Follow-up of Practiced Treatment Regimens & Health Conditions of Recovered Patients of COVID-19 Residing in Dhaka City: A Survey-based Descriptive Cross-sectional Study

By

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A thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of
Bachelor of Science in Microbiology

Department of Mathematics and Natural Sciences
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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
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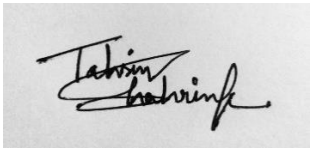

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Approval

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Ethics Statement

The study strictly maintained the principles and guidelines of the Helsinki declarations. Ethical clearance was obtained from the departmental review board of BRAC University, Dhaka, Bangladesh. Informed consent was obtained from the respondents before data collection. During data collection, the privacy of the respondents and confidentiality of the data were maintained strictly. Participation in the survey was completely voluntary, and the collected data was anonymously used only for this current study.

Abstract

Background and aim: Coronavirus disease 2019 (COVID-19), has spread worldwide like wildfire since late December 2019. Caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), this pandemic has induced a sense of panic and caused hundreds of thousands of deaths globally in short span of time. Bangladesh is not an exception regarding COVID-19; there have been several thousand COVID-19 cases and several hundreds of deaths reported so far. This survey-based descriptive cross-sectional study aims to study the prognosis of this viral infection, mainly focusing on the experienced symptoms, treatment regimens and post-recovery health conditions of the patients affected with COVID-19 residing in Dhaka city.

Materials and methods: All the respondents of this study were diagnosed at IEDCR from October to December 2020, and they resided in Dhaka city corporation area. The data were collected via an online survey using Google forms and were analyzed using SPSS version 26.00. The privacy of the respondents and confidentiality of the data were strictly maintained as per protocol.

Results: Among the 522 respondents mean age was 39.76±13.02 years. The respondents consisted of 70.31% males and 29.50% females. The mean BMI of the respondents was 26.4±6.52 kg/m^2. Among the respondents 39.3% were found to have various underlying health conditions. About 88.5% of the respondents suffered from a diverse range of symptoms including fever, fatigue, reduced sense of smell and taste, body pain, headache, dry cough etc. The respondents were on various medications that fell under the national guideline for COVID-19 management of Bangladesh. A mean of 19.71±7.56 days was required by the respondents to obtain a negative RT-PCR result. Various symptoms like fatigue, anxiety and/or depression, uneasiness, body pain, headache, dry cough etc. persisted in 76.3% of the respondents even after their recovery.

Conclusion: Males were more likely to be get affected by COVID-19 than females. Common symptoms of COVID-19 included fever, fatigue, headache, dry cough; less common symptoms like a reduced sense of smell and taste were also prevalent. Most respondents tend to take a longer time to get symptom-free than obtain a negative result. Further studies are required to provide more COVID-19 related information of Bangladesh.

Keywords: COVID-19; SARS-CoV-2; Bangladesh; Dhaka; Survey; Symptoms; Treatment regimens;

Dedication (Optional)

To my parents, Dr. Iqbal Ansary Khan & Dr. Razia Sultana

Thank you, for being the anchors of my life.

Acknowledgement

A humble gratitude to the respectful and cooperative individuals from Institute of Epidemiology, Disease Control and Research (IEDCR), which included: Prof. Dr. Tahmina Shirin, PhD (Director, IEDCR), Dr. Ahmed Nawsher Alam (Principal Scientific Officer, IEDCR) and other employees of the Virology lab. I solemnly thank Mohammad Rafiqul Islam, PhD (Associate Professor, Brac University) and Akash Ahmed (Lecturer, Brac University) for their kind suggestions along the way. Last but not the least, Md. Abdul Hannan and Fahmid Kaisar for their kind help.

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List of Acronyms

CDC	Center for Disease Control and Prevention
COVID-19	Coronavirus Disease 2019
HCQ	Hydroxychloroquine
HIV	Human Immunodeficiency virus
IEDCR	Institute of Epidemiology, Disease Control and Research
LSD	Least square difference
MH&FW	The Ministry of Health & Family Welfare
MERS-CoV	Middle east respiratory syndrome coronavirus
RT-PCR	Reverse transcription polymerase chain reaction
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus-2
SD	Standard deviation
WHO	World Health Organization

Chapter 1

Introduction

Since the late December of 2019 to the present day, the coronavirus disease or COVID-19 has been spreading globally like a wildfire. The World Health Organization (WHO) has declared this outbreak as a global health emergency; as on March 18, 2021, it has spread to 223 countries with 120,383,919 confirmed cases of COVID-19, including 2,664,386 deaths worldwide, reported to WHO [1]. The very first case of COVID-19 in Bangladesh was identified on Mach 8, 2020, and since then the cumulative case number has reached at 562,752 with 8,608 deaths and a total 515,989 recovered patients as on March 18, 2021[2]. Amidst the COVID 19 outbreak countries like Bangladesh is still facing the daunting challenge posed by a major segment of its populations who are still ignorant despite being informed and quite reluctant to follow the preventive measures such as wearing masks, maintaining social distancing etc. At the same time, limited testing opportunities and hospital facilities, lower literacy levels, ignorance and/or reluctance of the general population has shrouded the actual picture of COVID-19 and its impact on Bangladesh.

Clinical characteristics of the disease varies from person to person and about 80% cases stay symptomless (WHO). Symptoms such as fatigue, fever and dry cough, shortness of breath are most commonly prevalent in COVID-19 patients. Some patients even experience fewer common symptoms such as headaches, sore throat, loss of taste, loss off smell, nasal congestion, conjunctivitis, muscle or joint pain, nausea or vomiting, diarrhea, chills or dizziness and different types of skin rashes. Severe COVID-19 cases commonly have symptoms like shortness of breath, loss of appetite, confusion, persistent pain or pressure in chest, high temperature (above 38ºC). Many acute COVID-19 patients experienced persisting symptoms like fatigue or weakness, shortness of breath, headache, dyspepsia, joint pain, cough, chest

pain, anosmia, dysgeusia, depression, intermittent fever etc. for a long period of time even after they were tested negative for COVID-19 or got discharged from the hospitals [3,4]. The possibilities of reinfection are also present in many of the recovered patients of COVID-19 [5]. Treating COVID-19 affected patients are extremely challenging as very little is known about this novel coronavirus and the symptoms of this disease vary from case to case. In order to control the COVID-19 outbreak, on March 18, 2020, the WHO announced the launch of Solidarity, which is a global clinical trial to help find effective treatment for the coronavirus disease 2019 [6]. The global clinical trials for COVID-19 suggests the use of various antiviral drugs such as Remdesivir (an experimental antiviral drug), Chloroquine and Hydroxychloroquine (medications to treat the malaria virus), Lopinavir & Ritonavir (a combination of Human Immunodeficiency Virus (HIV) drugs) for treating COVID-19 patients [6,7,8]. In addition, some clinical trials suggest the use of Favipiravir, a next generation antiviral drug which showed results by acceleration of the viral clearance and improvement of the lung conditions of COVID-19 patients, Ivermectin, a broad-spectrum anti-parasitic drug which showed efficacious results for COVID-19 treatment in combination with Hydroxychloroquine, Ribavirin, a guanosine analogue and Corticosteroids [7,8]. Another suggested treatment method for acutely infected COVID-19 patients are the systemic transfusion of convalescent plasma (containing neutralizing antibodies) collected from healthy donors who recovered from COVID-19 to reduce the increasing cytokines and to replenish antibodies in the patient's system during the acute phase of the disease [9,10]. Following the National Guidelines on Clinical Management of Coronavirus Disease 2019 (COVID-19), the Ministry of Health & Family Welfare (MH&FW) recommends the use of paracetamol and antihistamine for symptomatic treatment; in addition use of chloroquine, hydroxychloroquine, favipiravir, remdesivir, lopinavir-ritonavir, corticosteroids, ribavain, tocilizumab, interleukin nebulizers,

zinc, melatonin, vitamin C, oseltamivir and empirical antibiotics are part of other recommended pharmacological treatments depending on the condition of the patient.

