

Sore Throat, an Early Sign in Covid-19? Prevalence and Changing Trends with New Viral Variants

Graça Coutinho MD, PhD* and Anuradha Kulasekaran MBBS, MD

Global Medical Science Respiratory, Reckitt Benckiser Healthcare Ltd, UK

*Corresponding author: Graça Coutinho MD, PhD, Global Medical Science Respiratory, Reckitt Benckiser Healthcare Ltd, Slough, UK

Received: September 15, 2021

Published: October 13, 2021

Abstract

Among the various manifestations of coronavirus (SARs-COV-2) infection 2019 (COVID-19), sore throat can be one of the early signs of the disease and is fairly common in both children and adults. Initial reports revealed that the prevalence of sore throat in COVID-19 patients varies by region, with different prevalence reported; for example, 29% in Asia and 7% in North America. However, more recent data from across the world have shown an increase in prevalence of sore throat to approximately 50% of patients. This may be explained by the spread of new strains, such as the Alpha and Delta variants, which are more frequently associated with otolaryngologic symptoms. Thus, in countries where the Delta variant is now predominant, sore throat is reported as one of the most common symptoms from severe respiratory COVID-19 infection. The emergence of these new variants of concern with changing associated symptoms, including sore throat, can be relevant for the individual patient's well-being as well as public healthcare. While symptoms of mild COVID-19, and in particular sore throat, can be managed with self-care medication, the recognition and accurate description of the current COVID-19 symptoms could, for instance, help direct patients to COVID-19 testing. The increased prevalence of sore throat with the Alpha and Delta variants should be considered for the diagnosis and early treatment of COVID-19, as well as the application of all relevant hygiene measures. This is particularly important during the cold and flu season, where sore throat could also be a symptom of other seasonal viruses. We reviewed recent literature regarding sore throat in patients with COVID-19 to better understand its prevalence and changing trends with new variants.

Keywords: sore throat; COVID-19; prevalence; SARS-CoV-2 variants; COVID-19 symptoms; COVID-19 symptoms treatment.

Introduction

In December 2019, the World Health Organisation (WHO) was informed of cases of pneumonia of unknown cause in Wuhan City, China. A novel coronavirus was identified as the cause and the virus spread globally, causing an outbreak of disease around the world. The coronavirus disease 2019 (COVID-19) pandemic was declared by WHO on 11 March 2020 [1]. COVID-19 is an infectious respiratory disease caused by SARS-CoV-2 and has been responsible for over 4.5 million deaths globally as of 8 September 2021 [2].

Global strategies such as mass testing, quarantine rules, regional lockdowns and large vaccination efforts have been put in place to control and prevent transmission. However, SARS-CoV-2 is constantly evolving giving rise to new variants that have increased the spread of infection globally and have been associated with the emergence of new symptoms. There is, therefore, a need to maintain monitoring of the disease and to evolve our understanding of COVID-19 as viral variants emerge.

The majority of COVID-19 patients suffer symptoms [3], which may be multifarious, touching practically all organ sys-

tems [4]. Initially, the most common symptoms of COVID-19 were reported as fever, dry-cough and fatigue [5]. However, during April 2020 a change or loss of taste or smell was added to the WHO's list of less-common COVID-19 symptoms. Shortly after, it was added to their list of most common symptoms after researchers identified it as a key symptom of disease, noting that people should isolate if they experience this change [6]. With new variants emerging and new knowledge acquired, it is important that the common list of symptoms is updated accordingly.

Sore throat (acute pharyngitis), although underreported earlier during the pandemic, is one of the early signs and common symptoms of COVID-19 [7-10]. Here we review the prevalence of sore throat in patients with COVID-19 and its evolution with different viral variants. As an early sign of COVID-19, we have also considered the potential implications for healthcare and early symptomatic treatment.

