

Comparison of the clinical differences between COVID-19, SARS, influenza, and the common cold: A systematic literature review

Jacek Czubak^{1,A,B,D}, Karolina Stolarczyk^{1,B,D}, Anna Orzeł^{2,C,D}, Marcin Frączek^{1,E,F}, Tomasz Zatoński^{1,E,F}

¹ Department and Clinic of Otolaryngology, Head and Neck Surgery, Wrocław Medical University, Poland

² Faculty of Medicine, Medical University of Lublin, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of the article

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Address for correspondence

Jacek Czubak

E-mail: jacekcz90@gmail.com

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Abstract

Background. This review focuses on the frequency of symptoms in COVID-19 in comparison to SARS, influenza and common cold.

Objectives. To evaluate and compare the knowledge about the clinical features, symptoms and differences between patients with COVID-19, SARS, influenza, and common cold. The research can help ear, nose and throat specialists and other health practitioners manage patients during the COVID-19 pandemic.

Material and methods. The biomedical databases used in the study included PubMed and MEDLINE. Statistical analysis using the Z-score test assessed which symptoms were more characteristic of COVID-19 than other viral diseases.

Results. Among individuals with COVID-19, the most frequently reported symptoms were cough (70%), fever (45%), muscular pain (29%), and headache (21%), whereas sore throat (12%), and rhinorrhea (4%) were observed at lower rates. Fever was identified as most frequent in COVID-19 (74%), appearing at a higher rate in those cases than in influenza (68%) or the common cold (40%) ($p < 0.05$). In comparison to other viral diseases, sore throat was rarely reported in COVID-19 and SARS (12% and 18%, respectively) ($p < 0.05$). In influenza and common cold, a cough was identified in 93% and 80% of cases ($p < 0.05$). Headache, rhinorrhea, muscular pain, and sore throat were more common in influenza (91%, 91%, 94%, and 84%, respectively) and common cold (89%, 81%, 94%, and 84%, respectively) than in COVID-19 (21%, 4%, 29%, and 12%, respectively) and SARS (45%, 12%, 55%, and 18%, respectively) ($p < 0.05$).

Conclusions. The results of the analysis show that a greater number of general symptoms should lead to a diagnosis of influenza or common cold rather than COVID-19.

Key words: influenza, ENT, common cold, COVID-19, SARS

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Introduction

The outbreak of the COVID-19 coronavirus epidemic in the Chinese city of Wuhan and its spread have become a global threat. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a β -coronavirus and the 7th coronavirus to be identified that causes human disease. Overall, SARS-CoV-2 was the 3rd zoonotic human coronavirus of the century.^{1,2} It is spread by human-to-human transmission via droplets over short distances (1.5 m), direct contact or (potentially) the gastrointestinal tract.^{3–5} It creates a high risk for virus transmission during ears, nose and throat (ENT) examination, especially during the direct examination of patients' respiratory tract. Moreover, recent studies indicate that ENT specialists are among the groups at a higher risk of exposure to the virus.⁶

COVID-19 is similar to the disease caused by SARS-CoV. Although SARS-CoV-2 is less virulent, it is more infectious and its rapid spread has led to the coronavirus pandemic.^{7,8} According to present clinical data about COVID-19, the symptoms of the disease may affect the upper respiratory tract, similarly to SARS, influenza and common cold. These similarities can pose a major diagnostic problem for any physician.

Every year, the world faces seasonal flu caused by influenza viruses. Three types of influenza viruses affect humans, the most common being type A and type B.⁹ Approximately 30–50% of cases of common cold are caused by rhinoviruses. The second-most common agents are human coronaviruses (HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63), which account for 10–15% of cases of this disease. The other causes associated with the common cold are adenoviruses, human respiratory syncytial virus (orthopneumovirus), enteroviruses, and human parainfluenza viruses.¹⁰

This review focuses on the frequency of symptoms in COVID-19 in comparison to SARS, influenza and common cold. Additionally, the research assesses the incidence of upper respiratory tract symptoms and influenza-like symptoms for the abovementioned viral diseases. To the best of our knowledge, no previous reports have focused on the differential diagnosis between those infectious diseases. The data presented herein are important for ENT specialists, who are often the first-line doctors for patients with upper respiratory tract infection.

Objectives

The aim of the study was to evaluate and compare information about the clinical features, symptoms and differences between patients with COVID-19, SARS, influenza, and common cold. The research can help ENT specialists and other health practitioners around the world manage patients in the current COVID-19 pandemic.

