Article Type: Concise Communication

Predicting asymptomatic SARS-CoV-2 infection rates of inpatients: a time series analysis.

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Running title: Predicting SARS-CoV-2 asymptomatic infections

Word count: 1216/1200
Abstract

Asymptomatic SARS-CoV-2 infections are often difficult to identify as widespread surveillance has not been the norm. Using time-series analysis, we examined if COVID-19-rates at the county-level could predict positivity rates among asymptomatic-patients at a large Health System. Asymptomatic-positivity rates at the system-level and county-level COVID-19-rates failed to show an association.
Introduction

Patients with Coronavirus Disease 2019 (COVID-19) have a wide range of clinical presentations, including asymptomatic infection. Asymptomatic SARS-CoV-2 infections play a critical role in transmission dynamics given the infectivity of SARS-CoV-2. The reported prevalence of asymptomatic individuals varies across settings, from 1% to 57%. Quarantining asymptomatic patients is a crucial strategy for stopping the spread of the SARS-CoV-2 virus. However, asymptomatic infections are often difficult to identify as widespread surveillance has not been the norm in the United States. Of particular concern is the rate of asymptomatic infections in healthcare settings, as they may expose healthcare providers or other patients at high risk of developing severe disease. In an effort to control SARS-CoV-2 transmission within the hospital setting, some hospitals have implemented universal SARS-CoV-2 testing among all consecutive admissions.

Our research group previously reported a 1% prevalence of asymptomatic infections at two large academic hospitals in Wisconsin from April to June 2020. However, as the pandemic intensified in Wisconsin, positivity rates among asymptomatic patients increased to 6% (data non-published). Predicting hospital-level asymptomatic rates using COVID-19 county-level data may be useful for individual facilities. Thus, we aimed to determine if COVID-19 rates reported at the county-level could predict the SARS-CoV-2 positivity rates among asymptomatic patients tested at a large academic health system.

Methods

This observational study was conducted from April 23, 2020 to December 10, 2020 at Froedtert Health (FH) hospitals. Located in the greater in Milwaukee County, FH is comprised of a large academic medical center and two community hospitals (961 beds & 46,206 admissions annually).

Asymptomatic SARS-CoV-2 infections

On April 23, 2020, FH implemented SARS-CoV-2 surveillances among all consecutive hospital admissions not suspected of COVID-19, all patients scheduled for elective procedures and deliveries, and all asymptomatic patients with known exposures. Test
orders were labeled with a different name than those tests used for symptomatic patients. Tests with orders used for symptomatic patients were excluded from this analysis. Providers collected nasopharyngeal and oropharyngeal swab specimens from patients according to institutional procedures, and samples were processed at Wisconsin Diagnostic Laboratory (WDL) using reverse transcription-polymerase chain reaction (RT-PCR). As previously described, both swabs were combined into a single container with viral transport media. Specimens were tested using the ThermoFisher TaqPath SARS-CoV-2 Assay or the Roche Cobas 6800 SARS-CoV-2 Assay according to the manufacturer’s instructions for use under Food and Drug Administration emergency use authorization.

COVID-19 cases in Milwaukee County
We accessed the Wisconsin Department of Health Services (WDHS) public COVID-19 database to obtain the daily number of newly COVID-19 cases confirmed in Milwaukee County. The WDHS defines confirmed cases as those unique persons with positive SARS-CoV-2 molecular tests. WDHS does not recognize a positive antigen or a positive antibody test as a confirmed COVID-19 case.

Statistical analysis
For the purposes of this study, COVID-19 rates or SARS-CoV-2 positivity rates were defined as the percentage of positive tests among all daily tests performed at the county-level or within FH, respectively. The association between daily positivity rates among SARS-CoV-2 asymptomatic patients at FH (dependent variable) and daily COVID-19 rates in Milwaukee County (independent variable) was assessed with autoregressive moving average time series analysis (ARIMA). First, we fit a linear regression model to obtain the residuals (estimated errors). We then examined the residuals using the autocorrelation function and partial auto-correlation function plots. Finally, we estimated the parameters for the daily COVID-19 incidence rate in Milwaukee County and the ARIMA model for the residuals and examined the residuals for the final model using auto-correlation function and partial auto-correlation function to confirm there was no autocorrelated residuals. Two-sided P-values <0.05 were considered to be statistically significant.
We used patients’ zip-codes to plot home addresses locations and to obtain their corresponding Area Disadvantage Index (ADI). Maps were created using Excel 2016 3D Maps (Microsoft Corp) and Inkscape 2020 (Inkscape Project).

