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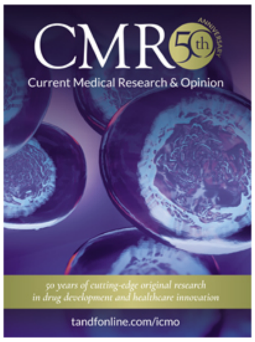


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RESEARCH ARTICLE

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# Evaluation of risk factors associated with SARS-CoV-2 transmission

Mai Ngoc Luu[a*], Shamael Thabit Mohammed Alhady[b*], Minh Duc Nguyen Tran[c*], Le Van Truong[d*], Ahmad Qarawi[e], U. Venkatesh[f], Ranjit Tiwari[g], Ian Christopher Naungayan Rocha[h], Le Huu Nhat Minh[i,j,k], Rohanti Ravikulan[l], Shyam Prakash Dumre[m], Hoang Thi Nam Giang[n], Dmytro Pavlenko[o], Fatmaelzahraa Yasser Ali[p], Bao-Tran Do Le[q], Sedighe Karimzadeh[r,s], Parshal Bhandari[t], Jaffer Shah[u], Jeza Muhamad Abdul Aziz[v,w], Nguyen Tien Huy[x] and the TMGH COVID-19 Collaborators[†]

[a]Department of Internal Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam; [b]Faculty of Medicine, University of Gezira, Wad Medani, Sudan; [c]Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam; [d]Ministry of the Public Security, Traditional Medicine Hospital, Hanoi, Vietnam; [e]Essen Healthcare, Bronx, NY, USA; [f]Department of Community Medicine & Family Medicine, All India Institute of Medical Sciences, Gorakhpur, India; [g]B.P. Koirala Institute of Health Sciences, Dharan, Nepal; [h]School of Medicine, Centro Escolar University, Manila, Philippines; [i]International Master/Ph.D. Program in Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; [j]Research Center for Artificial Intelligence in Medicine, Taipei Medical University, Taipei, Taiwan; [k]Global Clinical Scholars Research Training Program, Harvard Medical School, Boston, MA, USA; [l]Flinders Medical Centre, Bedford Park, South Australia, Australia; [m]Central Department of Microbiology, Tribhuvan University, Kathmandu, Nepal; [n]School of Medicine and Pharmacy, The University of Danang, Danang, Vietnam; [o]Department of Ophthalmology, Bogomolets National Medical University, Kyiv, Ukraine; [p]Faculty of Medicine, Zagazig University, Zagazig, Egypt; [q]Faculty of Chemistry and Biochemistry, University of California, Los Angeles, CA, USA; [r]Department of Neurology, University Hospital Cologne, Cologne, Germany; [s]Online Research Club, Nagasaki University, Nagasaki, Japan; [t]Department of Anesthesia and Intensive Care, PGMI/Lahore General Hospital, Lahore, Pakistan; [u]New York State Department of Health, New York, NY, USA; [v]Baxshin research center, Baxshin Hospital, Sulaymaniyah, Kurdistan Region, Iraq; [w]Medical Laboratory Science, College of Health Sciences, University of Human Development, Sulaymaniyah, Kurdistan Region, Iraq; [x]School of Tropical Medicine and Global Health, Nagasaki University, Nagasaki, Japan

**ABSTRACT**

**Objective:** Coronavirus disease 2019 (COVID-19) has caused high morbidity and mortality worldwide. Since there is not enough evidence of risk factors of SARS-CoV-2 transmission, this study aimed to evaluate them.

**Methods:** This survey-based study was conducted across 66 countries from May to November 2020 among suspected and confirmed individuals with COVID-19. The stepwise AIC method was utilized to determine the optimal multivariable logistic regression to explore predictive factors of SARS-CoV-2 transmission.

**Results:** Among 2372 respondents who participated in the study, there were 1172 valid responses. The profession of non-healthcare-worker (OR: 1.77, 95%CI: 1.04–3.00, $p = .032$), history of SARS-CoV or MERS-CoV infection (OR: 4.78, 95%CI: 2.34–9.63, $p < .001$), higher frequency of contact with colleagues (OR: 1.17, 95%CI: 1.01–1.37, $p = .041$), and habit of hugging when greeting (OR: 1.25, 95%CI: 1.00–1.56, $p = .049$) were associated with an increased risk of contracting COVID-19. Current smokers had a lower likelihood of having COVID-19 compared to former smokers (OR: 5.41, 95%CI: 1.93–17.49, $p = .002$) or non-smokers (OR: 3.69, 95%CI: 1.48–11.11, $p = .01$).