1.1 Objective

The objective of this survey based descriptive cross-sectional study is to help understand prognosis of COVID-19, which will mostly focus on the symptoms experienced, treatment received, post recovery health conditions of the coronavirus disease 2019 affected patients. It is expected that the proposed study will provide needed information for the development of a standard treatment regimens. Additionally, it may provide a revelation of the after-effects of COVID-19 infection on the patients residing in Dhaka City, and assist designing guidelines for the recovered patients to ensure better post-infection health conditions.

Chapter 2

Methodology

2.1 Study Design

Descriptive Cross-sectional study.

2.2 Sample Size

For this survey, the sample size was calculated to be around 384 based on the prevalence rate of 50%, 5% error and 95% confidence interval (CI).

Data was gained via an online survey embedded in Google forms. Challenges relating to online surveys include chances of low response rate due to technological disadvantages, lower literacy levels and lack of interest of the recipients to take part in the survey. Therefore, the survey link was sent to three times the sample size of recovered COVID-19 patients living within the two Dhaka City Corporation areas.

2.3 Study Population and Setting

This descriptive cross-sectional study based in Dhaka city corporation, Bangladesh, from October 1 to December 31, 2020, followed 522 patients (aged 1-76) who were diagnosed with PCR test-confirmed SARS-CoV-2 infection at the Institute of Epidemiology, Disease Control and Research (IEDCR) to assess the treatment regimens and COVID-19 symptom persistence.

3 inclusion criteria were applied while selecting the study population: (i) all patients were diagnosed with COVID-19 (confirmed by real-time PCR) at IEDCR from October 1 to December 31, 2020, (ii) all the patients resided in the Dhaka City Corporation North and Dhaka City Corporation South, Bangladesh, (iii) all patients provided their email address and phone number in the IEDCR database. The patients were requested to take part in the online survey via an e-mail containing the google form link to the survey. Baseline data on age, gender,

height, weight and comorbidities (diabetes, hypertension, asthma, cardiac diseases, respiratory diseases, kidney diseases, liver diseases, thyroid diseases, neurological disorders etc.) were collected via the online survey (by Google form). The data related to symptoms, treatment, healthcare provider, preventive practices and persisting symptoms were also collected via the online survey. This study focused on responses received from the patients after minimum 30 days of their diagnosis. Persisting symptoms were defined as fatigue, headache, lack of smell and taste, body pain, uneasiness, dry cough, productive cough, loss of appetite, diarrhea, shortness of breath, anxiety and depression etc.

2.4 Statistical Analysis

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

In bivariate analysis chi-square test was performed to test the association of two categorical variables. But, in respect of small cell frequency (<5), the Fisher exact test was run. To test the mean difference of different continuous variables by the categories of dichotomous variables, Independent sample-t test was performed. Similarly One-way ANOVA was done for the categorical variables with more than 2 categories. Least Square Difference (LSD) was used for post hoc pairwise comparison. Multiple linear regression was performed considering days to negative result for COVID-19 as dependent variable.

All statistical analysis were performed using SPSS version 26.0 (IBM SPSS Statistics Subscription Trial). A p value of less than 0.05 was regarded as statistically significant.

2.5 Ethical Considerations

The study strictly maintained the principles and guidelines of the Helsinki declarations. Ethical clearance was obtained from the departmental review board of BRAC University, Dhaka, Bangladesh. Informed consent was obtained from the respondents before data collection.

During data collection, the privacy of the respondents and confidentiality of the data were maintained strictly. Participation in the survey was completely voluntary, and the collected data was anonymously used only for this current study.

Chapter 3

Results

3.1 Basic Characteristics and Underlying Health Conditions

Table 1 Basic characteristics of the respondents

	Respondents n (%)	**Asymptomatic** n (%)	**Symptomatic** n (%)	***p*-value** (Fisher's Exact test)
	N=522	**n=60**	**n=462**	
Gender				
Male	367 (70.31)	48 (13.1)	319 (86.9)	0.202
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^2	**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)	

Total 522 COVID-19 patients responded to the survey. Among the respondents, 70.3% (n=367) respondents were male and 29.5% (n=154) were female and 0.2% (n=1) belonged to the others

category. The minimum age of the respondents was 1 year while maximum was 76 years, and the mean age of the respondents was 39.76 years with a standard deviation (SD) of ±13.02 years. Most of the respondents belonged to the 31 to 40 years age group which constitutes 29.5% of the total respondents (i.e., n=522). About 25.3% (n=132) belonged to 21 to 30 years, 20.9% (n=109) belonged to 41 to 50 years age group. The age group consisting 51 to 60 years formed 14.6% (n=76) of the respondents, while 7.1% (n=37) of the respondents were over 60 years and 2.7% (n=14) of the respondents were aged below 20 years. The mean BMI was 26.41 kg/m^2, standard deviation (SD) was ±6.52 kg/m^2. Most of the respondents (43.6%, n=221) belonged to the Normal BMI class; 39.6%, n=201 belonged to the Overweight class, 15.4%, n=78 belonged to the Obese BMI class and 1.4%, n=7 of the respondents were underweight according to their BMI. Fifteen respondents did not respond to the question on height and weight. (Table-1).

Table 2 Crosstabulation between BMI and gender

BMI	Gender			*p*-value **(Fisher's exact test)**
	Female	Male	Other	
Underweight, n (%)	5 (71.4)	2 (28.6)		0.009
Normal, n (%)	57 (25.8)	163 (73.8)	1 (0.5)	
Overweight, n (%)	53 (26.4)	148 (73.6)		
Obese, n (%)	34 (43.6)	44 (56.4)		

Among the BMI class, females consisted 71.4% (n=5) of the underweight class whereas male were higher in number in normal (73.8%, n=163), overweight (73.6%, n=148) and obese (56.4%, n=44) class. BMI and gender were found significantly associated with each other at 1% level of significance.

Among the 522 respondents, 39.3% (n=205) patients had various comorbidities. (Figure-1).

