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COVID-19 and Breakthrough infection among Physicians in a Tertiary Care Hospital of Dhaka, Bangladesh

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Key words:
COVID-19,4th wave, Breakthrough infection, N gene, ORF 1ab gene, Ct value, SARS-CoV-2

Abstract

Background: *Vaccination against SARS-CoV-2 is one of the major preventive ways of COVID-19 despite of that people become infected with SARS-CoV-2 after vaccination. The objective of this study was to observe the infection rate and Ct values of N and ORF 1ab gene of COVID 19 and breakthrough cases among physicians.* ***Methods****: A cross-sectional observational study was conducted at Department of Virology of SSMC, Dhaka, Bangladesh. A total of 64 vaccinated physicians of 4th wave (June- July 2022) for breakthrough cases and all the unvaccinated physicians (265) who tested for SARS CoV-2 in our laboratory during the same period of 1st wave (June- July 2020) were studied.* ***Results:*** *The percentage of breakthrough cases among vaccinated physicians was 46.9% (30); whereas the infection rate of COVID-19 among unvaccinated physicians was 18.5% (49).Majority of the (66.7%) breakthrough cases were female (20), while 65.3% of COVID-19 cases were male (32).A low mean Ct value for N genes was observed among breakthrough cases (24.8 ± SD 4.8) than the unvaccinated cases (27.8 ±SD 7.7). Among the breakthrough cases only 8.0 % of physicians became infected within 3 months, 63.0 % between 3-6 months and 29.0 % after 6 months of receiving last vaccine dose. Highest infection rate was observed during 1st (26.9%) and 3rd (22.6%) quarter of June for 1st and 4th wave of COVID-19 pandemic respectively.* ***Conclusion:*** *Higher percentage of breakthrough cases emphasizes that compliance with standard precaution along with vaccination is essential for the prevention of COVID-19.*

Introduction:

The coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first reported in December 2019 in Wuhan, China and spread rapidly worldwide since April 2020[1]. SARS Cov-2 is a non-segmented, single stranded, positive-sense RNA virus containing 32kb RNA genome and known to have extremely high mutation rates due to the lack of proofreading activity of viral RNA polymerase[2]. In humans, coronavirus infections may be asymptomatic or accompanied by fever, cough, shortness of breath and gastrointestinal symptoms[3]. The rapid spread, mortality and morbidity due to COVID-19 imposed a heavy disease burden on the health care system around world[4]. Health-care professionals (HCPs), especially physicians are the vital resource of the health-care system and focus on their professional duties for reducing the suffering of patients during COVID-19 pandemic[5]. Hospital becomes the one of the sources of secondary SARS-CoV-2 transmission due

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to viral contamination of hospital rooms from large number of infected individuals with SARS Cov-2[2]. So, working long periods in hospitals put the physicians at risk of reduced safety and some of them got infected[5].Medical staff makes up about 14% of people with COVID 19 in the world[5].Due to lack of specific antiviral treatment, maintaining standard precautions and vaccination against Covid-19 remain the most effective measures for controlling the pandemic[6]. Like many other countries in the world, Bangladesh also adopted the vaccination policies to combat COVID-19 pandemic. Different frontline workers and people at the age of over 55 years had been vaccinated during the initial phase of vaccination against SARS CoV-2 by the government of Bangladesh[7].With COVID-19, the CDC defines a vaccine breakthrough case as someone who tests positive for COVID-19 (with or without symptoms) 14 days or more after being up to date their vaccines[8].In RT-PCR assays for SARS CoV-2 relatively specific genes such as ORF1ab and N genes were targeted which encodes nonstructural proteins and structural protein respectively[9].N protein has functional RNA-binding domains which were crucial for viral replication process and also has role to increase viral replication[10].In general, the viral load of COVID-19 patient can be assumed indirectly from the Cycle threshold (Ct) value of the RT-PCR test. The real time RT-PCR (rRT-PCR) test amplifies the viral RNA from the patient's sample until it is at a detectable concentration that exceeds the threshold value and the number of amplification cycles necessary for that is known as Ct value which is inversely proportional to target RNA. Thus, the lower the Ct value, the higher the viral load and the higher the Ct value, the lower the viral load of a patient's sample[11]. Higher viral load is associated with a higher risk of viraltransmission[12]. So, this study was designed to observe the infection rate and Ct values of N and ORF1ab genes of COVID-19and breakthrough cases among physicians.