**Conclusions:** Our study suggests several risk factors for SARS-CoV-2 transmission including the profession of non-healthcare workers, history of other coronavirus infections, frequent close contact with colleagues, the habit of hugging when greeting, and smoking status.

**PLAIN LANGUAGE SUMMARY**

Since there is not enough evidence of risk factors of SARS-CoV-2 transmission, this study aimed to evaluate them. The risk of SARS-CoV-2 infection was higher among non-healthcare workers and among those who had a history of being tested positive for SARS-CoV or MERS-CoV before the COVID-19 outbreak. The habit of frequent contact with colleagues or hugging when greeting significantly increased the risk of being infected with SARS-CoV-2. The current smokers had a lower risk of getting infected with SARS-CoV-2 than others who had a habit of smoking tobacco in the past or who had never smoked.

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**CONTACT** Nguyen Tien Huy tienhuy@nagasaki-u.ac.jp School of Tropical Medicine and Global Health, Nagasaki University, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan.

*These authors contributed equally to this work. The authors wish it to be known that, in their opinion, the first 4 authors should be regarded as joint First Authors.

[†]For the list of Collaborators see Supplementary file S1.

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## Introduction

Coronavirus disease 2019 (COVID-19) is a contagious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Since December 2019, when initial cases were identified in Wuhan, China, the disease has rapidly spread across 220 countries and territories around the world and became a pandemic[2]. The ongoing pandemic has caused significant morbidity and mortality with 585,950,085 confirmed cases and 6,425,422 deaths worldwide as of August 12, 2022[3]. Therefore, there is an urgent need to control disease transmission.

Human transmission of SARS-CoV-2 is primarily *via* respiratory droplets through a mucosal or direct inhalation route[4]. While most coronaviruses are spread through respiratory droplets, SARS-CoV-2 shows environmental resistance, making transmission possible through surfaces, hands, air, water, and waste[5]. The aerosol transmission was reported to be another possible route[6]. However, this notion is still controversial. Some of the common factors that affect the transmission of this disease include non-compliance to public health protocols, attending social gatherings, staying in poorly ventilated areas, deprivation and population density[5,7]. Medical comorbidities such as chronic kidney disease, mental illness or cancer were shown to be associated with an increased risk of SARS-CoV-2 infection[8,9].

Despite various precautions (including border closures, social distancing, mask-wearing, and handwashing practices) that have been implemented to prevent the spread of SARS-CoV-2, there have been reports of several super-spreading events that led to many secondary infected cases and in some similar situations led to a community transmission of SARS-CoV-2[4,5,7,10]. Super-spreading may also be used to describe settings and events. Settings include cruise ships, airplanes, hospitals, care homes, schools, workplaces, and hotels, while events involve large gatherings or movements of groups or individuals[11,12]. These super-spreaders perhaps have some common characteristics that can be the risk factors of rapid transmission[10,11]. Identifying these factors will be very helpful in controlling disease transmission.

In the context of the ongoing COVID-19 pandemic, we conducted this study to evaluate the risk factors of COVID-19 transmission. The results can help to better understand the transmission dynamics of SARS-CoV-2 and potentially prevent and control the infection.

## Materials and methods

### Study design and participants

This multinational cross-sectional study aimed to detect the risk factors associated with transmission of SARS-CoV-2 infection. The data collection lasted for 7 months from May to November 2020 and reached 66 countries. The target population of this study was suspected and confirmed individuals with SARS-CoV-2 infection divided into two groups: the F0 group including individuals who were confirmed with SARS-CoV-2 infection; and the non-F0 group including individuals who had close contact with F0, who were suspected to be infected with SARS-CoV-2 during contact-tracing, who returned from affected geographic areas, or who lived, stayed, or worked at a place nearby F0. Additional selection criteria of the target population included individuals who were quarantined or isolated in hospitals or quarantine facilities. Those who were quarantined at home due to lockdown measures were excluded from the study.

A convenience sampling method was employed in this study with no restriction on age, gender, race, religion, marital status, education, and employment status. The recruitment of respondents was done *via* social media accounts of the authors and collaborators by sharing and posting the survey links. SurveyMonkey (SVMK Inc., San Mateo, CA, USA) was used as a platform to create the questionnaire and collect the data. The web-based survey data was extracted and encrypted for analysis ensuring confidentiality was maintained. All respondents filled out an informed consent indicated on the first page of the survey. The study obtained academic and ethical approval from the Institutional Review Board Office of the School of Tropical Medicine and Global Health, Nagasaki University, Japan (Reference number: NU_TMGH_2020_118_1).

