Late Diagnosis of COVID-19 in Patients Admitted to the Hospital

J Gen Intern Med 35(9):2829–31
DOI: 10.1007/s11606-020-05949-1
© Society of General Internal Medicine 2020

BACKGROUND

Testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is vital for identification of cases. Currently, the Centers for Disease Control and Prevention recommends that hospitalized patients with symptoms receive priority for testing.\(^1\)

Delayed testing could occur because patients have atypical presentations or the initial test is a false negative. Since test sensitivity depends on the site sampled\(^2\) and hospital protocols usually rely on nasal samples, patients with lower respiratory tract infections can have a false-negative result.\(^3\)

Understanding how often the diagnosis of SARS-CoV-2 is missed is essential for infection control. We describe the frequency and characteristics of hospitalized patients with COVID-19 diagnosed after admission.

METHODS

This retrospective cohort study included adults hospitalized before April 20, 2020, who tested positive for SARS-CoV-2. Testing became available for Cleveland Clinic Health System (CCHS) patients with suspected COVID-19 starting March 6 and was restricted to symptomatic, high-risk patients (e.g., hospitalized patients) on March 10. We identified patients with a positive SARS-CoV-2 test through CCHS’s COVID-19 registry. We compared patients whose first positive SARS-CoV-2 test was on the day of admission versus later (“late diagnosis”).

We collected demographic and health data from our electronic health record and the registry. We collected common symptoms of COVID-19. We also created a binary indicator of having none of the cardinal symptoms of COVID-19: cough, shortness of breath, or fever.

We report descriptive statistics. To identify factors associated with late diagnosis, we used a multivariable logistic regression model that included presenting symptoms, comorbidities, age, and sex. We used model building techniques to identify variables that were associated with late diagnosis and picked the model with the lowest AIC and BIC. To assess the association between late diagnosis and length of stay, intensive care unit (ICU) admission, discharge disposition, and mortality, we conducted multivariable regressions that included age, sex, and the variables associated with late diagnosis. CCHS’s IRB deemed this study exempt.

RESULTS

Our study included 356 patients; 86% with COVID-19 diagnosed on admission and 14% had a late diagnosis (\(n = 49\)). Patients diagnosed later presented without fever, shortness of breath, or cough 29% of the time (Table 1); 86% of the time they had \(\geq 1\) common symptom. They were similar in age, sex, and pre-existing comorbidities to patients diagnosed on admission. In the adjusted model, patients with late diagnosis presented less often with sputum (AOR 0.26, 95% CI 0.08–0.88) and more often with heart failure (AOR 2.36, 95% CI 1.15–4.84) and with none of the cardinal symptoms (AOR 2.89, 95% CI 1.30–6.43). Late diagnosis was not associated with length of stay, ICU admission, death, or discharge home (Table 2).

Eleven patients with late diagnosis had an initial negative result and 4 had two prior negative results. Four of 11 had their positive result collected from a non-nasal site. False negatives averaged 3.7 days to a positive result versus 2.2 days for others with late diagnosis (\(P > 0.05\)). False negatives were retested due to worsening symptoms (7/11), imaging suggestive of COVID-19 (2/11), and discharge protocol for skilled nursing facility (2/11).

