Original Article

PREVALENCE OF COVID-19 REINFECTION AND ASSOCIATED FACTORS: FINDINGS OF A COUNTRYWIDE CROSS-SECTIONAL STUDY IN BANGLADESH

Md. Ziaul Islam[1], Baizid Khoorshid Riaz[2], Shah Ali Akbar Ashrafi[3], Sharmin Farjana[4], Syeda Sumaiya Efa[5], Mohammad Adnan Khan[6]

ABSTRACT

Background: Information on the extent of COVID-19 reinfection and associated risk factors is scarce in Bangladesh. The present study aimed to determine the prevalence, severity, and associated risk factors of COVID-19 reinfection.

Methods: This countrywide cross-sectional study targeted all COVID-19 patients reported in May 2021 at the Health Information Unit (HIU), Directorate General of Health Services (DGHS), Bangladesh. The study identified 242 re-infected cases among 41408 confirmed COVID-19 patients by reviewing the medical records at HIU, and DGHS. Considering the selection criteria and informed consent, we enrolled 202 re-infected patients. Data were collected through telephone interviews and reviewing medical records using a semi-structured questionnaire and a checklist.

Results: The prevalence of COVID-19 reinfection was 0.58%, and most (98.0%) of them were urban residents. Of all, 37.1% had an interval of 3-6 months between two attacks of infections. The severity of reinfection included asymptomatic (6.4%), mild (67.8%), moderate (22.3%), and severe (3.5%) infections. The moderate and severe (25.9% and 7.4%) illness were significantly ($p<0.001$) higher in the patients having an interval of <3 months between two attacks. The moderate and severe illnesses (73.7% and 5.3%) were significantly ($p<0.001$) higher among the patients who didn't maintain social distance. The patients aged 30-39 years had more chance of having mild (AOR=9.26, p=0.009) and moderate (AOR=16.58, p=0.008) infection.

Conclusion: To avert COVID-19 reinfection and its severity, patients should be vigilant about preventive practices even after recovery. The study suggests effective interventions aligned with exposure, physical distancing, vaccination, and comorbidities to mitigate COVID-19 reinfection.

JOPSOM 2022; 41(1): 8-18
https://doi.org/10.3329/jopsom.v41i1.66639

Keywords: COVID-19, Reinfection; Severity, Associated factors, Bangladesh

---

1. *Professor and Head, Department of Community Medicine, National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka-1212, Bangladesh, ORCID ID: https://orcid.org/0000-0002-5582-2402*
2. *Professor and Head, Department of Public Health and Hospital Administration, National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka-1212, Bangladesh, ORCID ID: https://orcid.org/0000-0002-5843-6945*
3. *Chief, Health Information Unit, Directorate General of Health Services (DGHS), Mohakhali, Dhaka-1212, Bangladesh.*
4. *Department of Obstetrics and Gynecology, Shaheed Suhrawardy Medical College Hospital, Sher-E-Bangla Nagar, Dhaka-1207, Bangladesh.*
5. *Research Fellow, MPhil in Preventive and Social Medicine (PSM), National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka-1212, Bangladesh.*
6. *Assistant chief, Health Information Unit, Directorate General of Health Services (DGHS), Mohakhali, Dhaka-1212, Bangladesh.*

Corresponding author: *Md. Ziaul Islam, PhD, Department of Community Medicine, National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka-1212, Bangladesh. Cell: +8801726693778 Tel.: +8802222298898; E-mail address: dr.ziaul.islam@gamil.com (M.Z. Islam)*

INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic has infected more than 174 million patients, resulting in over 3.7 million deaths by June 2021 [1]. The pandemic has impacted negatively on the healthcare system and put a stop to socioeconomic activities [2]. COVID-19 was thought to be a disease caused by a stable virus that could provide immunity; similar to most respiratory viruses (with the notable exception of rhinoviruses) who provide immunity for a year or more. But it gradually became obvious that naturally acquired immunity to COVID-19 would not always provide security in the months following the initial infection. This may be due to a lack of effective natural immunity following infection or the presence of variants on major epitopes that could potentially contribute to infection resistance [3]. To date, almost 13 variants of COVID-19 were identified as variants being monitored (VBM)among them omicron variant was identified as a variant of concern (VOC) [4]. Due to the high transmissibility of these variants, they increase the risk of reinfection [5].

With the growing number of COVID -19 cases around the world, the main concern, apart from the vaccine, is several episodes of coronavirus infection in a single person, also known as COVID-19 reinfection [6]. Reinfection of COVID-19 is being increasingly reported in the present pandemic regarding COVID-19 despite the vaccination drive [7]. Many countries around the world have confirmed reinfections which raised questions about the vaccine's prospects and ability to protect the public from the disease [8].