### Survey questionnaire

The survey was carried out using a structured questionnaire prepared by the authors based on previous related studies, which included questions on demographic characteristics, disease-related characteristics, environmental factors, behavioral factors, knowledge of disease prevention, and past medical history[13–16]. The original English questionnaire was validated by a pilot survey of 30 medical students and 10 subjects who were quarantined during the COVID-19 pandemic to ensure the validity and reliability of the survey questions. The original questionnaire was then translated into 15 languages (Albanian, Arabic, Filipino, German, Hindi, Indonesian, Korean, Kurdish, Malayalam, Nepali, Russian, Spanish, Tamil, Ukrainian, and Urdu), to widen the reach of respondents. Both forward and reverse translation for each language was performed. The translated questionnaire in each language was pretested on five native speakers and modified if needed. The original English survey questionnaire and the 15 translated versions were detailed in Supplementary file S2.

### Statistical analysis

The gathered data were organized and collected in an Excel spreadsheet (Microsoft Corp., Redmond, Washington, USA), which was then processed and analyzed using R language version 4.0.2. In the descriptive statistics section, we compare the difference between the F0 and non-F0 groups using the Student's *T*-test, Mann-Whitney U, Chi-square, and Phi and

Crammer's V tests. We treated 5-Likert scale responses as continuous variables and calculated the Odds ratios (ORs) for each increase in frequency with values from 1 to 5 referring to the base factor level of 1 (never)[17]. Multivariable logistic regression analysis using the Stepwise Akaike information criterion (AIC) method on the MASS package was performed to explore the predictive factors of SARS-CoV-2 transmission. The potential explanatory variables were selected through AIC method to determine the optimal fit model in predicting the risk of getting SARS-CoV2.

## Results

### *Characteristics of study participants*

Among 2372 respondents who participated in the study, there were a total of 1172 (49.4%) valid responses. The median age of participants was 29 years (IQR 23–28.8). The male/female ratio was 1/1.1. Healthcare workers composed 40.3% of the respondents. Table 1 summarized the sociodemographic characteristics of participants, divided into F0 and non-F0 groups. The F0 and non-F0 groups were statistically different in their profession, race, religion, marital and employment status, history of having a positive test for SARS-CoV or MERS-CoV before the COVID-19 outbreak, medical history of high blood pressure, and history of getting influenza vaccination in the past 12 months ($p < .05$).

### *The habit of wearing a face mask*

Table 2 summarized the explored characteristics of the habit of wearing face masks among participants during two weeks before the quarantine or isolation period. Generally, F0 and non-F0 groups were not statistically different in their habit of wearing face masks, including the frequency of wearing face masks and the type of face mask. However, a higher proportion of respondents in the F0 group had the habit of wearing facemasks at the workplace compared to the non-F0 group (47.7% vs. 38.8%) ($p = .046$).

### *Environmental and behavioral factors*

The environmental and behavioral factors between F0 and non-F0 groups were compared and summarized in Supplementary Table S3. A higher proportion of respondents in the F0 group used a car to go to work/school compared to the non-F0 group (67.3% vs. 54.8%, $p = .005$), while more subjects in the latter group had a habit of going to work/school on foot (26.9% vs. 18.7%, $p = .042$). Compared to the non-F0 group, the F0 group reported more frequently being in close contact with colleagues as well as paying a visit to crowded places ($p = .025$ and $p = .002$, respectively). Regarding the hand-washing habit, the F0 group had a lower frequency of hand washing before or after caring for someone at home, who was sick with vomiting or diarrhea ($p = .022$), or after touching animals or animal-related wastes ($p = .041$) compared to the non-F0 group. Also, there was a higher proportion of subjects in the F0 group reported only cleaning their hands with hand sanitizer compared to the non-F0 group (29.7% vs. 20.8%, $p = .019$).

### *Knowledge related to preventing the spread of disease to others*

Table 3 summarizes and compares the knowledge related to preventing the spread of disease to others between F0 and non-F0 groups. All the explored knowledge characteristics were similar between F0 and non-F0 groups, except the knowledge of covering the nose and mouth when coughing or sneezing, and of sharing personal household items. Compared to the F0 group, there was a higher proportion of subjects in the non-F0 group who were aware that covering the nose and mouth when coughing or sneezing could help to prevent the disease transmission to others (80.6% vs. 71.8%, $p = .028$). Also, more subjects in the non-F0 group were aware that avoiding sharing personal household items could prevent the spread of airborne infectious diseases compared to the F0 group (71.7% vs. 62.2%, $p = .031$).