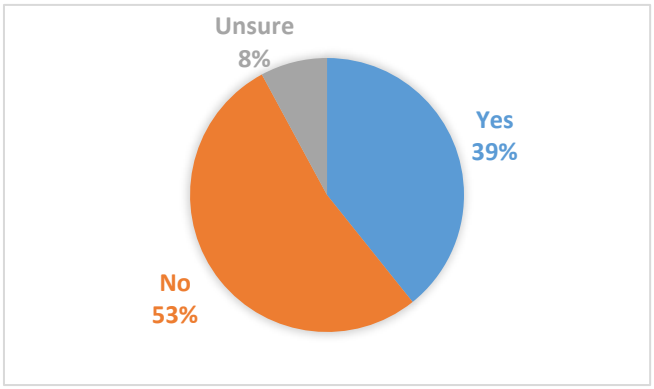

Figure 1 Presence of comorbidities among the respondents

Amidst the 205 respondents with underlying health conditions, 56.6% had Hypertension, 38.1% had Diabetes, 26.3% had Asthma, 12.2% had Cardiac diseases even before being diagnosed with COVID-19. Other comorbidities included thyroid diseases (6.9%), kidney diseases (5.9%), neurological disorders (5.4%), liver diseases (4.4%), respiratory diseases (2.9%), tuberculosis (0.5%), immunodeficiency or HIV (0.5%), malignant diseases or cancer (0.5%). (Figure-2).

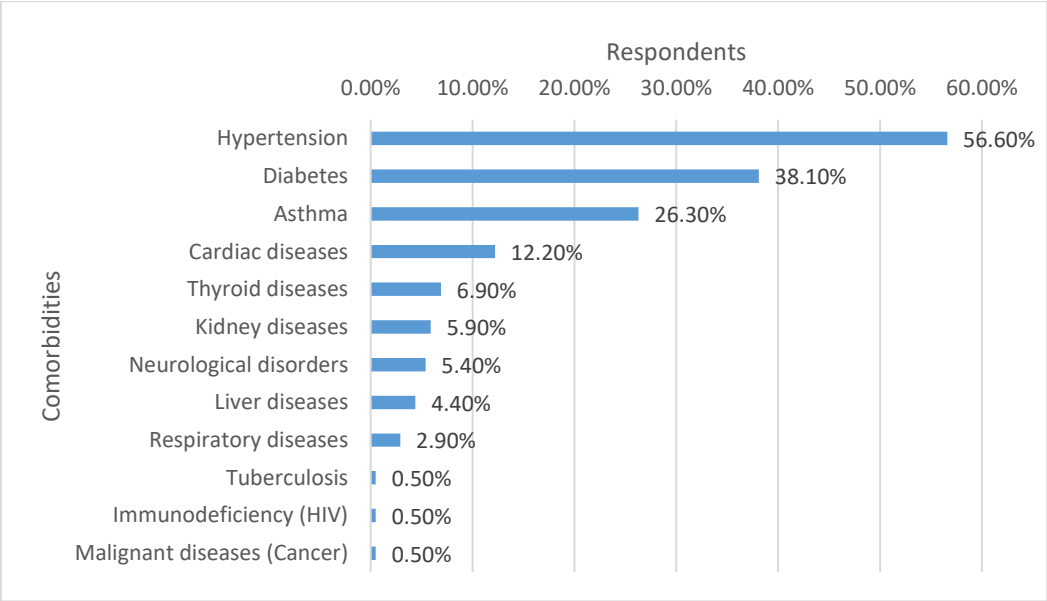

Figure 2 Underlying health conditions of the respondents

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

Respondents who previously had underlying health conditions mostly developed symptoms of COVID-19 (Table-3).

3.2 Symptom Status During Illness

Among the 522 respondents, 88.5% (n=462) were symptomatic while the rest, i.e., 11.5% (n=60) experienced no symptoms while being infected with SARS-CoV-2 (Table-1).

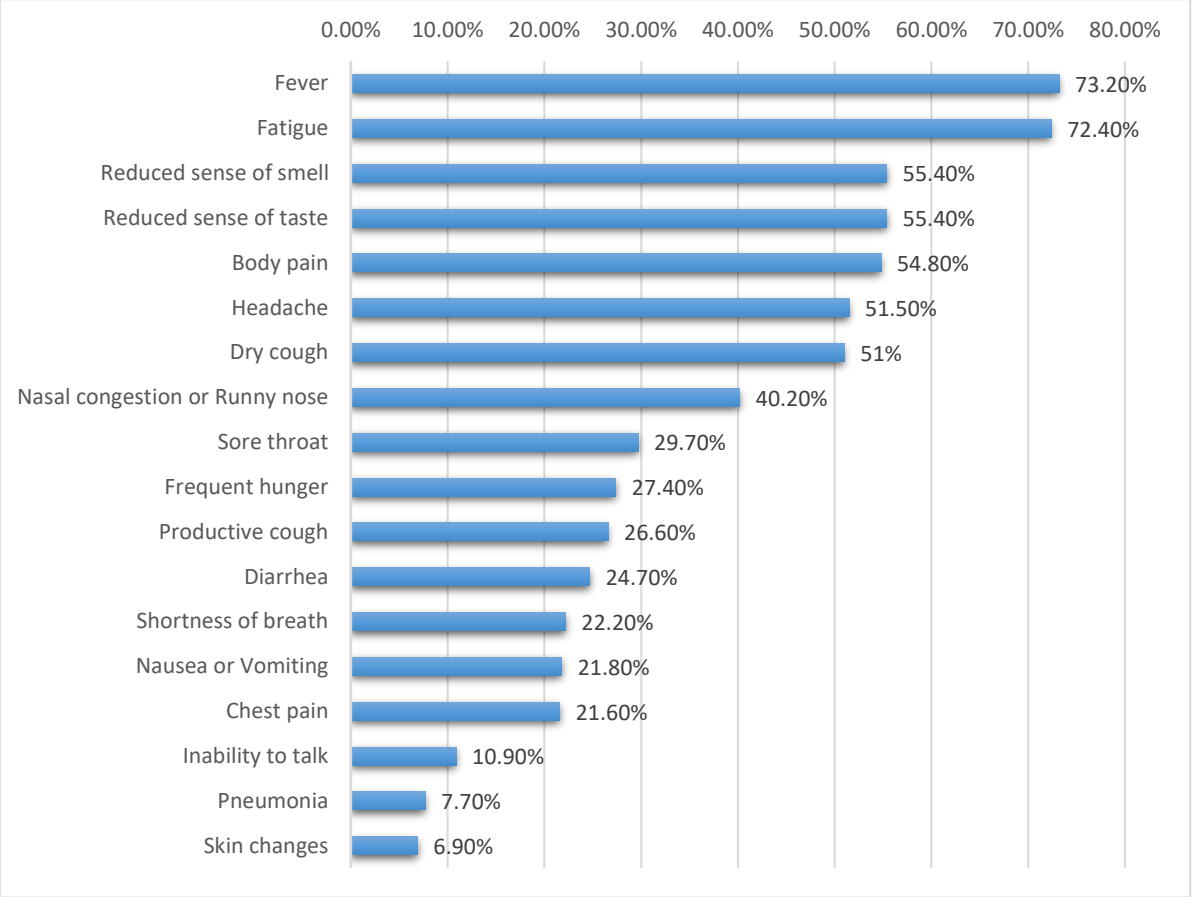

Figure 3 Clinical presentation of the respondents

Figure-3 records a wide range of symptoms reported by 89% (n=462) symptomatic respondents. The symptoms included fever 73.20% (n=382), fatigue 72.40% (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), sore throat 29.7% (n=155), frequent hunger 27.4% (n=143), productive cough 26% (n=139), diarrhea 24.7% (n=129), shortness of breath 22.2% (n=116), nausea or vomiting 21.8% (n=114), chest pain 21.6% (n=113), inability to talk 10.9% (n=57), pneumonia 7.7% (n=40), and skin changes 6.9% (n=36).

