

COVID-19 Infection and Endoscopy—Is Symptom-Based Screening Enough before Proceeding for Endoscopy?

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Background and study aim: The coronavirus disease 2019 (COVID-19) substantially affected healthcare systems including endoscopy services worldwide. Besides using PPE, pre-procedure symptom screening was adopted by the majority. The role of polymerase chain reaction (PCR) testing in addition to symptom-based screening over a longer period that includes a post-pandemic environment needed further investigation. This study aimed to evaluate the outcome of COVID-19 screening using PCR testing in low-risk patients narrowed down by a symptom-based pre-procedure screening tool during five waves of COVID-19.

Patients and Methods: This cross-sectional study was performed from June 2020 to March 2022. Patients aged ≥ 18 years with no symptoms screened via COVID-19 risk screening questionnaire, who underwent endoscopy procedures at Aga Khan University Hospital, Karachi, were reviewed. Patients who already had positive COVID-19 tests or had COVID-19 in the preceding month were excluded.

COVID-19 Reverse Transcriptase PCR on nasopharyngeal swabs was performed within 72 hours pre-procedure. World Health Organization (WHO) timelines were used to define time limits for five COVID-19 waves.

Results: Of 7198 patients booked for endoscopic procedures, 4967 (69.0%) patients were tested for COVID-19. The mean age was 47.6 ± 15.9 years and 44.9% were female. Overall COVID-19 positivity rate was 2.7% with the highest rate of 11.9% in the fifth COVID-19 wave followed by the first wave (2.4%).

Conclusion: There was a low overall occurrence of COVID-19 infection, apart from the fifth wave in asymptomatic patients undergoing endoscopic procedures. Therefore, increasing compliance with COVID-19 vaccination and conducting thorough symptom-based screening before endoscopic procedures could eliminate the necessity for RT-PCR testing.

INTRODUCTION

In December 2019, clusters of cases with severe acute respiratory distress syndrome (ARDS) emerged in Wuhan, China. The pathogen responsible, a novel coronavirus i.e., “severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2),” rapidly spread globally, leading to the declaration of a pandemic. Its highly contagious nature resulted in rapid outbreaks in numerous countries and across all continents [1–5].

The respiratory droplets generated during coughing, sneezing, or talking even at a distance of less than one meter are the primary source of

transmission for SARS-CoV-2. The virus could also be transmitted if a person makes direct contact with the mucous membrane of an infected patient, touches an infected surface, and then touches his or her eyes, nose, or mouth. The incubation period for SARS-CoV-2 is within 14 days following the exposure. Moreover, human-to-human transmission can occur from individuals in the pre-incubation period, asymptomatic carriers, or individuals with mild symptoms [6]. Additionally, the virus survives in aerosols (for hours), and on solid surfaces (up to days) adding the risk of aerosol and fomite transmission [7].

The most common signs and symptoms of this disease include fever, cough, sore throat, dyspnea, myalgia, diarrhea, loss of smell or taste, and pneumonia along with a history of travel or contact. The diagnosis of coronavirus disease 2019 (COVID-19) is made by the detection of SARS-CoV-2 ribonucleic acid by nucleic acid amplification tests (NAATs), primarily reverse transcription-polymerase chain reaction (RT-PCR) on specimens collected by nasopharyngeal or oropharyngeal swabs. A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19 [8].

While multiple ongoing trials to explore definitive treatment and vaccination have been done, currently, the one major established way to prevent this disease is to avoid cross-transmission. Hence, besides practicing social distancing and hygienic measures to prevent cross-transmission in communities, strategies have been adopted to minimize the risk of bidirectional transmission through healthcare facilities. Therefore, across the world, healthcare systems have prioritized the delivery of care to those requiring hospitalization, emergent, or urgent surgeries, and invasive procedures, while limiting outpatient clinics, and elective procedures [9–11].