SARS-CoV-2 reactivation or reinfection is a persistent and vexing problem and also a major public health concern in terms of global morbidity and mortality [9]. A recent study showed that most people infected with COVID-19 showed antibody response between 10 and 14 days after infection whereas in some mild cases, detection of antibodies requires a long time after symptoms, and in a few cases, antibodies are not detected at all. There is a lack of information regarding the longevity of the antibody response to SARS-CoV-2, but it is known that antibodies to other human coronaviruses wane over time, and reinfection occurs [10]. Some recent studies did not support the possibility of COVID-19 reinfection after 70 days following the initial infection and the evidence for COVID-19 recurrence due to viral relapse [11]. There is a possibility that recurrence of SARS-CoV-2 infection may occur from false-negative real-time reverse transcription polymerase chain reaction (RT-PCR) results which creates the need for a longer observation period for recovered COVID-19 patients. The possibility of discharged patients suffering reactivation or being re-infected with another SARS-CoV-2 strain also cannot be excluded [9].

According to European Centers for Disease Control and Prevention (ECDC) (2020), reinfection is defined as laboratory confirmation of two infections by two different strains (minimum distance to be determined or supported by phylogenetic and epidemiological data) with timely separated illness/infection episodes [12]. To create a standardized case definition of SARS-CoV-2 reinfection, the Centers for Disease Control and Prevention (CDC) has proposed some criteria for reinfection. According to CDC, 'a) persons with detection of COVID-19 infection by RT-PCR ≥90 days after the first detection of COVID-19 infection, whether or not symptoms were present, and paired respiratory specimens (one from each infection episode) are available, b) persons with detection of COVID-19 infection by RT-PCR ≥45 days after the first detection of COVID-19 infection and, with a symptomatic second episode and no obvious alternate etiology for COVID-19–like symptoms or close contact with a person known to have laboratory-confirmed COVID-19; and paired respiratory specimens (one from each infection episode) are available' is considered as reinfection [13].

No concrete evidence is available regarding the factors associated with COVID-19 reinfection. Systematic review and meta-analysis of nine studies had identified that fatigue; positive IgM, positive IgG, lower platelet count, etc., are associated with an increased risk of recurrent infection [12]. Another study revealed that the emergence of VOCs, pandemic fatigue, and disregard for infection prevention strategies are the factors related to the occurrence of reinfection [14]. Very little information is available regarding the factors which influence the severity of COVID-19 reinfection.

Several cases of COVID-19 reinfection have been reported in Bangladesh through piecemeal sources. But concrete data on prevalence, severity, and associated risk factors are not available. The present study aimed to determine the prevalence of COVID-19 reinfection and also to identify the associated risk factors.

METHODS

Study design and participants

This cross-sectional study was conducted among the listed patients of the Health Information Unit (HIU)

of the Directorate General of Health Services (DGHS), Bangladesh. The total duration of the study was 6 months (From March to August 2021). The target population was re-infected COVID-19 patients diagnosed by RT-PCR assay who reported to the HIU of the DGHS in May 2021. We reviewed the records of all the COVID-19 patients to find out the re-infected patients irrespective of their age, sex, and residence. We approached all the re-infected patients and collected data through a telephonic interview in the month of June 2021. The participants who did not respond to a phone call on three (03) separate occasions and who were unwilling to participate were excluded from the study.

Sample size and sampling

We reviewed the records of Health Information System (HIS) of 41,408 COVID-19 patients reported in May 2021 and identified 242 re-infected cases among them. We evaluated the present and previous history of illness, clinical findings, and socio-demographic characteristics of the re-infected cases. Due to failure of mobile contact or unwillingness or incomplete response, a total of 202 re-infected COVID-19 patients were enrolled purposively in the study.

Data collection

Data were collected through telephone interviews and reviewing records of HIS using a pretested semi-structured questionnaire and a checklist respectively. The semi-structured questionnaire was used to collect information on socio-demographic characteristics, clinical features, comorbidities, social exposure, preventive practices, and vaccination of the re-infected patients. The checklist was used to collect information on the severity of COVID-19 reinfection. To collect quality data, data enumerators were trained on the research procedure, data collection instruments and techniques, and data quality control. A digital recorder recorded each telephone interview session to stockpile the consent and response of each participant. The average duration of data collection through telephone interviews was 15-20 minutes. Infection severity was observed by reviewing relevant medical records, the records were requested to be sent via WhatsApp.

Measurements

The present study used the standardized definition of reinfection proposed by the CDC for identifying the reinfected cases. According to CDC, 'persons with COVID-19 infection detected by RT-PCR after ≥90 days of initial infection, with or without symptoms of COVID-19 and they have paired respiratory specimens (one from each infection episode), or, persons with COVID-19 infection detected by RT-PCR ≥45 days after initial infection with a symptomatic second episode and no obvious alternate etiology for COVID-19–like symptoms/close contact with a COVID-19 positive person, and they have paired respiratory specimens (one from each infection episode)' is considered as reinfection [13].

