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# Follow-up of practiced treatment regimens and health conditions of patients following recovery from COVID-19 residing in Dhaka City: a survey-based, descriptive, cross-sectional study



Tahsin Shahrin Khan<sup>a,b</sup>, Tahmina Shirin<sup>b</sup>, Ahmed Nawsher Alam<sup>b</sup>, Mohammad Abdul Hannan Shakhider<sup>c</sup>, Fahim Haque<sup>a,\*</sup>

<sup>a</sup> Department of Mathematics and Natural Sciences (Microbiology Programme), BRAC University, Dhaka, Bangladesh

<sup>b</sup> Institute of Epidemiology, Disease Control and Research, Dhaka, Bangladesh

<sup>c</sup> Transparency International Bangladesh, Dhaka, Bangladesh

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# ABSTRACT

*Objective:* To observe the prognosis of cases of coronavirus 2019 (COVID-19), focusing on symptoms, treatment and post-recovery health conditions.

*Methodology*: The respondents were residents of Dhaka City, Bangladesh who had a reverse transcription polymerase chain reaction (RT-PCR)-confirmed diagnosis of COVID-19 from the Institute of Epidemiology, Disease Control and Research from October to December 2020. They were followed up 1–3 months after diagnosis. Data were collected via Google forms sent directly by e-mail, and were analysed using SPSS. Participation was voluntary, and confidentiality of the respondents was strictly maintained.

*Results*: Five hundred and twenty-two of 3148 patients who had recovered from COVID-19 responded to the survey. The mean ( $\pm$ standard deviation) age and body mass index of the respondents were 39.8 $\pm$ 13 years and 26.4 $\pm$ 6.5 kg/m<sup>2</sup>, respectively. More males than females participated in this study (70.3% vs 29.5%). Approximately 39.3% of respondents had comorbidities. The majority (88.5%) of respondents had experienced symptoms, including fever, fatigue, anosmia and aguesia, body pain, headache and dry cough, for 1–5 days. Respondents were treated with antibiotics (72.4%), antiparasitics (47.9%) and antivirals (15.9%). Overall, respondents were RT-PCR positive for a mean of 19.7 $\pm$ 7.6 days. Symptoms such as fatigue, anxiety, depression, uneasiness, body pain and dry cough persisted in 76.3% of respondents when they were RT-PCR negative.

*Conclusion:* For most respondents, COVID-19 symptoms extended beyond the period of RT-PCR positivity. Further studies are needed to determine the changing status of COVID-19.

# Introduction

Following identification of the first case of coronavirus disease 2019 (COVID-19) in Bangladesh on 8 March 2020, the number of cases and deaths increased exponentially (World Health Organization, 2021).

According to the World Health Organization, the clinical characteristics of COVID-19 vary from person to person, and approximately 80% of cases remain asymptomatic. According to the Centers for Disease Control and Prevention (2021), symptoms may appear in an individual 2–14 days after exposure to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The symptoms range from mild to severe. Fatigue, fever and dry cough are the most common symptoms in patients with COVID-19 (World Health Organization, 2022). Some patients experience less common symptoms such as muscular or body pain, headache, sore throat, loss of taste, loss of smell, nasal congestion or runny nose, conjunctivitis, nausea or vomiting, and diarrhoea (World Health Organization, 2021). Severe cases often have symptoms such as shortness of breath, persistent pain or pressure in the chest, loss of speech or movement, and inability to wake or stay awake (World Health Organization, 2021).

Although most patients recover completely within weeks of illness, some experience long-term post-COVID conditions. Even after testing negative for COVID-19, patients can experience fatigue or weakness, shortness of breath, headache, dyspepsia, joint pain, cough, chest pain, change in taste or smell, depression, fever, etc., for  $\geq$ 4 weeks (Carfi et al., 2020; Centers for Disease Control and Prevention, 2020a). The possibility of re-infection is also present in many recovered patients

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<sup>\*</sup> Corresponding author. Address: Microbiology Programme, Department of Mathematics and Natural Sciences, BRAC University, 66, Mohakhali, Dhaka 1212, Bangladesh. Tel.: +8801715299027.

E-mail address: fahim.haque@bracu.ac.bd (F. Haque).

