Am J Transl Res 2021;13(4):3650-3657
www.ajtr.org /ISSN:1943-8141/AJTR0125446

*Original Article*

# Changes of clinical characteristics of asymptomatic patients with positive SARS-Cov-2 nucleic acid test during treatment cycle and related risk factors

Shuzhen Li[1*], Jiandong Li[2*], Dawei Cao[3], Xinli Hao[3], Yangyang Wei[3], Chaolu Hasi[4], Xinri Zhang[3], Xiaomei Kong[3]

*[1]Department of Infectious Disease Control and Prevention of Shenzhen Baoan Center for Disease Control and Prevention, Shenzhen, Guangdong Province, China; [2]Department of Respiratory and Critical Care Medicine, No. 7 Medical Center, Chinese PLA General Hospital, Beijing, China; [3]Department of Respiratory and Critical Care Medicine, The First Hospital of Shanxi Medical University, Taiyuan, Shanxi Province, China; [4]Inspection Center, The First Hospital of Shanxi Medical University, Taiyuan, Shanxi Province, China. [*]Equal contributors and co-first authors.*

Received November 2, 2020; Accepted December 4, 2020; Epub April 15, 2021; Published April 30, 2021

**Abstract:** Objective: This study was designed to explore the clinical characteristics, outcomes, and related influencing factors for asymptomatic patients with positive Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-Cov-2) nucleic acid test. Methods: Clinical data of 1568 patients with positive SARS-Cov-2 nucleic acid test (SNAT) were collected retrospectively. The patients were assigned to an asymptomatic group and a symptomatic group according to the existence of clinical symptoms when they got positive result in nucleic acid test, and the clinical data of the two groups were analyzed and compared. In addition, the data of asymptomatic patients who showed clinical symptoms later and the results of two-week follow-up after cure were analyzed. Results: Among all enrolled patients, there were 1489 patients with positive symptoms and 79 asymptomatic patients, including 34 patients who developed symptoms during treatment. Logistic analysis revealed that age ≤45 years (OR=2.722, P<0.001), history of diabetes mellitus (OR=0.446, P=0.007), and history of cancer (OR=0.259, P=0.008) were independent factors for asymptomatic presentation in patients with positive SNAT, and age ≥46 years (OR=1.562, P=0.012) and history of hypertension (OR=2.077, P<0.001) were risk factors for the occurrence of clinical symptoms in asymptomatic patients with positive SNAT during hospitalization. During the follow-up after cure, 8 patients got reoccurring positive SNAT result. Conclusion: Asymptomatic patients with positive SNAT are mostly young and middle-aged people, and old age and hypertension are risk factors for the occurrence of positive clinical characteristics in asymptomatic patients.

**Keywords:** Asymptomatic, Corona Virus Disease 2019-COVID-19, SARS-COV-2 nucleic acid test-SNAT, follow-up, risk factor, positive clinical symptoms

## Introduction

Corona Virus Disease 2019 (COVID-19) is the pandemic caused by infection of a newly discovered coronavirus, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2). It spreads to human beings through unknown intermediate hosts, damaging the respiratory system function, and finally endangering the health of patients and even causing death due to multiple organ failure [1]. Recent epidemiology showed that over 10 million patients suffer from COVID-19 worldwide [2-4]. COVID-19 is a highly contagious disease that can spread horizontally among people, which causes a consistent increase in the number of cases. At present, effective control of population flow is confirmed to be the most important measure to control the spread of the disease [5]. However, there is a class of asymptomatic patients who get positive SARS-Cov-2 nucleic acid test (SNAT) but have no clinical symptoms. Such patients also pose a potential risk of infection [6].