Considering almost a three times higher rate of SARS-CoV-2 infection reported among healthcare workers (HCWs) than the general population it became very obvious that healthcare facilities are at a higher risk of nosocomial spread [11–13]. Due to positive insufflation during endoscopic procedures and droplet generation with coughing, upper gastrointestinal (GI) endoscopy procedures are considered high aerosol-generating procedures and a potential source of airborne transmission for SARS-CoV-2 in the hospital setting. Moreover, fecal-oral transmission during lower GI endoscopy procedures emerged as a concern since the virus has been identified in the stools of infected patients [7,9]. Additionally, the droplets from infected patients could reach individuals present two meters or more from the source [14]. Therefore, direct contact with the secretions or aerosols generated during the endoscopy of an infected patient is likely to expose the endoscopist and the assisting staff to an increased risk of acquiring SARS-CoV-2 [15–17].

From the start, the primary focus was to prevent nosocomial transmission of SARS-CoV-2 among HCWs and patients while providing endoscopic services. Besides confirmation of SARS-CoV-2 infection among HCWs after endoscopies of infected patients in a multicenter survey conducted in Italy, endoscopy units also confirmed SARS-CoV-2 among physicians and nurses who required hospitalizations [18]. False-negative results for COVID-19 tests were also observed after testing 4,700 patients who underwent endoscopy [19]. Hence, in addition to the mandatory use of personal protective equipment (PPE), several international gastrointestinal (GI) societies recommended performing time-sensitive endoscopies and delaying elective endoscopies during the COVID-19 pandemic, substantially affecting endoscopy services worldwide [10,20–22].

At our tertiary care center, since June 8, 2020, pretesting for COVID-19 by RT-PCR on a nasopharyngeal swab was made mandatory within seventy-two hours before any endoscopic procedure. Such policies were not being practiced across Pakistan except at very few other institutions mainly due to the huge cost incurred with these tests. Furthermore, at that point, there was a lack of consensus on the utilization of PCR or antibody testing for SARS-CoV-2 before endoscopy to identify asymptomatic carriers [10,23]. Since the resumption of endoscopy services was of major concern, the American College of Gastroenterology and the British Society of Gastroenterology developed guidelines for the resumption phase. Screening by testing for SARS-CoV-2 via RT-PCR on nasopharyngeal swabs or antibody tests before endoscopy in all or selected cases to identify asymptomatic carriers is difficult to implement in all patients, especially in resource-constrained settings [10]. Hence, besides using PPE, triage using a pre-endoscopy COVID-19 clinical screening questionnaire was made mandatory. The American Gastroenterology Association (AGA) conducted a rapid review in 2021 which recommended against routine pre-procedural testing for SARS-CoV-2 in patients scheduled to undergo endoscopy stating that it causes unnecessary delays in patient care that may lead to increased overall morbidity and mortality [24]. Therefore, it is imperative to evaluate the usefulness of symptom-based screening with or without COVID-19 PCR testing to identify

asymptomatic patients with COVID-19 infection undergoing endoscopic procedures. This information is especially important in a post-pandemic world where COVID-19 cases are isolated or minimal, and only occur sporadically in a small subset of the population. This would allow us to adopt the best strategies for the early identification of patients asymptomatic for COVID-19 and minimize the risk of nosocomial transmission of SARS-CoV-2 to HCWs. This research would also aid in planning future COVID-19 transmission prevention initiatives cost-effectively and, based on the result of the study, further research can be conducted on a wider level. Hence this study aimed to evaluate the outcome of COVID-19 screening using PCR testing in low-risk patients narrowed down by a symptom-based pre-procedure screening tool during five waves of COVID-19.

