Comparison of Characteristics and Outcome in Asymptomatic COVID-19 Patients Before and After Hospitalization in Korea

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Abstract

Background: The progression of coronavirus disease-2019 (COVID-19) is less well-studied in asymptomatic patients. The study aimed to understand the clinical characteristics of asymptomatic COVID-19 patients at the time of admission and follow-up their occurrence of symptoms during hospitalization.

Methods: Patients were divided into two groups—those with no symptoms until discharge (group A) and those who had symptoms that developed during hospitalization (group B). Baseline and clinical characteristics were retrospectively measured, and logistic regression analysis was performed to identify risk factors for deterioration during hospital stay.

Results: Overall, 223 patients were enrolled in the study, including 42 and 181 patients in groups A and B, respectively. Patients were older in group B than in group A. They developed cough as the most common symptom. Abnormal initial chest X-ray (CXR) and higher levels of C-reactive protein were frequently observed in group B than in group A. Moreover, 5 patients required mechanical support, including hi-flow nasal cannular and mechanical ventilation in group B. Five patients were transferred to tertiary hospitals owing to deterioration, and 4 patients succumbed to COVID-19. The risk factors for deterioration were age over 75 years, diabetes mellitus, and C-reactive protein > 1.

Conclusions: Even when the patients have no symptoms at admission, we recommend close monitoring of symptoms during hospital stay in patients who present with risk factors at the time of admission.

Background

In December 2019, an outbreak of pneumonia with an unknown cause was observed in Wuhan, China. The causative agent was later identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease was named coronavirus disease (COVID-19) (1). COVID-19 can cause severe pneumonia that can lead to death in elderly patients (2). Additionally, asymptomatic infections have been reported in COVID-19 patients. The proportion of asymptomatic patients out of the total number of patients varied in different reports (3–5). Most of the studies have been conducted in patients without symptoms at the time of admission, and it remains unclear whether patients develop symptoms during hospitalization (6). Moreover, majority of the reports on asymptomatic patients included fewer patients (7, 8). Furthermore, Long et al. reported clinical and immunological characteristics of 37 COVID-19 patients without symptoms for 14 days and during hospital stay (8). Li et al. reported that about 9% of the asymptomatic and mild-symptomatic COVID-19 patients progressed to pneumonia in Wuhan, China (9). Thus, it is necessary to assess whether the clinical setting may change during the hospital stay among the asymptomatic patients. In this study, we compared the clinical characteristics of the COVID-19–positive patients who were asymptomatic at the time of admission but developed symptoms after hospitalization versus those who had no symptoms until they were discharged from hospital. Moreover,

we identified the risk factors that deteriorate the condition in asymptomatic COVID-19 patients during the hospital stay.

Methods

Study design

We conducted a retrospective observational study of COVID-19 patients admitted at the Keimyung University Dongsan Hospital, South Korea, between February 21 and May 29, 2020, and evaluated patients without symptoms at the time of admission. A questionnaire was prepared to determine whether symptoms were present at the time of admission, and the occurrence of newer symptoms in each patient was monitored every day during hospitalization. We excluded patients hospitalized for re-positivity of SARS-CoV-2 polymerase chain reaction (PCR) from this study. We excluded the patients who had symptoms at the time of admission. Further, patients without symptoms during hospitalization were included in group A, and those who developed symptoms during hospitalization were included in group B. Fever was defined as body temperature above 37.8 °C. Pneumonia was defined as pneumonic infiltration observed in the chest X-ray (CXR) along with respiratory symptoms experienced by the patients. The study design was approved by the Institutional Review Board of Dongsan Medical Center (IRB 2020-03-027), and requirement of informed consent was waived by the committee due to the retrospective nature of the study.

