Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Research note

Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19

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ABSTRACT

Objectives: Detailed knowledge on the prevalence of asymptomatic cases of coronavirus disease 2019 (COVID-19) and the clinical characteristics of mild COVID-19 is essential for effective control of the COVID-19 pandemic. We determined the prevalence of asymptomatic cases of COVID-19 and characterized the symptoms of patients with mild COVID-19.

Methods: Study participants were recruited from a community facility designated for the isolation of patients without moderate-to-severe symptoms of COVID-19 in South Korea. The prevalence of asymptomatic patients at admission and the detailed symptoms of mild COVID-19 were evaluated through a questionnaire-based survey. Diagnosis of COVID-19 was confirmed by real-time RT-PCR.

Results: Of the 213 individuals with COVID-19, 41 (19.2%) were asymptomatic until admission. Among the remaining patients with mild COVID-19, the most common symptom was cough (40.1%; 69/172), followed by hyposmia (39.5%; 68/172) and sputum (39.5%; 68/172). Of the 68 individuals with hyposmia, 61 (90%) had accompanying symptoms such as hypogeusia, nasal congestion or rhinorrhoea. Fever (>37.5°C) was only observed in 20 (11.6%) individuals.

Conclusions: As much as one-fifth of individuals with COVID-19 remained asymptomatic from exposure to admission. Hyposmia was quite frequent among individuals with mild COVID-19, but fever was not. Social distancing should be strongly implemented to prevent disease transmission from asymptomatic individuals or those with mild and inconspicuous symptoms. **G.-u. Kim, Clin Microbiol Infect 2020;26:948.e1–948.e3**

Introduction

In South Korea, the largest cluster of cases related to the religious group Shincheonji was recognized in Daegu city from 12 February 2020 [1]. Korean epidemiological teams meticulously sought out the close contacts of this religious group and performed extensive laboratory tests for SARS-CoV-2 in all the identified close contacts. As a result, 3081 cases of coronavirus disease 2019 (COVID-19) were confirmed in Daegu city alone as of 2 March 2020, approximately 70% of whom were related to this religious group [1].

As a result of the sharp increase in the number of patients with COVID-19 in Daegu, the Korean government decided to admit those without moderate-to-severe illness or risk factors for poor prognosis to a non-hospital facility for isolation and monitoring. This policy provided a unique chance to assess the prevalence of asymptomatic individuals in this outbreak and to characterize the symptoms of people with mild COVID-19.

Methods

As of 2 March 2020, a total of 19 636 diagnostic tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had been performed in the Daegu area [2]. Of these tests, 12 947 (66%) were performed in the general population in Daegu city and 6689 (34%) were performed in those related to the Shincheonji church; of the latter, about 60% had positive results [2]. As such, a total of 3081 individuals were diagnosed in the Daegu area, almost 70% (2136/

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3081) of whom were related to the religious group [2]. These 3081 individuals with confirmed COVID-19 were isolated in hospitals and community isolation facilities, depending on their risk assessment. Among 17 community isolation facilities, our facility housed 260 individuals. The Korean government and Daegu local government allocated individuals with mild COVID-19 to dedicated isolation facilities and the remaining individuals with moderate-to-severe COVID-19 (early warning score for SARS-CoV-2 infection patients ≥4) or those with high risk to hospitals [3]. The high-risk factors for COVID-19 were as follows: (a) ≥65 years, (b) chronic underlying diseases (e.g. diabetes mellitus, chronic renal failure, chronic liver disease, chronic lung disease, chronic cardiovascular disease), (c) haematological malignancy, and (d) those receiving chemotherapy or immunosuppressive agents. Regardless of their symptoms, all confirmed patients were isolated in hospitals or isolation facilities according to their risk assessment.

We conducted a questionnaire survey from 12 to 16 March 2020 in a community facility designated for the isolation of individuals with COVID-19; this facility is located approximately 50 miles from Daegu city. Diagnosis of COVID-19 was based on the results of real-time RT-PCR (Allplex 2019-nCoV Assay kit; Seegene, Seoul, South Korea), for SARS-CoV-2 E gene, RdRp gene and N gene using nasopharyngeal swab samples as authorized by the Korean government. Written informed consent was obtained from each participant who agreed to participate in this questionnaire study. Missing data were acquired with telephone interviews by trained doctors. The study protocol was approved by the Institutional Review Board of Asan Medical Centre (Seoul, Korea).

