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Technical Note

SARS-CoV-2 infection and COVID-19 severity in individuals with prior seasonal coronavirus infection

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ABSTRACT

We show that individuals with documented history of seasonal coronavirus have a similar SARS-CoV-2 infection rate and COVID-19 severity as those with no prior history of seasonal coronavirus. Our findings suggest prior infection with seasonal coronavirus does not provide immunity to subsequent infection with SARS-CoV-2.

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Understanding correlates of protective immunity against SARS-CoV-2 remains a top priority for management of the COVID-19 pandemic. Recent studies have identified a durable cross-reactive memory T cell immune response to SARS-CoV-2 in healthy blood donors, including those who donated prior to COVID-19 pandemic, which react with comparable affinity to seasonal coronaviruses (OC43, HKU1, 229E, and NL63) (Braun et al., 2020, Le Bert et al., 2020, Mateus et al., 2020). These cross-reactive T cells are detected in 20% to 50% of unexposed blood donors from geographically diverse locations such as Germany, Netherlands, Singapore, USA, and UK, and are thought to represent a lasting cellular immune response to past seasonal coronavirus infection (Braun et al., 2020, Le Bert et al., 2020, Grifoni et al., 2020, Meckiff et al., 2020, Weiskopf et al., 2020). The significance of a pre-existing cross-reactive cellular immune response to SARS-CoV-2 in terms of protection against infection with SARS-CoV-2 and severity of COVID-19 in those that do get infected remains speculative but has great implications for managing the pandemic and a rational vaccine strategy for the global community.

To investigate the impact of past infection with seasonal coronavirus on subsequent susceptibility to SARS-CoV-2 and severity of COVID-19, we retrospectively searched the electronic health records of 2.9 and 5.4 million patients at Stanford Health Care and University

of Washington, respectively, from January 1, 2016 to October 15, 2020 to identify individuals who had both seasonal coronavirus (OC43, HKU1, 229E and NL63) RT-PCR result prior to February 1, 2020 (pre COVID-19 pandemic), and subsequent SARS-CoV-2 RT-PCR result after February 1, 2020 (COVID-19 pandemic). At least one positive result and the last negative or positive result in those with multiple seasonal coronavirus RT-PCR results were included. Thus, if a patient had a positive result followed by negative seasonal coronavirus results, then only the positive result was counted. In total 2768 individuals (Northern California, $n = 1424$; Washington, $n = 1344$) met the inclusion criteria.

In 302 patients with a documented history of positive seasonal coronavirus test results, 3.3% (10) subsequently tested positive for SARS-CoV-2 compared with 3.1% (77) in 2466 patients with a history of negative seasonal coronavirus result ($P = 0.86$, χ^2 test; Table 1). Similar results were obtained when seasonal coronavirus results were analyzed per year to determine if more recent infection had an impact on SARS-CoV-2 positivity rate (Supplementary Table). We also did not observe a higher SARS-CoV-2 positivity rate in patients ≥ 65 versus < 65 years old in groups with a history of either positive or negative seasonal coronavirus result (data not shown). Lastly, in those with COVID-19, the proportion of patients with severe (defined as hospitalized and intubated) or moderate (defined as hospitalized but not intubated) infection was comparable to those with history of positive and negative seasonal coronavirus test results (40.0% (4/10) vs 48.1% (37/77), $P = 0.63$; Table 2).

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Table 1

SARS-CoV-2 RT-PCR positivity rate in patients with history of seasonal coronavirus (OC43, HKU1, 229E and NL63) prior to COVID-19 pandemic.

		Post-pandemic SARS-CoV-2			Pvalue
		Positive	Negative		
Pre-pandemic seasonal CoV	Northern California	Positive	4.3% (7)	95.7% (157)	0.81
		Negative	3.9% (49)	96.1% (1211)	
	Washington	Positive	2.2% (3)	97.8% (135)	0.95
		Negative	2.3% (28)	97.7% (1178)	
	Combined	Positive	3.3% (10)	96.7% (292)	0.77
		Negative	3.1% (77)	96.9% (2389)	

Table 2

Severity of COVID-19 in patients with history of seasonal coronavirus (OC43, HKU1, 229E, and NL63) prior to COVID-19 pandemic.

		Post-pandemic SARS-CoV-2			Pvalue
		Mild	Moderate/ Severe		
Pre-pandemic seasonal CoV	Northern California	Positive	71.4% (5)	28.6% (2)	0.83
		Negative	67.3% (33)	32.7% (16)	
	Washington	Positive	33.3% (1)	66.7% (2)	0.75
		Negative	25.0% (7)	75.0% (21)	
	Combined	Positive	60.0% (6)	40.0% (4)	0.63
		Negative	51.9% (40)	48.1% (37)	

Our findings suggest past infection with seasonal coronavirus, and thus by inference cross-reactive memory T cell immune response to SARS-CoV-2, do not provide protective immunity against subsequent infection with SARS-CoV-2 infection and also do not modulate the severity of COVID-19 in those that get infected by SARS-CoV-2. Our findings are consistent with the lack of protection against SARS-CoV-2 infection in children with prior infection with seasonal coronavirus based on seropositivity (Sermet et al., 2020). Retrospective studies with larger number of participants and prospective studies in individuals with pre-existing cross-reactive memory T cells are needed to confirm lack of protective immunity to SARS-CoV-2 or modulation of COVID-19 severity in individuals with pre-existing cross-reactive T cells to seasonal coronaviruses.

Author statement

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Declaration of competing interest

The authors report no conflicts of interest relevant to this article.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.diagmicrobio.2021.115338.

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