Prevalence of Sore Throat in Patients with COVID-19

Initially, prevalence of sore throat in patients with COVID-19 was either low, under reported, or may have been ignored be-

cause it is a relatively common symptom for many conditions, such as the common cold or the irritation from allergies [11]. In addition, the reported prevalence of sore throat in COVID-19 varied by region (Table 1), with the highest rates reported in Asian COVID-19 patients (except for China) compared with the lowest prevalence of sore throat in North American patients (29% vs 7%, respectively) [12]. However, during the course of the pandemic the prevalence of sore throat in COVID-19 patients has increased and sore throat is becoming an increasingly important early sign of COVID-19.

In more recent studies, sore throat was found in up to 56%, 47% and 46% of COVID-19 patients in Japan [13], Singapore [14] and Australia [15], respectively, and up to 45.8% of the patients in the United States [16]. Furthermore, a comprehensive analysis of COVID-19 in eight Latin America (LATAM) countries showed that the symptoms differed from the global data, where-in sore throat (44%) stood out as the third most common symptom with cough (60%) and fatigue or tiredness (52%) being foremost in hierarchy [17]. In Brazil, a retrospective analysis of nationwide data showed that sore throats were reported in 73% of hospitalised COVID-19 patients; the incidences differed in regions with 25% of Brazilian patients having sore throats [18]. Moreover, a retrospective and transversal study in 26 Mexican states from June 1 to September 30, 2020, showed that sore throat comprised 36% of outpatient's symptoms in those who tested positive for SARS-CoV-2 virus (46%) [19]. Those with post-COVID syndrome also suffer from persistence of symptoms including odynophagia (sore throats) with a relative risk of 2.3 [20].

A systematic international review identified sore throat as the most common otolaryngologic (ORL) manifestation of the disease, although the reported prevalence varied widely (4-81.6%) [21]. Beyond reporting issues [10] and regional variances [12], other reasons for the apparent differences of COVID-19 symptoms have been suspected, including the emergence of new viral strains [22]. The viral variants may explain some of the regional variances as well as the changing prevalence of certain symptoms, such as sore throat, during the course of the pandemic.

Table 1: Prevalence of sore throat in COVID-19 [12].

Continent	Number of studies	Prevalence, mean (95% confidence interval)
Asia (except China)	4	29% (19-39%)
Australia	1	24% (20-30%)
China	22	12% (9-15%)
Europe	5	24% (1-48%)
North America	2	7% (4-10%)

Table 2: Variants of concern causing COVID-19 [25, 26].

Variant	Country (date) of first discovery	Prevalence of sore throat
Alpha (B.1.1.7)	United Kingdom (September 2020)	Increased [23]
Beta (B.1.351)	South Africa (September 2020)	not known
Gamma (P1)	Brazil (December 2020)	not known
Delta (B.1.617.2)	India (December 2020)	Increased [24]

SARs-CoV-2 variants and Sore Throat

The four SARs-CoV-2 variants (Alpha, Beta, Gamma and Delta) that are currently (i.e., in Summer 2021) most concerning worldwide are listed in Table 2. Some SARS-CoV-2 variants, especially the Alpha and Delta variants, have become dominant because they spread more easily. This is of particular concern as the lifting of lockdown restrictions in many countries allows for the rapid spread of variants among both vaccinated and unvaccinated people, preventing the eradication of COVID-19.

In addition to transmission, these variants may also cause different symptoms than the initial strain (novel SARS-CoV-2; nSARS-CoV-2). Thus, among other symptoms (e.g., fatigue and myalgia), sore throat is reported more frequently with the new SARS-CoV-2 variants, such as the Alpha variant [23]. In the United Kingdom (UK) since May 2021, the Delta variant has become the dominant strain [27] and is found in over 99% of all COVID-19 cases [28]. In spring 2021, almost half of the patients with COVID-19 in the UK had sore throat, which was more common in 18–65-year-olds (49%) than in those >65 years (37%) or <18 years (40%) [29]. With the surge of the Delta variant, the prevalence of ORL symptoms has increased, and sore throat emerges as the second most common COVID-19 symptom after headache, before runny nose, fever and cough [24]. According to the leader of the UK COVID Symptom Study [24], Tim Spector (professor of genetic epidemiology at King's College London), the symptoms of COVID-19 infection (i.e., with the Delta strain) now resemble those of a bad cold [30]. These findings confirm previous reports that the new variants cause more frequently cough, sore throat, fatigue or myalgia than the preceding variants [23].

