The clinical characteristics of COVID-19: a retrospective analysis of 104 patients from the outbreak on board the Diamond Princess cruise ship in Japan

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Abstract

Background: The ongoing outbreak of the coronavirus disease 2019 (COVID-19) is a global threat. Identification of markers for symptom onset and disease progression is a pressing issue. We compared the clinical features on admission among patients who were diagnosed with asymptomatic, mild, and severe COVID-19 at the end of observation.

Methods: This retrospective, single-center study included 104 patients with laboratory-confirmed COVID-19 from the mass infection on the Diamond Princess cruise ship from February 11 to February 25, 2020. Clinical records, laboratory data, and radiological findings were analyzed. Clinical outcomes were followed up until February 26, 2020. Clinical features on admission were compared among those with different disease severity at the end of observation. Univariate analysis identified factors associated with symptom onset and disease progression.

Findings: The median age was 68 years, and 54 patients were male. Briefly, 43, 41, and 20 patients on admission and 33, 43, and 28 patients at the end of observation had asymptomatic, mild, and severe COVID-19, respectively. Serum lactate hydrogenase levels were significantly higher in 10 patients who were asymptomatic on admission but developed symptomatic COVID-19 compared with 33 patients who remained asymptomatic throughout the observation period. Older age, consolidation on chest computed tomography, and lymphopenia on admission were more frequent in patients with severe COVID-19 than those with mild COVID-19 at the end of observation.

Interpretation: Lactate dehydrogenase level is a potential predictor of symptom onset in COVID-19. Older age, consolidation on chest CT images, and lymphopenia might be risk factors for disease progression of COVID-19 and contribute to the clinical management.

Funding: Not applicable.

Research in context

Evidence before this study

We searched the PubMed database from its inception until March 1, 2020, for articles published in English using the keywords "novel coronavirus," "2019 novel coronavirus," "2019-nCoV," "Severe acute respiratory syndrome coronavirus 2," "SARS-CoV2," "COVID-19," "mass infection," "herd infection," "cruise ship," "Diamond Princess," "asymptomatic," and "subclinical." There were no published clinical studies featuring COVID-19 as a result of mass infection on board a cruise ship. We found published articles entitled "Characteristics of COVID-19 infection in Beijing" and "Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study," which compared patients with asymptomatic, mild, and severe COVID-19. However, none of the studies described potential markers for symptom onset or disease progression in patients with COVID-19.

Added value of this study

We present the differences in clinical characteristics of 104 patients with laboratory-confirmed COVID-19 as a result of mass infection on the Diamond Princess cruise ship who were treated at Self-Defense Forces Central Hospital, Japan from February 11 to February 25, 2020. On admission, 43, 41, and 20 patients had asymptomatic, mild, and severe COVID-19, respectively, whereas 33, 43, and 28 patients were determined to have asymptomatic, mild, and severe COVID-19, respectively, at the end of observation. During the observation period, 10 of the 43 (23.3%) asymptomatic patients on admission developed symptoms of COVID-19. Conversely, eight of the 84 (9.5%) patients with asymptomatic and mild COVID-19 on admission developed severe disease during the observation period. The serum lactate dehydrogenase (LDH) levels were significantly higher in 10 patients who were initially asymptomatic on admission to the hospital and developed symptomatic COVID-19 during the observation period compared with 33 patients who remained asymptomatic throughout the observation period. The prevalence rates of consolidation on chest computed tomography (CT) images and lymphopenia were significantly higher in eight patients who developed severe COVID-19 during the observation period compared with the 76 patients with asymptomatic or mild disease at the end of the observation. Older age, consolidation on chest CT, and lymphopenia on admission were more frequent in patients with severe COVID-19 (n = 28) than those with mild COVID-19 (n = 43) at the end of observation. LDH level might be marker for symptom onset in patients with COVID-19, whereas older age, consolidation on chest CT imaging, and lymphopenia are potential risk factors for disease progression. The current report findings will contribute to the improvement of clinical management in patients with COVID-19.

Implications of all the available evidence

Serum LDH level is a potential predictor of symptom onset of COVID-19, whereas older age, consolidation on chest CT imaging, and lymphopenia have potential utility as markers for disease progression.