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(Centers for Disease Control and Prevention, 2020b). Treating COVID-19 is extremely challenging as very little is known about this novel coronavirus, and because of the changing pattern of the symptoms. In 2020, global clinical trials suggested the use of various antiviral drugs such as remdesivir, chloroquine, hydroxychloroquine, lopinavir and ritonavir to treat COVID-19 (Esposito et al., 2020; Kumar and Al Khodor, 2020; World Health Organization, 2020). Additionally, clinical trials showed that favipiravir, a next-generation antiviral drug, accelerates viral clearance and improves the lung condition of patients; w and ivermectin, a broad-spectrum antiparasitic drug, showed efficacious results when combined with hydroxychloroquine, ribavirin, a guanosine analogue and corticosteroids (Esposito et al., 2020; Kumar and Al Khodor, 2020). The National Guidelines on Clinical Management of Coronavirus Disease (2019) in Bangladesh recommend the use of parac-

etamol and antihistamine for symptomatic treatment; chloroquine, hydroxychloroquine, favipiravir, remdesivir, lopinavir-ritonavir, corticosteroids, ribavirin, tocilizumab, interleukin nebulizers, zinc, melatonin, vitamin C, oseltamivir and empirical antibiotics are also recommended for pharmacological treatment depending on the condition of the patient.

The objective of this study was to help understand the prognosis of patients with COVID-19 in Dhaka City between October and December 2020. This study focused on symptoms, treatment and postrecovery health conditions. It was hoped that this study would provide an overview of the treatment regimens practiced for patients with COVID-19 in Dhaka City.

#### Methods

#### Study design

This was a descriptive cross-sectional study.

# Sample size

The sample size for this survey was calculated to be 384 based on 50% prevalence rate (p), 5% error (d) and 95% confidence interval (z).

# Samplesize $=\frac{z^2pq}{d^2} = 384.2$

Figure 1. Underlying health conditions.

# Study population and setting

This study followed-up 522 patients in Dhaka City, Bangladesh during January and February 2021, who had been diagnosed with COVID-19 between October and December 2020 at the Institute of Epidemiology, Disease Control and Research (IEDCR), in order to assess symptoms, treatment regimens and post-COVID-19 sequelae.

The inclusion criteria for this survey were: (i) patients diagnosed with COVID-19 (confirmed by RT-PCR) at IEDCR between 1 October and 31 December 2020; (ii) patients residing in Dhaka City (North and South), Bangladesh; and (iii) patients who provided their e-mail address and telephone number to the IEDCR database (Figure S1, see online supplementary material).

Patients were asked to take part in the online survey via an e-mail containing a link to the survey. In the case of children, the survey invitation and form were sent to their parent's e-mail address, taken from the IEDCR database. The survey was open for participation from January to February 2021; all data that were self-reported by patients within this period were used in the analysis. After February 2021, the survey was closed as the required representative sample size (n=384) had been reached.

# Statistical analysis

Descriptive data are shown as frequency (%), mean, standard deviation (SD), median and range, as appropriate. No imputation was made for missing data.

On bivariate analysis, Chi-squared test was used to test associations between two categorical variables. However, Fisher's exact test was used in cases of small cell frequency (<5). Similarly, Pearson's correlation test was used to test associations between variables. The independent sample *t*-test was used to test the mean difference between different continuous variables using the dichotomous variable categories.

All statistical analyses were performed using SPSS Version 26.0 (IBM Corp., Armonk, NY, USA). P<0.05 was considered to indicate significance.

#### Results

# Basic characteristics and underlying health conditions

Among the 3148 COVID-19-positive patients invited to participate in this survey, 522 patients responded and were enrolled in the study.

#### Table 1

Basic characteristics of the respondents

	Respondents, <i>n</i> (%)	Asymptomatic, n (%)	Symptomatic,n (%)	
	n=522	<i>n</i> =60	n=462	<i>P</i> -value(Fisher's exact test)
Gender				0.202
Male	367 (70.31)	48 (13.1)	319 (86.9)	
Female	154 (29.50)	12 (7.8)	142 (92.2)	
Other	1 (0.19)	0 (00)	1 (100)	
Age, years				
Mean (SD)	39.76 (±13.02)			
Median	37.00			
Minimum	1			
Maximum	76			
Distribution of age, n (%)				
≤20	14 (2.68)	2 (14.3)	12 (85.7)	0.007
21-30	132 (25.29)	26 (19.7)	106 (80.3)	
31-40	154 (29.50)	13 (8.4)	141 (91.6)	
41-50	109 (20.88)	6 (5.5)	103 (94.5)	
51-60	76 (14.56)	11 (14.5)	65 (85.5)	
>60	37 (7.09)	2 (5.4)	35 (94.6)	
BMI, kg/m <sup>2</sup>	n=507			
Mean (SD)	26.41 (±6.52)			
Median	25.68			
Category of BMI, n (%)				
Underweight (<18.5)	7 (1.38)	1 (14.3)	6 (85.7)	0.768
Normal (18.5–24.9)	221 (43.59)	28 (12.7)	193 (87.3)	
Overweight (25–29.9)	201 (39.64)	21 (10.4)	180 (89.6.)	
Obese (≥30)	78 (15.38)	8 (10.3)	70 (89.7)	