SNAT for asymptomatic SARS-Cov-2-positive patients have been listed as the focus of

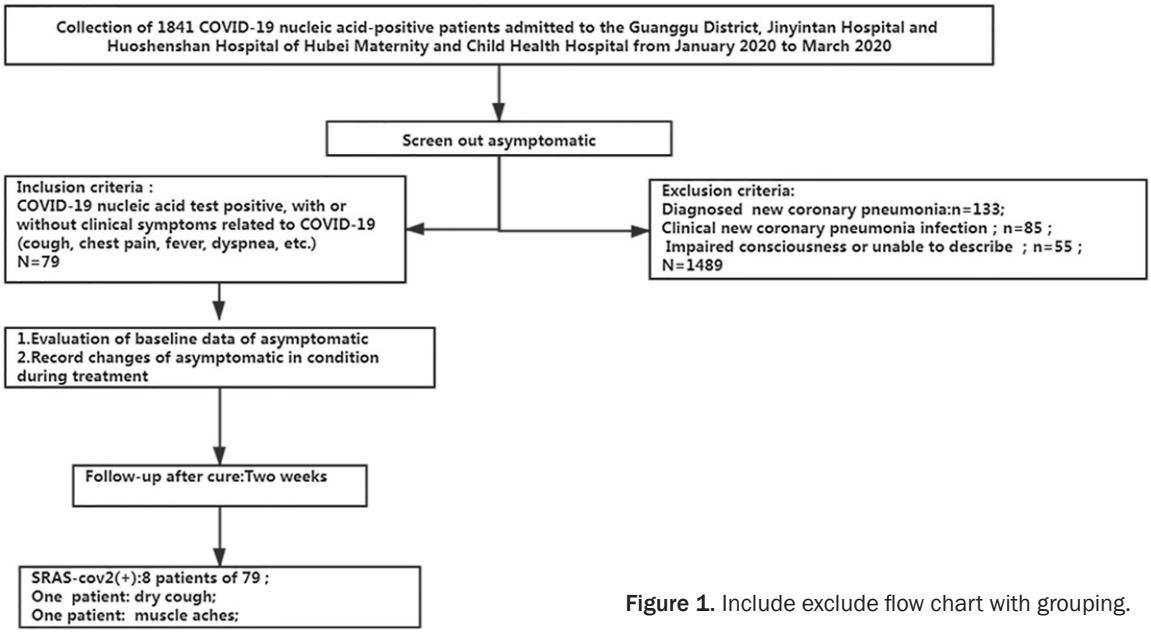


**Figure 1.** Include exclude flow chart with grouping.

COVID-19 prevention and control, but there are still few studies on the infection route and clinical characteristics of such patients and the reoccurring positive SNAT after discharge [7, 8]. The existing studies are mostly reports on individual cases [9, 10]. Therefore, this study aimed to explore the clinical characteristics of asymptomatic patients with positive SNAT through multi-center data analysis, with the goal of providing reference and suggestions for clinical treatment and prevention of this pandemic disease.

## Methods and methods

*Collection of clinical data*

In this study, clinical data of 1841 patients with positive SNAT from January 2020 to March 2020 were collected retrospectively. The data of 1568 patients were enrolled finally, with data of 273 patients excluded according to the criteria. Among the patients whose data were enrolled, there were 649 males and 919 females, including 1489 symptomatic SARS-Cov-2-positive patients and 79 asymptomatic SARS-Cov-2-positive patients in first SNAT. This study was conducted with permission from the Ethics Committees of our hospital. All enrolled patients agreed to participate in the study, and the study was in strict accordance with the Declaration of Helsinki [11].

*Inclusion and exclusion criteria*

The inclusion criteria of the study: Patients with positive SNAT at admission and with or without SARS-Cov-2-related clinical symptoms (cough, chest pain, fever, dyspnea, etc.) [12]. The exclusion criteria of the study: Patients diagnosed with SARS-Cov-2 who got negative result in SNAT, and those whose clinical data were missing [13]. See **Figure 1**.

*Determination of asymptomatic patients*

Asymptomatic patients met the Guidelines on the Novel Coronavirus-Infected Pneumonia Diagnosis and Treatment (7th Edition), namely, patients without symptoms including fever, dry cough, hypodynamia, nasal obstruction, pharyngodynia, myalgia, diarrhea got positive result in SNAT at admission.

*Follow-up*

After treatment, patients who got negative results in two nucleic acid tests in different time periods could be discharged, and they were followed up. Before April 12, 79 asymptomatic patients admitted to hospital on February 19th and discharged on March 30th were followed up by three trained experts through telephone interviews or electronic outpatient medical records. The principle was as

follows: In case of symptoms, the patient was required to go back to the hospital to receive reexamination of SARS-Cov-2 nucleic acid immediately. In case of no symptoms, the patient was required to receive SNAT once a week in the hospital. If the SNAT of the patient was positive (the patient was determined to be positive once his/her one test result was positive), he/she would receive reexamination of SARS-Cov-2 nucleic acid one week later. The follow-up period spanned two weeks after discharge.