Material and methods

The database presented in the study was built from the results of 9 studies published after March 2003.^{11–19} Only articles with data about symptoms of upper respiratory tract infection, such as fever, cough, muscular pain, headache, sore throat, and rhinorrhea, were included. Based on the search strategy, 1729 studies were found in the online database. Then, 1676 articles were excluded after the titles and abstracts were reviewed. The full texts of 53 articles were evaluated. Finally, 9 articles were included in the systematic literature review (Fig. 1).

The data was from 5400 patients with the following diseases: 1347 patients with COVID-19 (25.44%), 2470 patients with influenza (45.74%), 282 patients with SARS (5.22%), and 1274 patients with common cold (23.59%). Selected clinical presentation of patients with COVID-19, influenza, SARS, and common cold is also presented in Tables 1,2,3.

PubMed was the biomedical database used in the study. To identify the studies for potential review, the following search terms were used: "COVID-19," "SARS," "influenza," "common cold," "upper respiratory symptoms," "influenza-like symptoms," "otolaryngology," "ENT," and "otolaryngological manifestation." The Boolean operators "NOT," "AND" and "OR" were also used in succession to narrow and widen the search.

Only the following symptoms were taken into consideration while comparing the diseases: fever, sore throat, rhinorrhea, headache, cough, and myalgia. Our review was focused on studies about COVID-19, SARS, influenza, and common cold in which upper respiratory tract symptoms and influenza-like symptoms were considered, since they are the most common, mutual shared symptoms. Therefore, a large number of studies focusing on other symptoms (such as gastrointestinal symptoms or cardiologic symptoms) were excluded, which may have led to the omission of some important studies.

The search was limited to publications in English.

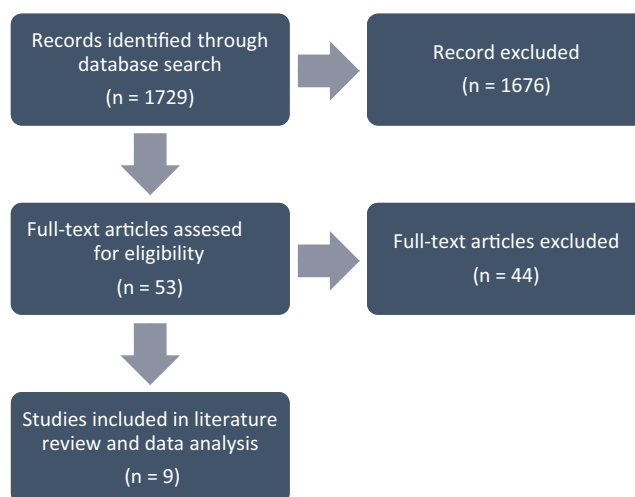


Fig. 1. A flow diagram of the inclusion criteria of studies eligible for the systematic literature review

Table 1. Selected clinical presentation of patients with COVID-19

Symptoms	Study							
	Wang et al. ¹¹ (n = 138) (%)	Chen et al. ¹² (n = 99) (%)	Huang et al. ¹³ (n = 41) (%)	Kim et al. ¹⁴ (n = 28) (%)	Jin et al. ¹⁵ (n = 74) (n = 577) no GI symptoms (n = 577) (%)	Jin et al. ¹⁵ (n = 577) (%)	Lechien et al. ¹⁶ (n = 417) (%)	Pooled data (n = 1374) (%)
Age, mean [years]	56	55.5	49	42.6	46.14	45.09	36.9	47.3
Sex								
female	63 (45.7)	32 (32)	11 (27)	13 (46.4)	37 (50)	283 (49)	263 (63)	702 (51)
male	75 (54.3)	67 (68)	30 (73)	15 (53.6)	37 (50)	294 (51)	154 (37)	672 (49)
Main symptom	fever	fever	fever	cough	fever	fever	cough	fever
Fever	136 (98.6)	82 (83)	40 (98)	7 (25.0)	63 (85.14)	482 (84)	204 (49)	1014 (74)
Sore throat	24 (17.4)	5 (5)	–	8 (28.6)	6 (8.11)	93 (16)	33 (7.93)	169 (12)
Rhinorrhea	–	4 (4)	–	2 (7.1)	2 (2.70)	35 (6)	18 (4.34)	61 (4)
Headache	9 (6.5)	8 (8)	3/38 (8)	7 (25.0)	16 (21.62)	51 (9)	196 (45)	290 (21)
Cough	82 (59.4)	81 (82)	31 (76)	8 (28.6)	53 (71.62)	382 (66)	329 (79)	966 (70)
Myalgia	48 (34.8)	11 (11)	18 (44)	7 (25.0)	10 (13.51)	61 (11)	246 (59)	401 (29)
Postnasal drip	–	–	–	–	–	–	29 (6.97)	29 (2.11)
Ear pain	–	–	–	–	–	–	13 (3.13)	13 (0.95)
Nasal obstruction	–	–	–	–	2 (2.70)	35 (6.07)	50 (12.02)	87 (6.33)
Facial pain/heaviness	–	–	–	–	–	–	54 (12.98)	54 (3.93)
Dyspnea	43 (31.2)	31 (31)	22 (55)	–	–	–	19 (4.57)	115 (8.36)
Diarrhea	14 (10.1)	2 (2)	1 (3)	3 (10.7)	53 (71.62)	–	51 (12.23)	124 (9.02)
Nausea	14 (10.1)	1 (1)	–	–	10 (13.52)	–	21 (5.03)	46 (3.34)
Vomiting	5 (3.6)	1 (1)	–	–	11 (14.86)	–	21 (5.03)	38 (2.76)
Abdominal pain	3 (2.2)	–	–	1 (3.6)	–	–	30 (7.19)	34 (2.47)
Dizziness	13 (9.4)	–	–	–	–	–	–	13 (0.95)