Data Collection

We collected data on patient demographics, including sex, age, exposure history, and overseas visits. Moreover, initial vital signs including body temperature, respiratory rate, pulse rate, and systolic blood pressure were measured. Additionally, data on clinical findings, including underlying diseases, symptoms, oxygen demand, laboratory tests, CXR, chest computed tomography (CT) findings, and PCR results were collected. The severity of pneumonia was evaluated based on hypoxemia and oxygen demand according to the World Health Organization (WHO) criteria. Deterioration was defined as the case when a patient was transferred to a tertiary hospital, died during hospital stay, or needed respiratory support using mechanical ventilation, hi-flow nasal canular, or extracorporeal membrane oxygenation during hospital stay.

Statistical Analysis

Categorical variables were described using frequencies and percentages, while continuous variables were described using mean value, median value, and interquartile range. All statistical analyses were performed using Statistical Package for the Social Sciences 20.0 software (SPSS Inc., IBM, Armonk, NY, USA). The Pearson χ^2 test and Fisher's exact test were used to compare qualitative variables. For continuous variables, normal distribution was tested by Kolmogorov-Smirnov test. Mann−Whitney U test

was performed for data that followed non-normal distribution, and independent t-test was performed for data that followed normal distribution. Logistic regression analysis was performed to identify the risk factors for deterioration during hospital stay. For unadjusted comparisons, $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics

A total of 1,022 patients were admitted at the hospital during the study period, of which 166 patients with re-positivity for SARS-CoV-2 and 633 who showed symptoms at the time of admission were excluded from the study. The remaining 223 patients (26.05%) were finally included. Of these, 42 patients (group A) showed no symptoms during hospitalization, while 181 (group B) developed symptoms (Fig. 1). Approximately 4.91% of total patients remained asymptomatic after hospitalization until discharge. Demographics of patients in both the study groups are provided in Table 1. Patients in group B had a higher median age than those in group A. The reason for PCR testing, such as an overseas trip or being a member of the Shincheonji Church, varied according to the group. Further, the incidence of hypertension was significantly higher in group B than in group A. However, the incidence of diabetes mellitus, neurologic disease, and solid tumor was higher without significance in group B than in group A (Table 1). Additionally, differences in initial vital signs were not observed between the two groups, except systolic blood pressure (SBP); median SBP of patients was higher in group B (136 mmHg) than in group A (129 mmHg).

Table 1
Baseline characteristics of patients

Characteristics	Group A (*n* = 42) n (%)	Group B (*n* = 181) n (%)	*P* value
Epidemiology			
Male sex	18 (42.9%)	70 (38.5%)	0.599
Age (median), years	21−57 (32.5)	24−72 (56.5)	0.006*
Cohort isolation	21 (50.0%)	126 (69.2%)	0.018*
Trip abroad	5 (11.9%)	7 (3.8%)	0.052
Exposure	19 (45.2%)	101 (55.5%)	0.23
Shincheonji Church	19 (45.2%)	49 (26.9%)	0.02*
Long-term care facility	3 (7.1%)	16 (8.8%)	0.999#
Underlying diseases			
Hypertension	3 (9.1%)	49 (28.2%)	0.021*
Diabetes mellitus	2 (6.1%)	25 (14.4%)	0.265#
Hyperlipidemia	3 (9.1%)	11 (6.3%)	0.472#
Chronic lung disease	0 (0.0%)	7 (4.0%)	0.600#
Chronic heart disease	3 (9.1%)	10 (5.7%)	0.440#
Neurologic disease	0 (0.0%)	17 (9.8%)	0.081#
Chronic liver disease	0 (0.0%)	1 (0.6%)	0.999#
Chronic kidney disease	0 (0.0%)	1 (0.6%)	0.999#
Autoimmune disease	0 (0.0%)	1 (0.6%)	0.999#
Malignancy	0 (0.0%)	10 (5.7%)	0.370#
Psychiatric disease	0 (0.0%)	4 (2.3%)	0.999#
Transplantation	0 (0.0%)	1 (0.6%)	0.999#
Pregnancy	0 (0.0%)	1 (0.6%)	0.999#

Fisher's exact test; *Group A* patients without symptoms during hospitalization; *Group B* patients who developed symptoms; * indicates *P* value less than 0.05 and statistically significant.