Results

Of the 260 PCR-confirmed individuals with COVID-19, 213 (81.9%) participated in this study. Of them, 41 (19.2%, 95% CI 14.5%–25.1%) had remained asymptomatic until admission.

Table 1
Clinical presentation of the 172 symptomatic individuals with mild COVID-19[a]

	n (%)
Age, median (IQR), years	26 (22–47)
Male sex	66 (38.4)
Fever (>37.5°C)	20 (11.6)
Cough	69 (40.1)
Sputum	68 (39.5)
Hyposmia[b]	68 (39.5)
Nasal congestion	59 (34.3)
Hypogeusia	58 (33.7)
Myalgia	54 (31.4)
Headache	54 (31.4)
Fatigue	46 (26.7)
Rhinorrhoea	45 (26.2)
Dizziness	32 (18.6)
Chills	31 (18.0)
Sore throat	31 (18.0)
Diarrhoea	27 (15.7)
Anorexia	23 (13.4)
Dyspnoea	7 (4.1)
Nausea	7 (4.1)
Abdominal pain	5 (2.9)
Pleuritic chest pain	3 (1.7)
Vomiting	2 (1.2)
Haemoptysis	1 (0.6)
Time from initial symptoms to diagnosis, median (IQR), days	14 (8–17)
Time from diagnosis to admission, median (IQR), days	3 (3–6)

COVID-19, coronavirus disease 2019; IQR, interquartile range.
[a] Of 213 participating individuals, 41 asymptomatic individuals were excluded from the analysis.
[b] Among 68 individuals with hyposmia, 32 (47.1%) complained of having nasal congestion.

In the remaining 172 individuals, the median duration from the first symptom to laboratory confirmation was 14 days (interquartile range 8–17), and the median duration from laboratory confirmation to admission was 3 days (interquartile range 3–6). Cough (40.1%; 69/172) was the most common symptom, followed by sputum (39.5%; 68/172), hyposmia (39.5%; 68/172), and nasal congestion (34.3%; 59/172). Of the 68 individuals with hyposmia, 61 (90%) had accompanying symptoms such as hypogeusia, nasal congestion or rhinorrhea. Fever (>37.5°C) was noted in only 20 (11.6%) individuals. The detailed clinical characteristics of the symptomatic patients are shown in Table 1 (and see Supplementary material, Fig. S1), and Table S1 (see Supplementary material) shows the distribution of the symptoms according to different time-points (i.e. symptom onset, at diagnosis, at admission).

Discussion

The presence of asymptomatic cases of COVID-19 was noted in early reports on the outbreak [4,5] and a large study on 72 314 Chinese patients reported that 1% were asymptomatic [6]. However, the majority of those cases were included from Hubei province, where the sudden shortage of health-care resources may have resulted in selection bias towards the exclusion of those with mild symptoms. Therefore, the actual prevalence of asymptomatic cases of COVID-19 could not be determined. We found that as much as one-fifth of individuals with COVID-19 had remained asymptomatic from potential exposure to laboratory confirmation and facility admission. Hence, our data fill an important gap concerning the prevalence of asymptomatic individuals, who constitute the base of the disease pyramid [7]. Previous studies reported that viable SARS-CoV-2 was isolated from asymptomatic individuals and that certain groups of infections had been transmitted from asymptomatic patients [8–10]; therefore, the notably high proportion of asymptomatic individuals in our data further supports the value of social distancing for the control of the current pandemic until a vaccine becomes available.

Separating individuals with suspected COVID-19 from other patients in outpatient clinics is critical for preventing a potential outbreak in the health-care setting. Therefore, it is important to delineate the epidemiological risk factors and clinical features of COVID-19. Furthermore, the pandemic spread of SARS-CoV-2 may weaken the role of epidemiological risk factors and clinical features of COVID-19 will become more important for screening. However, there are limited data on the symptoms of individuals with mild COVID-19. A recent Chinese study on 13 individuals with mild COVID-19 reported that nasal congestion (62%) was the most common symptom [11]. In our 172 individuals, the most common symptom was cough, followed by hyposmia and sputum, while fever (>37.5°C) was only observed in 11.6%.

