapat hubungan bermakna antara batuk ( $p=0,000$ ), pilek ( $p=0,001$ ), dan demam ( $p=0,000$ ) dengan hasil reaktif pemeriksaan *rapid test* antigen COVID-19. Pasien dengan gejala pilek memiliki risiko 8.67 kali lebih besar terjadinya reaktif pemeriksaan *rapid test* antigen COVID-19.

**Kesimpulan**

Terdapat hubungan antara gejala batuk, pilek, dan demam dengan hasil reaktif pada pasien berusia 17 tahun ke atas. Keluhan pilek memiliki risiko lebih tinggi terjadinya hasil reaktif pada pemeriksaan *rapid test* antigen COVID-19 dibandingkan batuk dan demam. Oleh karena itu pasien dengan keluhan pilek perlu lebih mewaspadai kemungkinan terinfeksi COVID-19.

**Kata Kunci:** batuk; pilek; demam; *rapid test* antigen; COVID-19.

**INTRODUCTION**

On December 31, 2019, the World Health Organization (WHO) China Country Office reported a case of pneumonia of unknown cause in Wuhan, Hubei, China. The cause of this case was only identified on January 7 2020, as a new type of coronavirus. Furthermore, on January 30, 2020, this event was designated as a Public Health Emergency of International Concern (PHEIC) until finally COVID-19 was declared a pandemic by WHO on March 11, 2020.

COVID-19 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a new type of coronavirus that has never been previously identified in humans.<sup>1</sup> Based on the WHO report as of July 17 2021, the total number of confirmed cases of COVID-19 worldwide was 188,655,968 cases, with 4,067,517 deaths. The Americas region has the most confirmed cases, namely 74,411,952 cases, followed by Europe with 57,636,847, Southeast Asia with 36,525,388, Eastern Mediterranean with 11,644,006, Africa with 4,531,636, and the West Pacific with 3,905,375. Reports on the same day showed that the daily number of confirmed cases in Indonesia was 54,000 people. Therefore, the total number of confirmed cases of COVID-19 in Indonesia is 2,780,803 cases with 71,397 deaths.<sup>2</sup> DKI Jakarta is recorded as the area with the highest number of confirmed cases, with a cumulative incidence of 6,107.56 per 100,000 people, followed by East

Kalimantan, North Kalimantan, DI Yogyakarta, and the Bangka Islands.<sup>3</sup> COVID-19 has a very diverse clinical spectrum.<sup>4</sup>

Infected patients can be asymptomatic, show very mild symptoms, and even have ARDS conditions requiring other mechanical ventilation support in the Intensive Care Unit (ICU).<sup>4</sup> Symptoms experienced by patients usually start with mild symptoms and appear gradually, including fever, tiredness, and dry cough. Some infected people are asymptomatic or don't show any symptoms. Some patients may experience nasal congestion, runny nose, myalgia, cephalalgia, sore throat, nausea, vomiting, diarrhea, conjunctivitis, anosmia, or rashes on the skin, or they can cough up blood.<sup>1,4-6</sup> Some of the symptoms caused by COVID -19 are similar to flu-like symptoms, such as fever, cough, difficulty breathing, tiredness, sore throat, runny nose, muscle aches, headache, nausea, vomiting, diarrhea, and loss of smell.<sup>4-6</sup>

Therefore, further tests are needed to determine the diagnosis of COVID-19, including a rapid antigen test. Decree of the Minister of Health of the Republic of Indonesia Number HK.01.07/Menkes/3602/2021 concerning Amendments to Decree of the Minister of Health Number HK.01.07/Menkes/446/2021 concerning the Use of Antigen Rapid Diagnostic Tests in Examination of COVID-19 states that in the context of contact tracing, enforcement diagnosis, and screening of COVID-19, Rapid Diagnostic Test Antigen can be applied as a method of examination. To improve the performance of the Rapid Diagnostic Test Antigen (later known as the Rapid Test Antigen (RTA)), the examination is carried out in the acute phase of infection, namely within the first seven days or week since the onset of symptoms.<sup>7</sup>

Based on the results of a study conducted by Brummer et al., it was found that high sensitivity was found (83.3%, 95% CI 76.3%-89.2%) at the first week of symptoms compared to one week after symptoms (61.5%, 95% CI 52.2% - 70.0 %).<sup>8</sup> However, a study conducted by Isikbay et al. found that patients with fever, cough, chills, myalgia, and diarrhea, which are symptoms that COVID-19 patients often experience, showed negative results in testing for COVID-19 with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).<sup>9</sup> Although RTA is recommended for rapid diagnosis of COVID-19, WHO still stipulates that the RT-PCR test is the gold standard of examination in diagnosing COVID-19.<sup>10</sup> This study aims to determine whether flu-like symptoms, namely cough, runny nose, and fever, correlated with a reactive outcome of the COVID-19 RTA.

