

Brief Communication

Neurological Events Following COVID-19 Vaccination: Does Ethnicity Matter?

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ABSTRACT: We conducted a retrospective cohort study in Ontario, Canada between December 1, 2020 and June 31, 2021 to compare the incidence of neurological events (hospitalization or emergency room visit) within six weeks of COVID-19 vaccination in Chinese, South Asian and Other ethnic groups. Compared to Others, the crude rates after the first dose for Bell's palsy, ischemic stroke and intracerebral hemorrhage were lower in Chinese (34, 159 and 48 per 1,000,000 doses) and in South Asians (44, 148 and 32), but similar after adjusting for age, sex and vaccine type. Our findings should help encourage vaccination for all, irrespective of ethnicity.

RÉSUMÉ : Incidents neurologiques consécutifs à la vaccination contre la COVID-19 : est-ce que l'origine ethnique des individus compte ?

Nous avons mené une étude de cohorte rétrospective en Ontario (Canada) entre le 1^{er} décembre 2020 et le 31 juin 2021 afin de comparer la fréquence d'incidents neurologiques (hospitalisation ou visite aux urgences) dans les six semaines suivant la vaccination contre la COVID-19, et ce, au sein des groupes ethniques chinois, sud-asiatique et autres. Par rapport à ces autres groupes, les taux bruts de paralysie faciale de Bell, d'AVC ischémique et d'hémorragie intracérébrale après une première dose étaient plus faibles chez les Chinois (34, 159 et 48 pour un million de doses) et les Sud-Asiatiques (44, 148 et 32 pour un million de doses), mais néanmoins similaires après ajustement pour l'âge, le sexe et le type de vaccin. Nos résultats devraient ainsi contribuer à encourager la vaccination pour tous, quelle que soit l'origine ethnique des individus.

Keywords: COVID-19; Bell's palsy; ethnicity; stroke; vaccine

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Introduction

Neurological events, particularly Bell's Palsy and transverse myelitis (TM), following vaccination, have been described in case reports or case series.^{1,2} While racial and ethnic differences in vaccine uptake have been observed,^{3,4} it is unknown if rates of neurological events following vaccination differ by ethnicity. As up to 76% of the world's population received at least one dose of COVID-19 vaccine (WHO estimate), it may be an ideal setting to evaluate rates of neurological events after a vaccine as well as potential ethnic differences. A large-scale study in the UK, involving 8 million people, found no association between COVID-19 vaccination and neurological events,⁵ but ethnic differences were not studied. Despite the lack of previous reports on ethnic differences in COVID-19 vaccine-related complications, concern about side effects was the most common cause for not getting vaccinated among ethnic groups compared to Whites in large-scale surveys in the UK and the US.⁶ Hence, it is important to evaluate if COVID-19 vaccine-related complications vary by ethnicity.

Our objective was to estimate the rate of neurological events within 42 days (6 weeks) of receiving COVID-19 vaccine in adult Ontarians, and its variation by ethnicity. We compared the rates of

neurological events in Chinese and South Asian ethnic groups because together they form the largest non-Caucasian ethnic group in Canada, making up 11.8% of its total population.

Methods

We conducted a retrospective cohort study in Ontario, Canada using linked health administrative databases. These datasets were linked using unique encoded identifiers and analyzed at Institute of Clinical Evaluative Sciences (ICES) (formerly known as the Institute for Clinical Evaluative Sciences). Use of these data is authorized under section 45 of the Ontario Personal Health Information Protection Act and does not require review by a research ethics board.

Ontario residents have access to the Ontario Health Insurance Program (OHIP), a universal, publicly funded health insurance plan that covers the cost of COVID-19 vaccines, inpatient care and emergency department (ED) visits.

Study population

We included all persons identified in the Ontario Registered Persons Database (RPDB) who were alive, eligible for OHIP and

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Table 1. Characteristics of the included cohort with at least one COVID-19 vaccine in Ontario, Canada