Clinical Characteristics

Laboratory findings of patients in both study groups are summarized in Table 2. Further, the initial levels of C-reactive protein (CRP) and procalcitonin were higher in group B, while those of albumin were higher in group A. The common symptoms that developed in patients in group B during the hospital stay are listed in Table 3. Cough was the most common symptom (59.9%), followed by sputum (46.3%), fever (36.7%), and myalgia (35.0%). Patients in group B had more abnormalities observed in the initial CXR than those in group A. However, the initial oxygen saturation and hypoxia levels were not different between the two groups. Further, CT imaging of the chest was performed in 22 and 111 patients in groups A and B, respectively, during the hospital stay. Of these, 3 (13.6%) and 46 (41.4%) cases in groups A and B, respectively, showed pneumonia in the chest CT (P = 0.007). Furthermore, follow-up chest CT was performed in 5 and 77 patients in groups A and B, respectively. Finally, in 43 patients in group B (55.8%), pneumonia was detected in the chest CT. In group B, the condition of several patients deteriorated during hospital stay, and failed to improve with nasal cannular oxygen therapy alone. Five patients required mechanical support to respirate, 2 had hi-flow nasal cannular, and 3 were assisted with mechanical ventilation. One patient required continuous renal replacement therapy. Additionally, 5 patients were transferred to a tertiary hospital for resuscitation, and 4 patients died.

Table 2
Initial laboratory and radiologic findings of patients

Findings	Group A (*n* = 42) n (%)	Group B (*n* = 181) n (%)	*P* value
Laboratory findings			
WBC (μL)	5750 ± 1314.05	5978.54 ± 1977.76	0.482
Hemoglobin (g/dL)	13.22 ± 2.00	11.70−14.30 (12.70)	0.199
Platelet (μL)	204−296.5 (251)	247.01 ± 81.48	0.316
ANC	2460−3980.5 (3320)	2610−4490 (3410)	0.277
ALC	1835 ± 602.52	1246−2150 (1710)	0.469
PT (INR)	0.99 ± 0.47	0.93−1.03 (0.97)	0.082
PT (sec)	11.77 ± 0.52	11.1−12.2 (11.7)	0.451
aPTT (sec)	28.95 ± 2.26	25.8−29.5 (27.9)	0.02*
BUN (mg/dL)	12.90 ± 4.21	11−17 (13)	0.277
Creatinine (mg/dL)	0.72 ± 0.18	0.60−0.88 (0.74)	0.418
Albumin (g/dL)	4.30−4.460 (4.40)	3.90−4.50 (4.30)	0.007*
AST (U/L)	17.5−25.0 (20.0)	16−27 (20)	0.31
ALT (U/L)	12.5−29.0 (17.0)	12−27 (18)	0.559
CRP (mg/dL)	0.03−0.11 (0.08)	0.03−0.50 (0.10)	0.022*
CPK (U/L)	59.65−122.0 (81.0)	47−110 (76)	0.186
LDH (U/L)	386.55 ± 90.60	344−476 (396)	0.075
Procalcitonin (ng/dL)	0.02−0.04 (0.02)	0.02−0.05 (0.03)	0.028*
Radiologic findings			
Abnormal initial CXR	1 (3.0%)	49 (27.8%)	0.002*

Group A patients without symptoms during hospitalization; *Group B* patients who developed symptoms; *WBC* white blood cell; *ANC* absolute neutrophil count; *ALC* absolute lymphocyte count; *PT* prothrombin time; *aPTT* activated partial thromboplastin time; *BUN* blood urea nitrogen; *AST* aspartate aminotransferase; *ALT* alanine aminotransaminase; *CRP* C-reactive protein; *CPK* creatine phosphokinase; *LDH* lactate dehydrogenase; *CXR* chest X-ray; [#] Fisher's exact test; * indicates *P* value less than 0.05 and statistically significant.