BMI, body mass index; SD, standard deviation.

#### Table 2

Cross-tabulation between body mass index (BMI) and gender

Gender	BMI Underweight	Normal	Overweight	Obese	P-value(Fisher's exact test)
Female, <i>n</i> (%)	5 (3.4)	57 (38.3)	53 (35.6)	34 (22.8)	
Male, n (%)	2 (0.6)	163 (45.7)	148 (41.5)	44 (12.3)	0.009
Other, <i>n</i> (%)	0	1 (100)	0	0	

Among them, 70.3% (*n*=367) were male and 29.5% (*n*=154) were female. The age range of the respondents was 1–76 years. The mean (±SD) age of the respondents was 39.8±13 years. Overall, 29.5% (*n*=154) of the respondents were aged 31–40 years, 25.3% (*n*=132) were aged 21–30 years, and 20.9% (*n*=109) were aged 41–50 years. A significant association was found between age and symptom status (1% level of significance). According to the guidelines of the Centers for Disease Control and Prevention, body mass index (BMI) was classified as underweight (<18.5 kg/m<sup>2</sup>), normal (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>) or obese ( $\geq$ 30 kg/m<sup>2</sup>). Mean (±SD) BMI was 26.4±6.5 kg/m<sup>2</sup>. Most respondents (43.6%, *n*=221) were classified as normal weight. Fifteen respondents did not respond to the question on height and weight (Table 1).

Females accounted for 71.4% (n=5) of the underweight respondents, and the proportion of males was higher among normal weight (73.8%, n=163), overweight (73.6%, n=148) and obese (56.4%, n=44) respondents. A significant association was found between BMI and gender (1% level of significance) (Table 2).

Among the 522 respondents, 39.3% (*n*=205) had pre-existing comorbidities. The main comorbidities were hypertension (56.6%), diabetes (38.1%), asthma (26.3%) and cardiac disease (12.2%) (Figure 1).

Respondents with pre-existing health conditions developed various symptoms of COVID-19 (Table 3).

#### Symptom status during illness

While infected with SARS-CoV-2, 88.5% (n=462) of respondents experienced multiple symptoms and 11.5% were asymptomatic (Table 1)

Figure 2 shows the wide range of symptoms reported by the symptomatic respondents. The symptoms included: fever (73.2%, n=382), fatigue (72.4%, n=378), reduced sense of smell (55.4%, n=289), reduced sense of taste (55.4%, n=289), body pain (54.8%, n=286), headache (51.5%, n=269), dry cough (51%, n=266), nasal congestion or runny nose (40.2%, n=210) and sore throat (29.7%, n=155). Moreover, the respondents suffered from various combinations of symptoms. The mean number of symptoms was 6.6, and 41% of respondents reported experiencing five to eight symptoms (Table S1, see online supplementary material). The respondents reported that most symptoms (i.e. fever, cough, headache, shortness of breath, nasal congestion or runny nose, nausea or vomiting, body pain, chest pain) lasted for 1–5 days from disease onset, whereas 33.3% of the respondents felt fatigue for >20 days (Table S2, see online supplementary material).

#### Treatment regimens

Regarding medications, acetaminophen (81.8%), montelukast (63.6%) and antihistamine (60.2%) were the most common medications taken by the respondents (Figure 3). For antibiotic treatment, 52.3% of the respondents took azithromycin, 41.4% took doxycycline and 7.9% took other antibiotics, including amoxicillin, ciprofloxacin, levofloxacin or penicillin-type antibiotics.

