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Clinical Features and Risk Factors of Post-COVID-19 Condition in Korea

Myungwon Jang[1], Dongkwon Choi[2], Jonghyuk Choi[2,3], Ho-Jang Kwon[2,3]

[1]Epidemic Intelligence Officer, Dangjin City Public Health Center, Dangjin, Korea; [2]Chungnam Center for Infectious Diseases Control and Prevention, Hongseong, Korea; [3]Department of Preventive Medicine, Dankook University College of Medicine, Cheonan, Korea

Objectives: Numerous studies have explored the causes and spread of outbreaks, yet there is a lack of research on post-coronavirus disease 2019 condition (PCC) in Korea. The goal of this study was to identify the various types of PCC and associated factors in discharged patients and to provide directions for the ongoing health management of confirmed patients.

Methods: A telephone survey was conducted among 680 coronavirus disease 2019 (COVID-19) patients diagnosed between July 7, 2021 and August 26, 2021, in Dangjin, Chungnam, Korea. A descriptive analysis of characteristics, univariate analysis, and regression were performed using data from basic epidemiological surveys conducted at the time of diagnosis and post-discharge questionnaires.

Results: Of the 585 patients who responded, 159 (27.2%) developed PCC. Of the 211 patients with no initial symptoms, 27 (12.8%) developed PCC, versus 132 (35.3%) of the 374 patients with initial symptoms. Among the initial symptoms, fever or chills, cough or sputum, loss of smell, and sore throat were associated with PCC. Compared to patients with less than 10 days of hospitalization, those with a hospitalization period of 21 days to 30 days (odds ratio [OR], 2.3; 95% confidence interval [CI], 1.0 to 5.2) and 31 days or more (OR, 5.8; 95% CI, 1.9 to 18.1) had a higher risk of PCC.

Conclusions: More than a quarter of COVID-19 patients, including those who had no initial symptoms, experienced PCC in Korea. People with the initial symptoms of fever, chills, and respiratory symptoms and those who had prolonged hospital stays had a high risk of PCC.

Key words: COVID-19, Post-acute COVID-19 syndrome, SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, in December 2019, is transmitted by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pathogen through droplets, surface contact, and airborne transmission in limited circumstances. Originating in China, it quickly spread globally, leading to its declaration as a pandemic on March 11, 2020. Korea reported its first domestic case of COVID-19 on January 20, 2020. By November 10, 2022, over 25 900 000 individuals had been infected with SARS-CoV-2.

According to the COVID-19 Mutant Virus Guidelines from the Korea Disease Control and Prevention Agency (KDCA), five major variants of concern have been identified to date: Alpha (α), Beta (β), Gamma (γ), Delta (δ), and Omicron (o) [1]. Each variant exhibits different levels of contagiousness and severity. As of March 2021, the Alpha variant, which was the first variant of concern in Korea, was reported to have the highest se-

verity among the Alpha, Beta, and Gamma variants [2]. The Omicron variant, which triggered the fifth wave of infections in Korea in the first half of 2022, was found to be 2-3 times more infectious but less severe than the Delta variant. This led to a significant surge in domestic cases in February 2022 and March of 2022.

The clinical manifestations of COVID-19 range from asymptomatic to severe, with primary symptoms including fever (above 37.5℃), cough, shortness of breath, chills, muscle pain, and loss of smell. Additional symptoms may encompass fatigue, loss of taste, sputum production, and gastrointestinal issues. A study on the clinical characteristics of COVID-19 revealed a median incubation period of 5.1 days. When exposed to an infected family member, fever and respiratory symptoms typically manifest within 3-7 days of exposure. However, symptoms such as a sore throat and muscle pain are comparatively rare [3].

The clinical symptoms of COVID-19 can manifest differently based on factors such as vital signs, sex, and age, and this variability has been the focus of numerous studies [4]. Additionally, with an increasing number of patients reporting persistent symptoms or the emergence of new symptoms after a certain period, the World Health Organization (WHO) formally defined the post-coronavirus disease 2019 condition (PCC) on October 21, 2021.