PATIENTS/MATERIALS AND METHODS

This cross-sectional study was performed from June 2020 to March 2022. Patients aged ≥ 18 years with no symptoms screened via COVID-19 risk screening questionnaire, who underwent endoscopy procedures as outpatient or inpatient at Aga Khan University Hospital, Karachi, were reviewed. Patients who declined to test COVID-19 PCR had positive COVID-19 tests, or had COVID-19 in the preceding month were excluded. Additionally, patients who were booked for an endoscopic procedure but did not have a COVID-19 PCR done within seventy-two hours of the scheduled procedure were not included in the study. COVID-19 Reverse Transcriptase PCR on nasopharyngeal swabs was performed within 72 hours pre-procedure. World Health Organization (WHO) timelines were used to define time limits for five COVID-19 waves. Patients with a positive PCR or who were asymptomatic were appropriately referred for further clinical assessment and care. Staff involved in the performance of the various endoscopy procedures were required to observe standard precautions as well as the use of PPE during the performance of endoscopy.

Records of these patients undergoing endoscopy were reviewed and data were collected using a standardized data collection tool which included: Age, gender, comorbid conditions, any symptoms of COVID-19, indication for endoscopy, and results of COVID-19 PCR test.

The symptom-based screening included a yes/no response to the following items: Fever, difficulty in breathing, cough, shortness of breath, runny nose/sneezing, chest pain, new onset loss of taste or smell, recent onset fatigue, nausea with or without diarrhea, and travel history. The rates of COVID-19 PCR positivity were determined according to the five waves of COVID-19 infection as per WHO timelines to determine any variations in COVID-19 positivity through the various waves of disease.

The data was entered and analyzed by using Statistical Package for Social Science (SPSS). A descriptive analysis was performed, and results were presented as mean with standard deviation for quantitative variables and frequency with percentage for qualitative variables. A comparative analysis was done using an independent t-test and Pearson's Chi-square test where applicable. All p-values were two-sided and considered statistically significant if < 0.05 .

RESULTS

Over the study period, which spanned from June 2020 to March 2022, 7198 patients had been booked for endoscopic procedures in outpatient and inpatient settings. Of these, 4967 patients (69%) had a COVID-19 PCR done within 72 hours before endoscopy and 2231 (31%) did not have a COVID-19 PCR done before endoscopy. Of the 4967 who had a COVID-19 PCR done, 4834 (97.3%) had a negative test and 133 (2.7%) had a positive test. The distribution of positive cases every year is shown below in Figure 1.

There was a progressive rise in the number of positive cases identified from 23 per year to 41 then 69 from 2020 to 2022. The total proportion of positive cases throughout the study period was 133/4967 (2.7%).

The distribution of positive cases was further analyzed and determined as per the waves of COVID-19 infection during the study period to determine whether there was any change in the trend of positive cases in patients who were asymptomatic for COVID-19 infection. The distribution was as follows: 15/616 (2.4%) during the first wave, 21/1313 (1.6%) during the second wave, 16/1197 (1.3%) during the third wave, 12/1263 (1.0%) during the fourth wave and 69/578 (11.9%) during the fifth wave. There was a sequential decline in positive rates from the first to the fourth wave and a spike during the fifth wave of COVID-19 infection. This is

summarized in Table 1 and illustrated graphically in Figure 2.

A total of 4967 patients were planned for procedures in the endoscopy unit during the study period. They included various diagnostic and therapeutic procedures and advanced endoscopy procedures such as endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS). An analysis of the procedures was done to determine the relative frequencies of the various procedures. The most common procedures were esophagogastro-duodenoscopy (EGD)

(2664/4967; 53.6%), colonoscopy (1237/4967; 24.9%), combined EGD and colonoscopy/sigmoidoscopy (398/4967; 8%), ERCP (201/4967; 4%) and flexible sigmoidoscopy (182/4967; 3.7%). Rates of positive cases depending on procedure were also determined and found to be as follows: EGD (81/2664; 3%), colonoscopy (24/1237; 1.9%), combined EGD and colonoscopy/sigmoidoscopy (12/398; 3%), ERCP (8/201; 3.9%) and flexible sigmoidoscopy (5/182; 2.7%). Frequencies of the various procedures and the rates of positive tests are summarized in Table 2.