Table 2. Selected clinical presentation of patients with influenza and the common cold

Symptoms	Study: Monto et al. ¹⁷	
	Laboratory confirmed tested negative for influenza (n = 2470) (%)	Influenza (common cold) (n = 1274) (%)
Age, mean [years]	34.8	34.5
Sex		
female	1223 (49.5)	697 (54.7)
male	1247 (50.5)	577 (45.3)
Main symptom	myalgia	myalgia
Fever	848 (68)	510 (40)
Sore throat	2075 (84)	1070 (84)
Rhinorrhea	2248 (91)	1032 (81)
Headache	2248 (91)	1134 (89)
Cough	2298 (93)	1019 (80)
Myalgia	2321 (94)	1198 (94)
Nasal obstruction	2248 (91)	1032 (81)
Loss of appetite	2272 (92)	1096 (86)
Weakness	2321 (94)	1198 (94)

Table 3. Selected clinical presentation of patients with SARS

Symptoms	Study		
	Booth et al. ¹⁸ (n = 144) (%)	Lee et al. ¹⁹ (n = 138) (%)	Pooled data (n = 282) (%)
Age, mean [years]	45	39.3	42.15
Sex			
female	88 (61)	72 (52)	160 (57)
male	56 (39)	66 (48)	122 (43)
Main symptom	fever	fever	fever
Fever	143 (99.3)	138 (100)	281 (100)
Sore throat	18 (12.5)	32 (23.3)	50 (18)
Rhinorrhea	3 (2.1)	31 (22.5)	34 (12)
Headache	51 (35.4)	31 (22.5)	128 (45)
Cough	100 (69.4)	79 (57.3)	179 (63)
Myalgia	71 (49.3)	84 (60.9)	155 (55)
Nausea	28 (19.4)	27 (19.6)	55 (19.5)
Vomiting	28 (19.4)	27 (19.6)	55 (19.5)
Diarrhea	34 (23.6)	27 (19.6)	61 (21.6)
Dizziness	6 (4.2)	59 (42.8)	65 (23)
Dyspnea	60 (41.7)	–	60 (21.3)
Malaise	45 (31.2)	–	45 (16)
Arthralgia	15 (10.4)	–	15 (5.3)
Chest pain	15 (10.4)	–	15 (5.3)
Abdominal pain	5 (3.5)	–	5 (1.8)

Articles that did not address the selected topics, low-quality studies, case reports, and studies based on non-significant cohorts were excluded. The full texts of the remaining high-quality articles were examined and elaborated on.

The data analysis involved frequency tables with numerical and percentage values, descriptive statistics, and statistical tests. Statistical analysis was performed using IBM SPSS Statistics v. 25 software (IBM Corp., Armonk, USA). The tests involved in the data analysis were the χ^2 and Z-score tests. The non-parametric χ^2 test was used to assess the differences in the appearance of symptoms in studied diseases: COVID-19, influenza, SARS, and common cold. The level of statistical significance was set at $p = 0.05$.

The Z-score test was used to compare the results of independent studies with large sample sizes. It was used to compare patients with COVID-19 and patients with other diseases under study in pairs in terms of the frequency of symptom appearance. Such an approach can determine which symptom was more likely to be observed in COVID-19, and can possibly lead to its diagnosis. Each studied disease was compared separately with COVID-19. The level of statistical significance was set at $p = 0.05$.