The WHO defines PCC as symptoms that typically appear 3 months following the onset of COVID-19 and persist for at least 2 months, which cannot be attributed to other diagnoses [5]. While most patients fully recover, approximately 10-20% continue to experience various symptoms during the mid-term to long-term course of the disease, even after the initial symptoms of infection have subsided. This phenomenon occurs regardless of the severity of the initial symptoms or hospitalization, and it is important to note that these patients are not infectious, even if PCC symptoms persist [6]. The Centers for Disease Control and Prevention (CDC) in the United States characterizes PCC as symptoms that persist for 4 or more weeks after the initial infection, encompassing new, recurring, or ongoing health issues [7].

A prospective study involving 130 patients in Korea identified changes in clinical features on chest CT images, dyspnea, and loss of smell and taste as PCC [8]. A separate study, which compared COVID-19 and influenza using data from the Health Insurance Review and Assessment Service, found that 19.1% of patients with COVID-19 and 28.5% of patients with influenza sought medical care due to complications [9]. Furthermore,

Kim et al. [10] reported that advanced age, female sex, and symptom severity were risk factors for PCC with persistent neurological symptoms.

Menges et al. [11] found a correlation between the severity of initial symptoms and comorbidities with PCC. Similarly, Zhang et al. [12] discovered an association between the severity of COVID-19 and PCC. Another study revealed an association between the number of symptoms in the acute phase of COVID-19 and PCC [13]. However, previous studies were somewhat limited, as they were either hospital-based or did not compare the effects on PCC in relation to the manifestation and type of initial symptoms. The aim of this study was to explore the distribution of PCC and to ascertain how factors such as initial symptoms, underlying diseases, and the length of hospitalization might impact the incidence of PCC.

METHODS

The US CDC defined PCC as a range of symptoms that can persist for at least four weeks, or even several months, following infection. We conducted a case analysis based on this definition at the time of our investigation. We chose to use the CDC's criteria over the WHO's because the latter's definition is more stringent, which would have reduced our study sample size; instead, our aim was to include a wide range of subjects. The case analysis used a questionnaire developed by the Dangjin City Public Health Center, and a survey was conducted to obtain basic data for follow-up management after discharge.

The survey was carried out at the Dangjin City Public Health Center from July 7, 2020, to September 25, 2021. It involved 750 patients who had been confirmed positive for COVID-19 through laboratory tests (reverse transcriptase polymerase chain reaction). To align with the US CDC definition, we included 680 confirmed cases diagnosed by August 26, 2021—4 weeks prior to the conclusion of the study—as our subjects. Data collection was conducted via basic epidemiological surveys, in accordance with local government guidelines for COVID-19, and through telephone questionnaires. Information such as sex, age, ethnicity, underlying health conditions, and, and initial symptoms at diagnosis were obtained from the basic epidemiological survey, and PCC information was obtained from a 1:1 telephone questionnaire.

PCC was categorized into 7 body systems corresponding to those used in the review of systems: systemic, skin, head/neck/ear/nose and throat, musculoskeletal, neuropsychiatric, respi-

ratory or circulatory, and digestive symptoms. Descriptive statistics were presented for the types and distribution of PCC, and associations between the general characteristics and PCC were analyzed through univariate analysis using the chi-square test. The effects of various risk factors on PCC were analyzed through multiple logistic regression adjusting for various factors, where *p*-value was the probability of PCC.

$$\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 sex + \beta_2 age + \beta_3 underlying\ disease + \sum \beta_i initial\ syptom_i$$
$$+ \sum \beta_j hospitalization\ period_j + \sum \beta_k ethnicity_k$$

The level of significance for all analyses was set at 0.05, and all analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Ethics Statement

This research was conducted using existing data or documents related to our research subjects, and it was carried out with the approval of an exemption from the Institutional Review Board of Dankook University (IRB No. DKU 2022-12-006).

RESULTS

A total of 585 confirmed cases were finally included, with the exclusion of 95 patients who refused to take part in the survey, changed their phone number, did not answer calls, or died before the survey took place. The response rate of the survey was 86.0% (585 out of 680).