Table 4 Distribution of symptoms in the respondents during illness

Number of symptoms	**n=522**
Mean (SD)	6.6 (±3.87)
Median	7.00
Distribution of count of symptoms, n (%)	
No symptoms	60 (11.5)
1-4 symptoms	87 (16.7)
5-8 symptoms	214 (41)
9-12 symptoms	127 (24.3)
>12 symptoms	34 (6.5)
***Common symptoms**, n (%)*	
Fever, Dry cough, Fatigue	204 (39.1)
***Less common symptoms**, n (%)*	
Reduced sense of smell and taste	245 (46.9)
***Severe symptoms**, n (%)*	
Shortness of breath, chest pain	52 (10)
Fever, Dry cough, Fatigue, Shortness of breath	64 (12.3)
Fever, Dry cough, Fatigue, Shortness of breath, chest pain	32 (6.1)

Mean number of symptoms were 6.6 among the respondents (522). Most of the respondents i.e., 41% (n=214) showed 5-8 symptoms; around 24.3% (n=127) had 9-12 symptoms, 16.7% (n=87) had 1 to 4 symptoms, and 6.5% (n=34) had more than 12 symptoms. About 39.1% (n=204) responded experienced a combination of common symptoms (fever, dry cough, fatigue), 46.9% (n=245) experienced less-common symptoms like reduced sense of smell and taste, and 6.1% (n=32) experienced a combination of severe symptoms (shortness of breath, chest pain) along with the common symptoms of COVID-19 (Table-4).

Table 5 Duration of symptoms among the respondents

Symptoms, n (%)	**1-5 Days**	**6-10 Days**	**11-15 Days**	**16-20 days**	**>20 Days**	n (100%)
Fever	285 (74.61)	63 (16.49)	23 (6.02)	7 (1.83)	4 (1.05)	**382**
Sore throat	108 (69.68)	25 (16.13)	10 (6.45)	3 (1.94)	9 (5.81)	**155**
Dry cough	108 (40.60)	77 (28.95)	28 (10.53)	13 (4.89)	40 (15.04)	**266**
Shortness of breath	61 (52.59)	31 (26.72)	11 (9.48)	3 (2.59)	10 (8.62)	**116**
Headache	167 (62.08)	58 (21.56)	18 (6.69)	10 (3.72)	16 (5.95)	**269**
Reduced sense of smell	90 (31.14)	107(37.03)	31 (10.73)	22 (7.61)	39 (13.49)	**289**
Reduced sense of taste	93 (32.18)	106(36.68)	34 (11.77)	20 (6.92)	36 (12.46)	**289**
Diarrhea	88 (68.22)	24 (18.61)	0 (0.00)	10 (7.75)	7 (5.43)	**129**
Fatigue/ Weakness	82 (21.69)	97 (25.66)	41 (10.87)	32 (8.47)	126(33.33)	**378**
Productive cough	65 (46.76)	33 (23.74)	14 (10.07)	10 (7.19)	17 (12.23)	**139**
Nasal congestion	117 (55.72)	54 (25.72)	12 (5.72)	9 (4.29)	18 (8.57)	**210**
Chest pain	46 (40.71)	24 (21.23)	15 (13.28)	6 (5.31)	22 (19.47)	**113**
Body pain	148 (51.75)	58 (20.28)	26 (9.09)	13 (4.55)	41 (14.34)	**286**
Nausea/ Vomiting	62 (53.91)	27 (23.48)	6 (5.22)	9 (7.83)	11 (9.57)	**115**
Frequent hunger	40 (27.97)	46 (32.17)	21 (14.69)	12 (8.39)	24 (16.78)	**143**

Among the symptomatic respondents, 74.6% respondents experienced fever, 69.7% had sore throat, 68.2% had diarrhea, 62.1% had headache, 55.7% had nasal congestion or runny nose, 53.9% felt nausea or vomited, 52.5% had shortness of breath, 51.8% had body pain, 46.8% had productive cough, 40.7% had chest pain, 40.6% had dry cough, for 1 to 5 days. About 37.0% symptomatic respondents experienced reduced sense of smell and 36.7% experienced reduced sense of taste for 6 to 10 days and 33.3% of patients felt fatigue for more than 20 days (Table-5).

