The Association Between Prior SARS-CoV-2 Infection and Incidence of Stroke

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BACKGROUND

- Long-term sequelae of COVID-19 are now well recognized, with over 60 physical and psychological signs and symptoms reportedly associated with prior SARS-CoV-2 infection.[1]
- Individuals with COVID-19 have an increased incidence of several comorbid conditions including diabetes and acute myocardial infarction.
- The association of SARS-CoV-2 vaccination with stroke is somewhat controversial, with some studies demonstrating a higher risk and other studies showing no association or even a protective effect.[2-6]
- The protective effect observed in vaccinated individuals may be due to the vaccination itself or reflect a healthy-survivor bias.

OBJECTIVES

We sought to determine the association between SARS-CoV-2 infection and subsequent incidence of stroke at a national level in Qatar.

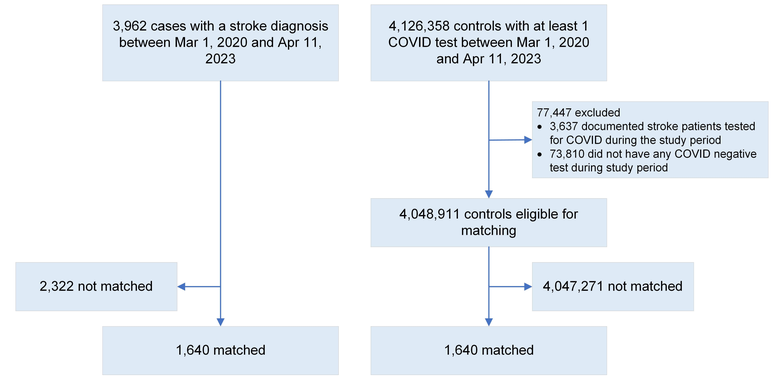
METHODS

- We linked the Qatar Stroke Database to the Qatar National COVID-19 database to retrieve the information on SARS-CoV-2 testing and vaccination.
- This database contains all records of RT-PCR and medically supervised antigen testing and vaccination in the State of Qatar since onset of the SARS-CoV-2 pandemic.
- Eligible individuals with stroke diagnosis were matched exactly 1:1 on 10-year age group, sex, nationality, type of comorbid condition, and number of vaccine doses received, to eligible controls who tested COVID-negative during the same week of the stroke diagnosis.
- We utilized a case-control design to determine the association of COVID-19 diagnosis with stroke.
- Adjusted odds ratios comparing odds of prior documented SARS-CoV-2 infection in cases relative to controls, and corresponding 95% confidence intervals, were estimated for the entire study population using conditional logistic regression.
- Subgroup analyses by age, nationality, comorbidity status, vaccine dose, prior infection type (pre-omicron, omicron, or both), and time since prior infection were further performed.

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2. Libruder C et al. An increased risk for ischemic stroke in the short-term period following COVID-19 infection: A nationwide population-based study. Neuroepidemiology 2023, 10.1159/0005311631.
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RESULTS

Dataset Construction



Baseline characteristics

Characteristics	Full eligible cohorts: Stroke cases N (%) N=3,962	Full eligible cohorts: Controls N (%) N=4,048,911	SMD†	Matched cohorts*: Stroke cases N (%) N=1,640	Matched cohorts*: Controls N (%) N=1,640	SMD†
Median age (IQR)—years	53.0 (44.0-63.0)	32.0 (25.0-40.0)	1.58‡	49.0 (42.0-56.0)	49.0 (41.0-56.0)	0.05‡
Age—years						
0-19 years	7 (0.2)	639,479 (15.8)		6 (0.4)	6 (0.4)	
20-29 years	63 (1.6)	992,449 (24.5)		40 (2.4)	40 (2.4)	
30-39 years	457 (11.5)	1,311,610 (32.4)		245 (14.9)	245 (14.9)	
40-49 years	1037 (26.2)	695,651 (17.2)	1.71	564 (34.4)	564 (34.4)	0.00
50-59 years	1079 (27.2)	282,603 (7.0)		499 (30.4)	499 (30.4)	
60-69 years	715 (18.0)	96,883 (2.4)		215 (13.1)	215 (13.1)	
70-79 years	389 (9.8)	23,961 (0.6)		50 (3.0)	50 (3.0)	
80+ years	215 (5.4)	6,275 (0.2)		21 (1.3)	21 (1.3)	
Sex						
Male	3,070 (77.5)	2,870,214 (70.9)	0.15	1,387 (84.6)	1,387 (84.6)	0.00
Female	892 (22.5)	1,178,697 (29.1)		253 (15.4)	253 (15.4)	
Nationality§						
Bangladeshi	516 (13.0)	297,003 (7.3)		231 (14.1)	231 (14.1)	
Egyptian	153 (3.9)	192,992 (4.8)		55 (3.4)	55 (3.4)	
Filipino	334 (8.4)	301,252 (7.4)		161 (9.8)	161 (9.8)	
Indian	847 (21.4)	1,131,295 (27.9)		525 (32.0)	525 (32.0)	
Nepalese	291 (7.3)	388,616 (9.6)	0.40	154 (9.4)	154 (9.4)	0.00
Pakistani	220 (5.6)	235,115 (5.8)		79 (4.8)	79 (4.8)	
Qatari	685 (17.3)	322,057 (8.0)		182 (11.1)	182 (11.1)	
Sri Lankan	126 (3.2)	135,284 (3.3)		64 (3.9)	64 (3.9)	
Sudanese	112 (2.8)	83,210 (2.1)		32 (2.0)	32 (2.0)	
Other nationalities¶	678 (17.1)	962,087 (23.8)		157 (9.6)	157 (9.6)	
Number of coexisting conditions						
None	1,022 (25.8)	3,564,973 (88.0)		944 (57.6)	944 (57.6)	
1	468 (11.8)	276,908 (6.8)		233 (14.2)	233 (14.2)	
2	615 (15.5)	108,598 (2.7)	1.71	220 (13.4)	220 (13.4)	0.00
3	757 (19.1)	45,023 (1.1)		172 (10.5)	172 (10.5)	
4+	414 (10.4)	24,943 (0.6)		50 (3.1)	50 (3.1)	
5	686 (17.3)	28,466 (0.7)		21 (1.3)	21 (1.3)	
Vaccine dose**						
0	2,138 (54.0)	2,704,895 (66.8)		783 (47.7)	783 (47.7)	
1	86 (2.2)	57,630 (1.4)		24 (1.5)	24 (1.5)	
2	1,261 (31.8)	1,033,188 (25.5)	0.29	603 (36.8)	603 (36.8)	0.00
3	459 (11.6)	250,712 (6.2)		229 (14.0)	229 (14.0)	
4	18 (0.5)	2,480 (0.1)		1 (0.1)	1 (0.1)	
5	0 (0.0)	6 (<0.01)		--	--	
Prior infection status**						
No prior infection	3,376 (85.2)	3,558,651 (87.9)		1,406 (85.7)	1,241 (75.7)	
Prior pre-omicron infection	390 (9.8)	285,702 (7.1)		150 (9.2)	213 (13.0)	
Prior omicron infection	172 (4.3)	186,591 (4.6)	0.10	75 (4.6)	163 (9.9)	0.27
Prior pre-omicron and omicron infections	24 (0.6)	17,967 (0.4)		9 (0.6)	23 (1.4)	

