

What Is the Predictive Value of a Single Nasopharyngeal SARS-CoV-2 PCR Swab Test in a Patient with COVID-like Symptoms and / or Significant COVID-19 Exposure?

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ABSTRACT:

Utilizing results of PCR testing and subsequent antibody titers, we report on the test characteristics of screening PCR test for Severe acute respiratory syndrome coronavirus-2 among hospital-workers. The PCR-test was found to be 87% sensitive, 97% specific, a positive predictive value of 0.98, and a negative predictive value of 0.80.

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INTRODUCTION

Since the first case of pneumonia was reported from Wuhan, China in December 2019¹, hospital workers have been at risk for exposure to the novel coronavirus currently named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)². During the early days of this pandemic, testing was administered selectively to identify and isolate those infected. Little objective evidence was available to determine pre-test probability and predictive value of these tests. We report a retrospective, cross sectional, observational study analyzing SARS-CoV-2 healthcare worker testing at a tertiary care hospital in Long Island, NY.

METHOD

From March 1 - April 30, 2020, Mount Sinai South Nassau tested healthcare workers with 'COVID-19 like' symptoms or significant exposure (defined as at least 15 minutes in close proximity) to a SARS-CoV-2 patient without wearing personal protective equipment using an established reverse transcription polymerase chain reaction (RT-PCR) test on a nasopharyngeal specimen. Due to the limited availability of testing supplies, only symptomatic employees were offered on-site testing. No "Patient Consent Statement" specific for this testing was obtained as this was part of routine care that all patients were receiving. This RT-PCR was performed by the cobas[®] SARS-CoV-2 Test on the Roche 6800 utilizing Light Cycler 480 II (Roche) and 2019-Novel Coronavirus (2019-nCoV) primers and Probes (IDT). The limit of detection of the assay is 1 genome copy/uL³. Subsequently, they underwent testing for presence of SARS-CoV-2 IgG antibodies using the Mount Sinai test looking at M spike protein at least 3 weeks after the onset of their symptoms. As shown by Zhou et al. (2020), most patients infected by SARS-CoV-2 develop a peak IgM response by day 9 and IgG response by 2 weeks⁴. Ni et.al (2020), further characterized the cellular and humoral immune response to SARS-CoV-2 and showed that the neutralizing antibody titers significantly correlated with the numbers of specific T cell response to the virus⁵. In turn, the SARS-CoV-2 antibody titers were correlated with invitro viral neutralization with a specificity of 100%. All staff also completed a questionnaire self-reporting symptoms experienced before the initial RT-PCR screening test using a questionnaire (See Figure 1). We analyzed data including date and result of SARS-CoV-2 PCR, symptoms on presentation, and date and result of antibody testing.

Symptoms reported were aggregated and compared with SARS-CoV-2 PCR and antibody tests. Symptoms were compared via two-tailed z-test with the threshold for significance defined as a p-value of 0.05.

RESULTS

105 healthcare workers underwent both SARS-CoV-2 PCR and antibody testing. 61 (58.1%) tested positive with the SARS-CoV-2 PCR test; 44 (41.9%) tested negative. Of the 61 that tested positive, 60 (98.4%) subsequently had antibody while only 1 (1.6%) had no antibody. Of the 44 healthcare workers with a negative SARS-CoV-2 PCR test, 9 (20.5%) were subsequently found to have antibody. Quantitative titers showed that 94% of subjects developed a robust immune response with a titer $>1:320$ (chosen as the level accepted by Mount Sinai for plasma donation). At the time of SARS-CoV-2 PCR testing, 76 healthcare workers reported symptoms, including fevers, chills, cough, dyspnea, wheezing, myalgia, pain, nausea, vomiting, diarrhea, fatigue, anosmia, throat pain, otalgia, tachycardia and hypersomnia. Statistical analysis of a larger group of employees ($n=461$, total tested for antibody including these 105 employees) revealed cough and myalgia to be the two symptoms significantly different between those with and without antibody (see Table 1a). The most common symptom reported was cough. The SARS-CoV-2 PCR test via nasopharyngeal swab was found to be 87% sensitive and 97% specific. The PCR test was also found to have a positive predictive value (PPV) of 0.98 and a negative predictive value (NPV) of 0.80 (see table 1b) among symptomatic patients.