3

Introduction

The coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). The first case was reported in Wuhan, China, in December 2019, [1] and the ongoing outbreak has been declared as a pandemic by the World Health Organization. Since specific treatment for COVID-19 is unknown, identification of patients at high risk for severe illness is critical to prepare and provide sufficient supportive therapy. Additionally, an explosive increase in case numbers has led to the collapse of healthcare systems. Therefore, triage of patients and their transportation to proper facilities are necessary. Although our knowledge of the clinical characteristics of COVID-19 and the pathogenicity of SARS-CoV2 are increasing, detailed clinical characteristics of the disease remain unknown; most of the published studies to date focus on patients with severe COVID-19. [2-5] In Japan, a large number of infections occurred among the passengers and crew members on board the Diamond Princess cruise ship in February 2020. By March 1, 2020, there were approximately 700 patients with laboratory-confirmed SARS-CoV2 infection. [6,7] Approximately 3700 passengers and crew members on the cruise ship were tested for SARS-CoV2 by reverse transcription (RT)-polymerase chain reaction (PCR), and all symptomatic and asymptomatic cases were referred to medical institutions designated for infectious diseases in accordance with the Infectious Diseases Control Law of Japan. [6,7] Approximately 15% of all laboratory-confirmed cases from Diamond Princess were admitted to the Self-Defense Forces Central Hospital in Japan.

In clinical settings, identifying patients who are at risk of symptom onset and clinical deterioration is essential. Therefore, understanding the clinical characteristics of patients with COVID-19 of different severity is necessary. To that end, we retrospectively analyzed the detailed clinical characteristics of hospitalized patients with COVID-19 as a result of the Diamond Princess outbreak, including those with asymptomatic, mild, and severe disease presentation, who were treated in the Self-Defense Forces Central Hospital in Japan.

Methods

Study design and patients

We conducted a retrospective review of the medical records of 104 patients with laboratory-confirmed COVID-19 who were admitted to the Self-Defense Forces Central Hospital in Japan between February 11 and February 25, 2020. Approximately 3700 passengers on the cruise ship were examined by quantitative RT-PCR or nested RT-PCR for SARS-CoV2 using pharyngeal swabs or sputum specimens at the public health institutes based on the recommendations protocol by the National Institute of Infectious Disease. [6-8] This study was reviewed and approved by the Japan Self-Defense Forces Central Hospital (approval number 01-011). Informed consent, both written and oral, was obtained from all enrolled patients.

Data collection

Patient information was retrospectively collected from the hospital medical records and included

126 clinical records, laboratory findings, and chest CT images. All data were collected and reviewed by

127 two study investigators (ST and KI).

128 **Definitions**

129 The geographical regions were classified according to the standard country or area codes for

130 statistical use (M49) by the United Nations Statistics Division

131 (https://unstats.un.org/unsd/methodology/m49/). Asymptomatic cases were defined as patients with

132 no history of clinical signs and symptoms. Severe symptomatic cases were defined as patients

133 showing clinical symptoms of pneumonia (dyspnea, tachypnea, peripheral capillary oxygen

134 saturation <93%, and need for oxygen therapy). [9] Patients with other symptoms were classified as

135 mild cases. The observation period was defined as the time interval between the date of admission

136 and the date of discharge or February 26, 2020.

137 **Statistical analysis**

138 Continuous variables were expressed as means with standard deviation or medians with interquartile

139 range (IQR) and compared using Student's *t* test and Wilcoxon rank-sum test for parametric and

140 nonparametric data, respectively. Categorical variables were expressed as numbers (%) and

141 compared by the χ^2 or Fisher's exact test. A two-sided *p* value of less than 0·05 was considered to be

142 statistically significant. All statistical analyses were calculated using Stata13 (Stata Corp, College

143 Station, TX, USA).

144 **Role of the funding source**

145 There was no funding source for this study. The corresponding author had full access to all

146 study-related data and had final responsibility for the decision to submit the study for publication.