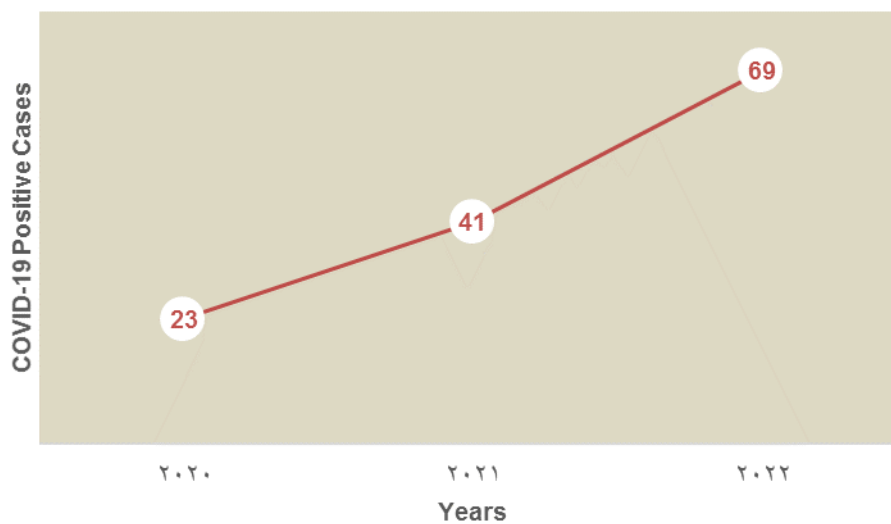


Figure 1. Yearly frequency distribution of COVID-19 positive cases

Table 1. Frequency distribution of positive and negative cases undergoing preprocedural PCR testing in the different waves of COVID-19, *n (%)*

	First	Second	Third	Fourth	Fifth	Total
Negative	601 (97.6)	1292 (98.4)	1181 (98.7)	1251 (99.0)	509 (88.1)	4834 (97.3)
Positive	15 (2.4)	21 (1.6)	16 (1.3)	12 (1.0)	69 (11.9)	133 (2.7)
Total	616	1313	1197	1263	578	4967

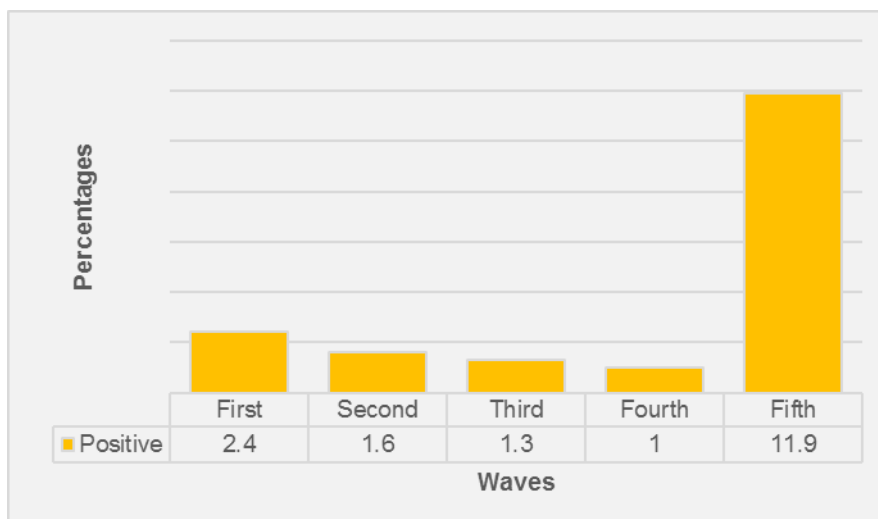


Figure 2. Graphical representation of COVID-19 positivity among asymptomatic endoscopy patients.

Table 2. Frequency distribution of COVID-19 positive and negative cases based on the procedure performed.

