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Short Communication

Clinical Characteristics of Patients with Coronavirus Disease (COVID-19): Preliminary Baseline Report of Japan COVID-19 Task Force, a Nationwide Consortium to Investigate Host Genetics of COVID-19

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ABSTRACT

Background and design: The coronavirus disease (COVID-19) pandemic is having a devastating effect worldwide. Host genome differences between populations may influence the severity of COVID-19. The Japan COVID-19 Task Force is conducting host genome analysis of hospitalized patients with COVID-19 from more than 70 institutions nationwide in Japan. This report describes the clinical characteristics of patients enrolled to date.

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The coronavirus disease (COVID-19) pandemic has had a devastating effect worldwide, including in Japan (see https://www.mhlw.go.jp/stf/covid-19/kokunainohasejoukyouyou.html). Host genome differences between populations may influence disease severity. This may explain why Asians, including Japanese, may have a lower risk of death (Price-Haywood, 2020; Zeberg and Pääbo, 2020). The Japan COVID-19 Task Force was established in early 2020 as a nationwide multicenter consortium. We collected and analyzed clinical specimens from patients in more than 70 institutions nationwide since February 2020 and reported the results of a genome-wide association study (Namkoong H et al., 2021).

This cross-sectional study aimed to determine the clinical characteristics of Japanese patients with COVID-19. The study facilities provide coverage for the most populous prefectural capital cities in Japan. We included 1645 (98.3%) patients with reverse transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19, 10 (0.6%) patients with rapid antigen test-confirmed COVID-19, and 19 (1.1%) patients who were considered as highly suspicious for COVID-19 by the physician. We collected information on patient demographics, laboratory test data, radiographic imaging, treatment, comorbidities, and outcomes for 1674 cases to construct a database for the Japan COVID-19 Task Force. The cases were not limited to inpatients; however, 1668 (99.6%) patients were hospitalized patients. All the patients in this study provided appropriate informed consent, which was approved by the ethics committee of the affiliated institutes. Symptoms and signs included not only those reported on referral or admission but also those observed during hospitalization. Laboratory and radiographic data were collected within 48 hours of the initial visit or admission. Disease outcome during hospitalization was assessed for fatality rate. We obtained information regarding any support using oxygen devices, invasive mechanical ventilation (IMV), and extracorporeal membrane oxygenation (ECMO) during the clinical course to determine the disease severity. In this report, disease severity was defined as follows: most severe, patients requiring support using high-flow oxygen devices, IMV, ECMO, or death; severe, patients requiring support using low-flow oxygen devices; mild, symptomatic patients not requiring oxygen support; asymptomatic, asymptomatic patients not requiring oxygen support (World Health Organization, 2020).

The patients’ clinical characteristics are shown in Table 1. Their median (interquartile range) age was 59 (45–71) years, 66.2% were male, and most patients were Japanese. Comorbidities included hypertension (34.6%), diabetes mellitus (22.9%), coronary artery disease (9.9%), and chronic kidney disease (7.0%). Moreover, 231 cases were categorized as most severe (13.8%), 459 cases as severe (27.4%), 933 cases as mild (55.7%), and 51 cases as asymptomatic (3.0%). The most common symptom was fever (>37.5°C), which was observed in 79.3% of patients. Cough, sputum, shortness of breath, dysgeusia, and dysosmia were observed in 58.2%, 24.7%, 30.7%, 18.7%, and 17.0% of patients, respectively. Most patients were enrolled in April 2020 (first wave), August 2020 (second wave), and December 2020 (third wave) (Figure 1). Supplementary Table 1 shows the patients’ characteristics in each epidemic. There was a high prevalence of elderly males among patients in the third epidemic. They also had a higher prevalence of comorbidities such as hypertension, diabetes, and chronic kidney disease, and a low prevalence of dysgeusia and dysosmia.

Laboratory findings showed an elevated inflammatory response, with median ferritin and C-reactive protein levels of 376 ng/mL and 2.69 mg/dL, respectively. Regarding radiographic findings, 81.3% of patients had ground glass opacity (GGO), and 39.8% had consolidation on chest computed tomography. The bilateral spread of GGOs was generally present during the acute phase of COVID-19. A total of 19.0% of patients were admitted to the intensive care unit, 11.1% were intubated, and 2.3% required ECMO. The fatality rate was 3.2%. Complications included bacterial infection and thrombosis in 11.9% and 3.6% of patients, respectively. The most commonly used antivirals were favipiravir and remdesivir, which were used in 35.0% and 18.3% of patients, respectively. Systemic corticosteroids were used in 40.9% of patients, especially in 58.9% of patients in the third epidemic.

Clinical characteristics of patients in this study were similar to those of other previously reported large-sample studies in Asian populations (Guan, 2020; Matsunaga N et al., 2020). The proportion of male patients was higher in this study than in other studies, which may be due to the relatively high disease severity in males (Chen N et al., 2020). The proportion of patients with comorbidities such as hypertension, diabetes, and chronic kidney disease was higher than that reported in another registry in Japan (Matsunaga N et al., 2020). We believe that this finding is due to a large number of patients registered in the third epidemic, unlike...
Table 1
Characteristics of 1674 patients with COVID-19 in Japan