Findings	Group A (*n* = 42) n (%)	Group B (*n* = 181) n (%)	*P* value
Pneumonic infiltration on CXR during hospital stay	2 (2.0%)	51 (43.2%)	0.194#

Group A patients without symptoms during hospitalization; *Group B* patients who developed symptoms; *WBC* white blood cell; *ANC* absolute neutrophil count; *ALC* absolute lymphocyte count; *PT* prothrombin time; *aPTT* activated partial thromboplastin time; *BUN* blood urea nitrogen; *AST* aspartate aminotransferase; *ALT* alanine aminotransaminase; *CRP* C-reactive protein; *CPK* creatine phosphokinase; *LDH* lactate dehydrogenase; *CXR* chest X-ray; # Fisher's exact test; * indicates *P* value less than 0.05 and statistically significant.

Table 3
Symptoms that developed in patients in
Group B

Symptoms	Total *n* = 181, n (%)
Cough	106 (59.9%)
Sputum	82 (46.3%)
Fever	65 (36.7%)
Myalgia	62 (35.0%)
Headache	55 (30.7%)
Sore throat	54 (30.2%)
Chilling sensation	45 (25.4%)
Diarrhea	45 (25.4%)
Rhinorrhea	42 (23.7%)
Dyspnea	38 (21.5%)
Chest pain	10 (5.6%)
Group B patients developed symptoms	

Risk factors indicating deterioration in asymptomatic COVID-19 patients during hospital stay

Multivariate analysis using variables with *P* < 0.05 in univariate analysis demonstrated that patients with age ≥ 75 years (odds ratio [OR], 18.564; 95% confidence interval [CI], 1.413−243.868; *P* = 0.026), diabetes mellitus (DM) (OR, 18.871; 95% CI, 1.390−256.288; *P* = 0.027), and CRP > 1 (OR, 19.563; 95% CI, 1.638−233.661; *P* = 0.019) were the risk factors for deterioration in asymptomatic patients at the time of admission (Table 4).

Table 4
Univariate and multivariate analysis of risk factors of deterioration among asymptomatic COVID-19 patients

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Male	0.627	0.181−2.806	0.627			
Age ≥ 75	61.650	7.607−499.657	0.001	18.564	1.413−243.868	0.026
RR > 20	6.850	1.898−24.716	0.003	7.881	0.849−73.179	0.069
HTN	4.418	2.371−8.230	0.001	0.48	0.052−4.453	0.518
DM	4.305	2.267−8.175	0.001	18.871	1.390−256.288	0.027
Neurologic disease	5.809	2.766−12.201	0.001	3.515	0.390−31.702	0.263
Malignancy	4.225	1.542−11.578	0.005			
Headache during hospital stay	3.597	1.011−12.793	0.048			
Dyspnea during hospital stay	1.406	0.289−6.835	0.673			
Initial CRP > 1	46.24	9.313−229.591	0.001	19.563	1.638−233.661	0.019
Initial abnormal CXR	11.617	2.898−46.562	0.001	1.272	0.143−11.298	0.829
Initial hypoxia	6.156	0.651−58.246	0.113			

COVID-19 coronavirus disease 2019; *OR* Odds ratio; *95% CI* 95% Confidence interval; *RR* respiratory rate; *LTCF* long-term care facility; *HTN* hypertension; *DM* diabetes mellitus; *CKD* chronic kidney disease; *CXR* chest X-ray

Discussion

In Korea, screening tests for SARS-CoV-2 have been extensively conducted to prevent the community transmission of COVID-19. In cases where a person was in contact with a COVID-19−positive person, traveled to a COVID-19 epidemic country, resided at long-term care facilities (LTCF) where COVID-19−positive patients were hospitalized, or was a member of the Shincheonji Church, a screening PCR test for SARS-CoV-2 was performed regardless of the symptoms (10). If the PCR showed a positive result even in

asymptomatic patients, they were isolated in hospitals or residential treatment centers. Thus, as several asymptomatic patients were hospitalized, we could investigate them in Korea. In other countries, asymptomatic patients have been identified through SARS-CoV-2 PCR screening tests for individuals who were in close contact with COVID-19 patients, and most of the reports have discussed the importance of screening and quarantine to prevent community transmission. Additionally, several reports suggest that a majority of the asymptomatic cases involved mild symptoms (7).