The severity of COVID-19 reinfection was categorized into asymptomatic, mild, moderate, severe, and critical illness following the clinical presentation of the patients. The asymptomatic patients included those individuals who were RT-PCR test-positive but had no symptoms consistent with COVID-19 [15].

We considered the national guideline of Bangladesh on the clinical management of COVID-19 patients to determine the severity of COVID-19 as mild, moderate, severe, and critical [16]. The mild illness included those individuals whose clinical symptoms (fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath or abnormal imaging) were mild and who had no evidence of pneumonia on imaging [16]. The moderate illness included those individuals who showed clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but had no sign of severe pneumonia, respiratory distress with <30 breaths/min, and peripheral capillary oxygen saturation (SpO2) ≥ 90% on room air [16].

The severe illness comprised those individuals who had clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: severe respiratory distress (respiratory rate ≥30 breaths/min) or finger oxygen saturation ≤90% at rest; or Arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2) ≦300mmHg [16]. The critical illness included those severe cases who had any of the following criteria: respiratory failure and requiring mechanical ventilation; or shock; or any organ failure that requires ICU care [16].

Those patients who had taken at least one dose of vaccine, irrespective of the type of vaccine, were regarded as vaccinated. Comorbidities included ischemic heart disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, asthma, malignant disease, and hypothyroidism. History of exposure was assessed considering the categories: performed outside activities, attended social gathering and used public transport. Categories of history of exposure were measured in the time interval between first and second attack. Practicing preventive measures was assessed by using a mask,

washing hands, and using hand sanitizer, and maintaining social distance. Preventive measures were measured between 1st and 2nd attack (reinfection) of COVID-19 disease.

Statistical analysis

All responses were checked for their completeness, and correctness to exclude missing or inconsistent data. All collected data were compiled together using the Statistical Package for the Social Science (SPSS) software (Version 25.0, IBM Statistical Product and Service Solutions, Armonk, NY, USA). Data analysis included descriptive statistics (frequency distribution, percentage, mean and standard deviation) and inferential statistics (Chi-square test, Fisher's Exact test, t-test, and multi-nominal logistics regression). Necessary tabulations were drawn for summarizing and smooth visual presentation of data.

The normality of the variables was tested with the Shapiro-Wilk test / Kolmogorov Smirnov tests of Normality. Continuous data were written in the form of mean and standard deviation. Categorical variables were reported as frequencies and percentages. Group comparisons of the variables were made and an association was tested with the Chi-square test or Fisher's exact test as appropriate. Finally, the strength of association among the variables was analyzed by multi-nominal logistic regression. A p-value < 0.05 was considered significant. All the statistical tests were two-sided and were performed at the 95% confidence interval (CI) with a significance level of $\alpha = 0.05$.

Ethical considerations

Participation in this study was voluntary and anonymous. We carried out all activities in conformity with the revised declarations of Helsinki. We explained the study purpose and procedure and the risk and benefits of participation to each participant. Informed verbal consent was obtained from each participant at the beginning of data collection and recorded with an audio recorder. We preserved the privacy of the participants along with anonymity and confidentiality of data.

RESULTS

The prevalence of COVID-19 reinfection was 0.58% (242 out of 41,408). Among 242 re-infected COVID-19 patients, 202 (83.5%) participated in the study, 6.2% didn't attend the telephone calls, 5.8% were unwilling to participate, and 4.5% had an incomplete interview (Fig. 1).

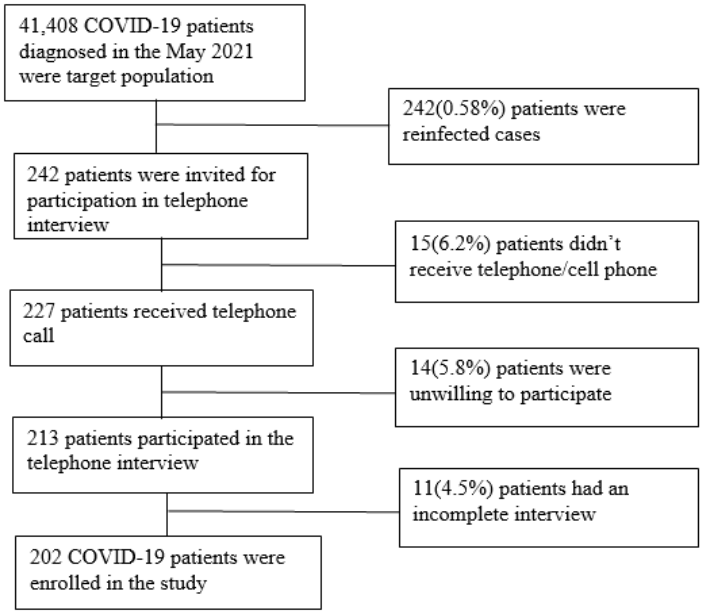

Fig 1. Flowchart of the study participants (COVID-19 reinfected patients)

The majority (50.5%) of the re-infected patients were aged 30-39 years. More than half (52.0%) of the patients were male, and the majority (79.7%) were married. Healthcare workers comprised 37.1% of re-infected patients, and 98.0% were urban residents. A majority (39.6%) of the patients had monthly family income within the range of BDT 50000 - 99000 (Table-1).