147

148 **Results**

149 During the observation period, a total of 107 patients on board the Diamond Princess cruise ship with

150 laboratory-confirmed COVID-19 were hospitalized in the Self-Defense Forces Central Hospital in

151 Japan. Three patients were excluded from the study because of withdrawal of consent to join the

152 study. Therefore, the remaining 104 patients were included in the final analysis. The patients' clinical

153 history, physical examination, and chest CT findings were evaluated on the day of admission, and all

154 blood tests were completed within the first 2 days following admission. The characteristics of 104

155 patients are presented in Table 1. Briefly, the patient age ranged from 25 to 93 years (median, 68

156 years; IQR, 46·75–75 years), and 54 (51·9%) patients were male. Most of the patients were from

157 Eastern Asia, with Japanese and Chinese ethnicities as the majority. The range of observation period

158 was 3–15 days (median, 10 days; IQR, 7–10 days). Fifty-two (50·0%) patients had comorbidities.

159 Based on their presentation on the day of admission, 43 patients (41·4%) who did not display any

160 symptoms were classified as asymptomatic, whereas 41 (39·4%) and 20 (19·2%) patients were

161 classified to have mild and severe COVID-19, respectively.

162

163   The clinical findings of the patients who were symptomatic on the day of admission and at the end of

164   observation period are shown in Table 2. At the end of the observation, there were 33 (31·7%), 43

165   (41·3%), and 28 (26·9%) patients with confirmed asymptomatic, mild, and severe COVID-19,

166   respectively. The most common clinical signs and symptoms on admission among the 71

167   symptomatic patients at the end of the observation were fever (42·3%) and cough (40·8%). Of the 43

168   patients who were asymptomatic on admission, 10 (23·3%) patients developed symptomatic

169   COVID-19 during the observation period, including three (7·0%) patients who developed severe

170   COVID-19 and required supplemental oxygen therapy. Conversely, five of the 41 (12·2%) patients

171   with mild disease on admission developed severe COVID-19 and required supplemental oxygen

172   therapy. Therefore, eight of the 84 (9·5%) patients with asymptomatic or mild presentation on

173   admission developed severe COVID-19 during the observation period. Additionally, of the 71

174   patients who were symptomatic at the end of the observation, 14 (13·5%) and one (1·4%) patient

175   required oxygen therapy and mechanical ventilation, respectively, whereas 10 (14·1%) and five

176   (7·0%) patients were treated by antibiotics and lopinavir/ritonavir, respectively. There were no

177   reports of complications or death during the observation period.

178

179   The characteristics of 10 patients who developed symptomatic COVID-19 during the observation

180   period among those who were asymptomatic on admission are presented in Table 3. Among these 10

181   patients who developed symptomatic COVID-19, the most frequent symptom was cough (n = 7,

182   70·0%). Conversely, 17 of the 33 (51·5%) patients never developed symptoms until the end of the

183   observation period had abnormal lung findings with various patterns on CT images (Table 3 and

184   Figure 1). By univariate analysis, there were no significant differences in the distribution of age, sex,

185   and comorbidities or the prevalence of abnormal lung findings and CT patterns between the

186   symptomatic and asymptomatic patients. The prevalence of elevated LDH levels above 230 IU/L was

187   significantly higher in patients who were initially asymptomatic but developed symptomatic

188   COVID-19 during the observation period (50·0% vs 12·1%; odds ratio [OR], 7·25; 95% confidence

189   interval [CI], 1·43–36·70; $p = 0.02$).

190

191   In the group of eight patients who developed severe COVID-19 during the observation period, the

192   age range was 42–87 years (median, 70 years; IQR, 70–77 years), and five (62·5%) patients were

193   male. The period from symptom onset to the reclassification of disease presentation as severe

194   COVID-19 ranged from 1 to 5 days (median, 4 days; IQR, 2·5–5 days). Additionally, all eight

195   patients (100·0%) developed radiographical abnormalities on CT prior to the emergence of

196   symptoms of typical pneumonia including tachypnea, dyspnea, and hypoxemia (Figure 2).

197   Furthermore, among these patients who developed severe COVID-19 during the observation period,

198   4 (50·0%) and 3 (37·5%) patients lacked the symptoms of cough and fever, respectively. We also

199   compared these eight patients who developed severe COVID-19 with 76 patients who remained

200   asymptomatic or had mild COVID-19 at the end of the observation period. By univariate analysis, no

201　significant differences were observed in the distribution of age, sex, and comorbidities between the

202　two groups. The prevalence rates of consolidation (75·0% vs 19·7%; OR, 12·20; 95%CI, 2·23–66·59;

203　$p = 0·04$) and lymphopenia (62·5% vs 25·0%; OR, 5·00; 95%CI, 1·10–22·92; $p = 0·04$) on the day of

204　admission were significantly higher in patients who developed severe COVID-19 during the

205　observation period than in those who were asymptomatic or had mild disease at the end of the

206　observation period.