Interestingly, hyposmia was quite frequent among individuals with mild COVID-19. Although hyposmia is caused by postviral olfactory dysfunction [12], further studies are needed for the specificity of this symptom in COVID-19. In addition, pathophysiological studies are needed to determine whether this unique symptom is associated with nasal congestion, dysfunction of the olfactory nerve due to SARS-CoV-2, or other co-morbidities.

This study has several limitations. First, the study population shows a dominance of young age and female sex, which is largely due to the fact that most individuals were associated with a single religious group. Therefore, the results of this study may not be directly applicable to older populations or to males. Nevertheless, this is the largest study to date on the prevalence of asymptomatic patients and the detailed clinical symptoms in individuals with mild COVID-19. Second, the study design has inherent recall bias. However, the study participants were well educated and cooperative, so this bias may not have substantially affected our main findings.

Third, we did not compare the symptoms of individuals with COVID-19 from those of patients with other respiratory viral infections, so further studies are needed on whether some dominant symptoms, such as hyposmia, are helpful to differentiate individuals with COVID-19 from those with other respiratory viral illnesses. Fourth, we did not perform other diagnostic tests to rule out the presence of co-infections. As a result, some of the symptoms presented in the study population might be associated with co-infections. A recent study reported that 20% of individuals with COVID-19 in northern California had one or more respiratory pathogens, including rhinovirus, respiratory syncytial virus, human coronavirus and influenza virus [13]. Therefore, our findings on the symptoms of individuals with mild COVID-19 should be considered with caution. Finally, some selection bias may have been introduced in this survey-based study considering that approximately 18% of patients at the isolation facility did not participate in the study.

In conclusion, approximately one-fifth of individuals with mild COVID-19 were asymptomatic at admission and the most common symptoms of mild COVID-19 were cough with or without hyposmia and sputum. Further research on the contribution of asymptomatic or mildly symptomatic individuals to the community spread of COVID-19 is essential for effective control of the pandemic spread of SARS-CoV-2.

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Transparency declaration

There are no potential conflicts of interest for any authors.

Authors' contribution

GK, SHR and SHK contributed to the analysis and interpretation of data; GK, MJK, SHR, JL, SB and JJ collected and assembled the data; GK, MJK, SHR, SHK were responsible for the concept and design of the study; and SHK drafted the article and obtained the funding. GK, MJK, SHR, JL, SB, JJ and SHK were responsible for the critical revision for important intellectual content and for the final approval of the article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2020.04.040.

References

[1] Korean Society of Infectious Diseases. Report on the epidemiological features of coronavirus disease 2019 (COVID-19) outbreak in the Republic of Korea from January 19 to March 2, 2020. J Korean Med Sci 2010;35:e112.
[2] [Korean, Daegu city home page], https://blog.naver.com/daegu_news/221835400627.
[3] Kim SW, Lee KS, Kim K, Lee JJ, Kim JY. A Brief Telephone Severity Scoring System and Therapeutic Living Centers Solved Acute Hospital-Bed Shortage during the COVID-19 Outbreak in Daegu, Korea. J Korean Med Sci 2020;35:e152.
[4] Chan JFW, Yuan S, Kok KH, Huang L. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395:514–23.
[5] Rothe C, Schunk M, Sothmann P, Bretzel G, Groeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med 2020;382:970–1.
[6] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. JAMA 2020. epub ahead of print.
[7] Munster VJ, Koopmans M, Doremalen NV, Riel DV, Wi ED. A novel coronavirus emerging in China—key questions for impact assessment. N Engl J Med 2020;382:692–4.
[8] Yu P, Zhu J, Zhang Z, Han Y, Huang L. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis 2020. epub ahead of print.
[9] Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. JAMA 2020. epub ahead of print.
[10] Hoehl S, Berger A, Kortenbusch M, Kortenbusch M, Cinatl J, Bojkova D, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. N Engl J Med 2020. epub ahead of print.
[11] Chang D, Lin M, Wei L, Xie L, Zhu G, Cruz CSD, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. JAMA 2020. epub ahead of print.
[12] Wang JH, Kwon HJ, Jang YJ. Detection of parainfluenza virus 3 in turbinate epithelial cells of postviral olfactory dysfunction patients. Laryngoscope 2007;117:1445–9.
[13] Kim Quinn J, Pinsky B, Sha NH, Brown I. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020. https://doi.org/10.1001/jama.2020.6266. epub ahead of print.