In this study, we compared the clinical characteristics between asymptomatic COVID-19 patients who developed symptoms during their hospital stay and those who remained asymptomatic until discharge. In the group of patients who developed symptoms during hospital stay, a higher proportion of patients had abnormal initial CXR. Over one fifth of the patients had bilateral pneumonia. Moreover, even if the patients had no symptoms at the time of admission, their condition had increased propensity to worsen during hospital stay. They required mechanical support to respirate or were transferred to tertiary hospitals. In case of asymptomatic patients, age over 75 years, DM, and CRP > 1 were the risk factors for deterioration during hospital stay. Thus, based on the results, we recommend careful observation because asymptomatic patients may experience deterioration rapidly, especially in those with the risk factors.

Screening tests for SARS-CoV-2 were conducted in other countries. The proportion of asymptomatic patients varied as per the countries and facilities. The mortality rate in asymptomatic or presymptomatic COVID-19 patients varied from 4.6–33% (11, 12). In Daegu, several COVID-19 outbreaks also occurred in LTCFs, and screening tests were conducted for those residents. In this study, although the proportion of individuals from LTCF was higher in group B than in group A, the differences were statistically insignificant. It is difficult to determine whether COVID-19 itself or the underlying disease was the cause of deterioration in patients during their hospital stay. Furthermore, a high proportion of relatively young and healthy individuals was observed in the group of patients without symptoms during the hospital stay, possibly because screening tests were conducted after their overseas travel or visit to the Shincheonji Church; these factors may have influenced their outcomes.

Many studies have reported the risk factors for progression of COVID-19. Age over 70 years and arrhythmia are poor prognostic factors for COVID-19 (13). Wei et al. reported that age and lower CD4 + T-cell counts were the risk factors for admission to intensive care units. Host immune response against the SARS-CoV-2 may contribute to COVID-19 pathogenesis; and immunologic reaction might decrease as persons get older (14) (Chen et al., 2020). In case of underlying diseases, patients with hypertension (HTN) or coronary artery disease may require intensive care (15), and DM, which makes patients susceptible to infections, is associated with mortality and severity in COVID-19 (16). DM has been associated with impaired immune responses, including reduced response to T cells, disorders in humoral immunity, and lower secretion of inflammatory cytokines (17, 18). Moreover, it might be associated with the use of angiotensin-converting enzyme (ACE) inhibitor. SARS-CoV-2 binds to target cells through the ACE2, which is expressed in the epithelial cells of the lung, heart, and blood vessels. In patients treated with ACE inhibitor, expression of ACE2 is increased (19). However, the pathogenesis is unclear, and thus,

further studies will be needed. In laboratory findings, several studies have suggested that initial high CRP level can be used as an early indicator for severe COVID-19. Elevated levels of CRP might be associated with an overproduction of inflammatory cytokines and tissue destructions. Therefore, higher levels of CRP indicate more severe disease course to lung injury and worse prognosis. Elevated plasma CRP level is associated with severity in COVID-19 patients, and higher CRP levels correlated with longer duration of hospital stay (13, 15). Most of the studies till now have been conducted on assessing the risk factors for progressing to severe COVID-19. However, this study assessed COVID-19 progression in patients who were asymptomatic at the time of admission, and identified risk factors associated with worsening of condition in patients who developed symptoms during the hospital stay.

This study has a few limitations. First, this was a retrospective observational study, and the symptom status was determined only from the medical records. Second, subjective symptoms such as chills, myalgia, and headaches may have been difficult to detect in elderly patients or those with decreased consciousness. Finally, immunological tests, such as detection of COVID-19 antibodies were not performed. Nevertheless, despite these limitations, the findings of the study make significant contribution as they indicate the necessity of careful monitoring of asymptomatic patients.