207

208　Finally, we performed analyses to identify differences in the clinical characteristics between patients

209　with mild and severe COVID-19 at the end of the observation period (Table 4). By univariate

210　analysis, age was significantly higher in the severe COVID-19 group than in the mild COVID-19

211　group (median, 72·5 years; IQR, 55·25–76·5 years vs median, 60 years; IQR, 40·0 –71·0 years;

212　$p = 0.03$). There were no significant differences in the distribution of sex, comorbidities, clinical

213　signs, and symptoms between the two groups. However, there was a significant difference in the

214　prevalence of consolidation as a CT pattern between the severe and mild cases (46·4% vs 20·9%; OR,

215　3·27; 95%CI, 1·15–9·30; $p = 0·03$). Among the blood tests, the rate of lymphopenia was higher in

216　patients with severe COVID-19 than in those with mild COVID-19 at the end of the observation

217　period (57·1% vs 23·3%; OR, 4·40; 95% CI; 1·57–12·32; $p = 0·005$).

218

219　**Discussion**

220　The present retrospective, single-center study provides a summary of the clinical features of patients

221　who developed COVID-19 of varying severity as a result of mass infection on board a cruise ship.

222　The LDH levels were significantly higher in 10 patients who were initially asymptomatic on

223　admission to the hospital and developed symptomatic COVID-19 during the observation period than

224　in 33 patients who remained asymptomatic throughout the observation period. Older age,

225　consolidation on chest CT images, and lymphopenia at the time of admission were significantly more

226　frequent among 28 patients with severe COVID-19 than among 43 patients with mild COVID-19 at

227　the end of the observation period. Overall, these findings suggest that serum LDH level might be a

228　marker of symptom onset and that older age, consolidation on chest CT images, and lymphopenia are

229　potential risk factors for disease progression in patients with COVID-19.

230

231　The predictors of symptom onset and risk factors for disease progression in COVID-19 remain

232　partially unclear because patients who are asymptomatic or are otherwise exhibiting mild symptoms

233　do not necessarily visit a hospital. During the COVID-19 outbreak on the Diamond Princess cruise

234　ship, approximately 3700 individuals on board were tested for SARS-CoV2 by RT-PCR, and all

235　laboratory-confirmed patients were referred to the hospitals. This unique situation allowed us to

236　observe the clinical course of asymptomatic patients as well as those with mild and severe symptoms,

237　which has not been reported to date. [2-5]

238

239 Based on the previously published findings of COVID-19 in China, old age, male sex, and presence
240 of comorbidities are considered as potential risk factors for disease progression and poor prognosis.
241 [1,10] Zhou *et al*. indicated that older age, high sequential organ failure assessment score, and elevated
242 d-dimer level were potential risk factors for death in patients with COVID-19. [11] Qin *et al*. reported
243 that lymphopenia and higher neutrophil–lymphocyte ratio were frequently observed in patients with
244 severe COVID-19 compared with those with mild disease. The present study findings support those
245 of previous reports suggesting older age and lymphopenia as potential risk factors for disease
246 progression in COVID-19. Lymphopenia, a common feature of symptomatic COVID-19, [12,13] can be
247 a direct consequence of SARS-CoV2 or might be mediated by cytokines. Qin *et al*. also suggested
248 that SARS-CoV2 infection might affect T lymphocytes and dysregulate the immune system,
249 consequently leading to secondary bacterial infections. [14] In the present study, we observed
250 lymphopenia in 27.3% of the patients who were asymptomatic at the end of observation period,
251 which suggests the development of immune system dysregulation as a direct consequence of
252 SARS-CoV2 infection in asymptomatic cases. However, the role lymphopenia in asymptomatic
253 patients remains unclear. Further cohort studies are warranted to determine the effect of lymphopenia
254 caused by SARS-CoV2 infection in the presence of secondary bacterial infection.