Out of a total of 585 subjects, 310 (53.0%) were male and 275 (47.0%) were female. Among them, 77 (24.8%) male and 82 (29.8%) female had PCC. There was no statistically significant difference in PCC by sex *(p*=0.177). Regarding the subjects' age distribution, 251 were under 40 years of age, 236 were between 40 years and 64 years of age, and 98 were over 65 years of age. The highest incidence of PCC was reported in the 40-64 age group (n=73, 30.9%), followed by those under 40 years old (n=62, 24.7%), and those 65 years old or above (n=24, 24.5%). There was also no significant association with PCC according to age group *(p*=0.245). Forty-six (31.5%) of 146 patients with underlying diseases and 113 (25.7%) of 439 patients without underlying diseases were found to have PCC. Hypertension showed a significant association with PCC *(p*=0.022), but no association was observed between the presence of at least 1 underlying disease and PCC *(p*=0.175). Furthermore, 374 of the 585 subjects had initial symptoms at

diagnosis. Among the 409 patients who did not have a fever as an initial symptom, 94 (23.0%) were diagnosed with PCC. Conversely, of the 176 patients who had a fever, 65 (36.9%) had PCC *(p*=0.001). Among the 421 patients without cough and sputum, 98 (23.3%) had PCC, while of the 164 patients with cough and sputum, 61 (37.2%) had PCC *(p*=0.001). Of the 570 patients who did not experience loss of smell, 150 (26.3%) had PCC, while 9 (60.0%) of the 15 patients who did experience loss of smell had PCC *(p*=0.004). Among the 489 patients without a sore throat, 123 (25.2%) had PCC, while 36 (37.5%) of the 96 patients with a sore throat had PCC *(p*=0.013). Of the 500 patients without muscle pain, 125 (25.0%) were diagnosed with PCC, while 34 (40.0%) of the 85 patients with muscle pain had PCC *(p*=0.004). No significant association was found between PCC and other initial symptoms. The hospitalization period and African ethnicity also showed statistically significant associations with PCC (Table 1).

In total, 49 types of PCC were investigated (Figure 1 and Table 2). Among the 585 subjects, 159 (27.2%) had PCC and 426 (72.8%) did not. PCC was most frequently reported with regard to respiratory or circulatory symptoms (n=64, 40.3%), followed by head/neck/ear/nose and throat symptoms (n=57, 35.8%), systemic symptoms (n=37, 23.3%), skin symptoms (n=14, 8.8%), neuropsychiatric symptoms (n=13, 8.2%), musculoskeletal symptoms (n=9, 5.7%), and gastrointestinal symptoms (n=6, 3.8%). Systemic symptoms included fatigue (n=15, 9.4%), dizziness (n=9, 5.7%), physical weakness (n=8, 5.0%), and appetite loss (n=6, 3.8%). Respiratory or circulatory symptoms included cough (n=29, 18.2%), sputum (n=14, 8.8%), dyspnea (n=17, 10.7%), and chest discomfort (n=8, 5.0%). For the head/neck/ear/nose and throat symptoms, 34 subjects (21.4%) were found to have loss of smell, while 15 patients (9.4%) had loss of taste. In addition, musculoskeletal symptoms such as muscle pain and joint pain, skin symptoms such as hair loss and dermatitis, and neuropsychiatric symptoms such as lethargy, anxiety, and depression, were identified as symptoms of PCC.

Out of the 211 patients who initially presented no symptoms, 27 (12.8%) eventually developed PCC, with cough and fatigue being the most frequently observed. Among the 374 patients who did exhibit initial symptoms, 132 (35.3%) were diagnosed with PCC. The most common symptoms in this group were loss of smell, cough, dyspnea, loss of taste, fatigue, and sputum production (Supplemental Material 1).

Upon analyzing the relationship between the length of hospitalization and PCC, we found no statistically significant asso-

Table 1. General characteristics and distribution of post-coronavirus disease 2019 condition (PCC)