Conclusions

The study describes the clinical and baseline characteristics of asymptomatic COVID-19 patients and compares the demographics between patients who developed symptoms after hospitalization versus those who remained asymptomatic until discharge. Based on the findings, we recommend thorough and careful observation of such asymptomatic patients to ensure a better disease outcome in this pandemic situation, especially in those aged over 75 years, diagnosed with DM, and having CRP > 1 mg/dL as these factors increase the risk of health deterioration.

Abbreviations

COVID-19, coronavirus disease-2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; CXR, chest X-ray; PCR, polymerase chain reaction; CT, computed tomography; SBP, systolic blood pressure; OR, odds ratio; CI, confidence interval; LTCF, long-term care facilities; DM, diabetes mellitus; CRP, C-reactive protein.

Declarations

Ethics approval and consent to participate

The study design was approved by the Institutional Review Board of Dongsan Medical Center (IRB 2020-03-027). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study.

Consent for publication

Not applicable.

Availability of supporting data

The datasets used and/or analyzed during the current study available from

the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Authors' contributions

J.Y.L., and J.S.P. collected epidemiological and clinical data. M.H. and J.Y.L. were responsible for statistical data. M.H. drafted the manuscript. H.A.K. was responsible for study design and revising the final manuscript.

Acknowledgements

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References

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708–20.
2. Lee JY, Kim HA, Huh K, Hyun M, Rhee JY, Jang S, et al. Risk Factors for Mortality and Respiratory Support in Elderly Patients Hospitalized with COVID-19 in Korea. J Korean Med Sci. 2020;35(23):e223.
3. Daniells JK, MacCallum HL, Durrheim DN. Asymptomatic COVID-19 or are we missing something? Commun Dis Intell (2018). 2020;44.
4. Ma Y, Xu QN, Wang FL, Ma XM, Wang XY, Zhang XG, et al. Characteristics of asymptomatic patients with SARS-CoV-2 infection in Jinan, China. Microbes Infect. 2020;22(4–5):212–7.
5. Noh JY, Yoon JG, Seong H, Choi WS, Sohn JW, Cheong HJ, et al. Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. J Infect. 2020.
6. Gao Z, Xu Y, Sun C, Wang X, Guo Y, Qiu S, et al. A Systematic Review of Asymptomatic Infections with COVID-19. J Microbiol Immunol Infect. 2020.
7. 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. Sci China Life Sci.

2020;63(5):706−11.

8. Long QX, Tang XJ, Shi QL, Li Q, Deng HJ, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med. 2020.

9. Li Y, Shi J, Xia J, Duan J, Chen L, Yu X, et al. Asymptomatic and Symptomatic Patients With Non-severe Coronavirus Disease (COVID-19) Have Similar Clinical Features and Virological Courses: A Retrospective Single Center Study. Front Microbiol. 2020;11:1570.

10. Kwon YS, Park SH, Kim HJ, Lee JY, Hyun MR, Kim HA, et al. Screening Clinic for Coronavirus Disease 2019 to Prevent Intrahospital Spread in Daegu, Korea: a Single-Center Report. J Korean Med Sci. 2020;35(26):e246.

11. Bigelow BF, Tang O, Barshick B, Peters M, Sisson SD, Peairs KS, et al. Outcomes of Universal COVID-19 Testing Following Detection of Incident Cases in 11 Long-term Care Facilities. JAMA Intern Med. 2020.

12. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med. 2020;382(22):2081−90.

13. Wang ZH, Shu C, Ran X, Xie CH, Zhang L. Critically Ill Patients with Coronavirus Disease 2019 in a Designated ICU: Clinical Features and Predictors for Mortality. Risk Manag Healthc Policy. 2020;13:833−45.

14. Chen Z, John Wherry E. T cell responses in patients with COVID-19. Nat Rev Immunol. 2020;20(9):529−36.

15. Wang CZ, Hu SL, Wang L, Li M, Li HT. Early risk factors of the exacerbation of Coronavirus disease 2019 pneumonia. J Med Virol. 2020.

16. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes Metab Syndr. 2020;14(4):535−45.

17. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). FEMS Immunol Med Microbiol. 1999;26(3−4):259−65.

18. Peleg AY, Weerarathna T, McCarthy JS, Davis TM. Common infections in diabetes: pathogenesis, management and relationship to glycaemic control. Diabetes Metab Res Rev. 2007;23(1):3−13.

19. Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271−80. e8.
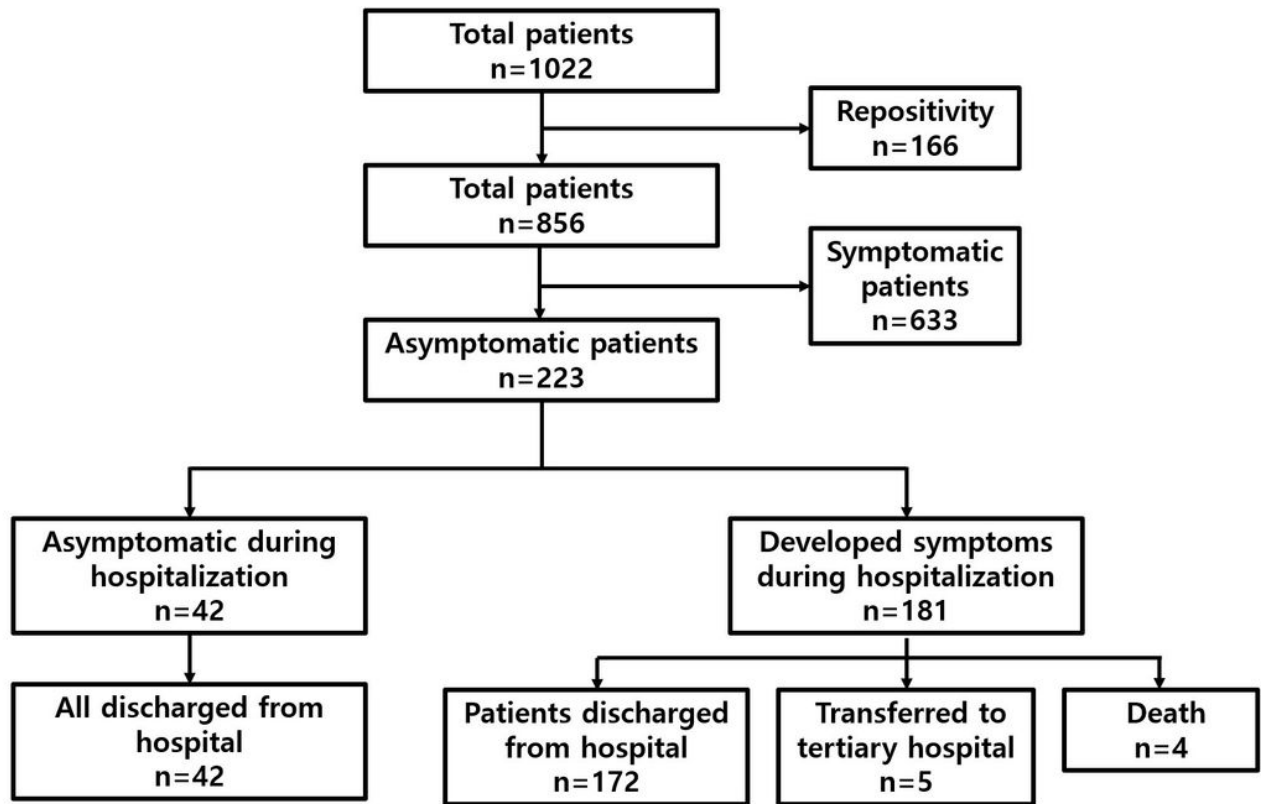
Figures

Figure 1

Flowchart of patients enrolled in the study.