DISCUSSION

Undiagnosed patients with COVID-19 can increase caregivers’ risk of infection, as protective equipment may not be used. We found that 14% of COVID-19 patients were diagnosed after admission and most presented with \(\geq 1\) common symptom. Few late diagnoses were due to a false-negative test. Retesting of false negatives often occurred after clinical deterioration, but 2 patients were not diagnosed until discharge. This study is limited because we could only identify false negatives if a patient was retested. Further, we could only include routinely collected clinical data. In conclusion, routine
| Demographics | At hospitalization | After hospitalization | \( P \) value<sup>a</sup> |
|--------------|-------------------|-----------------------|--------------------------|
| Race (%)     |                   |                       |                          |
| Asian        | 5 (2%)            | 0 (0%)                | 0.36                     |
| Black        | 112 (36%)         | 22 (45%)              |                          |
| Other        | 15 (5%)           | 4 (8%)                |                          |
| White        | 175 (57%)         | 23 (47%)              |                          |
| Male (%)     | 176 (57%)         | 27 (55%)              | 0.77                     |
| Hispanic (%) | 11 (4%)           | 5 (11%)               | 0.03                     |
| Smoking (%)  |                   |                       |                          |
| Current smoker | 25 (8%)     | 2 (4%)                | 0.05                     |
| Former smoker | 115 (38%)    | 20 (43%)              |                          |
| Non-smoker   | 146 (49%)         | 25 (53%)              |                          |
| Age (mean [SE]) | 66.0 (0.9) | 67.9 (2.2)            | 0.47                     |
| Exposure history |          |                       |                          |
| Exposed to COVID-19 | 82 (28%) | 7 (16%)               | 0.35                     |
| Family member w/ COVID-19 | 38 (13%) | 3 (7%)                | 0.23                     |
| Presenting symptoms |          |                       |                          |
| Cough (%)    | 226 (74%)         | 27 (55%)              | 0.01                     |
| Fever (%)    | 158 (51%)         | 22 (45%)              | 0.39                     |
| Shortness of breath (%) | 195 (64%) | 23 (47%)              | 0.03                     |
| Two or more of cardinal symptoms of COVID-19<sup>b</sup> | 209 (68%) | 29 (59%)              | 0.22                     |
| None of the cardinal symptoms of COVID-19<sup>b</sup> | 36 (12%) | 14 (29%)              | < 0.01                   |
| Fatigue (%)  | 167 (54%)         | 19 (39%)              | 0.04                     |
| Sputum production (%) | 74 (23%) | 4 (8%)                | 0.02                     |
| Flu-like symptoms (%) | 164 (53%) | 21 (43%)              | 0.17                     |
| Diarrhea (%) | 92 (30%)          | 11 (22%)              | 0.28                     |
| Loss of appetite (%) | 95 (31%) | 12 (24%)              | 0.36                     |
| Vomiting (%) | 37 (12%)          | 1 (2%)                | 0.04                     |
| At least one presenting symptom | 287 (93%) | 42 (86%)              | 0.06                     |
| Comorbidities |          |                       |                          |
| BMI (mean [SE])* | 30.4 (0.42) | 30.2 (1.1)            | 0.85                     |
| COPD/emphysema | 47 (17%)       | 6 (14%)               | 0.34                     |
| Asthma       | 63 (23%)          | 12 (30%)              | 0.35                     |
| Diabetes     | 125 (45%)         | 16 (36%)              | 0.26                     |
| Hypertension | 227 (78%)         | 35 (78%)              | 0.94                     |
| Coronary artery disease | 62 (23%) | 11 (27%)              | 0.58                     |
| Heart failure | 68 (25%)         | 16 (39%)              | 0.06                     |
| Cancer       | 53 (18%)          | 12 (27%)              | 0.19                     |
| Transplant history | 13 (5%)    | 0 (0%)                | 0.15                     |
| Connective tissue disease | 49 (18%) | 8 (20%)               | 0.79                     |
| Inflammatory bowel disease | 16 (6%) | 3 (7%)                | 0.76                     |
| Immunosuppressive disease | 69 (24%) | 13 (30%)              | 0.29                     |
| Vaccination history |          |                       |                          |
| Flu shot     | 158 (51%)         | 28 (57%)              | 0.46                     |
| Pneumovax shot | 103 (34%)        | 20 (41%)              | 0.32                     |
| Home medications |          |                       |                          |
| NSAIDS       | 105 (34%)         | 20 (41%)              | 0.37                     |
| Steroids     | 46 (15%)          | 10 (20%)              | 0.33                     |
| Carvedilol   | 17 (6%)           | 3 (6%)                | 0.87                     |
| ACE inhibitor | 39 (13%)          | 11 (22%)              | 0.07                     |
| ARB          | 35 (11%)          | 5 (10%)               | 0.81                     |
| Melatonin   | 19 (6%)           | 13 (27%)              | < 0.01                   |
| Hospital transfer |          |                       |                          |
| Hospital transfer | 3 (1%)           | 5 (10%)               | < 0.01                   |

<sup>a</sup>Body mass index (BMI) missing in 11 (3%) of respondents; presenting symptoms, comorbidities, vaccination history, and home medications are shown if they were positively identified

<sup>b</sup>Cardinal symptoms of COVID-19 include cough, shortness of breath, and fever

<sup>c</sup>P values were obtained using chi-square and Student's T tests

<sup>+</sup>Presenting symptoms, comorbidities, vaccination history, and home medications are shown if they were positively identified

\*Body mass index (BMI) missing in 11 (3%) of respondents; presenting symptoms, comorbidities, vaccination history, and home medications are shown if they were positively identified
testing on admission may reduce delayed identification of COVID-19. Retesting is also warranted.

Elizabeth R. Pfoh, PhD, MPH
Essa H. Hariri, MD
Anita D. Misra-Hebert, MD, MPH
Abhishek Deshpande, PhD, MD
Lara Jehi, MD
Michael B. Rothberg, MD, MPH

1Center for Value-Based Care Research, Cleveland Clinic Community Care, 9500 Euclid Avenue, Cleveland, OH 44195, USA
2Department of Internal Medicine, Cleveland Clinic Community Care, Cleveland, OH, USA
3Healthcare Delivery and Implementation Science Center, Cleveland Clinic, Cleveland, OH, USA
4Chief Research Information Officer, Cleveland Clinic, Cleveland, OH, USA

Corresponding Author: Elizabeth R. Pfoh, PhD, MPH; Center for Value-Based Care Research, Cleveland Clinic Community Care, 9500 Euclid Avenue, Cleveland, OH 44195, USA (e-mail: pfohe@ccf.org).

Author Contributions: All authors contributed to the study design. LJ and EH collected the data. EP conducted the data analysis and drafted the manuscript. All authors revised the manuscript for important intellectual content.

Compliance with Ethical Standards:

Conflict of Interest: The authors declare that they do not have a conflict of interest. Dr. Misra-Hebert reports funding from the Agency for Healthcare Research and Quality K08 HS024128 and reports grants from NHLBI, grants from Novo Nordisk, Inc, grants from Merck Inc., grants from Boehringer Ingelheim Pharmaceuticals, Inc outside the submitted work. Dr. Abhishek Deshpande has received research support from Clorox Healthcare not related to this study and is on the advisory board of Ferring Pharmaceuticals.

REFERENCES

1. Centers for Disease Control and Prevention. Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19). Available at: https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Accessed May 8, 2020

2. Wang W, Xu Y, Lu R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. 2020 Mar 11. doi: https://doi.org/10.1001/jama.2020.3786. [Epub ahead of print]

3. Xie, Xingbi, Zhong Z, Zhao W, et al. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology (2020): 200343.

Publisher’s Note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.