Characteristics	Subjects (n)	PCC Yes	PCC No	p-value[1]	Characteristics	Subjects (n)	PCC Yes	PCC No	p-value[1]
Total	585	159 (27.2)	426 (72.8)		Head-neck-ear-nose and throat				
Sex				0.177	Loss of taste				0.182
Male	310	77 (24.8)	233 (75.2)		No	571	153 (26.8)	418 (73.2)	
Female	275	82 (29.8)	193 (70.2)		Yes	14	6 (42.9)	8 (57.1)	
Age (y)				0.245	Loss of smell				0.004
<40	251	62 (24.7)	189 (75.3)		No	570	150 (26.3)	420 (73.7)	
40-64	236	73 (30.9)	163 (69.1)		Yes	15	9 (60.0)	6 (40.0)	
≥65	98	24 (24.5)	74 (75.5)		Headache				0.678
Underlying disease				0.175	No	506	136 (26.9)	370 (73.1)	
No	439	113 (25.7)	326 (74.3)		Yes	79	23 (29.1)	56 (70.9)	
Yes	146	46 (31.5)	100 (68.5)		Sore throat				0.013
Hypertension				0.022	No	489	123 (25.2)	366 (74.8)	
No	493	125 (25.4)	368 (74.6)		Yes	96	36 (37.5)	60 (62.5)	
Yes	92	34 (37.0)	58 (63.0)		Gastrointestinal symptoms				
Hyperlipidemia				0.116	Vomiting/nausea				0.922
No	536	141 (26.3)	395 (73.7)		No	581	158 (27.2)	423 (72.8)	
Yes	49	18 (36.7)	31 (63.3)		Yes	4	1 (25.0)	3 (75.0)	
Diabetes mellitus				0.092	Diarrhea				0.358
No	551	154 (27.9)	397 (72.1)		No	575	155 (27.0)	420 (73.0)	
Yes	34	5 (14.7)	29 (85.3)		Yes	10	4 (40.0)	6 (60.0)	
Rhinitis				0.717	Musculoskeletal symptoms				
No	580	158 (27.2)	422 (72.8)		Muscle pain				0.004
Yes	5	1 (20.0)	4 (80.0)		No	500	125 (25.0)	375 (75.0)	
Athsma				0.218	Yes	85	34 (40.0)	51 (60.0)	
No	575	158 (27.5)	417 (72.5)		Hospitalization period (day)				<0.001
Yes	10	1 (10.0)	9 (90.0)		≤10	199	50 (25.1)	149 (74.9)	
Others				0.112	11-20	337	83 (24.6)	254 (75.4)	
No	533	140 (26.3)	393 (73.7)		21-30	33	16 (48.5)	17 (51.5)	
Yes	52	19 (36.5)	33 (63.5)		≥31	16	10 (62.5)	6 (37.5)	
Initial symptoms at diagnosis				<0.001	Ethnicity				
No	211	27 (12.8)	184 (87.2)		Korean	470	138 (29.4)	332 (70.6)	-
Yes	374	132 (35.3)	242 (64.7)		Difference in PCC proportion from the reference		Reference		
Systemic symptoms					Asian	88	18 (20.5)	70 (79.5)	0.114
Fever/chills				0.001	Difference in PCC proportion from the reference		-8.9%p		
No	409	94 (23.0)	315 (77.0)		European	7	2 (28.6)	5 (71.4)	1.000
Yes	176	65 (36.9)	111 (63.1)		Difference in PCC proportion from the reference		-0.8%p		
Respiratory symptoms					African	20	1 (5.0)	19 (95.0)	0.035
Cough/sputum				0.001	Difference in PCC proportion from the reference		-24.4%p		
No	421	98 (23.3)	323 (76.7)						
Yes	164	61 (37.2)	103 (62.8)						
Dyspnea				0.387					
No	583	159 (27.3)	424 (72.7)						
Yes	2	0 (0.0)	2 (100)						