Procedure	Negative	Positive	Total
Argon plasma coagulation/sclerotherapy	7 (0.1)	0 (0.0)	7 (0.1)
Ascitic tap	5 (0.1)	0 (0.0)	5 (0.1)
Colonoscopy	1213 (25.1)	24 (18.0)	1237 (24.9)
EGD	2583 (53.4)	81 (18.9)	2664 (53.6)
EGD + Colonoscopy/sigmoidoscopy	386 (8.0)	12 (9.0)	398 (8.0)
EGD + Dilatation+ through-the-scope dilatation	27 (0.6)	0 (0.0)	27 (0.5)
EGD + Variceal band ligation	48 (1.0)	1 (0.7)	49 (1.0)
Enteroscopy	25 (0.5)	0 (0.0)	25 (0.5)
ERCP	193 (4.0)	8 (6.0)	201 (4.0)
EUS	57 (1.2)	2 (1.5)	59 (1.2)
Flexible sigmoidoscopy	177 (3.7)	5 (3.8)	182 (3.7)
Percutaneous Endoscopic Gastrostomy Tube placement	109 (2.2)	0 (0.0)	109 (2.2)
Polypectomy	4 (0.1)	0 (0.0)	4 (0.1)
Total	4834	133	4967

DISCUSSION

The COVID-19 pandemic has not only posed a significant burden of morbidity and mortality globally but has also significantly impacted healthcare delivery [25]. Studies indicate there seems to be a significant impact of the pandemic particularly in developing countries and limited resource settings with effects likely to persist longer due to relatively weaker health infrastructure and slower uptake of vaccines [26]. This effect on disruption of healthcare service delivery has significantly affected the

performance of important diagnostic and therapeutic procedures including endoscopy [21, 22].

The pandemic has been associated with a global reduction in the volume of endoscopies performed. A global 2020 survey of 155 endoscopy units distributed over 55 countries revealed up to a greater than 80% reduction in the volume of endoscopies done compared to baseline. Data from Asian endoscopy units reported a 16.3% rate of endoscopy performance

after the start of the pandemic compared to the baseline [22].

There has been concern about the possibility of COVID-19 transmission due to the aerosol-generating potential of the procedure and this has been thought to partly contribute to the reduction in endoscopy volume among other factors. In addition, COVID-19 infection appears to be transmitted via both symptomatic and asymptomatic individuals raising the concern about the need for screening asymptomatic patients before aerosol-generating procedures that are associated with a higher risk of infection transmission. For this reason, various pre-procedure testing strategies have also been explored [27].

The AGA issued guidance on the matter of COVID-19 testing in the pre-endoscopy setting [24]. The recommendations made were to implement universal COVID-19 symptom screening and avoid routine pre-procedure testing. This was based on a low prevalence of positive cases in asymptomatic individuals ranging from 0.0% to 1.5% even in the setting of surges of local rates in COVID-19 cases. The data was derived from developed countries with studies mostly from the USA and Europe [28–39].

To our knowledge, there is a lack of locally published data on pre-endoscopy COVID-19 testing strategy from Pakistan. This study was therefore done to evaluate a symptom-based screening approach to gain local data to add to the body of evidence in this area and guide decision-making in a limited-resource setting and a different epidemiological and potentially different clinical context. A study on waves of COVID-19 infection in Pakistan revealed five distinct waves of COVID-19 infection locally and this study also further sought to investigate for variations in positive PCR tests in asymptomatic individuals for the virus during the different waves of COVID-19 disease [40].

This study involved 4967 patients planned for various endoscopic procedures over 22 months with an overall positive rate for COVID-19 of 2.7% in asymptomatic patients. Previous studies on pre-procedure COVID-19 testing had revealed low rates of positive cases in asymptomatic individuals which formed the basis of the AGA recommendation against routine pre-procedure COVID-19 testing [24,28–40]. Subsequent further studies continued to

show low rates of positive tests in even larger cohorts [41,42]. However, one study from an Egyptian center revealed a positive COVID-19 PCR rate of 13%, although the sample population, in this case, was relatively smaller at 103 asymptomatic individuals screened before endoscopy [43].

