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ENHANCED EPIDEMIOLOGICAL SUMMARY

Estimates of Omicron Sub-lineage BQ.1 Severity in an Ontario-based Matched Cohort Study of Cases: August 4 – December 28, 2022

Published: March 2023

Purpose

Using data from Ontario's Public Health Case and Contact Management Solution (CCM) linked to Ontario Ministry of Health's COVaxON application, this report examines the risk of hospitalization and death among SARS-CoV-2 cases infected with the Omicron sub-lineage BQ.1, as compared to closely matched cases infected with the Omicron sub-lineage BA.5.

For more information on variants confirmed by whole genome sequencing in Ontario, refer to Public Health Ontario's (PHO's) SARS-CoV-2 Genomic Surveillance weekly report.

Highlights

- Among matched BQ.1 cases compared to BA.5 cases:
    - 83/2,457 (3.4%) matched BQ.1 cases were hospitalized or died compared to 77/2,457 (3.1%) BA.5 cases
    - 28/2,457 (1.1%) matched BQ.1 cases died compared to 34/2,457 (1.4%) BA.5 cases
- For BQ.1 cases compared to BA.5 cases, the risk of hospitalization or death was similar (adjusted hazard ratio, HR=1.04, 95%CI: 0.75, 1.43).
- For BQ.1 cases compared to BA.5 cases, the risk of death was similar (adjusted hazard ratio, HR=0.84, 95%CI: 0.51, 1.39).

Methods

A retrospective population-wide matched cohort study of Ontario cases infected with SARS-CoV-2 Omicron sub-lineages BQ.1 and BA.5 was conducted. Cases were included if symptom onset occurred between August 4 and December 28, 2022. Cases with a symptom onset date or specimen collection date after hospitalization were excluded. BQ.1 cases included all BQ.1 sub-lineages identified by whole-genome sequencing (WGS). BA.5 cases included the dominant BA.5 sub-lineages (BA.5.2 and BA.5.2.1). BQ.1 cases were matched to BA.5 cases using 1:1 matching on date of specimen collection (within 14 days), sex, age group in years (0-4, 5-11, 12-18, 19-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+), number of vaccine doses (0-5 doses), time since most recent vaccine dose (within 90 days), health region, long-term care home (LTCH) resident status, and healthcare worker status. Outcomes included hospitalization or death.

Cox proportional hazards models with robust 95% confidence intervals (CI) were used to determine hazards ratios (HR) for hospitalizations or deaths and deaths alone for BQ.1 compared to BA.5 cases. Prior documented infection was included as a covariate. Differences in risk by sex, age group, vaccination status, LTCH resident status and BQ.1 sublineages (BQ.1, BQ.1.1, and other BQ.1) were evaluated. In a sensitivity analysis, we adjusted for differential under-detection of prior infection by age group, using Canadian sero-prevalence estimates of infection-acquired immunity using previously described statistical methods.[1,2]

Results

There were 12,248 cases of BA.5 and 9,065 cases of BQ.1 during the period between August 4 and December 28, 2022. After 1:1 matching, there were 2,457 BQ.1 and BA.5 cases. The median follow-up time was 65 days (interquartile range [IQR]: 41, 79). There were 83 (3.4%) hospitalizations or deaths and 28 (1.1%) deaths among matched BQ.1 cases, compared to 77 (3.1%) hospitalizations or deaths and 34 (1.4%) deaths among matched BA.5 cases (Table 1). No change in comparative risk of hospitalization or death with BQ.1 was observed (HR=1.04, 95%CI: 0.75, 1.43). Results were similar when examining death alone (HR=0.84, 95%CI: 0.51, 1.39) (Table 2). Sensitivity analyses adjusting for estimated differential under-detection of prior infection led to similar point estimates of relative severity (hospitalization or death HR = 1.18, 95%CI 0.86, 1.63; death HR = 0.99, 95%CI: 0.60, 1.64).

Table 1. Characteristics of SARS-CoV-2 BQ.1 and BA.5 variant cases, overall and among matched cases (N, %).

	Full Cohort BA.5 N=12,248	Full Cohort BQ.1 N=9,065	Matched Cohort BA.5 N=2,457	Matched Cohort BQ.1 N=2,457
Age (median [IQR])	61.0 [41.0, 82.0]	58.0 [39.0, 80.0]	62.0 [43.0, 83.0]	61.0 [43.0, 83.0]
Sex				
Female	8,009 (65.4)	6,162 (68.0)	1,692 (68.9)	1,692 (68.9)
Vaccine doses				
0 doses	2,236 (18.3)	2,580 (28.5)	592 (24.1)	592 (24.1)
1 dose	86 (0.7)	51 (0.6)	1 (0.0)	1 (0.0)
2 doses	1,147 (9.4)	764 (8.4)	133 (5.4)	133 (5.4)
3 doses	3,988 (32.6)	2,419 (26.7)	770 (31.3)	770 (31.3)
4 doses	3,143 (25.7)	1,752 (19.3)	576 (23.4)	576 (23.4)
5 doses	1,642 (13.4)	1,494 (16.5)	385 (15.7)	385 (15.7)
Days since last dose (median [IQR])	343 [143, 385]	286 [104, 379]	322 [110, 378]	319 [110, 377]
LTCH resident	1,903 (15.5)	1,382 (15.2)	313 (12.7)	313 (12.7)
Health care worker	1,186 (9.7)	687 (7.6)	199 (8.1)	199 (8.1)
Prior infection*	1,237 (10.1)	1,763 (19.4)	363 (14.8)	406 (16.5)
Outcomes				
Hospitalization or death	440 (3.6)	254 (2.8)	77 (3.1)	83 (3.4)
Death	172 (1.4)	89 (1.0)	34 (1.4)	28 (1.1)

Note: IQR, inter-quartile range; LTCH, long-term care home

* Not included as a matching criterion; adjusted for using regression adjustment

Table 2. Risk of hospitalization or death associated with BQ.1 lineage infection relative to BA.5, Ontario, Canada.