255

256 In the present study, the prevalence of consolidation detected by chest CT was significantly higher in
257 severe cases than in mild cases. Consolidation was also frequently detected in patients who
258 developed severe COVID-19 during the observation period. Pan *et al*. and Shi *et al*. reported that
259 abnormal lung findings varied from ground glass opacities (GGOs) to consolidation during the
260 course of COVID-19 and that the appearance of consolidation was more frequent within 1–3 weeks
261 after the symptom onset. [15,16] Previous studies found that 55% of patients with COVID-19 developed
262 dyspnea in a median of 8 days (IQR, 5.0–13.0 days) after symptom onset; [1] thus, the development of
263 consolidation on CT is associated with disease deterioration. Generally, consolidation is easily
264 detectable by chest X-ray, which therefore might be useful for the evaluation of risk for disease
265 progression in patients with COVID-19 in settings with limited resources.

266

267 Additionally, CT imaging revealed a high prevalence of lung abnormalities in patients with
268 COVID-19. The various patterns of abnormal lung findings were observed in asymptomatic cases
269 (51·5%) as well as in symptomatic cases (69·0%) at the end of the observation period. In their report
270 focusing on CT imaging findings of COVID-19, Shi *et al*. also noted the presence of abnormal lung
271 findings in asymptomatic patients. [16] Bai *et al*. investigated the common radiological characteristics
272 of COVID-19 pneumonia and reported that chest CT had a diagnostic sensitivity of 73%–93% and a
273 specificity of 93%–100% in distinguishing COVID-19 from viral pneumonia. [17] Therefore, chest CT
274 imaging might also be useful diagnostic tool for the asymptomatic and symptomatic patients with
275 COVID-19. In the present study, all eight patients who developed severe COVID-19 during the
276 observation period presented with CT abnormalities, in advance of the appearance of typical

8

277   pneumonia symptoms such as dyspnea, tachypnea, and hypoxemia. Of these eight patients, four and

278   three patients lacked the symptoms of cough and fever, respectively. These findings highlight that

279   COVID-19 pneumonia silently progresses without any remarkable symptoms. Conversely, the

280   majority of asymptomatic patients with radiological abnormalities on CT imaging did not develop

281   severe pneumonia. The differences observed in the clinical outcomes might be associated with

282   patient background characteristics as well as the genetic and pathogenic diversity of SARS-CoV2.

283   Understanding CT abnormalities relevance to the duration of virus shedding and the incidence of

284   secondary bacterial pneumonia is important to improve the clinical management of COVID-19.

285   Further investigation is necessary to clarify the clinical impact of CT findings in patients with

286   asymptomatic or mild COVID-19.

287

288   Interestingly, there was a significant difference in the rate of patients with elevated LDH levels

289   between those who developed symptomatic COVID-19 during the observation period and those who

290   remained asymptomatic throughout the observation period, although there was no significant

291   difference in the prevalence of lymphopenia between the two groups. Elevated serum LDH levels are

292   associated with lung tissue damage, [18] and serum LDH is considered as a marker for disease activity

293   and progression in pneumonia due to various etiologies. [19,20] Given that abnormal lung findings are

294   frequently observed in patients with asymptomatic COVID-19, these findings implicate that an

295   elevated LDH level might also reflect lung tissue damage by COVID-19 and might be considered as

296   a predictor for symptom onset in COVID-19. Patient assessment with determination of serum LDH

297   levels and chest CT imaging might facilitate the successful dedication of medical resources to

298   patients who are at higher risk for disease progression in the setting of mass infections as well as in

299   normal clinical settings.

300

301   The major limitations of the present study were selection bias and low number of patients. We

302   enrolled an ideal, homogeneous cluster of relatively healthy individuals who could remain on board a

303   cruise ship for a relatively long term. Therefore, the patient population was not an exact

304   representation of normal clinical settings. Triage on the Diamond Princess cruise ship before

305   emergency transportation has also introduced a selection bias with an atypically large number of

306   patients. The Self-Defense Forces Central Hospital in Tokyo is close to the Yokohama port where the

307   cruise ship was docked, and the symptomatic cases were referred to the study hospital. However, the

308   critical cases were preferentially referred to neighboring hospitals in Yokohama. Likewise, several

309   clinical signs and symptoms, which have occurred and disappeared before the patients were referred

310   to our hospital, may be included or excluded from this study. In addition, laboratory tests and CT

311   images were obtained once in majority of the patients, and the present study was not able to

312   determine changes in lymphocyte count and radiological findings over the course of observation.