### *Risk factors associated with SARS-CoV-2 transmission in multivariable logistic regression*

After performing the multivariable logistic regression analysis, we found that the profession of non-healthcare-worker (OR: 1.77, 95% CI: 1.04–3.00, $p = .032$), history of being tested positive for SARS-CoV or MERS-CoV before the COVID-19 outbreak (OR: 4.78, 95% CI: 2.34–9.63, $p < .001$), higher frequency of being in contact with colleagues (OR: 1.17, 95% CI: 1.01–1.37, $p = .041$), and habit of hugging when greeting (OR: 1.25, 95% CI: 1.00–1.56, $p = .049$) significantly increased the odds of being infected with SARS-CoV-2. Participants who were suffering from diabetes mellitus were at higher risk of contracting SARS-CoV-2 but this finding only approached the borderline of significance (OR: 2.54; 95% CI: 0.92–6.34, $p = .055$). Participants who were smoking tobacco currently had a lower likelihood of having COVID-19 compared to those who smoked previously (OR: 5.41, 95% CI: 1.93–17.49, $p = .002$) or who never smoked (OR: 3.69, 95% CI: 1.48–11.11, $p = .01$) (Table 4).

## Discussion

Our study examined the risk factors associated with the transmission of SARS-CoV-2. In the current study, among those who were confirmed or suspected to be infected with SARS-CoV-2, non-healthcare workers were more likely to be infected with SARS-CoV-2 compared to healthcare workers. Although healthcare workers were at the frontline in the combat against the COVID-19 pandemic, our study showed that their risk of contracting SARS-CoV-2 infection may be lower than the general population when in close contact with an infected person. This may be attributed to the better awareness and preparedness of healthcare workers against COVID-19 compared to the general community[18,19].

We found that participants with a history of SARS or MERS infection before the COVID-19 outbreak significantly