## METHODS

This research was conducted using an observational analytic method with a cross-sectional approach at a clinic in South Tangerang from October to December 2021. Respondents in this study consisted of patients seeking treatment from January to June 2020, aged 17 years or older. Patients were taken with cough, runny nose, or fever complaints and carried out the RTA COVID-19 examination. The study did not include patients who performed COVID-19 RTA examinations and did not use tools with the Indonesian Clungene brand. The Clungene Indonesia brand was chosen because the tool is used in the clinic. Sampling was done by consecutive sampling. The collected data were analyzed and statistically tested using the chi-square test and logistic regression.

This research has passed the Ethical Review of the Research Ethics Committee of the Faculty of Medicine, Trisakti University, with Number 85//KER-FK/IX/2021 and has received research approval from the relevant clinic.

## RESULTS

A total of 85 respondents were involved in this study. Subjects aged 31 to 45 years are the age range of subjects with the highest number, and subjects with female gender have a slightly higher number than males, with a percentage of 51.8% (Table 1).

Table 1. Characteristics of research subjects

Characteristic	Frequency (total=85)	Percentage (%)
<b>Age (Year)</b>		
19 – 30	12	22,4
31 – 45	35	41,1
46 – 59	23	27,1
≥ 60	8	9,4
<b>Gender</b>		
Male	41	48,2
Female	44	51,8

Of the three symptoms studied, the most frequently examined symptom frequency by RTA was cough (88.2%), followed by fever (80%), and the least frequent was runny nose (60%). Meanwhile, of the 85 respondents who were examined with the rapid antigen test, 80% were found to be reactive (Table 2).

Subjects with cough symptoms were found to have positive COVID-19 antigen rapid test results (86.7%) compared to those who did not get a cough (Table 3). This is supported by Fisher's exact test, an alternative to the chi-square test, which shows a significant relationship between cough symptoms and a positive result on the COVID-19 rapid test antigen ( $p=0.000$ ). There were more subjects with cold symptoms with positive COVID-19 antigen rapid test results (92.2%) compared to subjects without a cold, which was proven by the results of the chi-square test, which showed a significant relationship between the two variables ( $p=0.001$ ). The latter is for symptoms of fever, where positive results on the COVID-19 antigen rapid test are dominated by subjects with fever symptoms (91.2%) compared to those without fever. This is also evidenced by Fisher's exact test results, which showed a significant relationship between the two variables ( $p = 0.000$ ).

Table 2. Distribution of symptoms and examination of the COVID-19 antigen rapid test

Variable	Frequency (total=85)	Percentage (%)
<b>Cough</b>		
Yes	75	88,2
No	10	11,8
<b>Running nose</b>		
Yes	51	60
No	34	40
<b>Fever</b>		
Yes	68	80
No	17	20
<b>COVID-19 Antigen Rapid Test Examination Results</b>		
Positive	68	80
Negative	17	20

Table 3. Relationship between symptoms and the results of the COVID-19 antigen rapid test

Variable	COVID-19 Antigen Rapid Test Examination Results		p-value
	Positive n (%)	Negative n (%)	
<b>Cough</b>			
Yes	65 (86,7%)	10 (13,3%)	0,000(**)
No	3 (30%)	7 (70%)	
<b>Running nose</b>			
Yes	47 (92,2%)	4 (7,8%)	0,001(*)
No	21 (61,8%)	13 (38,2%)	
<b>Fever</b>			
Yes	62 (91,2%)	6 (8,8%)	0,000(*)
No	6 (35,3%)	11 (64,7%)	

Table 4. Results of multivariate analysis of symptoms that are reactive to the COVID-19 antigen rapid test

Variable	p	OR	95% Confidence Interval	
			Lower Bound	Upper Bound
<b>Cough</b>	0,000	1,181E+10	1,678E+9	8,309E+10
<b>Running nose</b>	0,024	8,637	1,330	56,081
<b>Fever</b>	0,000	1,044E+10	1,044E+10	1,044E+10

Based on the logistic regression test, the cold variable was found to have an OR=8.637 value, which means that patients with cold symptoms are 8.6 times more likely to have a positive result on a positive COVID-19 rapid test antigen test, significantly compared to patients with symptoms of cough and fever (p=0.024). (Table 4)

## DISCUSSION

In this study, it was found that there was a significant relationship between symptoms of cough, runny nose, and fever with the results of a reactive test for the COVID-19 antigen rapid test. Based on the pathophysiology of COVID-19, the migration of neutrophils to the lungs and airways caused by viral proliferation in cells and tissues with many ACE-2 receptors results in the release of proinflammatory mediators.<sup>11</sup> Release of reactive oxygen species and proinflammatory mediators such as cytokines in the lungs and the airways, including the nasal mucosa, will irritate the airways, causing cough and runny nose symptoms.<sup>11</sup> This is also associated with ineffective airway clearance. The inability to clear the airway is characterized by coughing, accumulation of sputum in the airways, crackles, wheezing, and other respiratory symptoms.<sup>12</sup> Proinflammatory cytokines (such as TNF- $\alpha$ ) stimulate an immune response and induce the hypothalamus to release prostaglandins. The release of prostaglandins will cause an increase in body temperature set point by the body's thermoregulator played by the hypothalamus. The increase in the thermoregulatory set point functions to fight the infection that eventually causes fever.<sup>11</sup> This is in line with a cohort study by Huang et al. at Jin Yin-tan Hospital in Wuhan, China, at the start of the emergence of COVID-19 cases. Based on this study's results, fever and cough were the two symptoms that most often appeared in COVID-19 patients (98% and 76%, respectively).<sup>13</sup>