313   Therefore, multicenter, multi-national cohort studies should be conducted to determine predictive

314   markers for symptom onset and risk factors for diseases progression.

315

Conclusion

The present study highlights the clinical features of patients who developed COVID-19 as a result of mass infection on board the Diamond Princess cruise ship. Our analyses reveal serum LDH level as a potential predictor of symptom onset in COVID-19. Age, consolidation on chest CT images, and lymphopenia might be risk factors for disease progression. These findings contribute to a better understanding of the clinical course and access points to improve disease management in patients with COVID-19. Additional cohort studies are warranted to determine predictors for symptom onset and risk factors for disease progression.

Declaration of interests

The authors declare that they have no conflicts of interests.

Authors' contributions

TI and KT, study conception and design; ST and KI, collecting data and performing data analysis; ST, KI, MI, and KM manuscript drafting and editing; TaK, HO, SK, TsK, MK and SM, manuscript revision; MS, SS and UY, study supervision. All authors have read and approved the final manuscript.

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Figure Legends

Figure 1. Computed tomography (CT) patterns of abnormal lung findings among asymptomatic patients with the 2019 novel coronavirus disease (COVID-19). (A–D) A 73 year-old female patient. Patchy non-segmental GGOs are observed adjacent to the parietal pleura in the right upper lobe (A and B) and in both lower lobes (C and D). (E) A 70 year-old female patient. GGO with interlobular septal thickening (crazy-paving appearance) adjacent to the parietal pleura in both lower lobes. (F) A 76 year-old male. CT image shows GGO with consolidation, bronchial wall thickening, and bronchiectasis in left lower lobe.

Figure 2. Progression of CT findings in a 75 year-old male patient with COVID-19. The patient was asymptomatic on the day of admission. On the fourth day of admission, he developed tachypnea and hypoxemia and was administered oxygen therapy. (A–C) Chest CT images on the day of admission show multifocal GGO adjacent to the parietal pleura in multiple lobes with emphysematous changes. (D–F) Follow-up chest CT images on the tenth day of admission show an increase in the extent of GGO with crazy-paving appearance.

13

426 **Table 1. Baseline characteristics of patients with COVID-19 on the Diamond Princess cruise**
427 **ship**

Total number of patients (n = 104)	
Characteristics	
Age	68 [46·75–75]
Sex (male)	54 (51·9%)
Observation period (days)	10 [7–10]
Time from onset to admission (days)	5 [2–7]
Nationality	
Eastern Asia	55 (52·9%)
Southeast Asia	21 (20·2%)
Europe	4 (3·8%)
Northern America	14 (13·5%)
Oceania	4 (3·8%)
Others	6 (5·8%)
Smoking	
Yes	18 (17·3%)
Comorbid condition	
Total	52 (50·0%)
Cardiovascular disease	31 (29·8%)
Endocrine disorder	9 (8·7%)
Diabetes mellitus	7 (6·7%)
Respiratory disorder	7 (6·7%)
Malignancy	4 (3·8%)
Severity on admission	
Asymptomatic	43 (41·4%)
Mild	41 (39·4%)
Severe	20 (19·2%)

428 Data are presented as n (%), or median [interquartile range], unless otherwise specified.

429 **Table 2. Clinical findings and disease severity of 71 patients with symptomatic COVID-19**

	Number (%)	
	On admission	**At the end of observation**
Signs and symptoms		
Fever	30 (42·3%)	36 (50·7%)
Cough	29 (40·8%)	43 (60·6%)
Malaise	12 (16·9%)	22 (31·0%)
Headache	10 (14·1%)	18 (25·4%)
Sore throat	11 (15·5%)	11 (15·5%)
Runny nose	16 (22·5%)	24 (33·8%)
Diarrhea	8 (11·3%)	10 (14·1%)
Dyspnea	7 (9·9%)	19 (26·8%)
Tachypnea	16 (22·5%)	24 (33·8%)
$SpO_2 < 93\%$	3 (4·2%)	14 (19·7%)
Treatment		
Acetaminophen	4 (5·6%)	15 (21·1%)
NSAIDs	-	1 (1·4%)
Antibiotics	-	10 (14·1%)
Lopinavir/ritonavir	-	5 (7·0%)
Oxygen therapy	3 (4·2%)	14 (19·7%)
Mechanical ventilation	-	1 (1·4%)
Severity		
Asymptomatic	10 (14·1%)	-
Mild	41 (57·7%)	43 (60·6%)
Severe	20 (28·2%)	28 (39·4%)