| Characteristics of interest | Chinese <i>N</i> = 560,087 | South Asians <i>N</i> = 431,504 | General Population <i>N</i> = 9,071,875 |
|--|----------------------------|---------------------------------|---|
| Female, <i>n</i> (%) | 299,453 (53.5%) | 213,980 (49.6%) | 4,710,420 (51.9%) |
| Median age in years (Q1–Q3) | 48 (33–61) | 43 (31–57) | 50 (34–64) |
| Neighborhood-level income in quintiles, <i>n</i> (%) | | | |
| Q1 (lowest) | 100,715 (18.0%) | 70,784 (16.4%) | 1,699,277 (18.7%) |
| Q2 | 116,706 (20.8%) | 100,397 (23.3%) | 1,750,870 (19.3%) |
| Q3 | 101,946 (18.2%) | 117,352 (27.2%) | 1,819,542 (20.1%) |
| Q4 | 124,597 (22.2%) | 84,155 (19.5%) | 1,853,706 (20.4%) |
| Q5 (Highest) | 114,564 (20.5%) | 58,041 (13.5%) | 1,924,658 (21.2%) |
| Missing | 1,559 (0.3%) | 775 (0.2%) | 23,822 (0.3%) |
| Rural vs. urban residence, <i>n</i> (%) | | | |
| Missing | 1,551 (0.3%) | 773 (0.2%) | 20,353 (0.2%) |
| Rural | 3,642 (0.7%) | 3,650 (0.8%) | 1,008,899 (11.1%) |
| Urban | 554,894 (99.1%) | 427,081 (99.0%) | 8,042,623 (88.7%) |
| Charlson comorbidity score, <i>n</i> (%) | 0.07 ± 0.50 | 0.10 ± 0.55 | 0.14 ± 0.67 |
| 0 | 541,946 (96.8%) | 411,756 (95.4%) | 8,468,628 (93.4%) |
| 1 | 6,796 (1.2%) | 8,062 (1.9%) | 254,486 (2.8%) |
| >= 2 | 11,345 (2.0%) | 11,686 (2.7%) | 348,761 (3.8%) |
| Residence in a long-term residence, <i>n</i> (%) | 2,082 (0.4%) | 574 (0.1%) | 60,509 (0.7%) |

between 18 and 105 years of age on December 1, 2020 (index date) (e-figure 1). Non-Ontario residents, those who had no contact with the health system in the 5 years prior to index date, and those who were not continuously eligible for OHIP services in the year prior to index date were excluded. Information on the dates and types of COVID-19 vaccines administered were ascertained using the provincial COVID-19 vaccine registry (COVaxON). We collected data on first and second-dose vaccinations provided between the index date and June 30, 2021. Second-dose vaccinations administered less than 21 days after the first dose were excluded.

Exposure

We used the ETHNIC dataset, a version of the RPDB where a surname-based algorithm was used to classify Ontario residents as Chinese, South Asian or Others (regarded as “general population”) to define our exposure groups.⁷ Individuals who could not be linked to the ETHNIC database were excluded.

Outcomes

We used the Canadian Institute for Health Information Discharge Abstract Database and the National Ambulatory Care Reporting System to ascertain hospitalizations and ED visits for the following neurological conditions occurring within 42 days of either the first or second COVID-19 vaccination dose: Bell’s palsy, TM, Guillain Barre syndrome (GBS), ischemic stroke, intracerebral hemorrhage (ICH) and cerebrovenous sinus thrombosis (CVST). We included hospitalizations/ED visits where the diagnosis of an outcome of interest was suspected and/or included in any diagnostic code space on the record (e-Table 1 for details).

Covariates of interest

We obtained information on age, sex, rural residence and neighborhood-income quintile from the RPDB, and information

on residence in a long-term care home based on the Ontario Drug Benefit and Continuing Care Reporting System datasets. We used hospitalization data in the five years prior to index date to compute the Charlson Comorbidity score. These variables were only used to provide description of baseline characteristics of the cohort. Information on vaccine type was collected from COVaxON: Pfizer, Moderna or Other (e-Table 1).

Statistical analyses

We computed crude outcome rates (per 1,000,000 doses) of each outcome in the 42 days following first and second dose of COVID-19 vaccination for each exposure group. We used multivariable logistic regression to determine whether ethnicity was associated with outcome rates after controlling for age, sex and vaccine type. We used separate models for first and second-dose vaccinations. Given low event rates, we did not adjust for medical comorbidities.

Results

We included 10,063,466 Ontario residents aged 18 years and over, who received 19,933,221 vaccinations. Of these, 857,289 vaccinations were received by South Asians and 1,112,832 by Chinese. Compared to Chinese and the general population, South Asians were younger and less likely to live in the highest neighborhood-income quintile. Both Chinese and South Asians had lower comorbidity scores than the general population and were less likely to reside in long-term care homes (Table 1).

In total, 2,419 people developed ischemic stroke, 505 developed ICH and 542 developed Bell’s Palsy within 42 days following first dose of vaccine. The total number of people developing CVST (*n* = 52), GBS (*n* = 72) and TM (*n* = 25) was low which did not allow us to evaluate the differential effect of ethnicity on these outcomes.