**Table 1.** Sociodemographic characteristics of F0 and non-F0 groups.

| | Non-F0 | F0 | Total | *p*-value |
|---|---|---|---|---|
| Age (Median – IQR) | 29 (23–38.5) (*n* = 972) | 28 (23–39) (*n* = 155) | 29 (23–38.8) (*n* = 1127) | .884 |
| Gender (*n* = 1116) | | | | .078 |
| Female | 518 (53.8) | 70 (45.8) | 588 (52.7) | |
| Male | 445 (46.2) | 83 (54.2) | 528 (47.3) | |
| Profession (*n* = 1121) | | | | **<.001** |
| Healthcare worker | 365 (37.7) | 87 (56.5) | 452 (40.3) | |
| Non-healthcare worker | 602 (62.3) | 67 (43.5) | 669 (59.7) | |
| Race (*n* = 1121) | | | | **.003** |
| White/Caucasian | 310 (32.1) | 40 (25.8) | 350 (31.3) | |
| Asian | 418 (43.3) | 84 (54.2) | 502 (44.8) | |
| Hispanic/Latino | 74 (7.6) | 18 (11.6) | 92 (8.2) | |
| Others | 164 (17.0) | 13 (8.4) | 177 (15.7) | |
| Religion (*n* = 1126) | | | | **.005** |
| No religion | 218 (22.4) | 14 (9.1) | 232 (20.6) | |
| Buddhist | 37 (3.8) | 5 (3.2) | 42 (3.7) | |
| Christian | 272 (28.0) | 48 (31.2) | 320 (28.4) | |
| Hindu | 84 (8.7) | 15 (9.7) | 99 (8.8) | |
| Muslim | 329 (33.8) | 68 (44.2) | 397 (35.3) | |
| Others | 32 (3.3) | 4 (2.6) | 36 (3.2) | |
| Marital status (*n* = 1066) | | | | **.029** |
| Single | 476 (52.0) | 66 (43.7) | 542 (50.9) | |
| Divorced/ Widowed/ Separated | 41 (4.5) | 3 (2.0) | 44 (4.1) | |
| Married/ Domestic partnership | 398 (43.5) | 82 (54.3) | 480 (45.0) | |
| Education (*n* = 1126) | | | | .094 |
| Master/ PhD/ Doctoral | 81 (8.3) | 10 (6.5) | 91 (8.1) | |
| Undergraduate level | 219 (22.6) | 49 (31.6) | 268 (23.8) | |
| Primary school/ Secondary school/ High school | 270 (27.8) | 46 (29.7) | 316 (28.1) | |
| Vocational training | 365 (37.6) | 45 (29.0) | 410 (36.4) | |
| No formal education | 10 (1.0) | 0 (0.0) | 10 (0.9) | |
| Others | 26 (2.7) | 5 (3.2) | 31 (2.8) | |
| Employment status (*n* = 1126) | | | | **.043** |
| Full-time employment | 322 (33.2) | 69 (44.5) | 391 (34.7) | |
| Casual employment | 67 (6.9) | 8 (5.2) | 75 (6.7) | |
| Others | 22 (2.2) | 3 (1.94) | 25 (2.2) | |
| Part-time employment | 171 (17.6) | 27 (17.4) | 198 (17.6) | |
| Retired | 27 (2.8) | 6 (3.9) | 33 (2.9) | |
| Student | 260 (26.8) | 23 (14.8) | 283 (25.1) | |
| Unemployed | 102 (10.5) | 19 (12.3) | 121 (10.7) | |
| History of a positive test for SARS-CoV or MERS-CoV before COVID-19 outbreak (*n* = 1073) | 48 (5.2) | 25 (16.9) | 73 (6.8) | **<.001** |
| Past medical history | | | | |
| Diabetes mellitus | 40 (4.4) | 10 (7.0) | 50 (4.8) | .251 |
| Hypertension | 53 (5.9) | 17 (12.0) | 70 (6.7) | **.011** |
| Ischemic heart disease | 12 (1.3) | 3 (2.1) | 15 (1.4) | .444 |
| Heart failure | 14 (1.6) | 3 (2.1) | 17 (1.6) | .494 |
| Renal impairment | 9 (1.0) | 3 (2.1) | 12 (1.1) | .216 |
| HIV infection | 6 (0.7) | 1 (0.7) | 7 (0.7) | 1.000 |
| COPD | 3 (0.3) | 0 (0.0) | 3 (0.3) | 1.000 |
| History of allergy (*n* = 1073) | 321 (34.7) | 60 (40.5) | 381 (35.5) | .195 |
| Allergic rhinitis | 174 (42.3) | 41 (53.2) | 215 (44.1) | .100 |
| Asthma | 89 (21.7) | 17 (22.1) | 106 (21.7) | 1.000 |
| Eczema | 43 (10.5) | 10 (13.0) | 53 (10.9) | .650 |
| Drug allergy | 42 (10.2) | 14 (18.2) | 56 (11.5) | .069 |
| Food allergy | 105 (25.5) | 17 (22.1) | 122 (25.0) | .616 |
| Current tobacco smoking status (*n* = 801) | | | | .103 |
| Current tobacco smoking | 112 (16.0) | 10 (9.8) | 122 (15.2) | |
| Former tobacco smoking | 106 (15.2) | 22 (21.6) | 128 (16.0) | |
| Never smoking | 481 (68.8) | 70 (68.6) | 551 (68.8) | |
| History of getting influenza vaccination in the past 12 months (*n* = 897) | | | | **.004** |
| Yes | 195 (25.0) | 46 (39.3) | 241 (26.9) | |
| No | 512 (65.6) | 60 (51.3) | 572 (63.8) | |
| I do not remember | 73 (9.4) | 11 (9.4) | 84 (9.4) | |
| History of getting BCG vaccination in childhood (*n* = 1070) | | | | .645 |
| Yes | 409 (44.4) | 66 (44.6) | 475 (44.4) | |
| No | 161 (17.5) | 30 (20.3) | 191 (17.9) | |
| I do not remember | 352 (38.1) | 52 (35.1) | 404 (37.7) | |

Numbers in the parentheses indicate percentage (%), unless indicated otherwise. Abbreviations. BCG, Bacille Calmette-Guerin; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus Disease 2019; HIV, human immunodeficiency virus; IQR, Inter-quartile range; MERS-CoV, Middle East respiratory syndrome coronavirus; NS, not significant; SARS-CoV, Severe acute respiratory syndrome coronavirus; SD, standard deviation.

**Table 2.** The habit of wearing face masks during two weeks before the quarantine/isolation period.

| | Non-F0 | F0 | Total | *p*-value |
|---|---|---|---|---|
| Frequency of wearing a face mask during 2 weeks before quarantine/isolation ($n = 1066$) | | | | .283 |
| Never | 125 (13.7) | 13 (8.50) | 138 (12.9) | |
| Rarely | 68 (7.45) | 13 (8.50) | 81 (7.6) | |
| Sometimes | 144 (15.8) | 32 (20.9) | 176 (16.5) | |
| Usually | 204 (22.3) | 34 (22.2) | 238 (22.3) | |
| Always | 372 (40.7) | 61 (39.9) | 433 (40.6) | |
| Wear a face mask at home | 113 (12.1) | 25 (16.3) | 138 (12.7) | .185 |
| Wear a face mask at workplace | 362 (38.8) | 73 (47.7) | 435 (40.1) | **.046** |
| Wear a face mask in public places | 531 (56.9) | 91 (59.5) | 622 (57.3) | .613 |
| Wear a face mask whenever I go outside | 474 (50.8) | 91 (59.5) | 565 (52.0) | .057 |
| Using cloth face mask | 336 (35.9) | 53 (34.4) | 389 (35.7) | .791 |
| Using surgical face mask | 544 (58.1) | 92 (59.7) | 636 (58.3) | .772 |
| Using N95 respirator mask | 164 (17.5) | 36 (23.4) | 200 (18.3) | .104 |

Numbers in the parentheses indicate percentage (%), unless indicated otherwise. NS: not significant.

