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Diagnostic Value of Clinical Symptoms of COVID-19 in the Early Diagnosis of the Disease

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Abstract

Background: Early diagnosis of COVID-19 can have an important role in the decrease of mortality of patients. Symptoms such as fever and cough are the first diagnostic information. Due to the importance of early diagnosis of COVID-19, the current study aimed to assess the diagnostic value of different symptoms in detecting COVID-19 cases.
Materials and Methods: In the current cross-sectional study, 392 COVID-19 patients were confirmed based on RT-PCR (Reverse transcription-polymerase chain reaction) using nose and throat swab specimens and or Chest CT scan compatible with COVID-19 infection. The diagnostic value of symptoms in detecting COVID-19 was measured using the sensitivity, specificity, false alarm rate, likelihood ratio, and area under the receiver operating characteristics (ROC) curve (AUC).
Results: The highest sensitivity and lowest false negative in the detection of COVID-19 cases were seen in Dyspnea and cough with a sensitivity of 0.59 (95%CI: 0.51-0.66) and 0.57 (95%CI: 0.49-0.65) respectively. In terms of specificity, the Loss of consciousness with specificity 0.95 (95%CI: 0.92-0.98) had the best performance so this symptom had the lowest false positive in the detection of COVID-19 cases. The most positive likelihood ratio (LR+) was seen in cough (LR+:1.41) and fever (LR+:1.21), respectively. The most positive predictive value (PPV) was seen in cough (PPV: 0.49 (95%CI: 0.41- 0.56)), and fever (PPV: 0.45(95%CI: 0.37-0.53)) respectively.
Conclusion: Early symptoms among patients tested for SARS-CoV-2 identified those general non-respiratory symptoms were strongly associated with test positivity.

Keywords: COVID-19, Sensitivity, Specificity, Positive Predictive Value

Introduction

COVID-19 caused by the SARS-COV-2 virus. The majority of people with this infection have mild to moderate respiratory symptoms; others develop severe diseases, such as pneumonia. Accurate diagnosis requires laboratory analysis of nasal and throat specimens or imaging such as CT scans. However, the first diagnostic method is the signs and symptoms that result from a clinical examination [1]. As the virus spreads worldwide, governments' strategies will be to curb the transmission of the virus, which requires effective identification and treatment of patients. Physicians must correctly identify and triage COVID-19 patients, which are classified from mild to severe, to make optimal use of human resources, facilities, and equipment [2]. They can be used when there are sufficient resources for tests, but if these tests and additional tests are limited, making decisions based on clinical signs is necessary. Symptoms such as fever or cough and respiratory problems are the first and most accessible diagnostic information. Such information can be used to track COVID-19 or to select patients for more accurate diagnostic tests [1]. Fever, fatigue, muscle aches, nasal congestion, chills, sore throat, diarrhea are among the most common symptoms of COVID-19 [3]. These symptoms may not be sensitive enough. Many viral diseases, bacterial infections, and allergies can cause similar symptoms.

Many people with these symptoms tend to be able to do their job, but they quit for fear that they might pass COVID-19 on to others. Experimental limitations, unavailability of resources, and lack of evidence to inform the use of signs have exacerbated these challenges [4]. One study found that changes in smell and taste strongly predict positive COVID-19 test results. The presence of clinical signs of smell or taste change associated with fever is 75% accurate in predicting the results of the COVID-19 test [5]. However, this accuracy in predicting other symptoms is unclear. If accurate signs and symptoms made the initial diagnosis, the need for time-consuming tests and specialized diagnosis would be reduced. Due to the importance of early diagnosis of COVID-19, the current study was designed to evaluate the performance of different symptoms in detecting COVID-19 cases.

Materials and Methods

Data about the 392 patients with COVID-19 symptoms who were referred to a referral hospital in Tehran province, Iran, between 7 March to 8 Oct 2020. All hospitalized patients during the mentioned period were included in the census. However, this hospital was a military one, but during the pandemic, due to the priority of treating COVID-19 patients, the hospital received all patients from all over Tehran.