In the first case of COVID-19 in Wuhan, symptoms of nasal congestion were found. The SARS-CoV-2 infection has prominent signs and symptoms in the upper respiratory tract, such as rhinorrhea, sneezing, and sore throat.<sup>12</sup> The significant relationship between the symptoms of cough, runny nose, and fever and the results of the COVID-19 rapid antigen test is related to the theory diagnosis of COVID-19 where after passing the incubation period and reaching the peak of replication, mild symptoms will appear and can gradually develop into more severe symptoms. Starting from that period, patients infected with SARS-CoV-2 will show positive results on diagnostic tests, including rapid test antigen examinations.<sup>14</sup> During a pandemic, rapid test kits are widely used to help screen and diagnose COVID-19. The COVID-19 antigen rapid test was initially only used for initial screening and was eventually declared to be used as a diagnostic method.<sup>7,15</sup> This is undoubtedly related to the accuracy of the examination based on many studies where the sensitivity and specificity of the rapid antigen test were reported to be relatively high. as written by Chaimayo et al., based on their research results, the sensitivity and specificity of the COVID-19 rapid test antigen reached 98.33% and 98.73%.<sup>16</sup> The way the COVID-19 rapid test antigen works are by detecting antigen from a sample taken from a patient suspected of being infected with SARS-CoV-2. Examination of the COVID-19 antigen rapid test is carried out by taking a specimen from a nasopharyngeal swab. The antigen will be detected on the cassette provided, where usually the target of the COVID-19 antigen rapid test is the nucleocapsid of the virus, which has a large number. Although RT-PCR is the gold standard in the COVID-19 diagnosis method, the COVID-19 antigen rapid test is highly considered for its use considering the high accuracy, low price, and easy inspection procedure.<sup>16-17</sup>

Based on the results of multivariate analysis, it was found that of the variables studied, namely symptoms of cough, runny nose, and fever, with the results of the COVID-19 rapid test antigen examination, subjects with cold symptoms were significantly more likely to get reactive results on the COVID-19 rapid test antigen examination. ( $p=0.024$ ;  $OR=8.63$ ) compared with symptoms of cough and fever. Thus it can be concluded that although each of these symptoms, namely cough, runny nose, and fever, has a significant relationship with the results of the COVID-19 rapid test antigen based on bivariate analysis, it turns out that subjects with cold symptoms are eight times more likely to have a reactive result on a rapid test for COVID-19 antigen compared to cough and fever. As previously explained, a runny nose is one of the predominant symptoms in COVID-19 patients. Unlike SARS-CoV and MERS-CoV, which are variants of the coronavirus which previously caused outbreaks and caused many deaths, SARS-CoV-2 has very prominent respiratory symptoms.<sup>13</sup> SARS-CoV-2 infection has signs and symptoms in the respiratory tract. Prominent upper symptoms such as rhinorrhea, sneezing, and sore throat; where in the first case of COVID-19 in Wuhan, symptoms of nasal congestion were found.<sup>12</sup>

This study has limitations: it does not confirm the results of the rapid antigen test by RT-PCR, which is the gold standard for testing for COVID-19, so it cannot exclude false reactivity and false non-reactivity from the test results.

The results of this study can help medical personnel to think more about the possibility of a patient contracting COVID-19 if a cold is found compared to other symptoms so that treatment can be more appropriate. Likewise, these results can provide input for the public during the COVID-19 pandemic to remain aware of the possibility of contracting COVID-19 even if they only suffer from complaints of a cold, thereby preventing the broader spread of COVID-19.

## CONCLUSION

The distribution of reactive results on the COVID-19 antigen rapid test was 86.7% in cough subjects, 92.2% in cold subjects, and 91.2% in fever subjects. There is a significant relationship between the symptoms of cough, runny nose, and fever with reactive results on the COVID-19 rapid test antigen, where a cold is 8.67 times more likely to have a reactive result on the COVID-19 rapid test antigen.

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## AUTHORS CONTRIBUTION

JWM, plays a role in preparing research designs, data collection, data analysis, data interpretation, and is responsible for data collection in the field, preparing papers. TDS plays a role in drafting concepts, data analysis, data interpretation, preparing papers, revising final papers for publication.

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## CONFLICT OF INTEREST

There is no conflict of interest between the authors

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