**Table 3.** Comparison of knowledge related to preventing the spread of disease to others between F0 and non-F0 groups.

| Which of the following did you think you should do to prevent the spread of airborne infection disease to people around? | Non-F0 | F0 | Total | *p*-value |
|---|---|---|---|---|
| - Do not go to public places ($n = 1088$) | | | | .804 |
| Yes | 679 (72.4) | 105 (70.0) | 784 (72.1) | |
| No | 228 (24.3) | 39 (26.0) | 267 (24.5) | |
| I do not know | 31 (3.30) | 6 (4.00) | 37 (3.4) | |
| - Do not use public transportation ($n = 1079$) | | | | .534 |
| Yes | 643 (69.1) | 101 (68.2) | 744 (69.0) | |
| No | 225 (24.2) | 40 (27.0) | 265 (24.6) | |
| I do not know | 63 (6.77) | 7 (4.73) | 70 (6.5) | |
| - Stay away from others as much as possible ($n = 1080$) | | | | .422 |
| Yes | 708 (75.9) | 105 (71.4) | 813 (75.3) | |
| No | 195 (20.9) | 35 (23.8) | 230 (21.3) | |
| I do not know | 30 (3.22) | 7 (4.76) | 37 (3.4) | |
| - Use a separate bathroom if available ($n = 1082$) | | | | .624 |
| Yes | 659 (70.6) | 100 (67.1) | 759 (70.1) | |
| No | 198 (21.2) | 34 (22.8) | 232 (21.4) | |
| I do not know | 76 (8.15) | 15 (10.1) | 91 (8.4) | |
| - Limit contact with pets and other animals or wash your hands before and after handling pets ($n = 1074$) | | | | .406 |
| Yes | 569 (61.4) | 85 (57.8) | 654 (60.9) | |
| No | 265 (28.6) | 42 (28.6) | 307 (28.6) | |
| I do not know | 93 (10.0) | 20 (13.6) | 113 (10.5) | |
| - Wear a facemask when you are around other people ($n = 1082$) | | | | .192 |
| Yes | 701 (75.2) | 103 (68.7) | 804 (74.3) | |
| No | 206 (22.1) | 41 (27.3) | 247 (22.8) | |
| I do not know | 25 (2.68) | 6 (4.00) | 31 (2.9) | |
| - Cover your nose and mouth when coughing or sneezing ($n = 1079$) | | | | **.028** |
| Yes | 750 (80.6) | 107 (71.8) | 857 (79.4) | |
| No | 164 (17.6) | 37 (24.8) | 201 (18.6) | |
| I do not know | 16 (1.72) | 5 (3.36) | 21 (1.9) | |
| - Wash your hands often ($n = 1075$) | | | | .264 |
| Yes | 738 (79.6) | 110 (74.3) | 848 (78.9) | |
| No | 172 (18.6) | 36 (24.3) | 208 (19.3) | |
| I do not know | 17 (1.8) | 2 (1.4) | 19 (1.8) | |
| - Avoid sharing personal household items ($n = 1074$) | | | | **.031** |
| Yes | 664 (71.7) | 92 (62.2) | 756 (70.4) | |
| No | 203 (21.9) | 47 (31.8) | 250 (23.3) | |
| I do not know | 59 (6.4) | 9 (6.0) | 68 (6.3) | |
| - Clean all "high-touch" surfaces ($n = 1081$) | | | | .159 |
| Yes | 694 (74.5) | 100 (67.1) | 794 (73.5) | |
| No | 194 (20.8) | 39 (26.2) | 233 (21.6) | |
| I do not know | 44 (4.7) | 10 (6.7) | 54 (5.0) | |

Numbers in the parentheses indicate percentage (%), unless indicated otherwise. Abbreviation. NS, not significant.

had increased odds of being infected with SARS-CoV-2 too. To date, there are no adequate studies evaluating the immunity against COVID-19 following a prior coronavirus infection. Previous studies indicated that antibody responses to coronavirus were transient and waned rapidly after infection, contributing to the risk of reinfection[20,21]. The study of Anderson et al. also reported that antibodies against seasonal human coronavirus were boosted upon SARS-CoV-2 infection but were not associated with protection against this infection[22]. Another possible mechanism is the antibody-dependent enhancement (ADE) occurrence, similar to dengue infections when a second infection is caused by a