Age, Gender, comorbidity status, symptoms, and blood level O2 Saturation (O2S) (using Pulse oximetry) were the study variables. This variable was assessed at the time of referring to the hospital. In the current study, patients were confirmed by RT-PCR (Reverse transcription-polymerase chain reaction) at the time of hospitalization. The sensitivity and specificity of RT-PCR in detecting COVID-19 were estimated at 89 [6] and 99%, respectively [7]. The samples taken are tested in laboratories. This test is based on the so-called "polymerase chain reaction" method. In the PCR test method, a piece of DNA is amplified inside a thermocycler to search for specific pieces of DNA. The mentioned data was retrieved from the hospital's health information system (HIS). When patients were referred to the hospital, the disease's symptoms and other clinical and demographic variables, were recorded by a trained nurse in the HIS system.

The ethical committee at the Aja University of Medical Sciences approved the current study (and registered with ID: IR.AJAUMS.REC.1399.065.).

Measures of the algorithm's performance: Considering PCR test results in gold standard, the sensitivity, specificity, false alarm rate, likelihood ratio, and area under the receiver operating characteristics (ROC) curve (AUC) of symptoms were measured. Sensitivity indicates how well a test can identify true positives, and specificity indicates how well a test can identify true negatives.

A receiver operating characteristic curve, or ROC curve, shows the performance of a test. The closer the ROC curve is to the upper left corner of the graph, in the upper left corner, the sensitivity = 1 and the false positive rate = 0 (specificity = 1), so the higher the accuracy of the test. The ideal ROC curve thus has an AUC = 1.0 [8]. STATA 15 (Stata Corp LLC) and Excel 2010 were used to analyze the data.

Results

The most frequently reported symptoms among the understudied patients were Dyspnea (53%), cough (47%), and fever (38%) respectively (Table 1). The highest amount of sensitivity and lowest false negative were seen in Dyspnea (sensitivity = 0.59 (95%CI: 0.51-0.66)), and cough (sensitivity = 0.57 (95%CI: 0.49-0.65)), respectively. The Loss of consciousness with 0.95 specificity (95%CI: 0.92-0.98) had the best performance so this symptom had the lowest false positive in the detection of COVID-19 cases. The highest positive likelihood ratio (LR+) was seen in cough (LR+:1.41) and fever (LR+:1.21), respectively. The most positive predictive value (PPV) was seen in cough (PPV: 0.49 (95%CI: 0.41- 0.56)), and fever (PPV: 0.45(95%CI: 0.37-0.53)) respectively (Table2 and Fig.1).

Table 1. Most common symptoms of COVID-19 among understudied cases

Symptom	N	%
Fever	150	38
Cough	186	47
Muscular pain	74	19
Dyspnea (Respiratory distress)	209	53
Loss of consciousness	13	3
Fever+ Cough	75	20
Fever+ Dyspnea	65	17
Cough+ Dyspnea	90	23
Fever+O2 S	39	10
Cough+O2 S	45	12