3.3 Treatment Regimens

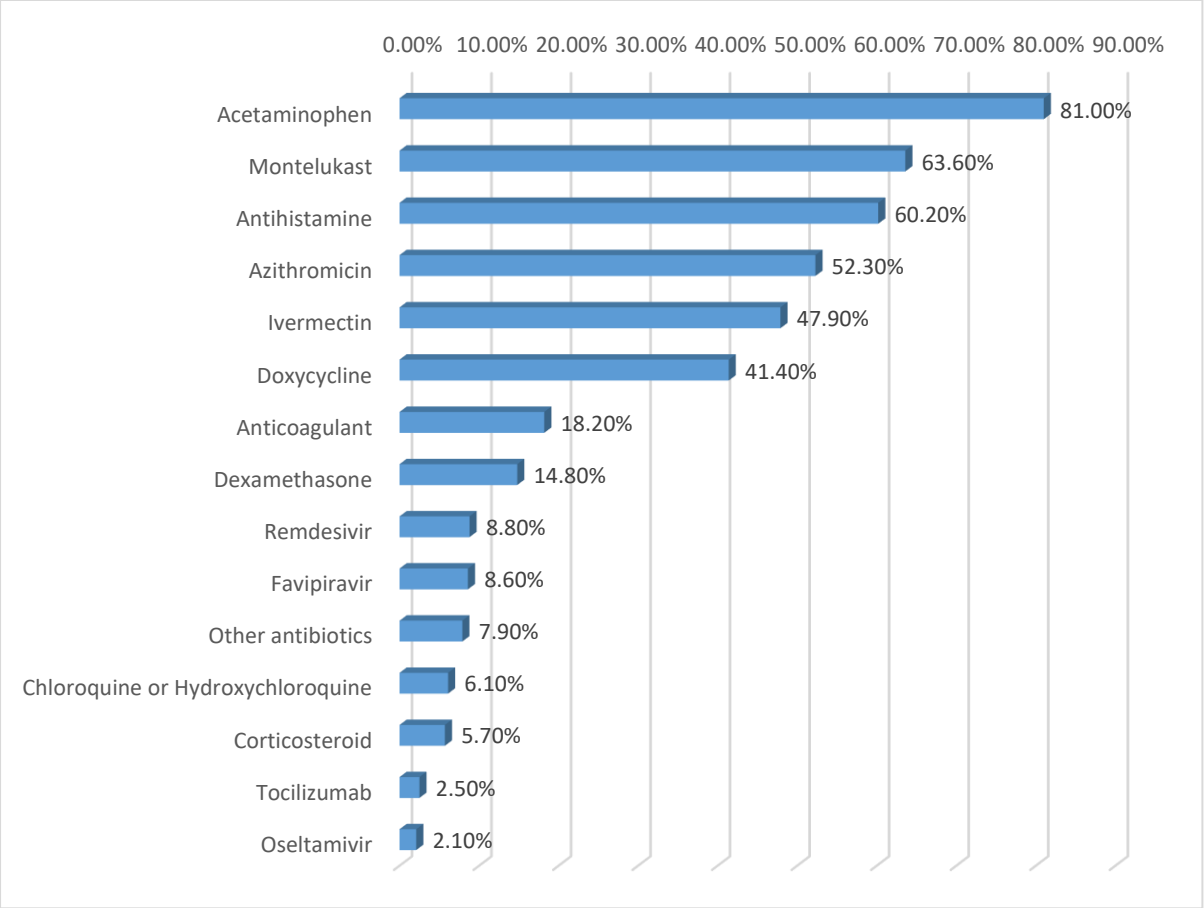

Figure 4 List of Medications taken by the respondents

Regarding medications, 81% of the respondents took Acetaminophen, 63.3% took Montelukast, 60.2% took Antihistamine 14.8% took dexamethasone. 52.3% took Azithromycin, 41.4% took Doxycycline, 7.9% took other antibiotics for example- Amoxycillin, Ciprofloxacin, Levofloxacin or Penicillin type antibiotics. Other medications taken by the respondents 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%). (Figure-4)

Table 6 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-6 shows the various combination of medications that were used to treat the respondents. It can be observed that most patients (44.3%, n=231) were on single antibiotic therapy, 28.2% (n=147) were on combination antibiotic therapy. 27.4% (n=143) were treated with a combination of Ivermectin and Doxycycline.

Table 7 Duration of different medication intake by the respondents

Medications, n (%)	**≤7 Days**	**14 Days**	**≤30 Days**	**>30 Days**	n (100%)
Acetaminophen	295 (69.09)	107 (25.06)	20 (5.69)	5 (1.17)	427
Antihistamine	142 (45.22)	120 (38.22)	33 (10.51)	19 (6.05)	314
Azithromycin	205 (75.09)	57 (20.88)	8 (2.93)	3 (1.10)	273
Doxycycline	138 (63.89)	58 (26.85)	11 (5.09)	9 (4.17)	216
Other Antibiotics	31 (75.61)	9 ((21.95)	1 (2.44)	0 (0.0)	41
Montelukast	107(32.23)	114 (34.34)	48 (14.46)	63 (18.98)	332
Chloroquine/ Hydroxychloroquine	17 (53.13)	10 (31.25)	4 (12.5)	1(3.13)	32
Favipiravir	25 (55.56)	15 (33.33)	3 (6.67)	2 (4.44)	45
Remdesivir	30 (65.22)	13 (28.26)	1 (2.17)	2 (4.35)	46
Oseltamivir	10 (90.91)	1 (9.09)	0 (0.0)	0 (0.0)	11
Tocilizumab	9 (69.23)	4 (30.77)	0 (0.0)	0 (0.0)	13
Ivermectin	235 (94)	13 (5.2)	1 (0.4)	1(0.4)	250
Corticosteroid	19 (63.33)	9 (30)	0 (0.0)	2 (6.67)	30
Anticoagulant	33 (34.74)	24 (25.26)	33 (34.74)	5 (5.26)	95
Dexamethasone	46 (59.74)	25 (32.47)	5 (6.49)	1 (1.29)	77

Most of the respondents were on various medication for 7 or less days. Among the respondents who took various kinds of medication, 69.1% (n=295) respondents took Acetaminophen, 45.2% (n=142) took Antihistamine, 75.1% (n=205) took Azithromycin, 63.9% (n=138) took Doxycycline, 32.2% (n=107) took Montelukast, 94.0% (n=235) took Ivermectin for less than 7 days (Table-7).

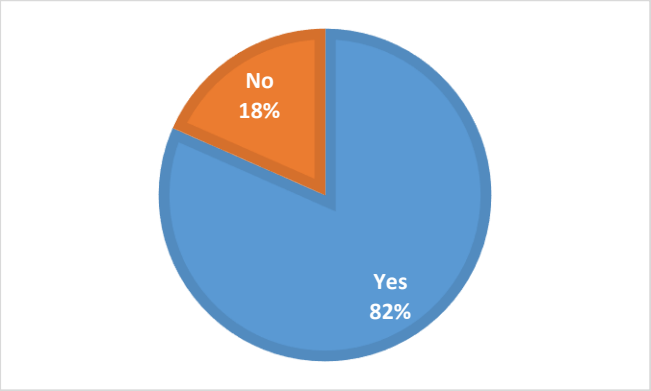

Figure-5 shows that, 81.6% of the respondents took Zinc supplements during their period of illness.

Figure 5 Zinc supplement intake by the respondents

Figure-6, shows that 63.0% of the respondents took vitamin D, 61.5% took vitamin C, 30.3% of the respondents took multivitamins, 10% took vitamin E and 7.3% took vitamin A supplements.

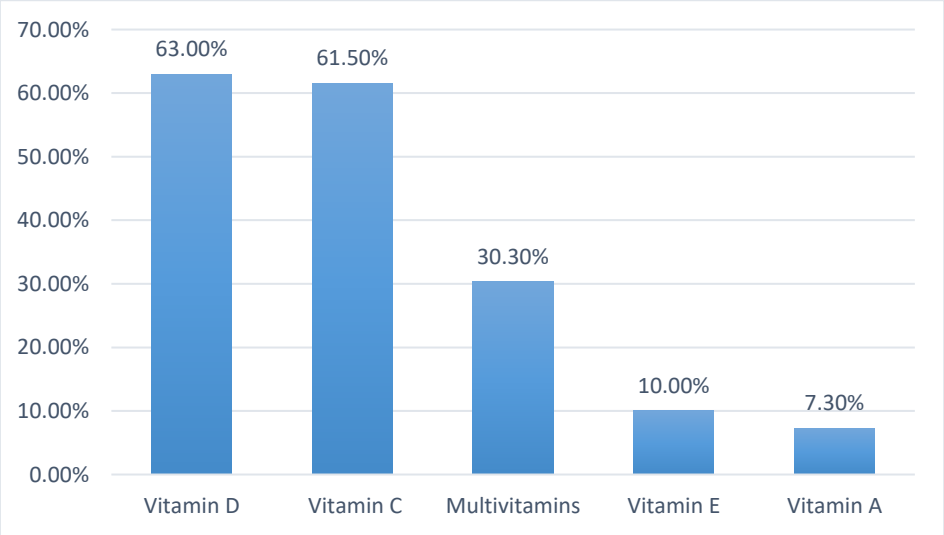

Figure 6 Different vitamin supplement intake by the respondents

Table 8 Treatments prescribed by Doctor

Type of treatment	**Prescribed by a Doctor, n (%)**	**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%)

Table-8 depicts that 92.1% (n=348) respondents took antibiotics, 96.9% (n=94) took antiviral treatment, 94.0% (n=235) took antiparasitic treatment as per a doctor's prescription, while 7.9% (n=30), 3.1% (n=3), 6.0% (n=15) took these types of medications respectively without doctor's instructions.