| Parameters                          | Number of patients with data | Subcategories                             | n (%) or median and IQR |
|-------------------------------------|------------------------------|-------------------------------------------|-------------------------|
| Severity classification             | 1674                         | Asymptomatic                              | 51 (3.0)                |
|                                     |                              | Mild                                      | 933 (55.7)              |
|                                     |                              | Severe                                    | 459 (27.4)              |
|                                     |                              | Most severe                               | 231 (13.8)              |
| Death at discharge                  | 1633                         |                                           | 52 (3.2)                |
| Age, years                          | 1674                         |                                           | 59 (45–71)              |
| Sex                                 | 1674                         | Male                                      | 1109 (66.2)             |
|                                     |                              | Female                                    | 565 (33.8)              |
| Population                          | 1674                         | Japanese                                  | 1629 (97.3)             |
|                                     |                              | Others                                    | 45 (2.7)                |
| BMI, kg/m²                          | 1525                         |                                           | 23.9 (21.6–26.9)        |
| Smoking history                     | 1547                         | Never                                     | 840 (54.3)              |
|                                     |                              | Previously or currently                    | 707 (45.7)              |
| Chronic medical conditions          |                              | Hypertension                              | 569 (34.6)              |
|                                     |                              | Diabetes mellitus                         | 379 (22.9)              |
|                                     |                              | Coronary artery disease                   | 164 (9.9)               |
|                                     |                              | Malignancy                                | 97 (5.9)                |
|                                     |                              | Autoimmune disease                        | 61 (3.7)                |
|                                     |                              | COPD                                      | 67 (4.1)                |
|                                     |                              | Chronic liver disease                     | 53 (3.3)                |
|                                     |                              | Chronic kidney disease                    | 110 (7.0)               |
| Symptoms at referral                |                              | Fever (≥37.5°C)                           | 1311 (79.3)             |
|                                     |                              | Cough                                     | 959 (58.2)              |
|                                     |                              | Sputum                                    | 405 (24.7)              |
|                                     |                              | Sore throat                               | 387 (23.8)              |
|                                     |                              | Rhinorrhea                                | 232 (14.2)              |
|                                     |                              | Dysgeusia                                 | 395 (18.7)              |
|                                     |                              | Dysosmia                                  | 278 (17.0)              |
|                                     |                              | Shortness of breath                       | 496 (30.7)              |
|                                     |                              | Fatigue                                   | 811 (49.4)              |
| Laboratory tests                    |                              | WBC [cells/µL]                            | 5200 (4100–6700)        |
|                                     |                              | LDH [IU/L]                                | 237 (190–314)           |
|                                     |                              | Ferritin [ng/mL]                          | 376 (171–711)           |
|                                     |                              | KL-6 [U/mL]                               | 234 (178–350)           |
|                                     |                              | PCT [ng/mL]                               | 0.06 (0.04–0.11)        |
|                                     |                              | CRP [mg/dL]                               | 2.69 (0.51–6.67)        |
| Radiographic imaging                |                              | Chest radiography findings                |                         |
|                                     |                              | Bilateral thoracic opacities              | 834 (53.6)              |
|                                     |                              | Unilateral thoracic opacities             | 180 (11.6)              |
|                                     |                              | Bilateral thoracic consolidation          | 305 (19.8)              |
|                                     |                              | Unilateral thoracic consolidation         | 121 (7.9)               |
|                                     |                              | Chest CT findings                         |                         |
|                                     |                              | Bilateral GGO                             | 1055 (71.3)             |
|                                     |                              | Unilateral GGO                            | 148 (10.0)              |
|                                     |                              | Bilateral consolidation                   | 465 (32.2)              |
|                                     |                              | Unilateral consolidation                  | 110 (7.6)               |
| Complications after referral        |                              | Bacterial infection                       | 196 (11.9)              |
|                                     |                              | Heart failure                             | 36 (2.2)                |
|                                     |                              | Thrombosis                                | 59 (3.6)                |
|                                     |                              | COVID-19 treatment                        |                         |
|                                     |                              | ICU admission                             | 314 (19.0)              |
|                                     |                              | Intubation                                | 183 (11.1)              |
|                                     |                              | ECMO                                      | 37 (2.3)                |
|                                     |                              | Antiviral drugs                           |                         |
|                                     |                              | Favipiravir                               | 595 (35.9)              |
|                                     |                              | Ritonavir                                 | 7 (0.4)                 |
|                                     |                              | Remdesivir                                | 311 (18.9)              |
|                                     |                              | Hydroxychloroquine                        | 18 (1.1)                |
|                                     |                              | Tocilizumab                               | 118 (7.2)               |
|                                     |                              | Systemic corticosteroid                   | 680 (40.9)              |

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease; CRP, C-reactive protein; CT, computed tomography; ECMO, extracorporeal membrane; GGO, ground glass opacity; ICU, intensive care unit; IQR, interquartile range; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; PCT, procalcitonin; WBC, white blood cell.
the situation in the previously reported registry. Our study suggests that a high proportion of hospitalized male patients with more comorbidities has gradually increased in Japan during the past year. Compared with the recent meta-analyses in other countries (Macedo A et al., 2021), we believe that the lower fatality rate in this study and in the previous report (Matsunaga N et al., 2020) may be explained by reasons specific to Japan. We consider the possibility that many inpatient cases of our study would have been treated as outpatients in other countries, because in Japan, the public health centers coordinated the hospitalization of many patients, including those with mild disease. The low fatality rate may also reflect the unique genetic characteristics of the Japanese. For example, the effect of DOCK2 on disease severity of COVID-19 has been reported (Namkoong H et al., 2021). Our study had a large group of patients treated with remdesivir, especially in the third epidemic. A relatively high proportion of patients were treated with systemic corticosteroids, based on the results of the RECOVERY trial (Horby, 2021). These treatments may have resulted in a lower fatality rate in this study than that in previous reports.

With this clinical information, characterization of the host genetic factors in a representative sample of Japanese patients may provide insights into new treatment approaches.

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Ethics Approval

This study was approved by the ethics committee of Keio University School of Medicine (20200061) and affiliated institutes.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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