430 Data are presented as n (%).

431 NSAID, non-steroidal anti-inflammatory drug; SpO_2, peripheral capillary oxygen saturation

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432 **Table 3. Clinical characteristics of 43 asymptomatic patients on admission**

	Total n = 43	At the end of observation		p value	OR (95% CI)
		Asymptomatic n = 33	Symptomatic n = 10		
Characteristics					
Age	69 [60·5–75]	70 [57–75]	67·5 [66·25–73·5]	0·96	
Sex (male)	19 (44·2%)	15 (45·5%)	4 (40·0%)	1·00	
Smoking					
Yes	7 (16·3%)	5 (15·2%)	2 (20·0%)	0·65	
Comorbid condition					
Total	21 (48·8%)	15 (45·5%)	6 (60·0%)	0·48	
Cardiovascular disease	12 (27·9%)	9 (27·3%)	3 (30·0%)	1·00	
Endocrine disorder	3 (7·0%)	2 (6·1%)	1 (10·0%)	0·56	
Diabetes mellitus	5 (11·6%)	5 (15·2%)	-	0·32	
Respiratory disorder	4 (9·3%)	2 (6·1%)	2 (20·0%)	0·22	
Malignancy	2 (4·7%)	1 (3·0%)	1 (10·0%)	0·42	
Signs and symptoms					
Fever	3 (7·0%)	-	3 (30·0%)	-	
Cough	7 (16·3%)	-	7 (70·0%)	-	
Malaise	2 (4·7%)	-	2 (20·0%)	-	
Headache	2 (4·7%)	-	2 (20·0%)	-	
Sore throat	-	-	-	-	
Runny nose	-	-	-	-	
Diarrhea	1 (2·3%)	-	1 (10·0%)	-	
Dyspnea	3 (7·0%)	-	3 (30·0%)	-	
Tachypnea	3 (7·0%)	-	3 (30·0%)	-	
$SpO_2 < 93\%$	3 (7·0%)	-	3 (30·0%)	-	
Radiographically findings on admission					
Abnormal lung findings	25 (58·1%)	17 (51·5%)	8 (80·0%)	0·15	
Lateral	13 (30·2%)	10 (30·3%)	3 (30·0%)	-	
Bilateral	12 (27·9%)	7 (21·2%)	5 (50·0%)	0·11	
GGO	15 (34·9%)	11 (33·3%)	4 (40·0%)	0·72	
Multifocal GGO	12 (27·9%)	9 (27·3%)	3 (30·0%)	1·00	
Consolidation	9 (20·9%)	6 (18·2%)	3 (30·0%)	0·41	
Crazy-paving appearance	5 (11·6%)	2 (6·1%)	3 (30·0%)	0·07	

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Nodular lesion	3 (7·0%)	2 (6·1%)	1 (10·0%)	0·56	
Laboratory findings on admission					
AST > 38 (IU/L)	4 (9·3%)	3 (9·1%)	1 (10·0%)	1·00	
ALT > 45 (IU/L)	5 (11·6%)	4 (12·1%)	1 (10·0%)	1·00	
LDH > 230 (IU/L)	9 (20·9%)	4 (12·1%)	5 (50·0%)	0·02*	7·25 (1·43–36·70)
CRP > 1.0 (mg/dL)	18 (41·9%)	11 (33·3%)	7 (70·0%)	0·07	
White blood cell count <4000 (/μL)	6 (14·0%)	4 (12·1%)	2 (20·0%)	0·61	
Platelet count <15 (×10^4/μL)	2 (4·7%)	1 (3·0%)	1 (10·0%)	0·41	
Lymphocyte count <1200 (/μL)	13 (30·2%)	9 (27·3%)	4 (40·0%)	0·46	

433   Data are presented as n (%), or median [interquartile range], unless otherwise specified.

434   Asterisk indicates statistical significance.

435   OR, odds ratio; 95% CI, 95% confidence interval; GGO, ground glass opacity; AST, aspartate

436   aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; CRP, C reactive

437   protein

Table 4. The clinical characteristics of patients with mild and severe COVID-19 at the end of observation