Methods:

This cross-sectional observational study was conducted at the department of Virology, Sir Salimullah Medical College, Dhaka, Bangladesh .Physicians who were symptomatic or had been exposed to an infected person, regardless of symptoms of COVID-19 and sent their samples to our department for confirmation of SARS CoV- 2 by rRT-PCR testing were studied. A total of 64 physicians who sent their samples to COVID-19 RT PCR laboratory of SSMC during the 4th wave of COVID-19 pandemic (June- July 2022) were included. To compare the breakthrough cases with unvaccinated cases of COVID-19, we included all the unvaccinated physicians (265) who tested for SARS CoV-2 in our laboratory during the same period of 1st wave (June- July 2020) as almost all physicians were vaccinated against SARS Cov-2 during 4th wave. In our laboratory, real time RT-PCR (Reverse transcriptase PCR) was done by Sansure Biotech Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit targeting ORF 1ab and N gene of SARS CoV-2 for confirmation of COVID 19 cases. Cycle threshold (Ct) values of < 40 from RT-PCR assays indicating detectable viral loads for both N and ORF 1ab RNA. We analyzed the COVID-19 RT PCR laboratory data of SSMC which were collected in a predesigned data collection sheet during the time of sample collection.

All the data were analyzed by using Excel Software 2016 and Microsoft word. Qualitative data were presented as numbers, percentages and pie diagram. Quantitative data were presented as mean ± standard deviation and line diagram.

Results:

A total of 64 vaccinated physicians of the 4th wave (June-July 2022) and 265 unvaccinated physicians of1st wave (June-July 2020) of COVID-19 pandemic were studied. The rate of breakthrough infection among physicians was 46.9% (30) whereas infection rate of COVID-19 among unvaccinated physicians was 18.5% (49). [Table I]

Table I: Distribution of COVID 19 and breakthrough cases among physicians during 1st wave and 4th wave of COVID-19 pandemic

Number of Physicians	COVID 19 and breakthrough cases	
	Positive cases, n (%)	Negative cases, n (%)
During 1st wave, n=265	49 (18.5)	216 (81.5)
During 4th wave, n=64	30 (46.9)	34 (53.1)

Among the breakthrough cases, 23.3% (7) and 76.7% (23) of physicians had received their 2nd and 3rddose (additional booster dose) of vaccine against SARS CoV-2 respectively. During 4th wave, female physicians were affected more (66.7%) than the 1st wave (34.7%). [Table II]

Table II: Gender distribution of rRT-PCR positive COVID 19 and breakthrough cases of physicians during 1st and 4th wave of COVID 19 pandemic

Cases	Gender	
	Male, n (%)	Female, n (%)
COVID-19, n= 49	32 (65.3)	17 (34.7)
Breakthrough infection, n=30	10 (33.3)	20 (66.7)

The mean Ct value of N and ORF 1ab genes were 27.8 and 31.3for COVID-19 and 24.8 and 33.3 for breakthrough cases respectively. **[Table III]**

Table III: Mean Ct value of N and ORF 1 ab genes of COVID-19 (1st wave) and breakthrough cases (4th wave) by rRT-PCR

Cases	N gene CT value Mean± SD	ORF lab gene CT value Mean± SD
COVID-19	27.8± 7.7	31.3± 4.8
Breakthrough infection	24.8± 4.8	33.3± 3.7