*Evaluation indexes*

*Primary outcome measures:* Related influencing factors on positive SNAT result without clinical symptoms were analyzed.

*Secondary outcome measures:* Related influencing factors on the occurrence of clinical symptoms in asymptomatic patients with positive SNAT were analyzed, and the rate of reoccurring positive SNAT in asymptomatic patients with positive SNAT after rehabilitation was recorded.

*Statistical analysis*

SPSS 26.0 was adopted for analyses. Bidirectional disordered enumeration data were analyzed using the chi-square test for R*C table, and unidirectional ordered data were analyzed using the multiple independent samples Kruskal-Wallis H test. In addition, risk factors for the reoccurrence of positive clinical symptoms in patients with positive SNAT and no symptoms of patients with positive SNAT were taken as dependent variables, and the indexes of univariate analysis ($P<0.05$) were taken as independent variables and included in binary logistic regression analysis. The conditional step-by-step method was used for statistical analysis. $P<0.05$ indicates a significant difference.

## Results

*Analysis of risks factors for asymptomatic patients and symptomatic patients*

A total of 1568 patients were enrolled in this study, including 79 asymptomatic patients and 1489 symptomatic patients. In both groups, there were more female patients than male patients, and hypertension and diabetes mellitus were the most common underlying diseases of all the patients. In addition, the two groups were not significantly different in comorbid hypertension, coronary heart disease, chronic renal function injury, CT imaging features, and disease classification (all $P>0.05$), while they were significantly different in the proportion of young and middle-aged people, history of diabetes mellitus, history of cancer, monocyte count, alanine aminotransferase (ALT), C-reactive protein (CRP), and clinical classification (all $P<0.05$). Multivariate logistic regression analysis revealed that young and middle age (≤45 years old), history of diabetes mellitus, time from exposure to patients to positive nucleic acid test, and history of cancer were independent risk factors for asymptomatic patients (**Tables 1**-**3**).

According to the statistical results, factor analysis and Logistic regression analysis were carried out.

On the above analysis of factors influencing the asymptomatic representation of patients with positive SNAT among groups, a model of factors influencing the asymptomatic representation with positive SNAT was established. Age, sex, ALT and CRP were assigned according to grade variables, and multivariate Logistic regression analysis was carried out to analyze the factors. In addition, the step-by-step (Ward) method was used to screen the variables, in which the inclusion standard was 0.05 and the exclusion standard was 0.10. The relative factors influencing the asymptomatic representation of patients with positive SNAT were expressed by the calibrated odds ratio (OR value; **Tables 2**, **3**).

*Comparison of clinical data between asymptomatic infected patients who became ill after hospitalization and recessive infected patients without symptoms all the time*

In this study, among the 79 asymptomatic infected patients at admission, 34 patients showed positive clinical features during the admission period. The 79 patients were divided into infected patients with long incubation period (n=34) and recessive infected patients without symptoms all the time (n=45). Further analysis revealed that there were significant differences between the two kinds of patients in age, hypertension and comorbid underlying