These findings from UK-based studies are supported by observations of the Delta variant in other areas of the world. LATAM countries have reported sore throat as one of the four most common symptoms. Mexico, now experiencing its own uptick in contagion, has the highest confirmed caseload [20] of the variant in the region with just around 600 cases; it is also present in Argentina, Brazil, Chile, and Peru with fewer than 25 cases identified in each country as of July 13. The rising cases of LATAM COVID-19 Delta variant is known from other countries to manifest with sore throat. For example, in a recent sample of COVID-19 patients in a tertiary care centre in India, where the Delta variant has become the dominant strain, most patients (77.8%) had throat-related symptoms, with sore throat representing the most common ORL symptom (49.2%) [31]. Thus, ensuring our knowledge of the circulating variants is up to date is required to understand how to control spread and to support management of patients with COVID-19. For the Delta variant, early treatment of sore throat symptoms may help patients with symptomatic relief.

Implications for Healthcare Professionals

Despite high vaccination rates in many countries, the COVID-19 pandemic continues unabated, with more cases reported already in the first 5 months of 2021 than in the whole of 2020 [32]. New strategies for the prevention, detection and treatment of the disease will, therefore, be needed to halt a rapid increase in cases as new variants emerge. It is important that the symptoms associated with the new variants are understood to ensure patients do not dismiss their symptoms or assume they are unrelated to COVID-19.

At present, a persistent cough is no longer the top indicator of having COVID-19 if you have had two vaccine doses; however, a sore throat is [24]. In addition, recent research in the UK

has suggested the Delta variant of COVID-19 may be presenting similar to a cold, with a sore throat being a more frequently observed symptom [30]. Despite this, WHO advice remains that the most common symptoms of the virus are a fever, a new cough, tiredness, and a loss or change in smell or taste; sore throat is listed as a less common symptom [6]. It is important that sore throat is recognised as a key symptom, and there have been calls from researchers for authorities to add sore throat to the existing three symptoms that trigger a COVID-19 test [33]. It is imperative that the significance of mild symptoms is recognised, in order to prevent people dismissing their symptoms and continuing with their daily lives whilst unknowingly passing on infection and causing the spread of the disease. Not only will this support prevention and control of the disease, but it will also support healthcare professionals to manage patients effectively. Furthermore, managing sore throat in the early stages may prevent the immune inflammatory response which facilitates bacterial co-infection to proceed [34,35].

Discussion and Conclusion

Sore throat has been recognised as one of the main symptoms of COVID-19 infection, especially with the Delta variant. This finding is relevant regarding both the individual patient's well-being and public healthcare. Further research regarding whether sore throat is an early indicator of COVID-19 is needed to support early testing and isolation of patients suffering from these symptoms, which may ultimately reduce the spread of infection.

Early management of symptoms that may appear minor, such as sore throat, can ultimately prevent the spread of infection and help to avoid bacterial co-infection, which may require antibiotics further down the line. Emerging evidence suggests that respiratory viral infections, such as SARS-CoV-2, predispose patients to bacterial co-infections, which leads to increased disease severity and mortality [35]. The increased inflammatory response produced by a viral infection facilitates bacterial infection by providing more sites for adhesion, impairing immune responses and causing cell and tissue destruction [34]. This allows for the spread of bacteria and development of invasive infection [34]. There are increasing reports of antibiotic resistant bacterial infections in European hospitals during COVID-19 surges [36]. This highlights the need to proactively manage early, mild symptoms to avoid huge healthcare burden and prevent severe patient infection. Bacterial co-infections showing resistance to antibiotics have the ability to cause severe illness, reducing patient quality of life (QOL), and increasing mortality. Understanding that patients are suffering from sore throat helps to relieve the patients suffering with this symptom, which is known to have an impact in their QOL in the short term [37].