Table 1. Baseline characteristics of the re-infected COVID-19 patients (n=202)

Baseline characteristic	Category	f (%)
Age group (Years)	18-29	28 (13.9)
	30-39	102 (50.5)
	40-49	44 (21.8)
	≥50	28 (13.9)
	Mean (± SD)	37.1 (± 8.5)
Gender	Male	105 (52.0)
	Female	97 (48.0)
Marital status	Married	161 (79.7)
	Unmarried	36 (17.8)
	Ever married	5 (2.5)
Education	Illiterate and primary	7 (3.5)
	Secondary/SSC	9 (4.5)
	HSC	12 (5.9)
	Graduate	112 (55.4)
	Post-graduate	62 (30.7)
Occupation	Homemaker	29 (14.4)
	Healthcare worker	75 (37.1)
	Business	31 (15.3)
	Service (Government and private)	59 (29.2)
	Others	8 (4.0)
Type of family	Nuclear	162 (80.2)
	Joint	40 (19.8)
Place of residence	Rural	04 (2.0)
	Urban	198 (98.0)
Monthly family income (BDT)	15000 – 49000	52 (25.7)
	50000 – 99000	80 (39.6)
	≥100000	70 (34.7)
	Mean (± SD)	81678.2 (± 50239.8)

f:frequency; %= Percentage; Ever married= Separated/Divorced/widow/widowed; SD= Standard deviation; BDT=Bangladeshi currency in Taka.

The majority (80.7%) had >94% oxygen saturation while 15.8% had 90 - 94% oxygen saturation. Around one-third of the patients (37.1%) had an interval of 3-6 months between the first and second attack, and most (90.6%) of re-infected patients were treated at home. In respect of severity of COVID-19 reinfection, 6.4% were asymptomatic, followed by 67.8% had mild, 22.3% had moderate, and only 3.5% had a severe infection. Regarding the history of exposure, most (94.6%) of the re-infected patients performed outside activities, 62.9% attended the social gathering, and 38.1% used public transport. Regarding preventive practices, most (90.6%) of the patients didn`t maintains social distance, 2.5% didn`t use a mask, and 1.5% didn't sanitize their hands. The study found that 24.8% of patients had comorbidities. Among all, 18.3% had hypertension (HTN), 19.8% had diabetes mellitus (DM), and 26.7% had the habit of smoking. Around two-thirds of (60.9%) were not vaccinated against COVID-19 and 34.2% of the patients got the 1st dose only (Table-2).

Table 2. Different categories of risk factors associated with COVID-19 reinfection (n=202)

Risk factors	Category	f (%)
Oxygen saturation (%)	>94	163 (80.7)
	90 - 94	32 (15.8)
	<90	7 (3.5)
Interval between the first and second	<3	54 (26.7)

attack (Month)	3-6	75 (37.1)
	7-12	73 (36.1)
Place of treatment	Home	183 (90.6)
	Hospital	19 (9.4)
Severity of COVID-19 reinfection	Asymptomatic	13 (6.4)
	Mild	137 (67.8)
	Moderate	45 (22.3)
	Severe	7 (3.5)
History of exposure	Performed outside activities	191 (94.6)
	Attended social gathering	127 (62.9)
	Used public transport	77 (38.1)
Preventive practices	Didn't maintain social distance	183 (90.6)
	Didn't use mask	5 (2.5)
	Didn't sanitize hand	3 (1.5)
Having comorbidity	Yes	50 (24.8)
	No	152 (75.2)
Types of comorbidity	CVD	6 (3.0)
	HTN	37 (18.3)
	DM	40 (19.8)
	COPD	3 (1.5)
	Hypothyroidism	8 (4.0)
Smoking history	Yes	54 (26.7)
	No	148 (73.3)
Having COVID-19 Vaccination	1 dose	69 (34.2)
	2 dose	10 (5.0)
	No vaccination	123 (60.9)

f: frequency; %: Percentage; CVD: Cardiovascular disease; HTN: Hypertension; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease

The asymptomatic illness was significantly (p=0.001) higher (32.1%) in patients aged ≥50 years. The moderate (25.9%) and severe (7.4%) illness were significantly (p<0.001) higher in the patients having an interval of <3 months between 1st and 2nd attack. The moderate and severe illness were significantly (p<0.001) higher among the patients who didn't maintain (73.7 and 5.3%) than those who maintained social distance (16.9% and 3.3%). The asymptomatic illness was significantly (p=0.019) higher in the patients having comorbidities (16.0%) than in the patients without comorbidities (3.3%). The severe illness was significantly (p=0.007) higher in the patients with CVD (33.3%) than in the patients without CVD (2.6%). The mild illness was significantly (p<0.049) higher in the non-hypertensive (71.5%) than in the hypertensive (51.4%) patients. The asymptomatic illness was significantly (p=0.001) higher in the diabetic (20.0%) than in the non-diabetic (3.1%) patients. The severe illness was significantly (p=0.033) higher in the patients with hypothyroid (25.0%) than in the patients without hypothyroid (2.6%) (Table-3).

Table 3. Association between risk factors and severity of COVID-19 reinfection

Risk factors		**Severity of COVID-19 reinfection**				**p-value****
		Asymptomatic f (%)	**Mild f (%)**	**Moderate f (%)**	**Severe f (%)**	
Age group (Years)	18-29	1 (3.6)	21 (75.0)	6 (21.4)	0 (0.0)	0.001*
	30-39	2 (2.0)	71 (69.6)	23 (22.5)	6 (5.9)	
	40-49	1 (2.3)	31 (70.5)	11 (25.0)	1 (2.3)	
	≥50	9 (32.1)	14 (50.0)	5 (17.9)	0 (0.0)	
Gender	Male	8 (7.6)	71 (67.6)	23 (21.9)	3 (2.9)	0.879
	Female	5 (5.2)	66 (68.0)	22 (22.7)	4 (4.1)	
Interval between the 1st	<3	0 (0.0)	36 (66.7)	14 (25.9)	4 (7.4)	0.001*

and 2nd attack (Month)	3-6	11 (14.7)	53 (70.7)	9 (12.0)	2 (2.7)	
	7-12	2 (2.7)	48 (65.8)	22 (30.1)	1 (1.4)	
Attended social gathering	Yes	8 (6.3)	80 (63.0)	33 (26.0)	6 (4.7)	0.196
	No	5 (6.7)	57 (76.0)	12 (16.0)	1 (1.3)	
Performed outside activities	Yes	10 (5.2)	130 (68.1)	44 (23.0)	7 (3.7)	0.067
	No	3 (27.3)	7 (63.6)	1 (9.1)	0 (0.0)	
Maintained social distance	Yes	12 (6.6)	134 (73.2)	31 (16.9)	6 (3.3)	0.000*
	No	1 (5.3)	3 (15.8)	14 (73.7)	1 (5.3)	
Used mask	Yes	12 (6.1)	133 (67.5)	45 (22.8)	7 (3.6)	0.375
	No	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)	
Sanitized hand	Yes	13 (6.5)	136 (68.3)	43 (21.6)	7 (3.5)	0.380
	No	0 (0.0)	1 (33.3)	2 (66.7)	0 (0.0)	
Used public transport	Yes	4 (5.2)	59 (76.6)	13 (16.9)	1 (1.3)	0.194
	No	9 (7.2)	78 (62.4)	32 (25.6)	6 (4.8)	
COVID-19 Vaccinated	1 dose	1 (1.4)	45 (65.2)	19 (27.5)	4 (5.8)	0.159
	2 dose	0 (0.0)	7 (70.0)	3 (30.0)	0 (0.0)	
	No	12 (9.8)	85 (69.1)	23 (18.7)	3 (2.4)	
Smoking history	Yes	1 (1.9)	35 (64.8)	15 (27.8)	3 (5.6)	0.194
	No	12 (8.1)	102 (68.9)	30 (20.3)	4 (2.7)	
Having comorbidity	Yes	8 (16.0)	29 (58.0)	11 (22.0)	2 (4.0)	0.019*
	No	5 (3.3)	108 (71.1)	34 (22.4)	5 (3.3)	
CVD	Yes	1 (16.7)	2 (33.3)	1 (16.7)	2 (33.3)	0.007*
	No	12 (6.1)	135 (68.9)	44 (22.4)	5 (2.6)	
HTN	Yes	5 (13.5)	19 (51.4)	11 (29.7)	2 (5.4)	0.049*
	No	8 (4.8)	118 (71.5)	34 (20.6)	5 (3.0)	
DM	Yes	8 (20.0)	19 (47.5)	11 (27.5)	2 (5.0)	0.001*
	No	5 (3.1)	118 (72.8)	34 (21.0)	5 (3.1)	
COPD	Yes	0 (0.0)	1 (33.3)	2 (66.7)	0 (0.0)	0.380
	No	13 (6.5)	136 (68.3)	43 (21.6)	7 (3.5)	
Hypothyroidism	Yes	0 (0.0)	6 (75.0)	0 (0.0)	2 (25.0)	0.033*
	No	13 (6.7)	131 (67.5)	45 (23.2)	5 (2.6)	

f: frequency; %: Percentage; CVD: Cardiovascular disease; HTN: Hypertension; DM: Diabetes Mellitus; COPD: Chronic obstructive Pulmonary Disease; *p<0.05 is significant at 95% confidence interval; **χ^2 test/Fisher's Exact test