	Total n = 71	Mild n = 43	Severe n = 28	p value	OR (95% CI)
Characteristics					
Age	67 [44–75]	60 [40–71]	72·5 [55·25–76·5]	0·03*	
Sex (male)	39 (54·9%)	22 (51·2%)	17 (60·7%)	0·47	
Smoking					
Yes	13 (18·3%)	6 (14·0%)	7 (25·0%)	0·35	
Comorbid condition					
Total	37 (52·1%)	19 (44·2%)	18 (64·3%)	0·14	
Cardiovascular disease	22 (31·0%)	11 (25·6%)	11 (39·3%)	0·3	
Endocrine disorder	7 (9·9%)	3 (7·0%)	4 (14·3%)	0·42	
Diabetes mellitus	2 (2·8%)	1 (2·3%)	1 (3·6%)	1·00	
Respiratory disorder	5 (7·0%)	2 (4·7%)	3 (10·7%)	0·38	
Malignancy	3 (4·2%)	2 (4·7%)	1 (3·6%)	1·00	
Acetaminophen on admission					
Yes	4 (5·6%)	4 (9·3%)	-	0·15	
Signs and symptoms on admission					
Fever	30 (42·3%)	19 (44·2%)	11 (39·3%)	0·8	
Cough	29 (40·8%)	16 (37·2%)	13 (46·4%)	0·49	
Malaise	12 (16·9%)	6 (14·0%)	6 (21·4%)	0·52	
Headache	10 (14·1%)	8 (18·6%)	2 (7·1%)	0·3	
Sore throat	11 (15·5%)	7 (16·3%)	4 (14·3%)	1·00	
Runny nose	16 (22·5%)	8 (18·6%)	8 (28·6%)	0·39	
Diarrhea	8 (11·3%)	5 (11·6%)	3 (10·7%)	1·00	
Dyspnea	7 (9·9%)	-	7 (25·0%)	-	
Tachypnea	16 (22·5%)	-	16 (57·1%)	-	
$SpO_2 < 9\%$	3 (4·2%)	-	3 (10·7%)	-	
Radiographically findings on admission					
Abnormal lung finding	49 (69·0%)	26 (60·5%)	23 (82·1%)	0·07	
Lateral	17 (23·9%)	11 (25·6%)	6 (21·4%)	-	
Bilateral	31 (43·7%)	15 (34·9%)	16 (57·1%)	0·09	
GGO	37 (52·1%)	18 (41·9%)	19 (67·9%)	0·05	
Multifocal GGO	34 (47·9%)	17 (39·5%)	17 (60·7%)	0·09	
Consolidation	22 (31·0%)	9 (20·9%)	13 (46·4%)	0·03*	3·27 (1·15–9·30)

Crazy-paving appearance	19 (26·8%)	8 (18·6%)	11 (39·3%)	0·1	
Nodular lesion	5 (7·0%)	4 (9·3%)	1 (3·6%)	0·64	
Laboratory findings on admission					
AST > 38 (IU/L)	15 (21·1%)	6 (14·0%)	9 (32·1%)	0·08	
ALT > 45 (IU/L)	13 (18·3%)	6 (14·0%)	7 (25·0%)	0·35	
LDH > 230 (IU/L)	23 (32·4%)	13 (30·2%)	10 (35·7%)	0·8	
CRP > 1.0 (mg/dL)	42 59·2%)	23 (53·5%)	19 (67·9%)	0·32	
White blood cell count <4000 (/μL)	15 (21·1%)	9 (20·9%)	6 (21·4%)	1·00	
Platelet count <15 ($\times 10^4$/μL)	7 (9·9%)	5 (11·6%)	2 (7·1%)	0·7	
Lymphocyte count <1200 (/μL)	26 (36·6%)	10 (23·3%)	16 (57·1%)	0·005*	4·4 (1·57–12·32)

440   Data are presented as n (%), or median [interquartile range], unless otherwise specified.

441   Asterisk indicates statistical significance.

442   OR, odds ratio; 95% CI, 95% confidence interval; GGO, ground glass opacity; AST, aspartate

443   aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; CRP, C reactive

444   protein

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