	Hospitalization or death, HR (95%CI)	Death, HR (95%CI)
Overall	1.04 (0.75, 1.43)	0.84 (0.51, 1.39)
Stratified Analyses*		
Sex		
Female	0.75 (0.48, 1.18)	0.87 (0.44, 1.69)
Male	1.48 (0.93, 2.35)	0.81 (0.38, 1.74)
Age Group		
<70 years	1.22 (0.52, 2.86)	NA
≥70 years	1.01 (0.71, 1.42)	0.76 (0.45, 1.29)
Vaccine doses**		
0 doses	0.90 (0.42, 1.93)	0.41 (0.10, 1.61)
3 doses	1.16 (0.58, 2.32)	1.47 (0.47, 4.60)
4 doses	1.70 (0.99, 2.92)	1.41 (0.62, 3.16)
5 doses	0.59 (0.27, 1.29)	0.58 (0.17, 1.96)
Time since most recent dose		
<90 days	0.60 (0.29, 1.23)	0.71 (0.25, 2.05)
90 - 179 days	1.68 (0.61, 4.62)	NA
180 - 269 days	2.86 (1.20, 6.74)	1.93 (0.58, 6.38)
≥270 days	0.78 (0.44, 1.40)	0.57 (0.24, 1.38)
LTCH resident		
No	1.08 (0.75, 1.56)	0.81 (0.43, 1.50)
Yes	0.89 (0.45, 1.75)	0.92 (0.39, 2.17)

	Hospitalization or death, HR (95%CI)	Death, HR (95%CI)
BQ.1 sub-lineage		
BQ.1	1.04 (0.63, 1.71)	0.91 (0.42, 1.97)
BQ.1.1	0.63 (0.37, 1.08)	0.44 (0.17, 1.12)
Other BQ	1.40 (0.96, 2.06)	1.15 (0.63, 2.12)

Note: CI, confidence interval; HR, hazard ratio; LTCH, long-term care home; NA, not applicable. All analyses are based on proportional hazards models, and presented as hazards ratios. Hazards ratios of 1 indicate equal risk for BQ.1 relative to BA.5, <1 indicate reduced severity of BQ.1, >1 indicate increased severity of BQ.1.
* Stratified hazard ratios represent relative risk of outcomes within a stratum. For example, among cases with 5 vaccine doses, risk of death is estimated to be 0.58 times lower (95%CI: 0.17, 1.96) among BQ.1 cases compared to BA.5 cases.
**Stratified estimates among cases with 1 or 2 vaccine doses only were not available due to small sample sizes.

Discussion

Despite concerns over increased antibody evasiveness of Omicron sub-lineage BQ.1 and its sub-lineages, our observations suggest little or no difference in real-world severity among BQ.1 cases compared to BA.5 cases after accounting for age, sex, vaccination status, and history of infection. These findings are in contrast to the decrease in severity observed following the transition from Delta to Omicron BA.1 lineage in late 2021, which led to an approximate 80% relative decrease in hospitalization and 90% relative decrease in infection-associated mortality.[3] The Omicron BA.1 wave nevertheless led to a high burden of SARS-CoV-2 mortality, due to the high incidence of infection. Estimates of severity changes in the transition from BA.1 to BA.5 have been mixed, with little or no changes detected in comparisons of BA.1 to BA.2[4] and heterogeneous findings comparing BA.2 to BA.4/5 sub-lineages.[5,6]

Limitations

Study limitations include the small number of outcomes observed, and imperfect ascertainment of prior infection status. Adjustment for estimated under-detection of prior infection, and estimates limited to LTCH residents (for whom SARS-CoV-2 testing was most complete), were congruent with our main findings.

Data Sources

- The data for this report were based on information successfully extracted from the Public Health Case and Contact Management Solution (CCM) for all public health units (PHUs) by PHO as of **January 3, 2023 at 1:00 p.m.**

- COVID-19 vaccination data were based on information successfully extracted from the Ontario Ministry of Health's COVaxON application as of **January 3, 2023 at approximately 7:00 a.m.** COVaxON data was subsequently linked to COVID-19 case data based on information successfully extracted from CCM for all PHUs by PHO as of **January 3, 2023 at 1:00 p.m.**

- Additional details on data caveats are documented in Technical Notes of the Ontario COVID-19 Data Tool.

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Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Estimates of Omicron sub-lineage BQ.1 severity in an Ontario-based matched cohort study of cases: August 24 – November 22, 2022. Toronto, ON: King's Printer for Ontario; 2023.

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