Multi-nominal logistics regression analysis revealed that in the patients aged between 30-39 years in comparison to patients aged ≥50 years, the chance of occurring mild illness was 9.26 times higher than asymptomatic illness (AOR=9.26, p=0.009); and the chance of occurring moderate illness was 16.58 times higher than asymptomatic illness (AOR=16.58, p=0.008). Also in the patients aged between 40-49 years in comparison to patients aged ≥50 years, the chance of occurring mild illness was 9.14 times higher than asymptomatic illness (AOR=9.14, p=0.022); and the chance of occurring moderate illness was 11.07 times higher than asymptomatic illness (AOR=11.07, p=0.032) (Table-4).

Table 4. Multinomial Logistic regression of risk factors of severity of COVID-19 reinfection

Risk factors		Mild			Moderate			Severe		
		AOR	95% CI	p-value	AOR	95% CI	p-value	AOR	95% CI	p-value
Age group (Years)	18-29	5.96	0.58-61.57	0.134	8.94	0.60-134.12	0.113	15.15	0.00-129970.8	0.556
	30-39	9.26	1.73-49.52	0.009*	16.58	2.08-131.96	0.008*	173.61	0.05-616682.9	0.216
	40-49	9.14	1.38-60.80	0.022*	11.07	1.24-99.02	0.032*	42.26	0.01-243794.9	0.397
	≥50	Reference								
Interval	>3	1.78	0.23-13.73	0.583	0.77	0.09-6.47	0.806	11.38	0.65-199.33	0.096

(Month) between 1st and 2nd attack	3-6	0.40	0.08-2.07	0.275	0.19	0.03-1.14	0.069	0.30	0.01-6.36	0.437
	7-12	Reference								
Maintained social distance	No	8.79	0.70-109.76	0.092	0.45	0.04-4.62	0.498	2.90	0.12-71.98	0.515
	Yes	Reference								
Having comorbidity	Yes	2.92	0.04-205.54	0.622	0.08	0.00-36.26	0.417	0.124	-	0.629
	No	Reference								
Hypertension	Yes	0.50	0.06-4.40	0.531	7.96	0.15-418.15	0.305	2.41	0.01-729.98	0.763
	No	Reference								
DM	Yes	0.27	0.01-12.66	0.502	2.54	0.02-340.45	0.710	0.78	0.00-284.76	0.934
	No	Reference								
Hypothyroid	Yes	9.56	0.00-123539.7	0.640	0.76	-	0.963	474.53	-	0.246
	No	Reference								

Reference category: Asymptomatic; AOR= Adjusted Odds Ratio; CI: Confidence interval; *p<0.05, significant at 95% CI;

DISCUSSION

Reinfection with SARS-CoV-2 is a burning public health issue. It is not well-addressed in Bangladesh, and thus this cross-sectional study aimed to identify the prevalence of COVID-19 reinfection and the risk factors associated with it. This current initiative withstands potential policy importance to devise decisive preventive strategies for the prevention of COVID-19 reinfection.

Based on the data collected from HIU of DGHS, Bangladesh, the estimated prevalence of COVID-19 reinfection was 0.58%. In this regard, the study conducted in France from June 2020 to January 2021 reported a little lower (0.47%) rate of reinfection [3]. This variation could be due to the differences in the study participants.

The present study found the mean (±SD) age of the re-infected patients to be 37±8.5 years. The study didn`t found any significant difference in reinfection rate between male and female patients (male=52.0%; female=48.0%). The study conducted in France shows similar results in terms of gender (male=51.2%); However, the mean age in that study was 50±22 years which may be due to the variation in immune status of the people of different ages in the two countries. Gender percentage was almost equal in both studies which indicates that gender differences didn't influence the occurrence of the reinfection.

The majority of the re-infected patients (37.1%) were healthcare workers. It could be argued that the healthcare workers working in different health facilities had to deal with COVID-19 patients and became exposed to the infective virus, which increased their vulnerability to reinfection. The study revealed that almost all (98.0%) of the patients was hailing from urban settings, which is supported by another study conducted in Bangladesh [17]. It could be claimed that the probability of disease transmission was higher in the urban areas due to high population density, overcrowded workplaces, industrialization, public transport use, and diverse religious and social gatherings. This study invites comprehensive preventive strategies for preventing COVID-19 reinfection in urban areas.