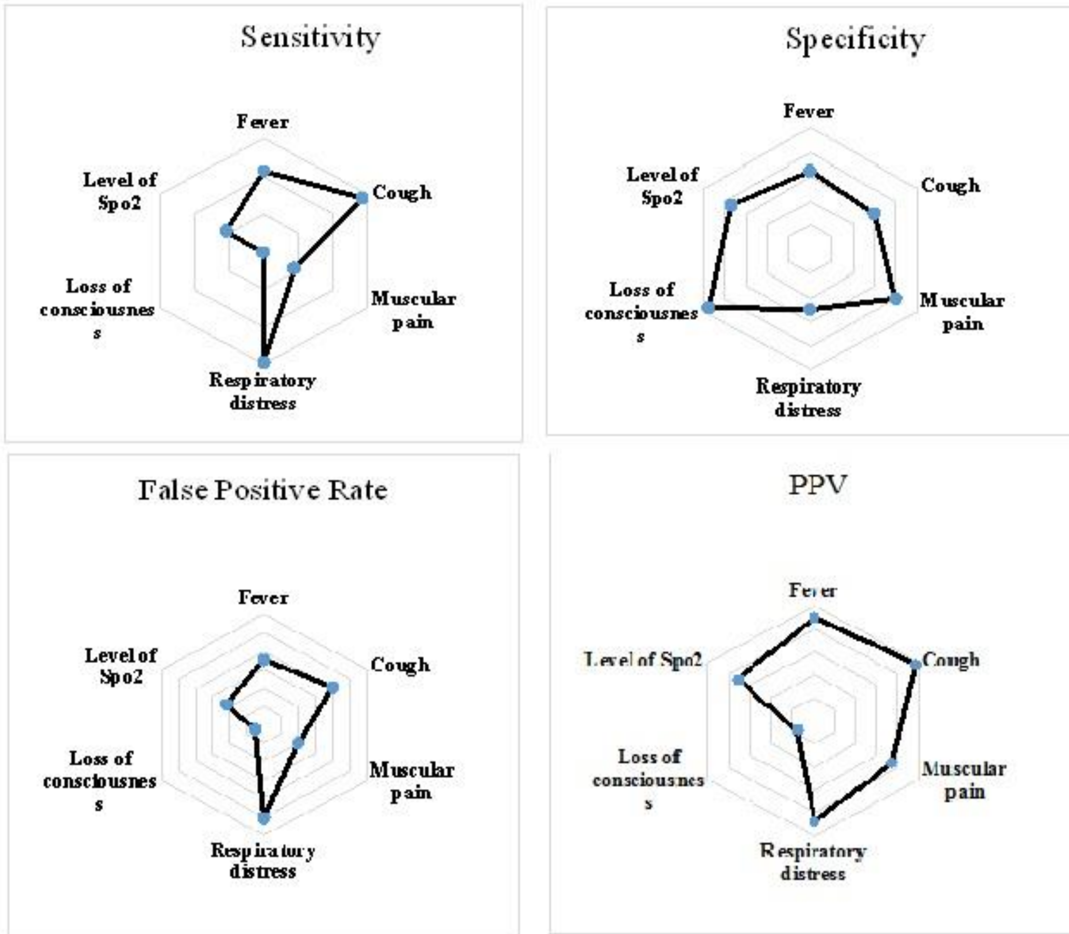

Fig.1. The performance of different symptoms in the detection of COVID-19

According to ROC areas, the Cough had the best performance in detecting COVID-19 (Under ROC areas 0.59). Fever and Dyspnea were in the next order according to Under ROC areas (0.54). AUC ranges from 0 to 1 (Fig. 2). According to multiple regression analysis, the odds ratio of COVID-19 for fever was 2.20(0.92-5.31). It means that the chance of COVID-19 among cases with a fever was twofold that of patients who didn't have these symptoms. The chance of COVID-19 among cough cases was twofold in patients who didn't have these symptoms 2.91(1.26-6.73). The odds ratio for COVID-19 among Dyspnea cases was 2.84(1.29-6.24) (Table3).

Table 2. The performance of different symptoms in the detection of COVID-19

Symptoms	Sensitivity	Specificity	False Alarm Rate	False Negative	LR+	LR-	PPV
Fever	0.43 (0. 35-0.50)	0.65 (0.59-0.71)	0.35 (0.29-0.41)	0.57 (0.50-0.65)	1.21	0.88	0.45 (0.37-0.53)
Cough	0.57 (0.49-0.65)	0.60 (0.53-0.66)	0.40 (0.34-0.47)	0.43 (0.35-0.51)	1.41	0.72	0.49 (0.41-0.56)
Muscular pain	0.17 (0.11-0.23)	0.80 (0.75-0.85)	0.20 (0.15-0.25)	0.83 (0.77-0.89)	0.87	1.03	0.37 (0.26-0.48)
Dyspnea (Respiratory distress)	0.59 (0.51-0.66)	0.49 (0.43-0.56)	0.51 (0.44-0.57)	0.41 (0.34-0.49)	1.16	0.84	0.44 (0.37-0.50)
Level of O_2S	0.22 (0.15-0.28)	0.74 (0.68-0.79)	0.26 (0.21-0.32)	0.78 (0.72-85)	0.83	1.06	0.36 (0.26-0.45)
Ansomia	0.01 (0.001-0.02)	0.95 (0.92-0.98)	0.05 (0.02-0.08)	0.99 (0.98-1.01)	0.12	1.05	0.08 (0.00-0.22)
Fever+ Cough	0.25 (0.18-0.32)	0.84 (0.80-0.89)	0.16 (0.11-0.20)	0.75 (0.68-0.82)	1.61	0.89	0.52 (0.41-0.63)
Fever+ Dyspnea	0.19 (0.13-0.26)	0.85 (0.80-0.89)	0.15 (0.11-0.20)	0.81 (0.74-0.87)	1.28	0.95	0.46 (0.34-0.58)
Cough+ Dyspnea	0.29 (0.22-0.36)	0.81 (0.75-0.86)	0.19 (0.14-0.25)	0.71 (0.64-0.78)	1.49	0.88	0.50 (0.40-0.60)
Fever+ O_2S	0.09 (0.05-0.14)	0.89 (0.85-0.93)	0.11 (0.07-0.15)	0.91 (0.86-0.95)	0.83	1.02	0.36 (0.21-0.51)
Cough+O_2S	0.13 (0.08-0.18)	0.89 (0.85-0.93)	0.11 (0.07-0.15)	0.87 (0. 82-0.92)	1.19	0.98	0.44 (0.30-0.59)