**Table 1.** Clinical date

| Characteristics | Value | | $\chi^2$/t | P |
|---|---|---|---|---|
| | Asymptomatic (n=79) | Symptomatic (n=1489) | | |
| Age (years) Distribution (%) | | | 7.488 | 0.006 |
| ≤45 years | 25 (31.65) | 276 (18.54) | | |
| ≥46 years | 54 (68.35) | 1213 (81.46) | | |
| Sex (%) | | | 0.002 | 0.907 |
| Male | 32 (40.51) | 617 (41.44) | | |
| Female | 47 (59.49) | 872 (58.56) | | |
| Coexisting disorder (%) | | | | |
| Respiratory disease | 1 (1.27) | 69 (4.63) | 1.284 | 0.258 |
| Time of contact with SARS-COV-2 (+) to test (d) | 9.5±2.6 | 5.1±1.8 | 20.622 | 0.000 |
| Coronary heart disease | 5 (6.33) | 77 (5.17) | 0.037 | 0.848 |
| Diabetes | 16 (20.25) | 174 (11.69) | 4.398 | 0.036 |
| Hypertension | 17 (21.52) | 406 (27.27) | 0.983 | 0.262 |
| Cerebrovascular disease | 4 (5.06) | 50 (3.36) | 0.243 | 0.647 |
| Chronic hepatopathy | 1 (1.27) | 22 (1.48) | 0.107 | 0.743 |
| Cancer | 5 (6.33) | 27 (1.81) | 5.560 | 0.022 |
| Chronic renal disease | 3 (3.80) | 14 (0.94) | 3.357 | 0.065 |
| Total with ≥2 comorbidity | 12 (15.19) | 299 (20.08) | 0.842 | 0.488 |
| Abnormalities on chest CT (%) | | | 5.110 | 0.078 |
| No abnormal | 7 (8.86) | 57 (3.83) | | |
| Unilateral | 12 (15.19) | 207 (13.90) | | |
| Bilateral | 60 (75.95) | 1225 (82.27) | | |
| Ground-glass opacity | 19 (24.05) | 410 (27.54) | 0.300 | 0.498 |
| Patchy shadowing | 47 (59.49) | 985 (66.15) | 1.197 | 0.224 |
| Interstitial abnormalities | 7 (8.86) | 65 (4.37) | 2.510 | 0.063 |
| Thickening of the adjacent pleura | 11 (13.92) | 186 (12.49) | 0.040 | 0.708 |
| Clinical classification (%) | | | 16.053 | 0.000 |
| Mild | 7 (8.86) | 57 (3.83) | | |
| Popular | 70 (88.61) | 1166 (78.31) | | |
| Severe | 2 (2.53) | 217 (14.57) | | |
| Critical | 0 (0.00) | 49 (3.29) | | |
| Clinical outcome | | | 0.445 | 0.505 |
| Discharged | 79 (100.00) | 1465 (98.39) | | |
| Died | 0 (0.00) | 24 (1.61) | | |

**Table 2.** Variable and assignment of COVID-19 nucleic acid positive asymptomatic influence indicators

| Variate | Name | Value | |
|---|---|---|---|
| Dependent variable | COVID-19 nucleic acid positive asymptomatic | 0= normal | 1= abnormal |
| Independent variable | Age | 0=≤45 years | 1=≥46 years |
| | Diabetes | 0= nonjoinder | 1= joinder |
| | Cancer | 0= nonjoinder | 1= nonjoinder |
| | ALT | 0=≤15 U/L | 1=>15 U/L |
| | CRP | 0=≤0.9 mg/L | 1=>0.9 mg/L |
| | Time from exposure to patients to positive nucleic acid test | 0=≤7 days | 1=>7 days |

Note: ALT: alanine aminotransferase; CRP: C-reactive protein; COVID-19: Corona Virus Disease.

**Table 3.** Influence factor ofCOVID-19 nucleic acid positive asymptomatic

| Factor | β | SE | Wals | P | OR | OR (95% CI) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower limit | Upper limit |
| Age ≤45 years | 1.001 | 0.262 | 14.566 | <0.001 | 2.722 | 1.628 | 4.553 |
| Diabetes | -0.806 | 0.300 | 7.208 | 0.007 | 0.446 | 0.248 | 0.804 |
| Cancer | -1.352 | 0.509 | 7.049 | 0.008 | 0.259 | 0.095 | 0.702 |
| Time from exposure to patients to positive nucleic acid test | 1.841 | 0.372 | 22.733 | <0.001 | 6.303 | 2.147 | 10.947 |

Note: COVID-19: Corona Virus Disease.

**Table 4.** Comparison of clinical data between asymptomatic infected patients who became ill after hospitalization and recessive infected patients without symptoms