Other medications taken were ivermectin (47.9%), anticoagulants (18.2%), dexamethasone (14.8%), remdesivir (8.8%), favipiravir (8.6%), chloroquine or hydroxychloroquine (6.1%), corticosteroids (5.7%), tocilizumab (2.5%) and oseltamivir (2.1%). Many respondents took zinc (81%), vitamin D (63%) or vitamin C (61.5%) as dietary supplements.

Table 4 shows various combinations of medications used to treat the respondents. Most patients (44.3%, n=231) received single antibiotic therapy, and 28.2% (n=147) received combination antibiotic therapy. One-quarter (27.4%, n=143) of respondents were treated with a combination of ivermectin and doxycycline.

Table 5 depicts the number of patients who took medications with or without doctor's instructions.

# Table 3

Distribution of underlying health conditions among the symptomatic and asymptomatic respondents

Comorbid conditions	Asymptomatic, n (%)	Symptomatic, n (%)	Total
Hypertension	9 (7.8)	107 (92.2)	116
Diabetes	8 (10.3)	70 (89.7)	78
Asthma	3 (5.6)	51 (94.4)	54
Cardiac diseases	3 (12.0)	22 (88.0)	25
Thyroid diseases	0 (0.00)	14 (100)	14
Kidney diseases	1 (8.3)	11 (91.7)	12
Neurological disorders	0 (0.00)	11 (100)	11
Liver diseases	1 (11.1)	8 (88.9)	9
Respiratory diseases	0 (0.00)	6 (100)	6
Tuberculosis	0 (0.00)	1 (100)	1
Immunodeficiency (HIV)	0 (0.00)	1 (100)	1
Malignant diseases (cancer)	0 (0.00)	1 (100)	1

HIV, human immunodeficiency virus.



#### Figure 2. Clinical presentation.

# Table 4

Combinations of medications taken by the respondents

Combination of medication	Respondents (n=522)
Single antibiotic therapy	231 (44.3)
Combination antibiotic therapy	147 (28.2)
Chloroquine or hydroxychloroquine + azithromycin	21 (4)
Ivermectin + doxycycline	143 (27.4)
Favipiravir + tocilizumab	9 (1.7)
Chloroquine or hydroxychloroquine + oseltamivir	7 (1.3)

# Table 5

Prescription of medications

Type of medication	Prescribed by a doctor, <i>n</i> (%)	Not prescribed by a doctor, $n$ (%)
Antibiotic treatment	348 (92.1%)	30 (7.9%)
Antiviral treatment	94 (96.9%)	3 (3.1%)
Antiparasitic treatment	235 (94.0%)	15 (6.0%)

#### Figure 3. Medications taken.



#### Table 6

Cross-tabulation of previous and persistent symptoms

Symptom status during illness, <i>n</i> (%)	Persistence of sympto	ms after recovery	P-value(Chi-
	Present, n (%)	Absent, <i>n</i> (%)	squared)
Asymptomatic, 60 (11.49)	39 (65.0)	21 (35.0)	0.030
Symptomatic, 462 (88.51)	359 (77.7)	103 (22.3)	

# RT-PCR negativity and post-recovery health conditions

Among the 522 respondents, 80.08% repeated the RT-PCR test a significant period of time after their first diagnosis (Figure S2, see online supplementary material). The mean ( $\pm$ SD) period to RT-PCR negativity for COVID-19 was 19.7 $\pm$ 7.6 days.

One-quarter (23.8%) of the respondents had no persistent symptoms after reaching RT-PCR negativity; however, others suffered with one or several persistent symptoms (Table S3, see online supplementary material) Figure 4. depicts the persistence of fatigue (54.8%, n=286), anxiety and/or depression (32.4%, n=169), uneasiness (30.3%, n=158), body pain (25.3%, n=132), headache (21.6%, n=113), dry cough (18.4%, n=96) and loss of appetite (14.6%, n=76) 3 months after diagnosis.

Among the asymptomatic respondents, 65% (n=39) developed various symptoms after testing negative for COVID-19, and 77.7% (n=359) of symptomatic respondents displayed various symptoms even after recovery. A significant association was found between past and persistent symptoms (3% level of significance) (Table 6).

# Correlation between respondent characteristics and days to negative RT-PCR result for COVID-19

Pearson's correlation coefficient showed a weak positive correlation between age and days to negative RT-PCR result [r(416)=0.135, P=0.006]; that is, days to negative RT-PCR result for COVID-19 increased with increasing age.