The current study portrayed that 80.7% of the patients had oxygen saturation >94% and the majority (90.6%) were treated at their homes. It could be explained by the fact that the majority of the mild to moderate patients didn't require hospitalized treatment. It was unveiled that 37.1% of the patients had an interval of 3-6 months between the first and second attack of COVID-19 infection and 36.1% had an interval of 7-12 months. This finding is similar to the study conducted in France that identified an interval of 3-10 months [3]. The results of both the studies indicate that possibility of reinfection was more during 3-12 months since the first attack of COVID-19. The present study exposed that severe reinfection was significantly higher among patients who had reinfection within <3 months (7.4%) in comparison to 7-12 months (1.4%) since the first incident. This study finding indicates that the severity of reinfection decreased with increasing intervals between the first and second episodes of infections.

The study depicted that most (94.6%) of the re-infected patients performed outside activities, 62.9% attended the social gathering, 38.1% used public transport, and 90.6% didn`t maintain social distance after recovery from the first COVID-19 attack. Some studies [18.19] claimed that COVID-19-infected

patients who acquired active immunity could prevent the severity of reinfection. But our study revealed that poor maintenance of social distance was significantly associated with the severity of COVID-19 reinfection, and the patients who maintained social distance had less chance of having a moderate infection. This finding forwards a strong recommendation for maintaining social distance even by the previously infected COVID-19 patients to avert reinfection.

The present study also revealed that 24.8% of patients had one or more comorbidities like hypertension (18.3%), diabetes mellitus (19.8%), and chronic obstructive pulmonary disease (1.5%). Another study conducted in Wuhan of China determined those comorbidities in different proportions; 40% hypertension, 20% diabetes mellitus, and 13% chronic obstructive pulmonary disease [20]. These disparities of comorbidities could be due to the social, environmental, cultural, and lifestyle variations between the two countries. But none of the studies reveal any association of the severity of COVID-19 reinfection with comorbidities.

The current study found that the majority (60.9%) of the re-infected patients were unvaccinated against COVID-19. Other studies claimed that vaccination boosts the immunity of previously infected patients and reduces the risk of COVID-19 reinfection [19]. Our extensive literature review confronted an enormous scarcity of relevant studies concerning the association between vaccination status and severity of COVID-19 reinfection. Multinomial logistic regression analysis revealed that the age of the re-infected patient was significantly associated with the severity of the reinfection.

As a cross-sectional study, it could not establish the association between COVID-19 and risk factors; rather it can only predict the causation. Interviews conducted through telephone pertains the chance of recall bias. Despite the limitation of telephone-interview, our study findings provide new insight into the COVID-19 reinfection and associated risk factors. The study also portrays information on the association of the severity of reinfection with preventive practices and the vaccination status of the patients. The study findings could contribute to designing an efficient preventive algorithm to alleviate COVID-19 reinfection with a more pragmatic approach. The study conserves decisive policy implications for devising effective interventions to prevent the severity of COVID-19 reinfection. Moreover, the study inspires future inclusive studies on COVID-19 reinfection and offers a scope of comparison considering geographical, demographical, socio-cultural, epidemiological, and clinical determinants.

CONCLUSION

The study findings found an association of severity of COVID-19 reinfection with age, comorbidity, and poor social distancing among the patients. To mitigate COVID-19 reinfection, infected patients should abide by preventive measures even after recovery and vaccination. The study also recommends future comprehensive research to correlate vaccination and immunity status with the severity of COVID-19 reinfection.

ACKNOWLEDGEMENTS

We are indebted to the Health Information Unit of DGHS for continuous and unrestricted support in sharing patients' records. We are obliged to the study participants for their participation in this study and sincere cooperation throughout the data collection process. We are also grateful to medRxiv for preprint publication of the article.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Board (IRB) of the National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka-1212, Bangladesh with reference no. NIPSOM/IRB/2021/06, date: 02/03/2021.All participants provided their written informed consent to participate in this study.

AUTHORCONTRIBUTIONS

Conception and design of the study: MZI, BKR. Data acquisition: MZI, SSE, SAAA, MAK.

Data analysis: MZI, SSE. Data interpretation: MZI, BKR, SAAA, MAK, SSE. The corresponding author MZI have accessed and verified the data. All the authors contributed to drafting the work or revising it critically, agreed to be accountable for all aspects of the manuscript, and approved the final version for submission.