Values are presented as number (%).
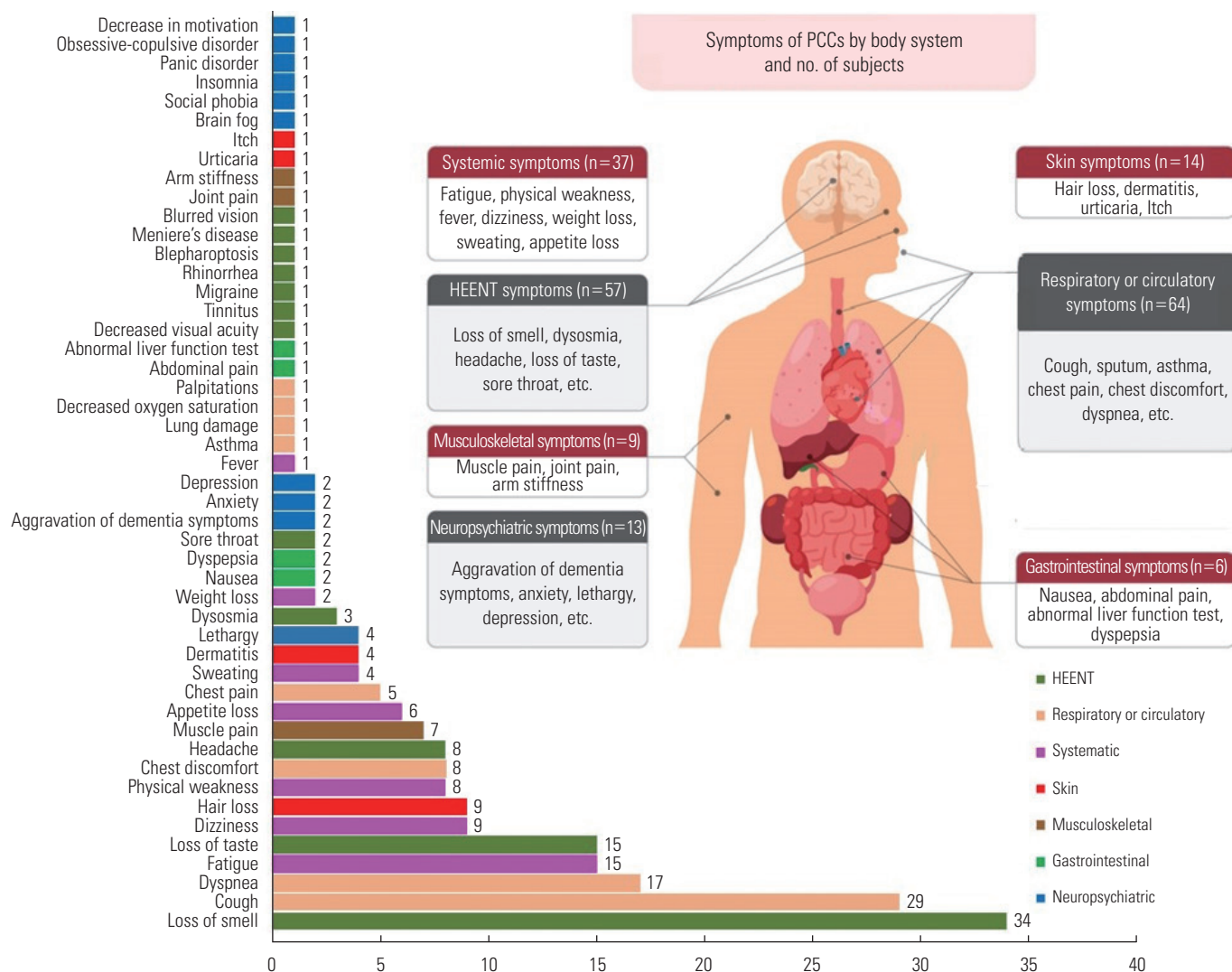[1]Chi-square test.

Figure 1. Symptoms of post-coronavirus disease 2019 conditions (PCC) by body systems. The bar graphs listed on the left show symptoms and the number of patients by PCC, and the human figure on the right shows body parts by system. HEENT, head, eyes, ears, nose, and throat.

ciation with systemic symptoms, or symptoms related to the head, neck, ear, nose, and throat, as well as musculoskeletal symptoms (Table 3). However, within the categories of respiratory and circulatory symptoms, statistically significant associations were observed with sputum and dyspnea. Similarly, among gastrointestinal symptoms, vomiting and nausea were significantly associated with the length of hospitalization (p=0.045, 0.001, and <0.001, respectively).

The multiple logistic regression performed to examine the relationships between various risk factors and PCC showed no statistically significant findings for sex, age, underlying disease, and ethnicity (Table 4). However, initial symptoms and length of hospitalization showed statistically significant rela-

tionships with PCC. Compared to subjects with no initial symptoms, those with initial symptoms of fever or chills, cough or sputum, loss of smell, and sore throat had a higher risk of developing PCC (odds ratio [OR] and 95% confidence interval [CI], 1.79 [1.17 to 2.74]; 1.67 [95% CI, 1.10 to 2.53]; 5.39 [95% CI, 1.80 to 16.09], and 1.69 [95% CI, 1.03 to 2.77], respectively). Compared to subjects with a length of hospitalization of 10 days or less, those with a length of hospitalization of 21 days to 30 days and those with a length of hospitalization of 31 days or more had a statistically significant higher risk of developing PCC (OR [95% CI], 2.32 [95% CI, 1.04 to 5.15] and 5.80 [95% CI, 1.85 to 18.15]).