**Table 4.** Summary of multivariable logistic regression analysis for F0 cases.

| Predictors | Univariable | | | Multivariable | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *p*-value | OR | 95% CI | *p*-value |
| Profession | | | | | | |
| Healthcare worker | *Reference* | | | *Reference* | | |
| Non-healthcare worker | 2.04 | 1.24–3.33 | **.005** | 1.77 | 1.04–3.00 | **.032** |
| Diabetes mellitus | | | | | | |
| No | *Reference* | | | *Reference* | | |
| Yes | 2.39 | 0.91–5.54 | .055 | 2.54 | 0.92–6.34 | .055 |
| Have you ever been tested positive for a coronavirus (SARS-CoV or MERS-CoV) before the COVID-19 outbreak? | | | | | | |
| No | *Reference* | | | *Reference* | | |
| Yes | 4.48 | 2.35–8.35 | **<.001** | 4.78 | 2.34–9.63 | **<.001** |
| How often did you have close contact with your colleagues?[a] | 1.16 | 1.01–1.34 | **.035** | 1.17 | 1.01–1.37 | **.041** |
| Did you hug when greeting?[a] | 1.29 | 1.05–1.59 | **.016** | 1.25 | 1.00–1.56 | **.049** |
| Which of the following is your current tobacco smoking status? | | | | | | |
| Current tobacco smoking | *Reference* | | | *Reference* | | |
| Former tobacco smoking | 3.55 | 1.41–10.21 | **.011** | 5.41 | 1.93–17.49 | **.002** |
| Never smoking | 2.09 | 0.94–5.57 | .099 | 3.69 | 1.48–11.11 | **.010** |
| Observations | | | | | 607 | |
| $R^2$ Tjur | | | | 0.093 | | |

[a]The frequency of close contact with colleagues and hugging when greeting with 5 specific levels (1 = never, 2 = rarely, 3 = sometimes, 4 = usually, 5 = always).
Abbreviations. COVID-19, Coronavirus Disease 2019; MERS-CoV, Middle East respiratory syndrome coronavirus; NS, not significant; SARS-CoV, Severe acute respiratory syndrome coronavirus; OR, odd ratio; CI, confidence interval.

different virus strain[23]. Longitudinal studies are required to evaluate the relationship between the risk of SARS-CoV-2 infection and the history of other coronavirus infections.

Previous studies reported that if there was an infected individual within the area of 400 $m^2$, their contact would imply a high risk for disease spreading, thus, reducing crowds in public spaces might help in deducting the infection rate[24,25]. We also have a similar observation. Those who were more frequently in close contact with one another (within 2 meters) had a higher possibility of being infected with SARS-CoV-2. In line with this, those who had a habit of hugging when greeting had a higher risk of having COVID-19.

The current study showed that current smokers had a lower possibility of getting infected with SARS-CoV-2 than others who had a habit of smoking tobacco in the past or who had never smoked. This accords with a previous study reporting that current smokers had a lower risk of contracting COVID-19 compared to former smokers and non-smokers (OR, 0.64, 95%CI: 0.49–0.84, $p < .001$) [26]. On the contrary, several previous studies reported the negative impact of smoking on COVID-19 progression and prognosis[27–29]. This discrepancy may be explained by the inadequate quality of collected data on smoking status. "Former smokers" and "non-smokers" may be misclassified as those who quit smoking a long time ago. Also, patients with COVID-19 may have quit smoking after having respiratory symptoms or before admission, thus, were not recorded as "current smokers". A meta-analysis of related papers using reliable self-report measures of smoking status showed that current smokers were at reduced risk of contracting COVID-19 compared to never smokers (RR = 0.74, 95% CI = 0.24–0.64) [30]. This meta-analysis also pointed out that there was no significant difference in hospitalization and disease severity of COVID-19 between current and never smokers. However, compared to never smokers, former smokers were at increased risk of hospitalization due to COVID-19 (RR = 1.20, 95% CI = 0.06–0.37) and of greater disease severity (RR = 1.52, 95% CI = 0.47-0.66)[30]. The angiotensin-converting enzyme 2 (ACE2) receptor has been confirmed to be the main entry of the SARS-CoV-2 to the host mucosa and an increase in the risk of SARS-CoV-2 infection has been observed in those receiving angiotensin-converting enzyme inhibitors[31]. To date, experimental models reported conflicting results regarding the ACE2 expression in the lung epithelium of smokers. The ACE2 expression in respiratory mucosa epithelia of smokers was shown to be downregulated compared with non-smokers, which may explain the lower proportion of smokers in COVID-19 patients[32]. On the contrary, the study of Liu et al. using a mouse model observed increased ACE2 levels in the bronchial epithelium but decreased ACE2 levels in the alveolar epithelium upon smoke exposure[33]. The controversial findings of the association between smoking and COVID-19 should be solved by further independent studies.