Results

The data regarding the symptoms in viral diseases was analyzed and the results are presented as descriptive and percentage values (Table 4). Moreover, the statistical significance was assessed with a p -value < 0.05 . The analyzed cases of patients with viral diseases indicated that the distribution of symptoms was differentiated. Among individuals with COVID-19, the most frequently reported symptoms were fever (74%), cough (70%), muscular pain (29%), and headache (21%), whereas sore throat (12%) and rhinorrhea (4%) were observed at lower rates (Table 4). Regarding patients with influenza, all of the symptoms were identified in the majority of cases: myalgia (94%), cough (93%), rhinorrhea (91%), headache (91%), sore throat (84%), and fever (68%) (Table 4). In common cold, 94% of patients endured muscle pain, the most frequent symptom in that disease. Furthermore, 89% of the patients reported headache, 84% sore throat, 81% rhinorrhea, and 80% cough; however, a fever was reported in only 40% of cases (Table 4). When it comes to individuals with SARS, fever was the symptom observed most often (100%). A cough was

reported in 179 patients (63%), headache in 128 (45%) and rhinorrhea in 34 patients (12%). On the other hand, sore throat was identified only in 18% of patients with SARS (Table 4). These results, showing differences in the frequency of symptoms in viral diseases were found to be statistically significant ($p < 0.05$; Table 4).

The statistical analysis using the Z-score test allowed us to assess which symptoms were more characteristic of COVID-19 than of other viral diseases. Fever was identified as the most frequent symptom in COVID-19 (74%), appearing at a higher rate than in influenza (68%) or common cold (40%) ($p < 0.05$). On the other hand, 100% of patients with SARS infection reported having a fever (Table 4). In comparison to the other viral diseases, patients with COVID-19 and SARS rarely reported sore throat (12% and 18%, respectively) ($p < 0.05$). However, in influenza and in common cold, cough was identified in 93% and 80% of patients, respectively ($p < 0.05$). Headache, rhinorrhea, muscular pain, and sore throat were more common in influenza (91%, 91%, 94%, and 84%, respectively) and in common cold (89%, 81%, 94%, and 84%, respectively) than in COVID-19 (21%, 4%, 29%, and 12%, respectively) or SARS (45%, 12%, 55%, and 18%, respectively) ($p < 0.05$; Table 4). Other symptoms are also presented in Tables 1,2,3.

Discussion

To the best of our knowledge, this review is the first to compare the upper respiratory tract and influenza-like symptoms in COVID-19, SARS, influenza, and common cold. Knowledge of the frequency of upper respiratory tract symptoms and influenza-like symptoms in COVID-19, SARS, influenza, and common cold could be used in the differential diagnosis.

The clinical classification divides COVID-19 into 4 types based on the severity of the symptoms. The 1st one, the mild type, is defined as having slight clinical symptoms without pneumonia in radiography, which can be asymptomatic or imitating the common cold.^{3,13,15} The 2nd one, the moderate type, is defined as presenting with fever and/or respiratory symptoms, plus pneumonia

Table 4. Comparison of symptom frequency between the studied diseases

Variable	COVID 19	Influenza	SARS	Common cold
Number of cases	1374	2470	282	1274
Fever	1014 (74%)	848 (68%)	281 (100%)	510 (40%)
Sore throat	169 (12%)	2075 (84%)	50 (18%)	1070 (84%)
Rhinorrhea	61 (4%)	2248 (91%)	34 (12%)	1032 (81%)
Headache	290 (21%)	2248 (91%)	128 (45%)	1134 (89%)
Cough	966 (70%)	2298 (93%)	179 (63%)	1019 (80%)
Myalgia	401 (29%)	2321 (94%)	155 (55%)	1198 (94%)

$p < 0.00001$; result are significant at $p < 0.05$.

in radiography, which may resemble influenza.^{3,13} The 3rd one, the severe type, is diagnosed based on dyspnea (a respiratory rate ≥ 30 times/min), a resting finger oxygen saturation $\leq 93\%$ and an arterial $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 300 mm Hg (1 mm Hg = 0.133 kPa). The last, the critical type, is defined as respiratory failure with shock and multiple organ failure, requiring mechanical ventilation and admission to the intensive care unit (ICU).^{3,14} The last 2 types can imitate SARS.