Among the breakthrough cases of physicians, 63% were infected with SARS-CoV-2 after 3 months (3-6 months) and 29% cases after 6 months of receiving vaccine against COVID-19. Only 8% cases were infected with SARS CoV-2 within 3 months of vaccination. [Figure-1]

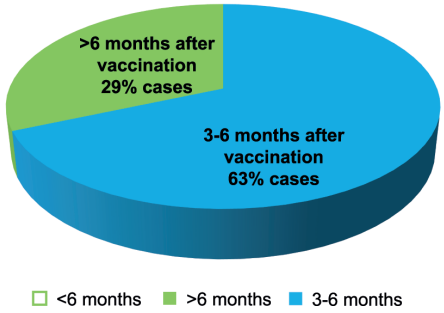

Figure-1: Pie diagram shows the percentage of physicians according to the time duration of detection of breakthrough cases from the last vaccine dose (2nd or 3rd dose) against COVID-19

According to our laboratory data, 4th wave (when majority cases were vaccinated) starts during 2nd quarter of June,2022 with infection rate of 5.9% which sharply rises upto 22.6% during 3rd quarter of June then gradually fell down and reaches 4.0% during 3rd quarter of July 2022. In contrast during 1st quarter of June 2020 (1st wave) the infection rate was 26.9% and throughout the duration of 2 months (June-July 2020) it remains approximately above 15.0%. During 4th quarter of July 2020 (1st wave) infection rate was 21.0% whereas during 4th quarter of July 2022 (4th wave) it was less than 3.0%.**[Figure-2]**

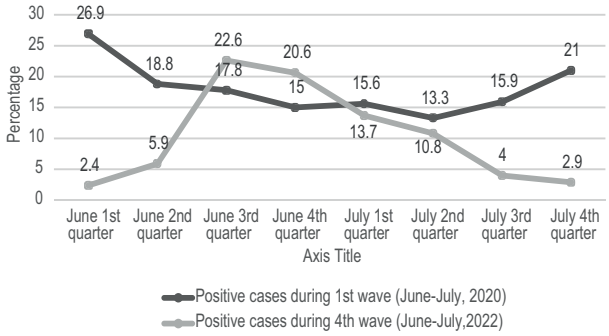

Figure 2: *Line diagram shows the percentages of rRT-PCR confirmed cases according to quarters of month (June and July) of 1st and4th wave of COVID 19 pandemic*

Discussion:

HCPs, particularly those works at the frontlines, are severely affected by SARS-CoV-2 and represent a high-risk category during theCOVID-19 pandemic crisis[13].In our study,18.5% of laboratory confirmed COVID-19 among unvaccinated physicians (1st wave) and 46.9% of breakthrough infections among completely vaccinated physicians (4th wave) for the same period(months of June and July) were observed. Breach in measures after vaccination and emergence of new variants during the study period may contribute to this finding. At the beginning of the pandemic, maintenance of proper hand hygiene and the use of proper personal protective equipment in the absence of suitable treatment against the virus constituted a significant measure of prophylaxis[14].Furthermore, during 1st wave physicians were under strict public health and preventive measures such as screening testing, isolation, contract tracing and quarantines after their hospital roster duty to prevent the