3.4 Re-diagnosis and Post-recovery Health Conditions

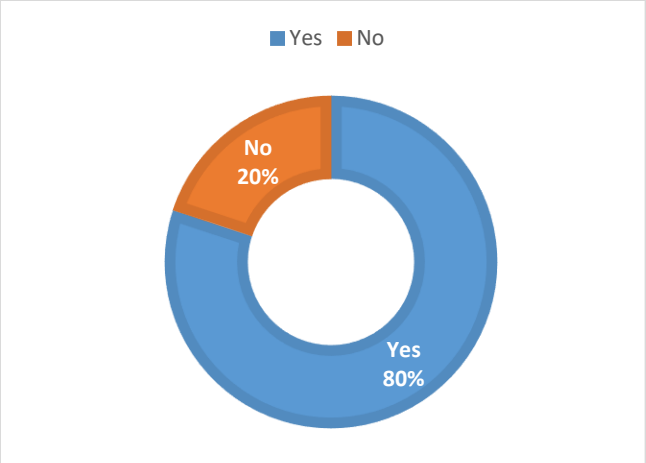

Figure 7 Repetition of RT-PCR tests among the respondents

Among the 522 respondents 80.08% repeated the COVID-19 PCR-test in hope to receive a negative test result. (Figure-7).

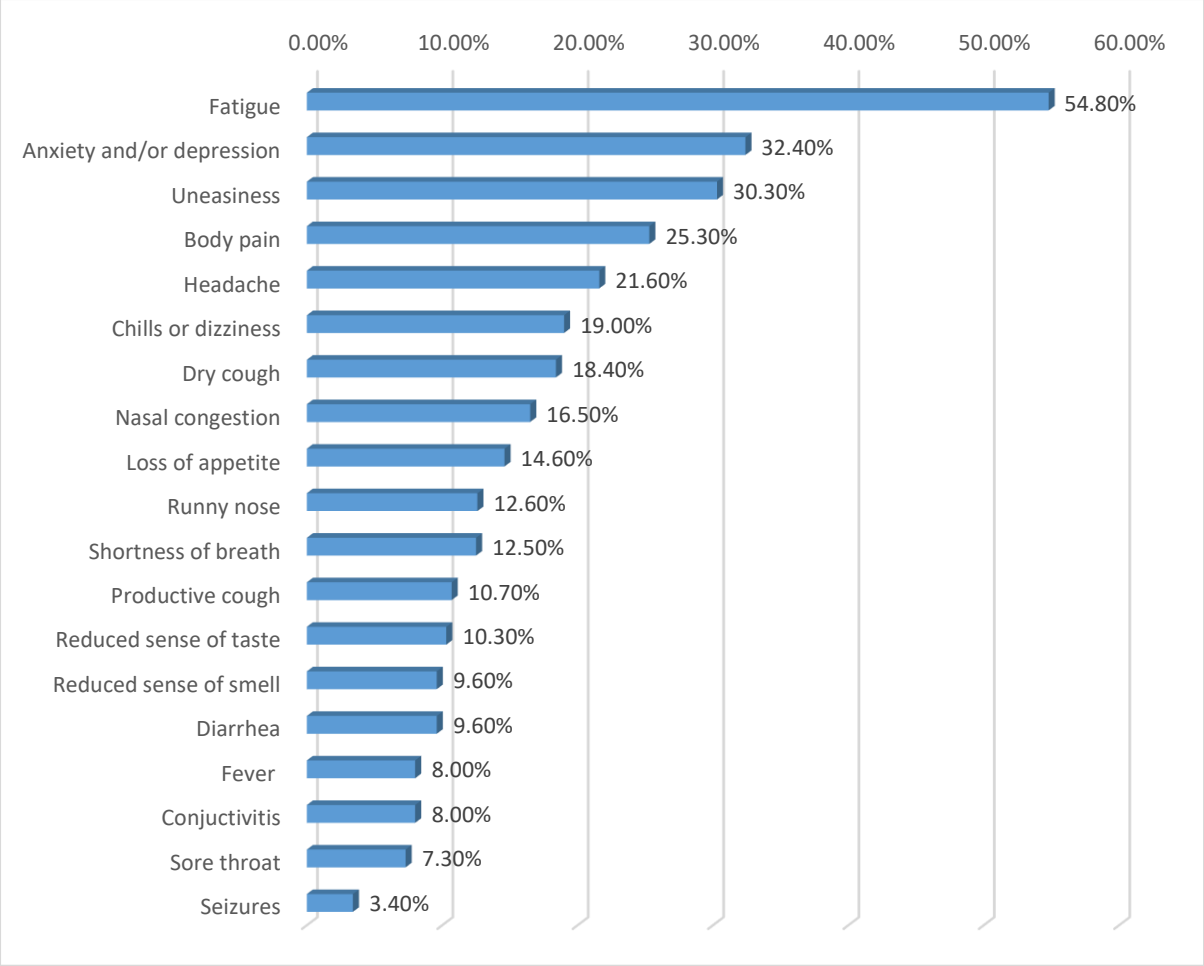

Figure 8 Persisting symptoms of the respondents after recovery

Figure-8 depicts persisting symptoms 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), loss of appetite 14.6% (n=76), shortness of breath 12.5% (n=65) of the 522 COVID-19 recovered respondents.

Table 9 Number of persisting signs and symptoms present in the respondents

Number of symptoms	**n=522**
Mean (SD)	3.28 (3.69)
Median	2.00
Distribution of count of symptoms, n (%)	
No symptoms	124 (23.8%)
1-3 symptoms	230 (44.1%)
4-6 symptoms	83 (15.9%)
7-9 symptoms	49 (9.4%)
>10 symptoms	36 (6.9%)

Table-9 shows the mean (SD) number of persisting symptoms was 3.28 (±3.69). About 44.1% (n=230) of the 522 respondents showed 1-3 symptoms, 15.9% (n=83) had 4 to 6 symptoms, 9.4% (n=49) had 7 to 9 symptoms and 6.9% (n=36) had more than 10 symptoms.

Table 10 Cross-tabulation of past and present symptoms

Symptom status during illness	**Persisting symptoms after recovery**		***p*-value** (chi-square)
	Present, n (%)	Absent, n (%)	
Asymptomatic	39 (65.0)	21 (35.0)	0.030
Symptomatic	359 (77.7)	103 (22.3)	

Among the asymptomatic respondents, 65% (n=39) developed various symptoms after recovering from COVID-19. These various symptoms included fatigue 56.4% (n=22), anxiety and depression 41.0% (n=16), uneasiness 33.3% (n=13), body pain 33.3% (n=13), headache 28.2% (n=11) etc. Whereas 77.7% (n=359) respondents who suffered from various symptoms during their period of illness continued to suffer from various symptoms even after recovery. A significant association exists between past and persisting symptoms of the respondents which is significant at the level of 3%. (Table-10)

3.5 Correlation Between Respondent's Characteristics and Days to Negative RT-PCR Result for COVID-19

Table 11 Association between respondent's characteristics and days to negative RT-PCR result

	Days to negative result for COVID-19	
Respondent's characteristics	Pearson's correlation	*p*-value
Age	0.135	0.006
BMI	-0.036	0.471
Number of comorbidities	0.144	0.003
Number of symptoms during illness	0.140	0.004

From Pearson's correlation coefficient, there was weak positive correlation between age and days to negative RT-PCR result for COVID-19, r (416) =0.135, p = 0.006; i.e., with the increase of age, the days to negative RT-PCR result for COVID-19 also increase.