A weak positive correlation was found between the number of comorbidities and days to negative RT-PCR result [r(416)=0.144,

# Table 7

Association between respondent characteristics and days to negative reverse transcription polymerase chain reaction (RT-PCR) result

Respondent characteristics	Days to negative RT-PCR re Pearson's correlation	esult <i>P</i> -value
Age	0.135	0.006
Body mass index	-0.036	0.471
Number of comorbidities	0.144	0.003
Number of symptoms during	0.140	0.004
illness		

P=0.003); that is, days to negative RT-PCR result increased with increasing number of comorbidities.

A weak positive correlation was found between the number of symptoms during illness and days to negative RT-PCR result [r(416)=0.140, P=0.004]; that is, days to negative RT-PCR result increased with increasing number of symptoms (Table 7).

#### Association between days to negative RT-PCR result and medications

Associations between days to negative RT-PCR result and medications taken by the respondents were tested using independent *t*-test.

Except for antibiotic therapy, the *P*-value was >0.05 for the other medications (Table 8). Therefore, for those medications, the null hypothesis cannot be rejected at the 5% level of significance. The tests (except for the test for antibiotic therapy) did not find a significant difference between the average days to RT-PCR negativity of respondents who received these various medications and those who did not.

#### Discussion

This study investigated the clinical characteristics and treatment of 522 patients with RT-PCR-confirmed COVID-19, diagnosed at IEDCR between 1 October and 31 December 2020 and followed-up within 3 months of diagnosis. The study presents an overview of the treatment regimens practiced, and previous and persistent clinical presentations

Figure 4. Persistent symptoms after recovery.



#### Table 8

Association between days to negative reverse transcription polymerase chain reaction result and medication type

Medication type		Mean (SD)	Mean difference	P-value
Antibiotic	Yes	20.51 (7.91)	-3.12	< 0.001
	No	17.38 (5.85)		
Antiviral	Yes	21.07 (6.48)	-1.66	0.146
	No	19.40 (7.75)		
Antiparasitic	Yes	20.73 (7.37)	-1.96	0.235
	No	18.77 (7.62)		
Anticoagulant	Yes	22.93 (7.896)	-3.91	0.417
	No	19.02 (7.32)		
Corticosteroids	Yes	21.31 (7.95)	-1.93	0.714
	No	19.38 (7.44)		
Zinc	Yes	19.84 (7.22)	-0.813	0.412
	No	19.03 (9.08)		
Vitamin D	Yes	20. 23 (7.064)	-1.43	0.063
	No	18.796 (8.298)		
Vitamin C	Yes	20.52 (7.24)	-2.11	0.407
	No	18.41 (7.89)		
Multivitamin	Yes	19.78 (7.056)	-0.12	0.217
	No	19.67 (7.805)		

SD, standard deviation.

of individuals who had recovered from COVID-19 residing in North and South Dhaka City.

Given the dense population, the highest number of COVID-19 cases in Bangladesh is detected in Dhaka (World Health Organization 2022); hence, Dhaka is considered the core of disease transmission in Bangladesh. For the same reason, Dhaka was the focus area of this study.

Overall, 70.3% of respondents were male and 29.5% were female. Similar findings were found in patients with COVID-19 in China (Guan et al., 2020b; Chen et al., 2021), India (Gupta et al., 2020) and Bangladesh (Hossain et al., 2020; Mowla et al., 2020). Previously, it has been noted that males are more vulnerable to SARS-CoV and MERS-CoV than females (Badawi and Ryoo, 2016; Mowla et al., 2020). Reduced susceptibility of females to such viral infections could be attributed to protection from the X chromosome and sex hormones, which play an important role in innate and adaptive immunity (Channappanavar et al., 2017). Males are generally more involved in outdoor activities which involve being in crowded areas compared with females in the context of Bangladesh; therefore, males are more likely to be affected.

The mean (±SD) age of the study respondents was  $39.8\pm13$  years, which is consistent with studies conducted in India (mean age 40.3 years) (Gupta et al., 2020) and Bangladesh (mean age  $41.7\pm16.3$  years) (Mowla et al., 2020). The age groups most affected were 31-40 years (29.5%) and 21-30 years (25.3%). These factors indicate that active populations are at greater risk of contracting COVID-19, potentially due to outdoor social exposures. Around 2.7% and 7.1% of the patients were aged <20 years and >60 years, respectively.