| Factor | Infected patients who became ill (n=34) | Recessive infected patients without symptoms (n=45) | $\chi^2$/t | P |
|---|---|---|---|---|
| Age distribution (%) | | | 9.932 | 0.002 |
| ≤45 years | 12 (35.29) | 33 (73.33) | | |
| ≥46 years | 22 (64.71) | 12 (26.67) | | |
| Sex (%) | | | 1.594 | 0.135 |
| Male | 17 (50.00) | 15 (33.33) | | |
| Female | 17 (50.00) | 30 (66.67) | | |
| Coexisting disorder (%) | | | | |
| Asthma | 0 (0.00) | 1 (2.22) | 0.002 | 1.000 |
| Diabetes | 10 (29.41) | 6 (13.33) | 2.184 | 0.078 |
| Hypertension | 15 (44.12) | 2 (4.44) | 15.777 | <0.001 |
| Coronary heart disease | 3 (8.82) | 2 (4.44) | 0.106 | 0.076 |
| Cerebrovascular disease | 2 (5.88) | 2 (4.44) | 0.053 | 1.000 |
| Cancer | 3 (8.82) | 2 (4.44) | 0.106 | 0.076 |
| Chronic renal disease | 3 (8.82) | 0 (0.00) | 2.065 | 0.151 |
| Abnormalities on chest CT (%) | | | 1.789 | 0.453 |
| Unilateral | 7 (20.59) | 5 (11.11) | | |
| Bilateral | 25 (73.53) | 35 (77.78) | | |
| No abnormal | 2 (5.88) | 5 (11.11) | | |
| Ground-glass opacity | 6 (17.65) | 13 (28.89) | 0.795 | 0.247 |
| Patchy shadowing | 23 (67.65) | 24 (53.33) | 0.746 | 0.199 |
| Interstitial abnormalities | 4 (11.76) | 4 (8.89) | 0.002 | 0.720 |
| Thickening of the adjacent pleura | 6 (17.65) | 5 (11.11) | 0.253 | 0.406 |
| Nucleic acid and antibody detection results | | | 0.090 | 0.956 |
| Qpcr+igm- | 6 (17.65) | 7 (15.56) | | |
| Qpcr+igm+ | 24 (70.59) | 32 (71.11) | | |
| Qpcr-igm+ | 4 (11.76) | 6 (13.33) | | |
| Nucleic acid detection results after discharge | | | 0.002 | 0.966 |
| Qpcr+ | 3 (8.82) | 5 (11.11) | | |
| Qpcr- | 31 (91.18) | 40 (88.89) | | |

diseases (all P<0.05; **Table 4**). Then indexes with differences were selected for multivariate logistic regression analysis. It was found that hypertension and age (≥46 years old) were main independent risk factors for asymptomatic patients with positive SNAT (**Tables 5**, **6**).

*Tracing of medical history and follow-up after discharge*

In this study, 79 patients got negative result in nucleic acid test after treatment, but 8 patients of them showed reoccurring positive SNAT

**Table 5.** COVID-19 nucleic acid positive symptoms in no clinical symptoms index variable names and the influence of the assignment sheet

| Variate | Name | Value | |
|---|---|---|---|
| Dependent variable | Clinical symptoms | 0= exist | 1=no exist |
| Independent variable | Age | 0=≤45 years | 1=≥46 years |
| | Hypertension | 0= nonjoinder | 1= joinder |

Note: COVID-19: Corona Virus Disease.

**Table 6.** Analysis of clinical data infection risk factor in the hospital after the onset of asymptomatic

| Factor | β | SE | Wals | P | OR | OR (95% CI) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower limit | Upper limit |
| Age (≥46 years) | 0.446 | 0.129 | 2.142 | 0.012 | 1.562 | 1.237 | 2.184 |
| Hypertension | 0.731 | 0.571 | 1.420 | <0.001 | 2.077 | 1.534 | 3.187 |

(10.13%), including 1 patient with dry cough and 1 patient with positive symptoms including muscle soreness. In addition, the medical history of the 79 patients was traced, with a traceability rate of 100.00%, in which 60 patients had a definite contact history, including 36 patients contacting the disease in familial aggregation, 11 patients in nursing homes, 8 patients in workplace, 4 patients in public places, and 1 patient in an isolation point, and 19 patients had no definite contact history.

## Discussion

Asymptomatic patients with positive SNAT are special people among infected patients [14]. Such patients get positive result of SNAT, but have no pneumonia-related features, which leads to negligence in epidemic prevention. They are also infectious with potential to develop positive and typical clinical symptoms [15]. However, how occur the development of asymptomatic patients with positive SNAT remains unclear [16]. Therefore, this study analyzed the general data and course development of patients with positive SNAT but without positive clinical symptoms at admission so as to find clues that would contribute to the overall study of COVID-19 pandemic.