Diabetes was reported to be a major risk factor contributing to severity and mortality in COVID-19 patients but did not increase the risk of COVID-19[34]. However, diabetes was showned to be more common in patients with severe COVID-19[34]. In the present study, diabetes status was self-reported by the participants through the survey questions. Participant self-report of a diagnosis of diabetes has been validated to be a reliable method to evaluate diabetes status in previous studies[35,36]. Although participants with diabetes had higher odds of getting infected with SARS-CoV-2 but this finding only approached the borderline of significance ($p = .055$). The non-association between diabetes and the risk of getting COVID-19 may be due to the under-reported rate of diabetes among the patients with COVID-19 or due to the analysis not considering the severity of diabetes.

Results from our current findings may have some implications for policymakers in offering preventive measures for COVID-19 such as health information dissemination to enhance the awareness of COVID-19 among the community and physical distancing during the pandemic. Although the current study showed that smoking was protective against SARS-CoV-2 infection, smoking was reported to be associated with worse outcomes among COVID-19 patients[27,29]. As a result, recommendation of smoking cessation should be maintained during the COVID-19 pandemic.

The current study had several limitations. Firstly, as it was a cross-sectional survey-based study, our results only suggested possible associations between risk factors and COVID-19 but did not determine the exact risk factors of getting COVID-19. Secondly, although our study covered a large population from various geographical locations (66 countries), which ultimately strengthened the study results and made it a global study, the limited number of participants who were confirmed to have COVID-19 compared to non-infected participants might have partially affected the results. Further studies are needed to evaluate the risk factors of SARS-CoV-2 transmission during the ongoing second wave of the pandemic.

## Conclusions

Our study findings obtained from a wide geographic population suggest several possible risk factors of SARS-CoV-2 transmission including the profession of non-healthcare worker, history of other coronavirus infection, frequent close contact with colleagues, habit of hugging when greeting, and tobacco smoking status. These observations required further investigations to offer preventive measures for COVID-19.

## Transparency

### Declaration of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Declaration of financial/other relationships

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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### Author contributions

NTH, MNL, STMA, NTMD, and LVT conceived the study and designed the study protocol. MNL, STMA, NTMD, and LVT performed the data curation, software, formal analysis, validation, and drafted the manuscript. AQ, VU, RT, ICNR, LHNM, RR, SPD, HTNG, DP, FYA, BTDT, SK, PB, JS, JMAA, and the TMGH COVID-19 Collaborators carried out the data investigation and critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. NTH supervised the study project.

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### Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

### Ethics statement

The study obtained academic and ethical approval from the Institutional Review Board Office of the School of Tropical Medicine and Global Health, Nagasaki University, Japan (Reference number: NU_TMGH_2020_118_1).

## ORCID

Mai Ngoc Luu http://orcid.org/0000-0002-8129-1764
Shamael Thabit Mohammed Alhady http://orcid.org/0000-0001-7463-3300
Minh Duc Nguyen Tran http://orcid.org/0000-0002-9333-7539
Le Van Truong http://orcid.org/0000-0002-7474-0453
Ahmad Qarawi http://orcid.org/0000-0001-7278-9889
U. Venkatesh http://orcid.org/0000-0001-8059-9364
Ranjit Tiwari http://orcid.org/0000-0002-2148-4839
Ian Christopher Naungayan Rocha http://orcid.org/0000-0002-8775-6876
Le Huu Nhat Minh http://orcid.org/0000-0002-7728-1539
Shyam Prakash Dumre http://orcid.org/0000-0002-4072-0745
Hoang Thi Nam Giang http://orcid.org/0000-0002-8648-483X
Dmytro Pavlenko http://orcid.org/0000-0001-8761-9559
Bao-Tran Do Le http://orcid.org/0000-0003-3233-8965
Sedighe Karimzadeh http://orcid.org/0000-0002-9981-4404
Parshal Bhandari http://orcid.org/0000-0001-8311-8466
Jaffer Shah http://orcid.org/0000-0002-8961-218X
Jeza Muhamad Abdul Aziz http://orcid.org/0000-0002-1522-1880
Nguyen Tien Huy http://orcid.org/0000-0002-9543-9440

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