Our study revealed a low overall COVID-19 positivity rate of 2.7% with the highest rate of 11.9% in the 5th COVID-19 wave followed by the 1st wave (2.4%). The positive rate in asymptomatic patients was particularly high in the 5th wave, thus a possible basis to perform PCR testing in addition to symptom-based screening. We hypothesize that the higher positive rate may be due to several reasons including reduced compliance with standard precautions for reducing COVID-19 transmission in the general population, decreased compliance with vaccination, and acceleration of transmission of mutated variants of the virus during 1st and 5th wave. Moreover, considering the low prevalence in asymptomatic patients, symptom-based screening without PCR tests will improve compliance and turnover rate.

PCR-based COVID-19 screening before endoscopy may have to therefore take into consideration a regional burden of infection, vaccination status of HCWs and the general population, availability of PPE, as well as mutated forms of the virus to mitigate the risk of transmission to HCWs, other patients and at the same time, form a basis for rational use of PPE. However, studies do suggest that even in the absence of testing in asymptomatic, transmission risk to HCWs appears to be minimal. In the retrospective study by Hann et al, 15 750 procedures were assigned to either no screening (n=4543), screening using antigen testing (n=682), or screening by PCR testing (n=10 465) [44]. Over the 20-month study period, however, there was no incident case of COVID-19 disease among twenty-nine vaccinated staff involved in the performance of procedures. However, the risk when prevalence is high as was in the case in this study during the fifth wave of infection may need further investigation.

While the study was conducted during the pandemic, it still holds importance in a post-pandemic world for several reasons. Insight into the prevalence and screening of asymptomatic COVID-19 cases during endoscopic procedures is valuable information in helping to prepare for

potential future outbreaks or similar infectious diseases, ensuring appropriate screening protocols and infection control measures are in place. Furthermore, it highlights the importance of implementing standardized screening procedures and testing protocols within healthcare settings, enhancing the preparedness of healthcare systems in identifying and managing infectious diseases, even when positivity rates fall below 0.5%. This can help guide risk assessment and decision-making processes, ensuring the safety of both patients and HCWs. Understanding these numbers can assist in optimizing resource allocation which helps healthcare institutions allocate precious resources effectively, especially in resource-constrained settings. Moreover, our findings highlight the need for adaptability according to the state of the pandemic. This flexibility is crucial for adjusting screening and testing strategies as needed, considering the dynamic nature of infectious diseases.

Our study has a large sample size and spans five waves of the pandemic, which increases the generalizability of our results and provides a comprehensive picture of the impact of the disease, capturing all potential variations in data. Standardized data collection and institution-wide policy of preprocedural testing ensure that data is consistent and decrease the likelihood of missing relevant cases. Limitations of our study include reduced generalizability due to a single-center setting, selection bias due to the strict 72-hour PCR testing inclusion criteria, and the retrospective study design. Moreover, our study did not explore the incidence of new COVID-19 infection among endoscopy staff during the period.

CONCLUSION

There was a low overall occurrence of COVID-19 infection, apart from the fifth wave in asymptomatic patients undergoing endoscopic procedures. Therefore, increasing compliance with COVID-19 vaccination and conducting thorough symptom-based screening before endoscopic procedures could eliminate the necessity for RT-PCR testing.

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Conflict of Interest: None.

Ethical approval of the study was obtained from the Aga Khan University Ethical Review

Committee (ERC) (ERC reference 2021-6504-18861). Patient anonymity was maintained. Patient data was stored on secured files that were accessible by only the primary investigator and coinvestigators.

HIGHLIGHTS

- The overall incidence of COVID-19 infection in low-risk patients screened via the COVID-19 PCR before endoscopic procedures was low except during the fifth COVID-19 wave .
- Increasing compliance with a thorough symptom-based screening before endoscopic procedures could eliminate the necessity for RT-PCR testing
- Screening strategies for COVID-19 before endoscopy need to take into consideration contextual factors such as local prevalence of disease, compliance with vaccination, and prevalence of mutated virus species.

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