DISCUSSION

Determining likelihood of COVID illness using diagnostic PCR testing has not been fully determined. The lack of availability of adequate SARS-CoV-2 testing, reports of high false negative tests⁶ and variability of symptoms on presentation⁷ hinder accurate diagnosing. The high PPV seen in this study reinforces the rationale for PCR testing to identify new active cases. However, one fifth (20.5%) of symptomatic or significantly exposed staff were incorrectly labeled as not having SARS-CoV-2 after a single negative nasopharyngeal swab. This could be due to sub-detectable viral load at the time of screening, poor collection technique, and quality of specimen collected (depth of swab, and quality of sweep of nasopharyngeal region).

Our study had some notable limitations. Symptoms were self-reported thus failed to preclude recall bias and lacked objective verification. Antibody titers were thus not correlated by symptoms due to the subjective nature of symptoms reporting. The calculated specificity was dependent on the assumption that employees did not become infected between the screening test and antibody testing and applies only to symptomatic employees. However, our study showed the value and the limitations of relying on a single PCR nasopharyngeal swab to diagnose SARS-CoV2 illness.

TABLE 1a. *Distribution of Reported Symptoms and their statistical significance*

Symptom	total	pos	neg	p-value
Chills	6 (0.08)	4 (0.08)	2 (0.09)	0.864560133
Fever	27 (0.36)	17 (0.32)	10 (0.43)	0.33998196
Cough	60 (0.79)	46 (0.87)	14 (0.61)	0.010878595
SOB	23 (0.30)	15 (0.28)	8 (0.35)	0.572089927
Wheezing	2 (0.03)	1 (0.02)	1 (0.04)	0.53806803
Headache	21 (0.28)	18 (0.34)	3 (0.13)	0.060999114
Diarrhea	7 (0.09)	5 (0.09)	2 (0.09)	0.918556266
Nausea/vomiting	3 (0.04)	3 (0.06)	0 (0.00)	0.244338211
Myalgias	35 (0.46)	31 (0.58)	4 (0.17)	0.000958949
Fatigue/malaise/weakness	6 (0.08)	4 (0.08)	2 (0.09)	0.864560133
Anosmia	6 (0.08)	6 (0.11)	0 (0.00)	0.092694007
Sinus	8 (0.11)	6 (0.11)	2 (0.09)	0.731918328
Sore throat	23 (0.30)	14 (0.26)	9 (0.39)	0.26764694
Lightheaded/dizzy	3 (0.04)	1 (0.02)	2 (0.09)	0.161385004
Otalgia	1 (0.01)	0 (0.00)	1 (0.04)	0.126489104
Tachycardia	1 (0.01)	0 (0.00)	1 (0.04)	0.126489104
Hypersomnia	1 (0.01)	0 (0.00)	1 (0.04)	0.126489104

Table 1b. *Distribution of subjects with both SARS Cov2 PCR and Antibody Result (n=105)*

PATIENTS	(n)	ANTIBODY POSITIVE TITER	POSITIVE TITER <1:320	POSITIVE TITER ≥1:320	ANTIBODY NEGATIVE TITER
SARS CoV2 PCR (+)	61	60	2	58	1
SARS CoV2 PCR (-)	44	9	2	7	35

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Potential conflicts of interest. All authors report no conflicts of interest relevant to this article

Patient Consent specific for this testing was not obtained as all care was provided as part of routine patient care.

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Figure 1

Date: _____


**Mount
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Nassau**
Covid-19

1. Name: _____ Phone# _____ Email _____

2. D.O.B: _____

3. Date of Onset Symptoms: _____

4. Were you Covid Tested? Yes ☐ or No ☐

<u>Headache</u> ☐	☐ <u>Medications</u>
<u>Fever</u> ☐	
<u>Flu-like</u> ☐	☐ <u>Chest X Ray</u>
<u>Body Ache</u> ☐	☐ <u>Hospitalization</u>
<u>Cough</u> ☐	
<u>Chest Tightness</u> ☐	
<u>Shortness of breath</u> ☐	
<u>Sore Throat</u> ☐	
<u>Loss of Smell/Taste</u> ☐	
<u>GI Symptoms</u> ☐	
<u>Other</u> ☐	