Although the influence of the other variants on COVID-19 symptoms remains to be elucidated, the increased prevalence of sore throat with the Alpha and Delta variants should be considered for both the diagnosis and the treatment of COVID-19. As the virus that causes COVID-19 will continue to mutate and new variants will spread, close tracking is key to maintain and improve the performance of diagnostic tools, vaccines, therapeutic medicines and other healthcare measures [38]. It is important that healthcare guidance available to the public is updated frequently with emerging information on treatment guidance in accordance with the changing symptoms associated with viral variants.

Author contributions: GC and AK conducted the search, analysis and interpretation of the literature included within this review. They revised the manuscript critically for important intellectual content and approved the final version to be published.

Competing interests: GC and AK are employees of Reckitt Benckiser Health Ltd.

Grant information: The author(s) received no specific funding for this work.

Acknowledgements: Medical Writing support was provided by Don Dreher, MD, PhD, ECPM (Totzke & Dreher Scientific SA) and Donna Carre (Reckitt).

References

1. WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020. World Health Organisation. 2020 (consulted on 15 September 2021): WHO Director-General's opening remarks at the media briefing on COVID-19 - 2020.
2. WHO. WHO Coronavirus (COVID-19) Dashboard. World Health Organisation, 2021.
3. Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *J Assoc Med Microbiol Infect*, 2020; 5(4): 223-234.
4. Duerden M, Coutinho G, Kulasekaran A. Worldwide Comparison of Symptoms and Symptomatic Treatment Recommendations in Mild COVID-19. *Curr Med Res Opin*, 2021; 04(08): 1009-1025.
5. WHO. Coronavirus Disease (COVID-19): What are the symptoms of COVID-19? World Health Organisation. 2020: Coronavirus disease (COVID-19) (who.int), 2021.
6. WHO. Coronavirus: Symptoms. World Health Organisation. 2021: Coronavirus (who.int), 2021.
7. Weng LM, Su X, Wang XQ. Pain Symptoms in Patients with Coronavirus Disease (COVID-19): A Literature Review. *J Pain Res*, 2021; 14: 147-159.
8. Meyer-Friessem CH, Gierthmühlen J, Baron R, Sommer C, Uceyler N, Enax-Krumova EK. Pain during and after COVID-19 in Germany and worldwide: a narrative review of current knowledge. *Pain reports*, 2021; 6(1): e893.
9. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. *PloS one*, 2020; 15(6): e0234765.
10. Lovato A, Rossetti G, de Filippis C. Sore throat in COVID-19: Comment on "Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis". *J Med Virol*, 2020; 92(7): 714-715.
11. Harris, K. Is my sore throat COVID-19 or not? OSF Healthcare. 2021: Is my sore throat COVID-19 or not? OSF HealthCare, 2021.
12. Singhavi H, Pai A, Mair M, Singhavi J, Gandhi P, Baker A, et al. SARS-Cov2: a meta-analysis of symptom distribution by continent in 7310 adult COVID-19 infected patients. *Virusdisease*, 2021: 1-10.
13. Kimura Y, Nogami K, Watanabe K, Yoshimura T, Asai H, Fujioaka O, et al. COVID-19 findings revealed via otolaryngological examination: Findings of a Japan Otorhinolaryngologist Association questionnaire. *Auris, nasus, larynx*. 2021; 48(6): 1176-1180.
14. Pung R, Chiew CJ, Young BE, Chin S, Chen MI, Clapham HE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. *Lancet (London, England)*, 2020; 395(10229): 1039-1046.
15. Covid-19 National Incident Room Surveillance Team. COVID-19, Australia: Epidemiology Report 7 (Reporting week ending 19:00 AEDT 14 March 2020). *Communicable diseases intelligence*. 2020; 44.
16. Lan FY, Filler R, Mathew S, Buley J, Iliaki E, Bruno-Murtha LA, et al. COVID-19 symptoms predictive of healthcare workers'