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RESULTS (contd.)

Association between prior COVID-19 and stroke

	Stroke cases* Prior infection	Stroke cases* No prior infection	Controls* Prior infection	Controls* No prior infection	Adjusted odds ratio (95% CI)
Main analysis					
Any prior infection	234	1,406	399	1,241	0.48 (0.40 to 0.58)
Subgroup analyses					
By nationality					
Qataris	44	138	72	110	0.45 (0.28 to 0.74)
Non-Qataris	190	1,268	327	1,131	0.48 (0.39 to 0.60)
By age					
<40 years	9	37	8	38	1.17 (0.39 to 3.47)
40-59 years	156	907	260	803	0.49 (0.39 to 0.63)
60+ years	38	248	65	221	0.52 (0.33 to 0.81)
By comorbidity status					
None	118	826	214	730	0.45 (0.34 to 0.59)
1	39	194	57	176	0.62 (0.39 to 0.98)
2	40	180	64	156	0.48 (0.29 to 0.79)
3	23	149	41	131	0.45 (0.25 to 0.84)
4+	14	57	23	48	0.47 (0.20 to 1.09)
By vaccine dose					
0 dose	56	727	108	675	0.43 (0.29 to 0.62)
2 doses	114	489	202	401	0.46 (0.35 to 0.60)
3+ doses	61	169	82	148	0.63 (0.42 to 0.96)
By prior infection type					
Prior pre-omicron infection	129	1,265	202	1,192	0.59 (0.46to 0.75)
Prior omicron infection	64	1,214	144	1,134	0.36 (0.26 to 0.51)
Prior pre-omicron & omicron infections	4	1,105	16	1,093	0.25 (0.08 to 0.75)
By time since prior infection					
<90 days	49	1,169	90	1,128	0.49 (0.33 to 0.71)
≥90 days-6 months	14	1,136	47	1,103	0.30 (0.16 to 0.54)
≥6 months-1 year	34	1,165	82	1,117	0.37 (0.24 to 0.57)
≥1 year	88	1,203	131	1,160	0.62 (0.46 to 0.84)
Additional analyses					
<90 days	49	1,169	90	1,128	0.49 (0.33 to 0.71)
≥90 days	168	1,326	292	1,202	0.48 (0.38 to 0.60)
<6 months	67	1,216	141	1,142	0.42 (0.30 to 0.58)
≥6 months	142	1,279	233	1,188	0.52 (0.41 to 0.66)
<1 year	111	1,292	233	1,170	0.40 (0.31 to 0.52)
≥1 year	88	1,203	131	1,160	0.62 (0.46 to 0.84)

POSSIBLE EXPLANATIONS

- Inclusion of individuals who survived a previous COVID-19 infection may indicate a healthier population at a lower risk of stroke.
- Those with stroke may have considered themselves at a higher risk of severe COVID-19 if infected and therefore taken extra precautions to avoid infection.
- We mitigated these factors by matching the cases and controls on demographic characteristics as well as the type of coexisting comorbid conditions, but this matching may not have fully controlled for effects of these factors.

CONCLUSIONS

Individuals with acute stroke were less likely to have had previous confirmed SARS-CoV-2 infection. The lower risk of stroke in this population with prior SARS-CoV-2 infection does not appear to be explained by demographic characteristics, comorbidities, or prior vaccination status.

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