Mean ( $\pm$ SD) BMI was 26.4 $\pm$ 6.5 kg/m<sup>2</sup>, and the proportion of males was higher in normal weight, overweight and obese BMI classes. Thus, gender was found to be independently and significantly associated with BMI ( $x^2$ = 17.012, *P*=0.003) Kim et al. (2020). reported that underweight and obesity were significantly associated with severe clinical outcomes, including death, among patients with COVID-19. However, it was not possible to find such associations in the present study due to lack of data on disease severity.

Overall, 39.3% of the respondents had diverse underlying health conditions. Hypertension, diabetes, asthma and cardiovascular diseases were the most common comorbidities, similar to the findings of other studies of patients with COVID-19 (Ahmed et al., 2020; Mowla et al., 2020; Yang et al., 2020) as well as MERS-CoV (Badawi and Ryoo, 2016).

In this study, 11.5% of patients were asymptomatic and 88.5% were symptomatic. Further study is required to verify the percentage

of asymptomatic patients found in the present study because it is not an overview of the entire population. Only symptomatic patients, individuals who were in close contact with a patient with COVID-19, and patients who came forward with complaints or suspicion of being infected were tested for COVID-19 during the study period. As such, the number of symptomatic patients was higher than the number of asymptomatic patients; however, this might not be the actual case. Fever, fatigue, body pain, headache, dry cough, sore throat, productive cough, shortness of breath and chest pain were the main symptoms reported. Patients also experienced reduced sense of smell and taste, and skin changes. Gastrointestinal symptoms included diarrhoea, and nausea and vomiting; some respondents complained of loss of appetite and abdominal pain. The responses regarding the symptoms during illness were consistent with Guan et al. (2020a), Hossain et al. (2020) and Ahmed et al. (2020).

As there was inadequate evidence-based specific therapy against COVID-19, a still-unfamiliar virus, during the study period, diverse medications were used where the mainstay was to relieve symptoms, such as acetaminophen, antihistamines and various supplements (e.g. zinc; vitamins D, C, E and A; multivitamins). The respondents received single or combination antibiotic therapy that mainly included azithromycin, doxycycline and other antibiotics (i.e. amoxicillin, ciprofloxacin, levofloxacin). Antiviral therapy included remdesivir, favipiravir and oseltamivir. Other medications included antiparasitic ivermectin, anticoagulants, dexamethasone or corticosteroids, antimalarial drugs (chloroquine or hydroxychloroquine) and immunosuppressive drugs (tocilizumab). The medications used by the respondents were in line with the makeshift national guidelines of clinical management of COVID-19 set by the Ministry of Health and Family Welfare, Bangladesh (2020), and other studies related to the treatment of COVID-19 globally which were not approved by any acceptable regulatory authorities, such as the World Health Organization (Esposito et al., 2020; Kumar and Al Khodor, 2020).

Million et al. (2020) used a combination of hydroxychloroquine and azithromycin to treat COVID-19, and the combination was reported to be safe and to induce low mortality during the peak of the COVID-19 pandemic in France. Similar evidence-based favourable results were reported by Al Mahtab et al. (2020) in a study of 33 patients with COVID-19 in a medical college in Bangladesh (Al Mahtab et al., 2020). However, some studies have raised concerns regarding the use of hydroxychloroquine-azithromycin combination therapy for COVID-19 (Molina et al., 2020) Chowdhury et al. (2021). found that ivermectin-doxycycline combination therapy was more effective than hydroxychloroquine-azithromycin combination therapy in terms of recovery time (mean duration 8.9 days for ivermectin-doxycycline, 9.3 days for hydroxychloroquine-azithromycin), outcome ratio (100% for ivermectin-doxycycline, 96.4% for hydroxychloroquine-azithromycin), and the symptomatic recovery rate in a hospital setting at Chakoria Upazilla Health Complex, Cox's Bazar, Bangladesh with 116 patients with COVID-19 (Chowdhury et al., 2021). In this study, 27.4% of respondents were on ivermectin-doxycycline combination therapy, and 4% were treated with chloroquine or hydroxychloroquine with azithromycin.

As well as the injudicious use of antibiotics, antiparasitic drugs and antivirals by the physicians, it was found that 7.9%, 6.0% and 3.1% of the respondents who were treated with medications took antibiotics, antiparasitic drugs and antivirals, respectively, without a doctor's prescription; this finding is alarming given the increase in antibacterial resistance in the population.