Table 2. Types of post-coronavirus disease 2019 condition (PCC)

Types	Classification	Subjects (n=585)
PCC	No	426 (72.8)
	Yes	159 (27.2)
Systemic symptoms		37 (23.3)
	Fatigue	15 (9.4)
	Appetite loss	6 (3.8)
	Physical weakness	8 (5.0)
	Fever	1 (0.6)
	Dizziness	9 (5.7)
	Weight loss	2 (1.3)
	Sweating	4 (2.5)
Respiratory or circulatory symptoms		64 (40.3)
	Cough	29 (18.2)
	Sputum	14 (8.8)
	Chest pain	5 (3.1)
	Chest discomfort	8 (5.0)
	Dyspnea	17 (10.7)
	Others[1]	5 (3.1)
Gastrointestinal symptoms		6 (3.8)
	Nausea	2 (1.3)
	Abdominal pain	1 (0.6)
	Abnormal liver function test	1 (0.6)
	Dyspepsia	2 (1.3)
Head-neck-ear-nose and throat symptoms		57 (35.8)
	Loss of smell	34 (21.4)
	Loss of taste	15 (9.4)
	Dysosmia	3 (1.9)
	Headache	8 (5.0)
	Sore throat	2 (1.3)
	Others[2]	7 (4.4)
Musculoskeletal symptoms		9 (5.7)
	Muscle pain	7 (4.4)
	Joint pain	1 (0.6)
	Arm stiffness	1 (0.6)
Skin symptoms		14 (8.8)
	Hair loss	9 (5.7)
	Dermatitis	4 (2.5)
	Urticaria	1 (0.6)
	Itch	1 (0.6)
Neuropsychiatric symptoms		13 (8.2)
	Aggravation of dementia symptoms	2 (1.3)
	Anxiety	2 (1.3)
	Lethargy	4 (2.5)
	Depression	2 (1.3)
	Others[3]	5 (3.1)

Values are presented as number (%); The percentage for each symptom was expressed as a proportion among subjects with PCC.
[1] Asthma, lung damage, decreased oxygen saturation, and palpitations.
[2] Migraine, blepharoptosis, Meniere's disease, blurred vision, decreased visual acuity, tinnitus, and rhinorrhea.
[3] Brain fog, social phobia, insomnia, panic disorder, obsessive-compulsive symptoms, and low motivation.

Table 3. Associations between length of hospitalization and post-coronavirus disease 2019 condition (PCC)

PCC	Length of hospitalization (day)				p-value[1]
	≤10	11-20	21-30	≥31	
Total	199 (34.0)	337 (57.6)	33 (5.6)	16 (2.7)	
Systemic symptoms					0.890
Yes	56 (31.8)	104 (59.1)	11 (6.3)	5 (2.8)	
No	143 (35.0)	233 (57.0)	22 (5.4)	11 (2.7)	
Fever					0.980
Yes	47 (33.6)	82 (58.6)	7 (5.0)	4 (2.9)	
No	152 (34.2)	255 (57.3)	26 (5.8)	12 (2.7)	
Chills					0.374
Yes	15 (24.6)	39 (63.9)	5 (8.2)	2 (3.3)	
No	184 (35.1)	298 (56.9)	28 (5.3)	14 (2.7)	
Respiratory or circulatory symptoms					0.601
Yes	51 (30.9)	97 (58.8)	12 (7.3)	5 (3.0)	
No	148 (35.2)	240 (57.1)	21 (5.0)	11 (2.6)	
Cough					0.766
Yes	46 (30.9)	89 (59.7)	10 (6.7)	4 (2.7)	
No	153 (35.1)	248 (56.9)	23 (5.3)	12 (2.8)	
Sputum					0.045
Yes	13 (32.5)	21 (52.5)	6 (15.0)	0 (0.0)	
No	186 (34.1)	316 (58.0)	27 (5.0)	16 (2.9)	
Dyspnea					0.001
Yes	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	
No	199 (34.1)	336 (57.6)	33 (5.7)	15 (2.6)	
Head-neck-ear-nose and throat symptoms					0.513
Yes	59 (36.2)	87 (53.4)	12 (7.4)	5 (3.1)	
No	140 (33.2)	250 (59.2)	21 (5.0)	11 (2.6)	
Loss of taste					0.397
Yes	3 (21.4)	11 (78.6)	0 (0.0)	0 (0.0)	
No	196 (34.3)	326 (57.1)	33 (5.8)	16 (2.8)	
Headache					0.335
Yes	29 (36.7)	40 (50.6)	6 (7.6)	4 (5.1)	
No	170 (33.6)	297 (58.7)	27 (5.3)	12 (2.4)	
Sore throat					0.642
Yes	31 (32.3)	54 (56.3)	8 (8.3)	3 (3.1)	
No	168 (34.4)	283 (57.9)	25 (5.1)	13 (2.7)	
Gastrointestinal symptoms					0.026
Yes	3 (25.0)	6 (50.0)	1 (8.3)	2 (16.7)	
No	196 (34.2)	331 (57.8)	32 (5.6)	14 (2.4)	
Vomiting and nausea					<0.001
Yes	0 (0.0)	2 (50.0)	0 (0.0)	2 (50.0)	
No	199 (34.3)	335 (57.7)	33 (5.7)	14 (2.4)	
Diarrhea					0.878
Yes	3 (30.0)	6 (60.0)	1 (10.0)	0 (0.0)	
No	196 (34.1)	331 (57.6)	32 (5.6)	16 (2.8)	
Musculoskeletal symptoms					0.382
Yes	35 (41.2)	42 (49.4)	6 (7.1)	2 (2.4)	
No	164 (32.8)	295 (59.0)	27 (5.4)	14 (2.8)	