According to ROC areas, the Cough had the best performance in detecting COVID-19 (Under ROC areas 0.59). Fever and Dyspnea were in the next order according to Under ROC areas (0.54). AUC ranges from 0 to 1 (Fig. 2). According to multiple regression analysis, the odds ratio of COVID-19 for fever was 2.20(0.92-5.31). It means that the chance of COVID-19 among cases with a fever was twofold that of patients who didn't have these symptoms. The chance of COVID-19 among cough cases was twofold in patients who didn't have these symptoms 2.91(1.26-6.73). The odds ratio for COVID-19 among Dyspnea cases was 2.84(1.29-6.24) (Table3).

Table 3. Multiple analysis of symptomatology of 392 patients presenting for COVID-19 suspicion*

Variable	OR	Se	Z	P	95% CI for OR	
Fever	2.20	0.99	1.76	0.08	0.92	5.31
Cough	2.91	1.24	2.50	0.01	1.26	6.73
Muscular pain	0.92	0.26	-0.30	0.76	0.52	1.61
Dyspnea (Respiratory distress)	2.84	1.14	2.60	0.01	1.29	6.24

* Adjusted for age and gender

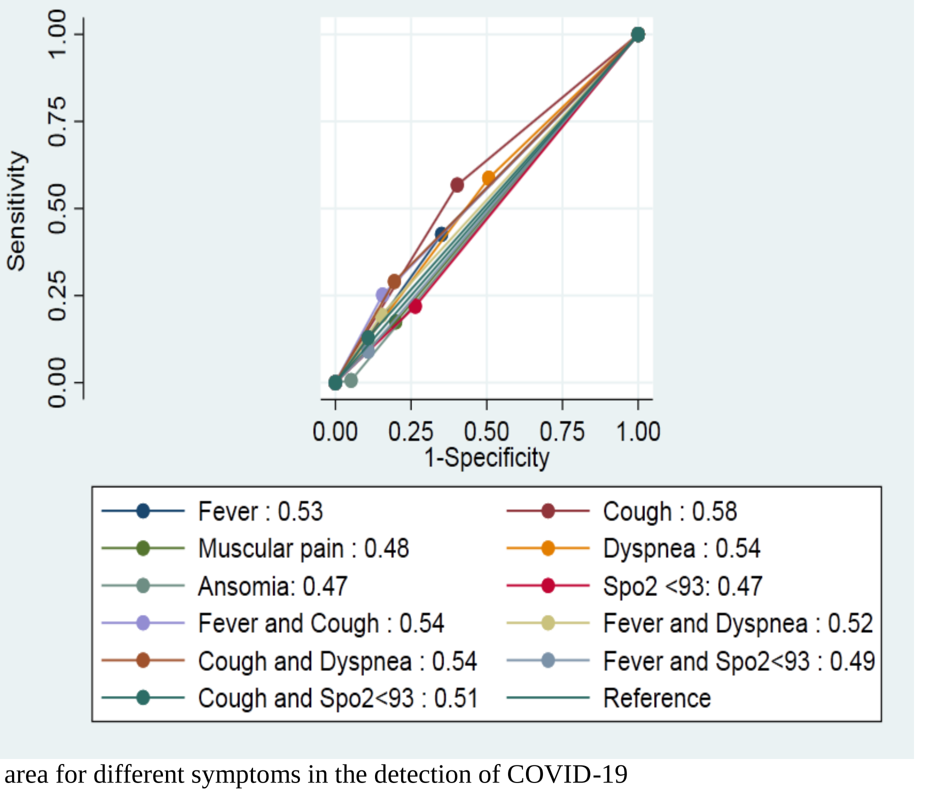

Fig. 2. The Under-ROC area for different symptoms in the detection of COVID-19

Discussion

This study provides beneficial findings about the syndromic diagnosis of COVID-19 in 446 patients. General symptoms (Dyspnea (53%), cough (47%), and fever (38%) were commonly reported by patients. Cough and fever have been previously reported as early symptoms in mild cases [9], and fever occurs in most hospitalized patients [10]. In the present study, fever was not the most sensitive in detecting COVID-19 among suspect patients, which is consistent with other study findings [11, 12]. While the accuracy of a diagnostic test is a characteristic of the test, the Positive and Negative Predictive Values are affected by the prevalence of the disease in the population.