This study compared the clinical data between asymptomatic patients and symptomatic patients. Our results suggest that young and middle age, contact history more than one week, history of diabetes mellitus, and history of cancer are the influencing factors for asymptomatic infection with SARS-Cov-2, which may be related to immune-related mechanisms. Young and middle-aged people resist SARS-Cov-2 infection because of their good immune system function. The general incubation period of SARS-Cov-2 infection is 3-5 days, so contact history of more than one week indicates that the body has presented active and effective immune response. In addition, patients with diabetes mellitus may have taken metformin hypoglycemic drugs that have certain anti-inflammatory effects, and patients with cancer are asymptomatic, with positive SNAT, because they have received medicine that would enhance immune system function. It is verified that young and middle age, diabetes mellitus, contact history of more than one week, and history of cancer are influencing factors for negative symptoms of patients with positive SNAT. However, the number of individuals enrolled in this study is small, and further in vitro experiments are needed to confirm the above research results. Similar research conclusions have been reported previously [17].

In this study, according to analysis of the disease course of the 79 patients with positive SNAT at admission, 34 patients showed positive clinical symptoms during treatment. Data analysis revealed that history of hypertension and old age were main risk factors for positive signs of patients with positive SNAT, which indicated that hypertension and old age were main influencing risk factors for the occurring of positive clinical symptoms in patients with positive SNAT but negative clinical symptoms, and combination of the two had a good predictive value. Therefore, measures should be actively taken to regulate the blood pressure of patients with positive SNAT but negative clinical symptoms and comorbid hypertension and old-age patients with positive SNAT but negative clinical symptoms, and their diseases changes should be monitored closely. It also

has been reported that hypertension and old age may be influencing factors for the occurrence of positive clinical symptoms in patients with positive SNAT but negative clinical symptoms [18, 19].

At the end of the study, the asymptomatic patients were followed up, and the results revealed that the COVID-19 appeared in aggregation, and the incidence of it increased in families and public places [20, 21]. Therefore, effective prevention and control of population mobility is an important means to prevent disease spread and transmission [2, 22, 23].

To sum up, patients with positive SNAT but without symptoms long termly can be found in individuals at all ages, but are more common in young individuals. Old-age asymptomatic patients with underlying diseases face a higher risk of showing clinical symptoms than young asymptomatic patients without underlying diseases, which can be used as clinical observation reference. However, we notice that the sample size of the study is small, so it is required to expand the sample size to further evaluate the relevant epidemiological characteristics of asymptomatic patients. Moreover, whether hypoglycemic drugs and immune adjuvant drugs for tumor treatment have actual effects on patients suffer from COVID-19 needs further confirmation.

## Acknowledgements

This work was supported by A special COVID-19 Project Initiated by Shanxi Provincial Education Department.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Xiaomei Kong, Department of Respiratory and Critical Care Medicine, The First Hospital of Shanxi Medical University, No. 85 Jiefang South Road, Taiyuan 030001, Shanxi Province, China. Tel: +86-18835157355; E-mail: kongxiaomei0609@163.com

## References

[1] Lai CC, Shih TP, Ko WC, Tang HJ and Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. Int J Antimicrob Agents 2020; 55: 105924.

[2] Shi Q, Dorling D, Cao G and Liu T. Changes in population movement make COVID-19 spread differently from SARS. Soc Sci Med 2020; 255: 113036.

[3] Li B, Yang J, Zhao FM, Zhi LL, Wang XQ, Liu L, Bi ZH and Zhao YH. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020; 109: 531-538.

[4] Falcoz PE, Monnier A, Puyraveau M, Perrier S, Ludes PO, Olland A, Mertes PM, Schneider F, Helms J and Meziani F. Extracorporeal membrane oxygenation for critically Ill patients with COVID-19-related acute respiratory distress syndrome: worth the effort? Am J Respir Crit Care Med 2020; 202: 460-463.

[5] Ahn DG, Shin HJ, Kim MH, Lee S, Kim HS, Myoung J, Kim BT and Kim SJ. Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). J Microbiol Biotechnol 2020; 30: 313-324.

[6] Hu ZL, Song C, Xu CJ, Jin GF, Chen YL, Xu X, Ma HX, Chen W, Lin Y, Zheng YS, Wang JM, Hu ZB, Yi YX and Shen HB. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci 2020; 63: 706-711.