There was weak positive correlation between number of comorbidities and days to negative RT-PCR result for COVID-19, r (416) =0.144, p = 0.003. Which indicates that with the increase of number of comorbidities in respondents, days to negative RT-PCR result for the infection will also increase.

There was a weak positive correlation between number of symptoms during illness with days to negative RT-PCR result for COVID-19, r (416) =0.140, p = 0.004. i.e., with the increase of number of symptoms, days to negative RT-PCR result for the infection will also increase.

3.6 Association between Days to negative RT-PCR result for COVID-19 and medications

The association of days to negative RT-PCR result for COVID-19 and medications taken by the respondents were tested by independent t-test. The results are shown in the table below.

Table 12 Association of days to negative RT-PCR results with medications

Medications		Mean (SD)	Mean difference	*p*-value
Antibiotic therapy	Yes	20.51 (7.91)	-3.12	<0.001
	No	17.38 (5.85)		
Antiviral therapy	Yes	21.07 (6.48)	-1.66	0.146
	No	19.40 (7.75)		
Antiparasitic therapy	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 supplements	Yes	19.84 (7.22)	-0.813	0.412
	No	19.03 (9.08)		
Vitamin D supplements	Yes	20. 23 (7.064)	-1.43	0.063
	No	18.796 (8.298)		
Vitamin C supplements	Yes	20.52 (7.24)	-2.11	0.407
	No	18.41 (7.89)		
Multivitamin supplements	Yes	19.78 (7.056)	-0.12	0.217
	No	19.67 (7.805)		

Except antibiotic therapy, as *p*-value is >0.05 for rest of the medications including, antiviral therapy, antiparasitic therapy, anticoagulants, corticosteroids, zinc and vitamin supplements, the null hypothesis cannot be rejected at 5% level of significance. The tests (except for the test with antibiotic therapy) indicates that the average days to negative RT-PCR result for COVID-19 of respondents who took these various medications and who did not take them are not significantly different.

The mean days to negative RT-PCR result for COVID-19 was found significantly (*p*-value ,0.001) higher among the respondents who were on antibiotic therapy compared to their counterpart.

From Pearson's correlation coefficient, there was a weak positive correlation between antibiotic therapy and days to negative RT-PCR result for COVID-19, r (416) =0.199, $p<$ 0.001. Which indicates, with the increase of number of antibiotic therapies, the days to negative RT-PCR result for COVID-19 increased as well.

There was a statistically significant effect of number of antibiotic intakes on days to negative RT-PCR result of COVID-19 at the $p<0.05$ level by one-way ANOVA (F (3,414) =5.844, p =0.001).

Table 13 Antibiotic combination vs Days to negative RT-PCR result for COVID-19

One-way ANOVA (Post-Hoc test)					
Mean difference (I-J) (*p*-value)					
		I			
		None	Single antibiotic	Double antibiotic	Three or more antibiotic
J	None				
	Single antibiotic	-2.53 (0.005)			
	Double antibiotic	-4.03 (<0.001)	-1.50 (0.088)		
	Three or more antibiotics	-5.87 (0.122)	-3.34 (0.374)	-1.84 (0.627)	

The mean difference is significant at the level of 0.05. There was a significant difference between the increased days to negative RT-PCR result scores with the increase of number of antibiotics taken. Days to negative RT-PCR result for COVID-19 were found significantly higher in respondents who took antibiotic therapy compared to those who did not. Moreover, respondents who were on double antibiotic therapy took more days to recover from the infection than who were not on any antibiotic therapy. Respondents who were treated with

double antibiotic therapy took longer time than respondents taking single antibiotic therapy, though this difference was not significant at 5% level of significance.

Table 14 Effect of Antibiotic therapy on days to negative RT-PCR result for COVID-19

Independent variables	Coefficient	*p*-value	95% CI
Antibiotic therapy (Ref: No)	2.081	0.018	0.353 - 3.809
Age	0.009	0.783	-0.056 – 0.075
BMI	-0.058	0.275	-0.163 – 0.047
Presence of comorbidities	0.402	0.631	-1.244 – 2.049
Presence of symptoms during illness	3.122	0.011	0.734 – 5.510
Acetaminophen	-1.204	0.235	-3.193 – 0.784
Vitamin C	1.182	0.146	-0.414 – 2.778
Vitamin D	0.304	0.726	-1.403 – 2.012
Zinc supplements	0.073	0.944	-1.999 – 2.146
Antiviral therapy	1.209	0.244	-0.826 – 3.244
Antiparasitic therapy	0.547	0.491	-1.013 – 2.106
Anticoagulant	3.330	0.001	1.313 – 5.347
Corticosteroids	-0.598	0.580	-2.720 -1.524
Presence of persisting symptoms	1.466	0.102	-0.292 – 3.224
***Dependent variable: Days to negative RT-PCR result for COVID-19**			

- **Antibiotic therapy=2.081:** After adjusting the effect of other related independent variables, for the use of antibiotic therapy the mean days to negative RT-PCR result for COVID-19 would increase by 2.081 days.
- **Presence of symptoms during illness=3.122:** After adjusting other independent variables, for the presence of symptoms during illness the mean days to negative RT-PCR result for COVID-19 would increase by 3.122 days.
- **Anticoagulant therapy=3.330:** After adjusting the effect of other related independent variables, for the use of anticoagulant therapy the mean days to negative RT-PCR result for COVID-19 would increase by 3.330 days.

Chapter 4

Discussion

This is a survey-based descriptive cross-sectional study on the demography, clinical characteristics and treatment of 522 RT-PCR-test-confirmed patients of SARS-CoV-2 who were diagnosed at IEDCR during October to December 2020. The study presents an overview of the practiced treatments regimens, previous and current clinical presentations of SARS-CoV-2 infected patients residing in the Dhaka city corporation area.

One of the main pathogens of respiratory diseases are Human Coronaviruses; including SARS-CoV, MERS-CoV which are responsible for causing severe respiratory syndrome in humans and four other human coronaviruses (HCoV-OC43, HCoV-229E, HCoV-NL63 and HCoV-HKU1) which are responsible for mild upper respiratory diseases. Previously SARS-CoV and MERS-CoV caused two consecutive major global outbreaks with high mortality rates in the year of 2002-03[10,11] and 2012[12, 13], respectively. However, compared to previous similar outbreaks, SARS-CoV-2 has proven to overpass when it comes to infection and mortality rate. After first being identified as a novel coronavirus on Jan 7, 2020 by the Chinese Center for Disease Control and Prevention (CDC) SARS-CoV-2 was initially named as 2019-nCoV by WHO. [14] Belonging to the beta-coronavirus group, 2019-nCoV has a relatively unique sequence from the other six subtypes; however, it has a closer relation to SARS-CoV than MERS-CoV, and it is very well adapted to the human cell receptors, allowing it an easy access to invade human cells and cause infection in humans.[15]

Given the dense population, highest number of COVID-19 cases is detected in Dhaka [16]; hence, Dhaka can be considered as the core of disease transmission in Bangladesh, for the very same reason it is the focus area of this study.