Rapid diagnoses of COVID-19 infection are essential for detecting and early isolating infected patients and decreasing the growth of infection in society. Therefore, finding some easy-access diagnostic tools such as syndromic detection may be crucial, especially in middle and low-income countries with no laboratory test facilities [13]. RT-PCR is the gold standard method for COVID-19 diagnosis [14]. Its false negative rate is 1.5% to 58%, and the test positive result depends on the time after COVID-19 symptoms (the positive test rate on the first and 8th day is 38% and 20%, respectively) [15]. To our knowledge, this is the first research about the sensitivity and specificity of COVID-19 syndromes in the Middle East. However, some countries conducted it earlier [12, 13]. We found the most frequent symptom was Dyspnea(53%), close to the French study that was performed on 391 patients (58.2%) [16], and the prevalence of cough (47%) and fever (38%) were lower than other studies (60%-70% and 78.2% respectively) [13, 16]. The difference between prevalence might be due to ignorance of fever and cough as COVID-19 symptoms in our patients; they just report COVID-19 symptoms after appearing dyspnea (as alarm sign). So, our patients probably referred to the health system at the late stage of infection, and during this period the risk of spreading the virus in society would be high. According to this study, the sensitivity of cough and fever was 57% and 43%, respectively, they were lower than two previous French [16, 17] researches in which the sensitivity of cough and fever was 70.4% and 78% respectively [16, 17]. In a recent study, sensitivity of dyspnea was 59%, higher than French research (32%) [16]. The difference between the sensitivity of the present research and other studies might be due to the later attendance of our patients in the health centers. The patients might ignore fever and cough as COVID-19 clues, but just after the dyspnea (as important complaints), persons return to covid-19 center and report them. Regarding specificity of symptoms, we found anosmia the most specific symptom for COVID-19 (95%). Anosmia is dominant in European youth, and we found the specificity of it nearly the same as in French and German studies (91% and 97% respectively) [16, 17]. Mexican and Netherlands researchers proposed multiple symptoms for syndromic diagnosis of COVID-19 [13,18]. We also used a combination of two symptoms for the evaluation of syndromic diagnosis proficiency in COVID-19 patients . We found that "cough and dyspnea" were the most sensitive syndrome (29%) .

Meanwhile, the most specific syndromes for COVID-19 diagnosis were both "low O2S and cough" and " low O2S and fever "(89%). On the other hand, we found that "cough and fever" sensitivity was 25% lower than the Mexican investigation (44.8%) [13]; however, the specificity of this syndrome ("cough and fever") was 84%, similar to another study [13]. We found that the "fever and dyspnea" sensitivity was 19%, lower than the Mexican study (33.4%). Meanwhile, the specificity of "fever and dyspnea" syndrome was 85%, close to the Mexican investigation (88.07%) [13]. The current study had some limitations, which include being a single center and a relatively small sample size.

Regarding the PCR test, which was used as the gold standard in this study, it is important to mention that it can cause false negatives and positives. Therefore, a negative result in a person cannot rule out the possibility of viral infection. So, our results may be affected by this issue. In future studies, it is better to use a combination of PCR test results and clinical characteristics to diagnose the disease. The strength of the present work is that this is the first study on syndromic diagnosis of COVID-19 in Middle East countries that are overwhelmed with COVID-19 infection.

Conclusion

According to the results, some symptoms showed acceptable performance in diagnosing the COVID-19 case. So, using different symptoms to diagnose COVID-19 can be a cost-effective method, especially in less developed and developing countries. Therefore, these symptoms can be used as a primary and inexpensive tool for initial screening of suspects. More detailed tests can be performed in later stages to confirm the diagnosis.

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Conflict of interest

None declared.

Funding

None declared.

Ethical Considerations

The ethical committee at the Aja University of Medical Sciences approved the current study.

Code of Ethics

The ethical committee at the Aja University of Medical Sciences approved the current study (and registered with ID: IR.AJAUMS.REC.1399.065.).