[7] Al-Tawfiq JA. Asymptomatic coronavirus infection: MERS-CoV and SARS-CoV-2 (COVID-19). Travel Med Infect Dis 2020; 35: 101608.

[8] Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M, Drosten C, Vollmar P, Zwirglmaier K, Zange S, Wölfel R and Hoelscher M. Transmission of 2019-nCoV infection from an asymptomatic contact in germany. N Engl J Med 2020; 382: 970-971.

[9] Zhang JJ, Tian SJ, Lou J and Chen YG. Familial cluster of COVID-19 infection from an asymptomatic. Crit Care 2020; 24: 119.

[10] Bai SL, Wang JY, Zhou YQ, Yu DS, Gao XM, Li LL and Yang F. Analysis of the first cluster of cases in a family of novel coronavirus pneumonia in Gansu province. Zhonghua Yu Fang Yi Xue Za Zhi 2020; 54: E005.

[11] Issue information-declaration of helsinki. J Bone Miner Res 2017; 32: BM i-BM ii.

[12] Gousseff M, Penot P, Gallay L, Batisse D, Benech N, Bouiller K, Collarino R, Conrad A, Slama D, Joseph C, Lemaignen A, Lescure FX, Levy B, Mahevas M, Pozzetto B, Vignier N, Wyplosz B, Salmon D, Goehringer F and Botelho-Nevers E; in behalf of the COCOREC study group. Clinical recurrences of COVID-19 symptoms after recovery: viral relapse, reinfection or inflammatory rebound? J Infect 2020; 81: 816-846.

[13] Zimmermann P and Curtis N. Coronavirus infections in children including COVID-19: an

overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J 2020; 39: 355-368.
[14] Tian SJ, Hu N, Lou J, Chen K, Kang XQ, Xiang ZJ, Chen H, Wang DL, Liu N, Liu D, Chen G, Zhang YL, Li D, Li JR, Lian HX, Niu SM, Zhang LX and Zhang JJ. Characteristics of COVID-19 infection in Beijing. J Infect 2020; 80: 401-406.
[15] Zhuang GH, Shen MW, Zeng LX, Mi BB, Chen FY, Liu WJ, Pei LL, Qi X and Li C. WITHDRAWN: potential false-positive rate among the 'asymptomatic infected individuals' in close contacts of COVID-19 patients. Zhonghua Liu Xing Bing Xue Za Zhi 2020; 41: 485-488.
[16] Ye F, Xu SC, Rong ZH, Xu RH, Liu XW, Deng PF, Liu H and Xu XJ. Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster. Int J Infect Dis 2020; 94: 133-138.
[17] Chang D, Xu H, Rebaza A, Sharma L and Dela Cruz CS. Protecting health-care workers from subclinical coronavirus infection. Lancet Respir Med 2020; 8: e13.
[18] Liang SY. Sepsis and other infectious disease emergencies in the elderly. Emerg Med Clin North Am 2016; 34: 501-522.
[19] Cassini A, Colzani E, Pini A, Mangen MJ, Plass D, McDonald SA, Maringhini G, van Lier A, Haagsma JA, Havelaar AH, Kramarz P, Kretzschmar ME and Behalf BC. Impact of infectious diseases on population health using incidence-based disability-adjusted life years (dalys): results from the burden of communicable diseases in Europe Study, European Union and European Economic Area Countries, 2009 to 2013. Euro Surveill 2018; 23: 17-00454.
[20] Xia XY, Wu J, Liu HL, Xia H, Jia B and Huang WX. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. J Clin Virol 2020; 127: 104360.
[21] Yang HY and Duan GC. Analysis on the epidemic factors for the corona virus disease. Zhonghua Yu Fang Yi Xue Za Zhi 2020; 54: E021.
[22] Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, Sun C, Sylvia S, Rozelle S, Raat H and Zhou H. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis Poverty 2020; 9: 29.
[23] Liu K, Ai SQ, Song SX, Zhu GH, Tian F, Li H, Gao Y, Wu YL, Zhang SY, Shao ZJ, Liu QY and Lin HL. Population movement, city closure in Wuhan and geographical expansion of the 2019-ncov pneumonia infection in China in January 2020. Clin Infect Dis 2020; 71: 2045-2051.