The analysis of clinical data in the study indicated significant similarities in the frequency of the symptoms fever and cough in infections caused by SARS-CoV (100% and 63%, respectively) and SARS-CoV2 (74% and 70%, respectively). The results show that it may not be possible to distinguish among the viral diseases under study judging only by the clinical presentation. The study reveals that general symptoms, like headache and myalgia, or non-specific upper respiratory tract inflammation symptoms, such as sore throat and rhinorrhea, are more likely to be found in patients with influenza or common cold than in patients with COVID-19. Ninety-four percent of patients with both influenza and the common cold reported myalgia, whereas in the case of COVID-19 patients, this symptom was observed in 29% of cases. The results show that an increased number of general symptoms should lead to a diagnosis of influenza rather than COVID-19. In the case of common cold, symptoms like headache, myalgia, rhinorrhea, and sore throat will appear more likely than fever. As in a study by Monto et al., comparing influenza and common cold, those factors can be used in common cold and COVID-19 for the initial differential diagnosis.¹⁷ Therefore, a lack of fever and the presence of headache, myalgia, rhinorrhea, and sore throat could suggest a diagnosis of common cold.

Anosmia and gustatory dysfunction are characteristic signs of SARS-CoV-2 infection. Recently published studies have demonstrated that anosmia and hyposmia can appear before the respiratory symptoms of COVID-19, or even as the only sign of the infection.²⁰ It should also be pointed out that anosmia and gustatory dysfunction can occur in patients who do not complain of nasal blockage or any other rhinitis symptoms.²¹ That could indicate direct damage from the virus on the olfactory and gustatory receptors. Researchers from South Korea, China, Germany, France, and Italy have found that a significant number of individuals with COVID-19 were affected by hyposmia or anosmia. For example, in a study by Lechien et al., anosmia occurred in 86% of patients and gustatory dysfunction was present in 88.8% of patients.¹⁶ Further, in a study by Klopfenstein et al., anosmia occurred in 47% of patients and was associated with dysgeusia in 85% of cases.²¹ Those smell disorders are very rare in SARS or other coronavirus infections.²² Therefore, the British Association of Otorhinolaryngology (ENT-UK) includes a loss of the sense of smell in their list of COVID-19 markers of infection.²⁰ Lechien et al. also observed that 3% of COVID-19 patients complained

of ear pain, 6.97% of postnasal drip and 13% of facial pain/heaviness. In the other articles analyzed, those symptoms were not found; therefore, these symptoms were not taken into consideration.¹⁶ However, it has to be considered that asymptomatic and mild infections of SARS-CoV-2 are frequent. That is why a physician should always treat their patients as potentially infected and follow appropriate precautions to avoid the further spread of the virus. Due to the non-specific symptoms presented in COVID-19, patients cannot be diagnosed solely by clinical presentation; only laboratory tests can confirm a diagnosis. The presence of a wide range of general symptoms (headache, rhinorrhea, myalgia, and sore throat) should lead physicians to clinically suspect influenza or common cold rather than COVID-19. This could then guide medical decisions to be made before confirmatory tests are available.


Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) is a specific molecular examination for SARS-CoV-2. It is performed on specimens which are obtained mainly from nasopharyngeal swabs or oropharyngeal swabs, but also from the stool.^{23,24} Wang et al. recommend samples from the lower respiratory tract of the patients (sputum and bronchoalveolar lavage fluid), although nasopharyngeal swab is more commonly used and easier to obtain.^{24,25} Recent studies suggest that chest computed tomography (CT) is a sensitive diagnostic tool for COVID-19 diagnosis with a sensitivity of 97% in a patient with positive RT-PCR tests.^{24,26} Interestingly, even asymptomatic patients with COVID-19 had radiological changes in their lungs 1 day after exposure, which is also helpful in differential diagnostics.¹⁴ In influenza, RT-PCR and viral culturing have a sensitivity close to 100%, but the turnaround time for a viral culture is 3–10 days compared to 1–8 h for RT-PCR.⁹ In SARS, RT-PCR is the method of the first choice for detection.²⁷

Conclusions


Although further investigation is required to strengthen the observation made in the present study, our results add some evidence that could be used in the differential diagnosis of COVID-19, SARS, influenza, and common cold.


ORCID iDs

Jacek Czubałak  <https://orcid.org/0000-0003-0205-1955>

Karolina Stolarczyk  <https://orcid.org/0000-0002-4514-0387>

Anna Orzeł  <https://orcid.org/0000-0002-5908-6967>

Marcin Frączek  <https://orcid.org/0000-0003-0181-122X>

Tomasz Zatoński  <https://orcid.org/0000-0003-3043-4806>

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