Authors' Contributions

Yousef Alimohamadi: Wrote the manuscript, Contributed to data collection, Critically reviewed the manuscript, and Approved the final version, Analyzed the data, Critically reviewed, Edited the manuscript. Mojtaba Sepandi: Wrote the manuscript, Contributed to data collection, Critically reviewed the manuscript, and Approved the final version, Analyzed the data, Critically reviewed, Edited the manuscript. Homeira Sedighi Nezhad: Wrote the manuscript, Contributed to data collection, Critically reviewed the manuscript, and Approved the final version, Analyzed the data, Critically reviewed, Edited the manuscript.

References

1. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. Cochrane Database Syst Rev. 2020;7(7):CD013665.

2. Jain V, Yuan JM. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. Int J Public Health. 2020;65(5):533-46.
3. Yombi JC, De Greef J, Marsin AS, Simon A, Rodriguez-Villalobos H, Penaloza A, et al. Symptom-based screening for COVID-19 in health care workers: The importance of fever. J Hosp Infect. 2020;105(3):428-9.
4. Clemency BM, Varughese R, Scheafer DK, Ludwig B, Welch JV, McCormack RF, et al. Symptom Criteria for COVID-19 Testing of Heath Care Workers. Acad Emerg Med. 2020;27(6):469-74.
5. Roland LT, Gurrola JG 2nd, Loftus PA, Cheung SW, Chang JL. Smell and taste symptom-based predictive model for COVID-19 diagnosis. Int Forum Allergy Rhinol. 2020;10(7):832-8.
6. Marando M, Tamburello A, Gianella P, Taylor R, Bernasconi E, Fusi-Schmidhauser T: Diagnostic sensitivity of RT-PCR assays on nasopharyngeal specimens for detection of SARS-CoV-2 infection: A Systematic Review and Meta-Analysis. Caspian J Intern Med. 2022;13(Suppl 3):139-47.
7. Kostoulas P, Eusebi P, Hartnack S. Diagnostic Accuracy Estimates for COVID-19 Real-Time Polymerase Chain Reaction and Lateral Flow Immunoassay Tests With Bayesian Latent-Class Models. Am J Epidemiol. 2021;190(8):1689-95.
8. Sepandi M, Heidarian Miri H, Rajaeefard A. Receiver operating characteristic curve's application and interpretation in medical research. Jentashapir J Cell Mol Biol. 2010;1(1):e94039.
9. Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic Transmission of SARS-CoV-2 - Singapore, January 23-March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(14):411-5.
10. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Science China. Sci China Life Sci. 2020;63(5):706-11.
11. Tostmann A, Bradley J, Bousema T, Yiek WK, Holwerda M, Bleeker-Rovers C, et al. Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020. Euro Surveill. 2020;25(16):2000508.
12. Kluytmans-van den Bergh MFQ, Buiting AGM, Pas SD, Bentvelsen RG, van den Bijllaardt W, van Oudheusden AJG, et al. SARS-CoV-2 infection in 86 healthcare workers in two Dutch hospitals in March 2020. medRxiv. 2020:2020-03.
13. Romero-Gameros CA, Colin-Martínez T, Waizel-Haiat S, Vargas-Ortega G, Ferat-Osorio E, Guerrero-Paz JA, et al. Diagnostic accuracy of symptoms as a diagnostic tool for SARS-CoV 2 infection: a cross-sectional study in a cohort of 2,173 patients. BMC Infect Dis. 2021;21(1):255.
14. Romero-Gameros CA, Waizel-Haiat S, Mendoza-Zubieta V, Anaya-Dyck A, López-Moreno MA, Colin-Martinez T, et al. Evaluation of predictive value of olfactory dysfunction, as a screening tool for COVID-19. Laryngoscope Investig Otolaryngol. 2020;5(6):983-91.
15. Beeching NJ, Fletcher TE, Fowler R. Coronoavirus disease 2019 (COVID-19). BMJ Best Practices. 2020.
16. Peyrony O, Marbeuf-Gueye C, Truong V, Giroud M, Rivière C, Khenissi K, et al. Accuracy of emergency department clinical findings for diagnosis of coronavirus disease 2019. Ann Emerg Med. 2020;76(4):405-12.
17. Salmon Ceron D, Bartier S, Hautefort C, Nguyen Y, Nevoux J, Hamel AL, et al. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter Coranosmia cohort study. J Infect. 2020;81(4):614-20.
18. Tostmann A, Bradley J, Bousema T, Yiek WK, Holwerda M, Bleeker-Rovers C, et al. Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020. Euro Surveill. 2020;25(16):2000508.