Although some research papers provide new insight regarding the effectiveness or risks of using various medications, it is not good practice to rely on these scattered studies which were not authenticated by regulatory authorities while dealing with novel organisms and consequential diseases. This study indicates that if treatment regimens are not set judiciously, ethically and based on evidence, the haphazard management of cases during a pandemic may have a severe impact on the health and wellbeing of the entire population. This shows that, in future, there is a need to prepare more meticulously and follow a particular evidencebased treatment regimen approved by accepted regulatory authorities to avoid misuse of medications.

Among the self-reporting respondents (Figure S2, see online supplementary material) who repeated the COVID-19 RT-PCR test, it took a mean (±SD) of 19.7±7.6 days to achieve a negative test result after the initial positive result; the range of days required for a negative result was 2-50 days. However, 76.2% of the respondents had persistent symptoms even after they had reached RT-PCR negativity. The persistent symptoms included fatigue, anxiety and/or depression, uneasiness, body pain, headache, dry cough, nasal congestion, loss of appetite, runny nose, shortness of breath, productive cough, and reduced sense of smell and taste; this was consistent with the findings of Carfi et al. (2020). The mean number of persistent symptoms was 3.3, and 44.1% of respondents experienced one to three persistent symptoms (Table S3, see online supplementary material). Among the asymptomatic respondents, 65% developed various symptoms after testing negative. Among the symptomatic respondents, 77.7% continued to suffer from various symptoms after testing negative. Symptoms during illness were found to be significantly associated with persistent symptoms (Table 6).

This study revealed that time to reach RT-PCR negativity increased with increasing age, increasing number of comorbidities, and increasing number of symptoms during illness; these associations were significant at the level of 1%. A significant association was also found between the use of antibiotics and days to negative RT-PCR result. Respondents who had undergone antibiotic treatment took significantly longer to recover than their counterparts. However, related studies could not be found to discuss these findings in greater detail.

#### Limitations

This study had a few limitations. The findings need to be verified by a larger sample in a multicentre study. Challenges relating to online surveys include the risk of a low response rate due to technological disadvantages, lower literacy levels and lack of recipient interest to participate. Due to these challenges, all the patients who met the study inclusion criteria were asked to take part in this survey via e-mail, and only those who self-reported within the 2-month survey period were selected for inclusion in this study. The authors could not collect data from physical examinations (e.g. respiratory rate, oxygen saturation, blood pressure, temperature, etc.) and laboratory findings (i.e. chest X-ray, computed tomography scans, D-dimer, etc.) due to time constraints. Thus, severity of disease could not be assessed. Further studies are needed to provide more COVID-19-related information for Bangladesh.

# Conflict of interest statement

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

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None.

# Ethical approval

Ethical approval was obtained from the Departmental Review Board of BRAC University, Dhaka, Bangladesh. Informed consent was obtained from the respondents before data collection. There was an informed consent section at the start of the Google survey form (https://docs.google.com/forms/d/e/1FAIpQLSe4cgix-a2t0tAIDT604KK89demb1nkR92sLixK7g4xwzXIfA/viewform); only those who agreed to take part in the survey self-responded and provided their data. The consent form was originally written in Bengali for the convenience of the participants; the translated consent form can be found at: https://docs.google.com/document/d/1Zx-mnW6cPpq96T21n2JjAqWw5a\_G7-keMGg0BPswV4I/edit. In the case of children, the survey invitation and form were sent to their parent's e-mail address, taken from the IEDCR database. During data collection and analysis, the privacy of the respondents and confidentiality of the data were strictly maintained. Participation in the survey was entirely voluntary, and the collected data were used anonymously.

# Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2022.03.005.