**Results**

Over the 8 months of observation, there were 2,347 new asymptomatic infections at FH and 75,196 new confirmed cases in Milwaukee County. Figure 1 shows the time series plots of SARS-CoV-2 asymptomatic positivity rates at FH and COVID-19 rates in Milwaukee County. The overall positivity rate of asymptomatic infections at FH was 37.8 per 1,000 people tested and the overall positivity rate of COVID-19 infections in Milwaukee County was 172.3 per 1,000 people tested. Both monthly SARS-CoV-2 infection rates at FH and the county-level COVID1-9 rates peaked in November 2020. In December 2020, the county-level COVID-19 rates were elevated while rates of asymptomatic SARS-CoV-2 infections began to decline at FH. The lowest COVID-19 rate at FH was observed in May 2020 while the lowest COVID-19 rate for the county was observed in August 2020. To examine the association between the daily positivity rate of asymptomatic infections at FH and the daily COVID-19 rate in Milwaukee County, we fitted a seventh-order autoregression for the residuals based on autocorrelation function and partial auto-correlation function. As the COVID-19 rate in Milwaukee County increased by one unit, the asymptomatic infection rate in FH decreased by 0.024 unit (95% CI -0.053-0.004, p-value=0.095) after accounting for autocorrelation over time. Thus, there was no strong association between positivity rates among SARS-CoV-2 asymptomatic patients at FH and COVID-19 incidence rates in Milwaukee County. Supplementary Figure 1 shows the auto-correlation function and partial auto-correlation function plots of the residuals after fitting a seventh-order autoregression for error terms, which indicate no autocorrelated errors in the final model. Finally, we observed that the majority of asymptomatic cases were located in Milwaukee County (Figure 2A) even though the catchment area for all tests was fairly large (Figure 2B). Based on ADIs, hot-spots of asymptomatic patients occurred in the most disadvantaged areas in the county (Figure 2B).
Discussion

Using time series analyses, we found that COVID-19 positivity rate at the county-level was not associated with asymptomatic SARS-CoV-2 infections at a regional medical center after accounting for autocorrelation over time. Universal testing for SARS-CoV-2 infections may help to identify asymptomatic infections and reduce COVID-19 transmission. However, implementing screening programs in cities or counties is difficult because it is expensive and logistically challenging. In addition, there are no national or international guidelines that define who, where, or when is most feasible to perform massive screening for asymptomatic infections. In response, hospitals have implemented infection control and preventive measures based on how the COVID-19 pandemic behaves within the community, strengthening or relaxing restrictions based on COVID-19 epidemic curves at the state, county or city-level. However, it is important to consider that the patient population at an individual Health System may not be representative to the population at the county-level.

Our study used data from a single health system and a single county, which may have limited our analysis. We did not analyze individual-level data, and thus we were unable to explore if differences among patients could impact the association between COVID-19 rate and asymptomatic infection rate. Also, we did not evaluate the effects of test availability at the county-level and how this may have affected the incidence rates. Based on our findings, we suggest that COVID-19 rates at the county-level may not be reflective of asymptomatic infection rates in local health systems. Hospitals need to test their population to implement specific policies to reduce SARS-CoV-2 transmission regardless of county-level spread, especially when their patient population does not reflect the composition of the population at the county-level.
References


Acknowledgments

Financial Support
This study was performed in part with support from the Advancing a Healthier Wisconsin Foundation.

Conflict of interest
All authors report no conflicts of interest relevant to this article.
Figure 1. Time series plots of positivity rates.
A) SARS-CoV-2 asymptomatic patients at Froedtert Health and B) COVID-19 in Milwaukee County. The red line indicates moving average over time.
Figure 2. Map of zip-code addresses corresponding to Froedtert Health patients with positive SARS-CoV-2 asymptomatic patients (Panel A) and total SARS-CoV-2 asymptomatic patients tested (Panel B) with an overlay of area deprivation indexes at the county-level. The number of positive asymptomatic cases (Panel A) or total patients tested (Panel B) are represented by circles with colors green, yellow, and red, representing lowest to highest number of tests, respectively. ADI scores in Wisconsin counties were shaded using colors blue (lowest) to red (highest). The red cross indicates the location of hospitals that belonged to the Froedtert Health network. The map was created using Excel 2016 3D Maps (Microsoft Corp) and Inkscape 2020 (Inkscape Project).
Supplemental Material

Supplementary Figure 1. Auto and Partial auto-correlation function plots of the residuals after fitting a seventh-order autoregression for error terms. A) Auto-correlation function and B) Partial auto-correlation function plots. The x-axis indicates the number of lags in days. Dotted blue lines indicates 95% confidence interval. ACF: auto-correlation function.