Values are presented as number (%).
[1] Chi-square test.

Table 4. Effect of risk factors on post-coronavirus disease 2019 conditions (PCC)

Variables	n	PCC, n (%)	aOR (95% CI)[1]	*p*-value
Sex				
Male	310	77 (24.8)	1.00 (reference)	
Female	275	82 (29.8)	1.28 (0.86, 1.90)	0.229
Age (y)				
<40	251	62 (24.7)	1.00 (reference)	
40-64	236	73 (30.9)	1.21 (0.78, 1.87)	0.404
≥65	98	24 (24.5)	0.83 (0.45, 1.53)	0.553
Underlying disease				
None	439	113 (25.7)	1.00 (reference)	
Yes	146	46 (31.5)	1.22 (0.77, 1.94)	0.391
Initial symptoms				
Fever/chills				
No	409	94 (23.0)	1.00 (reference)	
Yes	176	65 (36.9)	1.79 (1.17, 2.74)	0.007
Cough/sputum				
No	421	98 (23.3)	1.00 (reference)	
Yes	164	61 (37.2)	1.67 (1.10, 2.53)	0.016
Loss of smell				
No	570	150 (26.3)	1.00 (reference)	
Yes	15	9 (60.0)	5.39 (1.80, 16.09)	0.003
Sore throat				
No	489	123 (25.2)	1.00 (reference)	
Yes	96	36 (37.5)	1.69 (1.03, 2.77)	0.036
Muscle pain				
No	500	125 (25.0)	1.00 (reference)	
Yes	85	34 (40.0)	1.67 (1.00, 2.80)	0.051
Length of hospitalization (day)				
≤10	199	50 (25.1)	1.00 (reference)	
11-20	337	83 (24.6)	0.87 (0.56, 1.35)	0.529
21-30	33	16 (48.5)	2.32 (1.04, 5.15)	0.039
≥31	16	10 (62.5)	5.80 (1.85, 18.15)	0.003
Ethnicity				
Korean	470	138 (29.4)	1.00 (reference)	
Asia	88	18 (20.5)	0.67 (0.37, 1.23)	0.199
European	7	2 (28.6)	1.62 (0.29, 9.07)	0.585
African	20	1 (5.0)	0.21 (0.03, 1.76)	0.151

aOR, adjusted odds ratio; CI, confidence interval.
[1]The aORs were estimated from a multiple logistic regression mutually adjusted for each other.

DISCUSSION

This study found that characteristics such as sex, age, underlying disease, and ethnicity did not significantly affect the occurrence of PCC. Patients with initial symptoms of fever or chills, cough or sputum, loss of smell, and sore throat were more likely to develop PCC than patients without initial symptoms. Throughout the study period, all COVID-19 patients were admitted to either residential treatment centers or medical facilities; the longer the hospitalization (21 days or more), the greater the likelihood of experiencing PCC. Furthermore, the study found that various forms of PCC could occur in individuals without initial symptoms (Supplemental Material 1). The study also revealed that initial symptoms of COVID-19, such as cough, loss of smell, headache, and sputum production, could persist until the period identified as PCC.