The socio-demography findings of this study depict that 70.31% were male, 29.50% were female. Similar findings were also found in other studies conducted in China [17, 18], India [19] and Bangladesh [20,21]. Previously, it has also been notable that males are infected with SARS-CoV and MERS-CoV more than females [21,22]. The reduced susceptibility of females to these viral infections could be attributed to the protection from the X chromosome and sex hormones, which play an important role in innate and adaptive immunity.[23] Besides this, it is evident that males are more involved in outdoor activities than females in the context of Bangladesh, therefore males are more likely to be affected than females.

According to the findings of the study, the mean age of the respondents was 39.76±13.02 years which was in consistent with other studies conducted in India [19] (mean age: 40.3 years) and Bangladesh [21] (mean age: 41.67±16.3 years). In this study, the age group mostly affected were 31-40 years (29.50%) and 21-30 years (25.29%). Around 2.68% of the total respondents were aged below 20 years. Meanwhile, 7.09% of all were above 60 years old. The youngest patient was of 1 year of age and the oldest was 76 years.

The mean BMI of the respondents were 26.4±6.52 kg/m^2. About 43.59% were normal, 39.64% overweight, 15.38% obese and 1.38% were underweight among the respondents. In the underweight class female respondents were higher (71.4%, n=7) in number than male. However, the number of males were higher in normal (73.8%), overweight (73.6%) and obese (56.4%) class. Gender was found independently and significantly associated with BMI of the respondents (x^2= 17.012, *p*-value= 0.003). Kim et al. reported in their study that underweight and obesity were statistically associated with severe clinical outcomes including death among patients with COVID-19[25]. However, in this study such association were not possible to find due to lack of data on disease severity.

Among the total respondents, 39.3% of the respondents had diverse underlying health conditions. Hypertension (56.6%), diabetes (38.1%), asthma (26.3%) and cardiovascular diseases (12.2%) was found to be the most common comorbidities among the respondents of this study, which was similar to the findings of other covid-19 related studies [21, 26, 27] as well as MERS-CoV [22].

Among the respondents of this study some patients (11.49%) were asymptomatic whereas most (88.51%) showed a various number of symptoms. Among the symptoms during illness fever (73.20%), fatigue (72.40%), body pain (54.80%), headache (51.50%), dry cough (51%), sore throat (29.70%), productive cough (26.60%), shortness of breath or dyspnea (22.20%), chest pain (21.60%), pneumonia (7.70%), skin changes (6.90%) were predominantly reported by the symptomatic respondents. Reduced sense of smell and taste, occurred in 55.40% of the respondents. Gastrointestinal symptoms included diarrhea (24.70%) and nausea or vomiting (21.80%); some respondents complained about having anorexia and abdominal pain. The responses regarding the symptoms during illness were consistent with Guan et al. [18], Hossain et al. [20], Ahmed et al. [28].

Though there is no specific therapy against this virus yet, the respondents of this study reported that they were treated with a diverse set of medications. The respondents were on single (44.3%) or combination (28.2%) antibiotic therapy including azithromycin, doxycycline, and some other antibiotics (i.e., amoxycillin, ciprofloxacin, levofloxacin). Antiviral therapy included remdesivir, favipiravir, oseltamivir. Other medications included acetaminophen, montelukast, antihistamine, antiparasitic e.g., ivermectin, anticoagulants, dexamethasone or corticosteroids, antimalarial drugs like chloroquine or hydroxychloroquine, immunosuppressives like tocilizumab, supplemental zinc, Vitamin-C, Vitamin-D, multivitamins and other vitamins (A, E). The medications used by the respondents were in line with the national guidelines of Clinical Management of COVID-19 set by the Ministry of

Health and Family Welfare, Bangladesh, and other studies related to treatment of COVID-19. [7, 8, 9]

Million et al. practiced using a combination of hydroxychloroquine (HCQ) and azithromycin therapy to treat COVID-19 and the combination were reported as safe and induced low mortality during the of peak of COVID-19 pandemic in France [28]. Similar evidence-based favorable results were reported by Al Mahtab and Bhuyan et al. in study consisting 33 COVID-19 infected patients, set in a medical college of Bangladesh [29]. However, some studies have provided concerns regarding using HCQ-azithromycin combination therapy for COVID-19 [30]. Chowdhury et al. found the combination therapy of ivermectin and doxycycline more effective than HCQ-azithromycin combination in terms of recovery time (mean duration of 8.933days for ivermectin-doxycycline, 9.33 days for HCQ-azithromycin), outcome ratio (100% for ivermectin-doxycycline, 96.36% for HQ-azithromycin) and symptomatic recovery rate in a hospital setting at Chakoria Upazilla Health Complex, Cox's Bazar with 116 patients with COVID-19.[31] In this study 27.4% respondents (n=143) were on combination therapy of ivermectin-doxycycline, 4% (n=21) were treated with chloroquine or hydroxychloroquine with azithromycin; favipiravir and tocilizumab were combinedly taken by 1.7% of the respondents. 6.1% (n=32) of the total respondents were on external oxygen supplementation therapy, 0.4% (n=2) in need of mechanical ventilation and 0.5% (n=3) were treated in the intensive care unit where needed.

Among the respondents who were treated with medications, 7.9%, 6.0% and 3.1% took antibiotics, antiparasitic and antiviral treatments respectively without any prescription from a doctor; this is quite alarming given the increase of antibacterial resistance in our population.

Among the respondents (n=418, 80.08%) who repeated the COVID-19 RT-PCR test, it took mean 19.71±7.56 days to get a negative RT-PCR test result; the minimum number of days

required to obtain a negative result came down to 2 days for certain individuals while it escalated to 50 days for some. However, 76.2% (n=398) of the respondents had persisting symptoms even after being tested negative. The persisting 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, reduced sense of smell and taste, diarrhea, fever, conjunctivitis, sore throat etc. which was consistent with the findings of Carfi et al. [3]. The mean number of persisting symptoms in the patients were 3.28 and most (44.1%) respondents suffered from one to three persisting symptoms even after they were tested negative for COVID. Even among the asymptomatic respondents, 65% developed various symptoms including fatigue, anxiety and/or depression, uneasiness, body pain, headache etc. after their recovery. Amidst the symptomatic ones 77.7% continued to suffer from various symptoms even after recovery from the infection. Symptoms during illness were found significantly associated with the persistent symptoms (Table-10).

It was found in this study that, with the increase of age, number of comorbidities and symptoms during illness, the respondents required more days to obtain a negative RT-PCR result, which was statistically significant at level of 1%. A significant association was also found between the use of antibiotics and days to negative RT-PCR results of the respondents. It seems from the results that the respondents who had undergone antibiotic treatment significantly took longer to recover than their counterparts. It was also found that with the increased number of antibiotics, the days to negative RT-PCR result had also increased (mean days increased by 2.081 days) significantly. Anticoagulant therapy and presence of symptoms during illness also played a role in the increase of days to negative RT-PCR results; the mean days significantly increased by 3.30 and 3.122 days respectively due to the application of anticoagulants and presence of symptoms during illness. However, related studies couldn't be found to discuss these findings further in details.

4.1 Limitations

The outcome of this study needs to be further verified by a larger sample with a multi-center study. This study could not collect data on physical examinations (e.g., Respiratory rate, oxygen saturation, blood pressure, temperature etc.) and laboratory findings (i.e., chest X-ray, CT-scans, D-dimer etc.). Thus, the disease severity of the respondents couldn't be assessed. Further study would provide more COVID-19 related information about Bangladesh.

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