#### References

- Ahmed N, Islam M, Kabir M, Rahman M, Sadat S. Clinico-pathological findings of Bangladeshi COVID-19 patients with their clinical outcome: study of a cohort of 201 cases. J Bangladesh College Physicians Surgeons 2020;38:37–42.
- Al Mahtab M, Akbar S, Mahtab M, Choudhury N, Islam M, Bhuyan M, et al. Treatment of COVID-19 patients at a medical college hospital in Bangladesh. Euroasian J Hepato– Gastroenterol 2020;10:27–30.
- Badawi A, Ryoo S. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. Int J Infect Dis 2016;49:129–33.
- Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. JAMA 2020;324:603.
- Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19). Atlanta, GA: CDC; 2020a Available at: https://www.cdc.gov/coronavirus/2019-ncov/ long-term-effects.html accessed 18 November 2020.
- Centers for Disease Control and Prevention. COVID-19 and your health. Atlanta, GA: CDC; 2020b Available at: https://www.cdc.gov/coronavirus/2019-ncov/ your-health/reinfection.html accessed 18 November 2020.
- Centers for Disease Control and Prevention. Defining adult overweight and obesity. Atlanta, GA: CDC; 2021 Available at: https://www.cdc.gov/obesity/ adult/defining.html accessed 25 February 2022.
- Channappanavar R, Fett C, Mack M, Ten Eyck P, Meyerholz D, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol 2017;198:4046–53.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2021;395:507–13.

- Chowdhury A, Shahbaz M, Karim M, Islam J, Guo D, He S. A randomized trial of ivermectin-doxycycline and hydroxychloroquine-azithromycin therapy on COVID-19 patients. Eurasian J Med Oncol 2021;5:63–70.
- Esposito S, Noviello S, Pagliano P. Update on treatment of COVID-19: ongoing studies between promising and disappointing results. Infez Med 2020;28:198–211.
- Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020a;382:1708–20.
- Guan W, Liang W, Zhao Y, Liang H, Chen Z, Li Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020b;55.
- Gupta N, Agrawal S, Ish P, Mishra S, Gaind R, Usha G, et al. Clinical and epidemiologic profile of the initial COVID-19 patients at a tertiary care centre in India. Monaldi Arch Chest Dis 2020;90. doi:10.4081/monaldi.2020.1294.
- Hossain I, Khan MH, Rahman MS, Mullick AR, Aktaruzzaman MM. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in Bangladesh: a descriptive study. J Med Sci Clin Res 2020;8:544–51.
- Kim T, Roslin M, Wang J, Kane J, Hirsch J, Kim E. BMI as a risk factor for clinical outcomes in patients hospitalized with COVID-19 in New York. Obesity 2020;29:279–84.
- Kumar M, Al Khodor S. Pathophysiology and treatment strategies for COVID-19. J Translat Med 2020;18:353.
- Million M, Lagier J, Gautret P, Colson P, Fournier P, Amrane S, et al. Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: a retrospective analysis of 1061 cases in Marseille, France. Trav Med Infect Dis 2020;35.
- Molina J, Delaugerre C, Le Goff J, Mela-Lima B, Ponscarme D, Goldwirt L, et al. No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. Méd Malad Infect 2020;50:384.
- Mowla S, Azad K, Kabir A, Biswas S, Islam M, Banik G, et al. Clinical profile of 100 confirmed COVID-19 patients admitted in Dhaka Medical College Hospital, Dhaka, Bangladesh. J Bangladesh Coll Physicians Surgeons 2020;38:29–36.
- World Health Organization. "Solidarity" clinical trial for COVID-19 treatments. Geneva: WHO; 2020 Available at: https://www.who.int/emergencies/diseases/ novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarityclinical-trial-for-covid-19-treatments accessed 19 November 2020.
- World Health Organization. Coronavirus disease (COVID-2019) Bangladesh situation reports. Geneva: WHO; 2021 Available at: https://www.who.int/ bangladesh/emergencies/coronavirus-disease-(covid-19)-update/coronavirusdisease-(covid-2019)-bangladesh-situation-reports accessed 23 April 2021.
- World Health Organization. COVID-19 Situation Report No. 10. Geneva: WHO; 2022 Available at: https://www.who.int/docs/default-source/searo/bangladesh/ covid-19-who-bangladesh-situation-reports/who-ban-covid-19-sitrep-10.pdf? sfvrsn=c0aac0b8\_4 accessed 18 February 2022.
- World Health Organization. Coronavirus disease (COVID-19). Geneva: WHO; 2022 Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/ question-and-answers-hub/q-a-detail/coronavirus-disease-covid-19 accessed 25 February.
- Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 2020;94:91–5.
- National Guidelines on Clinical Management of Coronavirus Disease, 2019 (Covid-19) [Internet]. Mohfw.gov.bd. 2022 [cited 22 March 2022]. Available from: http://www.mohfw.gov.bd/index.php?option=com\_docman&task=doc\_download& gid=22424&lang=en