spread of SARS-CoV-2 infections. Approximately 14.0 % of asymptomatic health care workers (HCW) COVID-19 cases in Egypt and 9% HCWs cases were reported from Italy during the early period of pandemic[13].In India, during the second wave,13.3% of breakthrough infections were observed among completely vaccinated HCWs in a dedicated COVID-19 tertiary care hospital ofDelhi[15]. In another study of Pakistan,17.27% of COVID-19 cases among HCWs after vaccination were reported. The high percentages of COVID-19 infections among HCPs were due to their continuous or recurrent exposure to COVID-19 infected individuals and the environment[16].There is a higher possibility of pathogen-loaded droplets to be shed at hospitals and other healthcare units due to overcrowded healthcare facilities[14].Among the physicians with breakthrough infections of this study, 66.7% were females. A study of India also reported 66.7 % female HCWs with breakthrough infections[17]. Male dominance of HCWs (60.6%) with breakthrough infections were reported in another study of Pakistan[16].A Ct value of N gene less than 30 indicated an increased viral load and was used to determine infectivity[18]. In our study, we observed a low Ct value of N gene among breakthrough cases (24.8 ± SD 4.8) than the unvaccinated cases (27.8 ±SD 7.7) which may be one of the contributing factors for the higher number of breakthrough cases during 4th wave as low Ct value is related to high viral load. Mean Ct value of 29.96 (SD 4.90) and 28.48 (SD 5.04) for N and ORF 1ab genes were reported in unvaccinatedCOVID-19 patients in Changzhou, China[19]. A total of 74% of breakthrough cases of HCWs with a high viral load (Ct value of N gene<30) at some point during their infection were reported in a study of largest medical center in Israel[18]. Among the physicians with breakthrough infections of this study, 23.3% had received two doses of vaccine and 76.7% had received an additional booster dose against SARS CoV-2. Another study reported 94.8% of HCWs with breakthrough infections had received a minimum of two doses of vaccination, while only 1.9%had received 3rd dose[16].Vaccines are critical tool in the fight against COVID-19 infection as they work by generating an immune response but it may be somewhat less effective against some of the COVID-19 virus variants. As no vaccine accords 100% protections, a small proportion of individuals will contract COVID-19 infection despite complete vaccination[20]. In our study, 8.0% of breakthrough cases of physicians were infected with SARS-CoV-2 within 3 months, 63% after 3 months (3-6 months) and 29% cases after 6 months from the last (2nd/ booster) vaccine dose. Approximately 47.8% of HCPs with breakthrough infections within 3 months, 40.9% after 3 months (3-6 months) and 11.3 % after 6 months from the second dose of vaccination were also reported in another study of Pakistan[16].The median interval of 39 days and 69 days from the second vaccine dose to SARS-CoV-2 detection were reported in the study conducted in Israel and India respectively[17,18].Less efficacy of vaccines against the newer variants that were produced for the initial strain of SARs-CoV-2 may be a contributing factor[21].A study of Bangladesh reported that June 2020 of 1st wave had the highest number of cases and July 2020 was most fatal months due to highest death which made Bangladesh the second most affected country in Southeast Asia after India[22].According to our study, we found high infection rate of 26.9% during 1st quarter of June, 2020 which remains approximately above 15.0 % throughout the duration of 2 months (June-July, 2020).In contrast,4th wave (when majority cases were vaccinated) starts with infection rate of 5.9% which sharply rises upto 22.6% within one week and persists only approximately 1.5 months (2nd quarter of June to 2nd quarter of July,2022) and then droped to 2.9% in4th quarter of July, 2022.During 1st wave all the cases were unvaccinated and had no previous immunity to SARS CoV-2 which may be responsible for the persistent high infection rate of COVID-19. The government of Bangladesh had almost achieved the vaccination target during 4th wave but due to emergence of omicron sub-variants BA.4 and BA.5 in that time may be responsible for the high rise of the infection in that time. The new omicron sub-variants spread very fast and notably evade the neutralizing antibody elicited by SARS-CoV-2 infection and vaccination[23].Though the infection rate was high during 4th wave but duration was short which may be due to vaccination and previous Covid-19 infections of the study population.

Conclusion:

Compliance with non-pharmacological measures such as hand washing, wearing face mask and

physical distancing along with vaccination is essential for the prevention of COVID-19 breakthrough infection among physicians.

Single-center and the relatively short study duration might limit validity. Future multi-center studies with longer follow-up periods will provide more comprehensive insights.

Data Availability:
The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:
The authors stated that there was no conflict of interest in this study.

Funding:
This research received no external funding.

Ethical consideration:
The study was approved by the Ethical Review Committee of Sir Salimullah Medical College Mitford Hospital (SSMCMH) Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; had agreed on the journal to which the article had been submitted; and agreed to be account able for all aspects of the work.

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