Table 2. Neurological events within 42 days following the first and second COVID-19 vaccine

| Outcomes of interest | Overall population Crude rate [§] | Ethnicity | | | | | |
|--|---|-------------------------|------------------------|-------------------------|-------------------------------|-------------------------|------------------------------|
| | | Other (ref) | | Chinese | | South Asians | |
| | | Crude rate [§] | Odds ratio [reference] | Crude rate [§] | Adjusted odds ratio* (95% CI) | Crude rate [§] | Adjusted odds ratio* (95%CI) |
| First dose of COVID-19 vaccine | | | | | | | |
| Bell's palsy | 53.9 (49.4–58.6) | 55.6 (50.8–60.6) | 1.00 | 33.9 (20.4–53.0) | 0.62 (0.39–0.98) | 44.0 (26.5–68.8) | 0.83 (0.52–1.31) |
| Ischemic stroke | 240.4 (230.9–250.2) | 249.8 (239.6–260.3) | 1.00 | 158.9 (127.6–195.5) | 0.74 (0.59–0.91) | 148.3 (114.2–189.4) | 0.84 (0.65–1.08) |
| Intracerebral hemorrhage | 50.2 (45.9–54.8) | 51.2 (46.6–56.0) | 1.00 | 48.2 (31.8–70.1) | 1.07 (0.72–1.57) | 32.4 (17.7–54.4) | 0.85 (0.50–1.44) |
| Second dose of COVID-19 vaccine | | | | | | | |
| Bell's palsy | 52.1 (47.7–56.8) | 53.7 (48.9–58.7) | 1.00 | 32.6 (19.3–51.5) | 0.63 (0.39–1.01) | 44.6 (26.9–69.7) | 0.90 (0.57–1.42) |
| Ischemic stroke | 232.8 (223.4–242.6) | 242.0 (231.9–252.5) | 1.00 | 137.5 (108.3–172.1) | 0.66 (0.53–0.83) | 164.4 (128.2–207.7) | 0.98 (0.77–1.24) |
| Intracerebral hemorrhage | 47.4 (43.2–51.9) | 49.0 (44.5–53.9) | 1.00 | 39.8 (24.9–60.3) | 0.93 (0.60–1.42) | 23.5 (11.3–43.2) | 0.65 (0.35–1.21) |

[§]Crude rates are per 1,000,000 people. *Adjusted for age, sex and type of COVID-19 vaccine (Pfizer [ref], Moderna vs Other).

Overall, crude rates of ischemic stroke and ICH after the first dose of COVID-19 were lowest in South Asians while Bell's palsy were the lowest in Chinese (Table 2). Chinese ethnicity was associated with a lower adjusted odds of ischemic stroke (adjusted odds ratio [aOR] 0.74; 95% CI, 0.59–0.91) and Bell's Palsy (0.62, 0.39–0.98). Compared to the general population, South Asians had lower adjusted odds for each of the three complications albeit with wide confidence intervals that included null values (Table 2). Similar results were observed for crude rates after second dose (Table 2). Again, Chinese ethnicity was associated with a lower adjusted odds of ischemic stroke compared to the general population (0.66; 0.53–0.83), but not Bell's Palsy (0.63; 0.39–1.01); whereas, like the first dose, odds of ICH were non-significantly lower in South Asians compared to the general population.

Discussion

In this population-based retrospective cohort study in Ontario, rates of neurological events following the first or the second dose of COVID-19 were low and were largely similar after both doses. The crude rates were lower in South Asians and Chinese, with no ethnic differences in these rates after accounting for age, sex and vaccine type.

In Georgia, United States of America (USA), the rate of ischemic stroke within 21 days of COVID-19 vaccination was 8.14 to 10.48 per 100,000 doses, depending on vaccine type.⁸ In a large-scale study across the entire US, among people ≥ 65 years with Medicare benefits, rates of ICH were 48% higher (IRR 1.48; 1.41–1.56) and that of ischemic stroke were 7% lower (IRR 0.93; 0.90–0.96) in Asians compared to Whites. We too found a lower rate of ischemic stroke in Chinese in Ontario, but no difference in the rate of ICH. Further, our observed rates of these events are similar to the baseline rates observed in Ontario in the years preceding COVID-19 infection,⁹ and the known ethnic differences in the incidence of stroke and its subtypes.¹⁰

While our strength includes use of population-based registry to track COVID-19 vaccination, and linked health records to identify incident neurological events, the use of latter can lead to some misclassification inherent to use of health administrative data.¹¹

Also, some neurological events such as Bell's Palsy may rarely require emergency visit or hospitalization, i.e., patients get diagnosed as an outpatient, not requiring ER visit or hospitalization.¹² Thus, our observed estimates of the incidence of these conditions could be underestimated. Our surname algorithm is specific although for those with hyphenated names or those who change surnames after marriage could be incorrectly classified. Lastly, the incidence of a neurological event in the weeks after vaccination cannot be attributed directly to the vaccine itself.

We observed overall low rates of neurological events following COVID-19 vaccine in Ontario adults, without significant ethnic differences. This should encourage all ethnic groups to be vaccinated by showing lack of vaccine-associated complications by ethnicity.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/cjn.2024.299>.

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