- SARS-CoV-2 PCR results. PloS one. 2020; 15(6): e0235460.
17. Miguel A Fernández-Rojas, Luna-Ruiz-Esparza MA, Campos-Romera A, Calva-Espinosa DY, Moreno-Camacho JL, Ariadna P, et al. Epidemiology of COVID-19 in Mexico: Symptomatic profiles and presymptomatic people. *Int J Infect Dis*, 2021; 104: 572-579.
 18. Ranzani OT, Bastos LSL, Gelli JGM, Marchesi JF, Baião F, Hamacher S, et al. Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. *Lancet Respir Med*, 2021; 9(4): 407-418.
 19. Galván-Tejada CE, Herrera-García CF, Godina-González S, Villagrana-Bañuelos KE, Amaro JDDL, Herrera-García K, et al. Persistence of COVID-19 Symptoms after Recovery in Mexican Population. *Int J Environ Res Public Health*, 2020; 17(24): 9367.
 20. Chase H. Explainer: Covid Variants in Latin America. Americas Society/Council of the Americas, 2021.
 21. Al-Swiahb JN, Motiwala MA. Upper respiratory tract and otolaryngological manifestations of coronavirus disease 2019 (COVID-19): A systemic review. *SAGE open medicine*, 2021; 9: 20503121211016965.
 22. Kim SY, Kim DW. Does the Clinical Spectrum of Coronavirus Disease 2019 (COVID-19) Show Regional Differences? *Clin Exp Otorhinolaryngol*, 2020; 13(2): 83-84.
 23. Mahase E. Covid-19: Sore throat, fatigue, and myalgia are more common with new UK variant. *Br Med J (Clinical research ed)*, 2021; 372: n288.
 24. COVID Symptom Study. What are the symptoms of COVID-19 if you're unvaccinated? ZOE COVID Study - UK Data. 2021; What are the new top 5 COVID symptoms?, 2021.
 25. CDC. About Variants of the Virus that Causes COVID-19. Centers for Disease Control and Prevention - United States. 2021; Your Health. About COVID-19, 2021.
 26. ECDC. SARS-CoV-2 variants of concern as of 26 August 2021. European Centre for Disease Prevention and Control. 2021; All topics: A to Z. Situation updates on COVID-19, 2021.
 27. Torjesen I. Covid-19: Delta variant is now UK's most dominant strain and spreading through schools. *Br Med J*, 2021; 373: n1445.
 28. O'Dowd A. Covid-19: Cases of delta variant rise by 79%, but rate of growth slows. *Br Med J*, 2021; 373: n1596.
 29. COVID Symptom Study. Is a sore throat a symptom of COVID-19? ZOE COVID Study - UK Data. 2021; Symptom Series. Sore throat, 2021.
 30. Grover N. Delta variant Covid symptoms include headaches, sore throat and runny nose. *The Guardian*. 2021; International edition (online). Europe – Coronavirus, 2021.
 31. Gosavi S, Nagarajan S, Shah NJ, Thomas NAT, Kumar KR, Sangole V. ENT Symptomology in Active COVID-19 Patients in our Tertiary Care Centre. *Indian J Otolaryngol Head Neck Surg*, 2021: 1-6.
 32. Sergeant J, Stucka M, Thorson M. Coronavirus cases in 2021 are already higher than 2020 worldwide. These seven charts break down the spread. *USA Today*, 2021.
 33. Schraer R. Covid: Seven symptoms should trigger virus test, study says. *BBC News* 2021: Covid: Seven symptoms should trigger virus test, study says - BBC News, 2021.
 34. Mirzaei R, Goodarzi P, Asadi M, Soltani A, Aljanabi HAA, Jeda AS, et al. Bacterial co-infections with SARS-CoV-2. *IUBMB Life*, 2020; 72(10): 2097-2111.
 35. Morris DE, Cleary DW, Clark SC. Secondary Bacterial Infections Associated with Influenza Pandemics. *Front Microbiol*, 2017; 8: 1041.
 36. Westblade LF, Simon MS, Satlin MJ. Bacterial CoinfectionS in Coronavirus Disease 2019. *Trends Microbiol*, 2021; 29(10): 930–941.
 37. Ware JE Jr, Coutinho G, Smith A, Tselenti E, Kulasekaran A. The Effects of Increased Acute Respiratory Symptom Frequency on Health-related Quality of Life in the 2020 US General Population. Manuscript in preparation, 2021.
 38. WHO. Tracking SARS-CoV-2 variants. World Health Organization, 2021.