A national survey conducted in Malta found that PCC was associated with female sex, hospitalization, and initial symptoms [14]. In this study, it was found that there was no statistically significant association between PCC and sex, which was inconsistent with the Malta study [14]. This result, however, is consistent with a study of the US CDC Morbidity and Mortality Weekly Reports based on electronic medical records, which found no significant association with sex [15]. A study on the non-hospitalized population reported that the number of initial symptoms was related to PCC [16]. This study showed a strong relationship between initial symptoms and PCC, which is consistent with the Malta study but inconsistent with the WHO announcement that initial symptoms are not related to PCC. According to a study by the US CDC COVID-19 Emergency Response Team, PCC was experienced by 20.8% of those aged 18 to 64 and 26.9% of those aged 65 or older with respiratory symptoms and muscle pain [15]. In addition, a study conducted in Korea reported that advanced age was a risk factor for PCC [10], but this is not consistent with our study.

In this study, 49 PCC symptoms, including fatigue, cough, and shortness of breath, were investigated. These symptoms were identified through an open-ended question and were found in similar proportions and types as in other studies [17-20]. The results are similar to those of previous research, including a systematic review and meta-analysis [1,2,19,21]. One of the outcomes of that study was that a longer hospitalization period was associated with PCC, a finding that is in agreement with the results of this study [16].

In another study focusing on outpatients and inpatients, it was found that the majority of patients sought hospital care following the onset of initial symptoms. Consequently, the percentage of subjects initially classified as "asymptomatic" among those with PCC was as low as 1.2% [10, 21]. Therefore, in other studies, it has been challenging to examine meaning-

ful data about individuals who did not exhibit initial symptoms, as the study participants were individuals diagnosed with the disease in a hospital setting. However, in Korea, an epidemiological investigation was carried out through an integrated health and disease management system for COVID-19 patients at a local public health center. This approach made it possible to confirm the presence and type of initial symptoms, revealing that 12.8% of those without initial symptoms eventually developed PCC.

Several potential biological mechanisms for PCC have been identified. These include damage to the autonomic nervous system, inflammation, autoimmunity, endothelial dysfunction, viral persistence, and coagulation activation [22]. However, the precise mechanisms responsible for PCC are not yet fully understood. Further research is required to gain a more comprehensive understanding of these conditions.

This study has some limitations. First, the survey was only conducted once due to the unplanned nature of the study, which made it impossible to identify any symptoms that may have initially presented, disappeared, and then recurred. A more extensive investigation over a longer period could have allowed for a more detailed analysis of the duration of the sequelae. Second, the survey was not integrated with clinical practice, which may have led to the inclusion of subjective opinions in the classification of initial symptoms and PCC. Symptoms might have been ambiguously categorized by body systems, such as respiratory or circulatory, due to the absence of a clear clinical evaluation. Finally, symptoms that manifest after a certain period may be indicative of other diseases, like influenza, rather than being post-COVID-19 symptoms. This implies the necessity of a differential diagnosis.

Nevertheless, this study has several implications. It involved subjects whose age distribution mirrored that of the national confirmed cases at the time of the survey (Supplemental Material 2), and participants were surveyed about various initial symptoms and PCC through open-ended questions. In addition, the survey was conducted by telephone on a 1:1 basis for all age groups, unlike a previous study that focused on subjects who were between 17 years to 29 years old [10].

In conclusion, this study identified specific factors linked to the incidence of PCC. These factors include initial symptoms such as fever, chills, cough, sputum production, loss of smell, and sore throat, as well as extended hospital stays. Moreover, the emergence of PCC in initially asymptomatic patients underscores the necessity for robust guidance and monitoring systems. Given the ongoing COVID-19 epidemic in Korea, there is a notable dearth of research on PCC and its associated risk factors. As such, there is a pressing need for further research in various areas, including the PCC investigation currently being spearheaded by the KDCA.

SUPPLEMENTAL MATERIALS

Supplemental materials are available at https://doi.org/10.3961/jpmph.23.124.

CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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AUTHOR CONTRIBUTIONS

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ORCID

Myungwon Jang   *https://orcid.org/0000-0002-7367-3180*
Dongkwon Choi   *https://orcid.org/0000-0002-8827-1483*
Jonghyuk Choi   *https://orcid.org/0000-0002-8661-493X*
Ho-Jang Kwon   *https://orcid.org/0000-0003-3029-5674*

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