FUNDING

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

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY

The corresponding author will share the de-identified dataset on demand

REFERENCES

1. Mao Y, Wang W, Ma J, Wu S, Sun F. Reinfection rates among patients previously infected by SARS-CoV-2: systematic review and meta-analysis. Chinese Medical Journal. 2022 Jan 20;135(02):145-52.
2. To KK, Hung IF, Ip JD, Chu AW, Chan WM, Tam ARet al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2020 Aug 25 (In press).
3. Brouqui P, Colson P, Melenotte C, Houhamdi L, Bedotto M, Devaux Cet al. COVID-19 re-infection. European journal of clinical investigation.2021 May;51(5).https://doi.org/10.1111%2Feci.13537.
4. Centers for Disease Control and Prevention (CDC). SARS-CoV-2 Variant Classifications and Definitions. Updated on: 26 April, 2022. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html [Accessed: 08 august, 2022].
5. Fakhroo A, AlKhatib HA, Al Thani AA, Yassine HM. Reinfections in COVID-19 patients: impact of virus genetic variability and host immunity. Vaccines. 2021 Oct 12;9(10):1168. https://doi.org/10.3390/vaccines9101168.
6. Dickson M, Mathews RA, Menon GG. Analysis of COVID-19 Reinfection Rates and Its Underlying Causes: A Systematic Review. Research Gate. Available at: https://www.researchgate.net/publication/345990650 (Accessed: 28 October 2021).
7. G Das M, Borkakoty B, Borgohain M, Das AK. Suspected SARS-Cov-2 reinfections in health care workers from Assam, India: Are they true reinfections? Indian J Pathol Oncol. 2021; 8(1): 10-16. Available at: https://www.ipinnovative.com/open-access-journals.
8. Hoang VT, Dao TL, Gautret P. Recurrence of positive SARS-CoV-2 in patients recovered from COVID-19. Journal of medical virology. 2020 Nov; 92(11): 2366-7.
9. Zare F, Teimouri M, Khosravi A, Rohani-Rasaf M, Chaman R, Hosseinzadeh A et al. COVID-19 Reinfection in Shahroud, Iran; A follow up Study. Epidemiology & Infection. 2021 Jan; 1: 1-2. Available at: https://doi.org/10.1017/S095026882100087X.
10. Mukherjee A, Anand T, Agarwal A, Singh H, Chatterjee P, Narayan J et al. SARS-CoV-2 re-infection: development of an epidemiological definition from India. Epidemiology & Infection. 2021; 149.Available at: https://doi.org/10.1017/S0950268821000662.
11. Yahav D, Yelin D, Eckerle I, Eberhardt CS, Wang J, Cao B et al. Definitions for coronavirus disease 2019 reinfection, relapse and PCR re-positivity. Clinical Microbiology and Infection 2021 Mar 1; 27(3): 315-8. https://doi.org/10.1016/j.cmi.2020.11.028.
12. Hoang T. Systematic review and meta-analysis of factors associated with re-positive viral RNA after recovery from COVID-19. Journal of Medical Virology. 2021 Apr; 93(4): 2234-42. Available at: https://doi.org/10.1002/jmv.26648.
13. Centers for Disease Control and Prevention (CDC). Investigative Criteria for Suspected Cases of SARS-CoV-2 Reinfection (ICR). SARS-CoV-2 Variant Classifications and Definitions. Updated on: 27 October, 2020. Available at: https://stacks.cdc.gov/view/cdc/96072.
14. Jain VK, Iyengar K, Garg R, Vaishya R. Elucidating reasons of COVID-19 re-infection and its management strategies. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021 May 1;15(3):1001-6. https://doi.org/10.1016/j.dsx.2021.05.008
15. National Institutes of Health (NIH). Coronavirus Disease 2019 (COVID-19) Treatment Guidelines, 2021. Available form: https://www.covid19treatmentguidelines.nih.gov/(Accessed: 16 September, 2021).
16. Directorate General of Health Services (DGHS). National Guidelines on Clinical Management of COVID-19, 2020. Available at: https://covidlawlab.org/wp-

content/uploads/2021/01/Bangladesh_2020.11.05_Guideline_National-Guidelines-on-Clinical-Management-of-COVID-19_EN.pdf (Accessed: 25 October 2021).

17. Islam MZ, Riaz BK, Islam AN, Khanam F, Akhter J, Choudhury R et al. Risk factors associated with morbidity and mortality outcomes of COVID-19 patients on the 28th day of the disease course: a retrospective cohort study in Bangladesh. Epidemiology and Infection. 2020 Oct 29; 148: e263. Available at: https://doi.org/10.1017/S0950268820002630.
18. Spellberg B, Nielsen TB, Casadevall A. Antibodies, immunity, and COVID-19. JAMA internal medicine. 2021 Apr 1; 181(4): 460-462. doi:10.1001/jamainternmed.2020.7986.
19. Abbasi J. Study suggests lasting immunity after covid-19, with a big boost from vaccination. JAMA 2021 Aug 3; 326(5) :376-7. doi:10.1001/jama.2021.11717.
20. He S, Zhou K, Hu M, Liu C, Xie L, Sun S et al. Clinical characteristics of "re-positive" discharged COVID-19 pneumonia patients in Wuhan, China. Scientific reports. 2020 Oct 15;10(1):1-9. Available at: https://doi.org/10.1038/s41598-020-74284-6.