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ABSTRACT

Methods Hospitalised CAP patients at St. Paul’s Hospital, Vancouver, Canada pre-COVID-19 (fiscal years 2018/2019 and 2019/2020) and during COVID-19 pandemic (2020/2021 and 2021/2022) were evaluated.

Results In 5219 CAP patients, there was no significant difference prepanvirus versus during pandemic in mean age, gender and Charlson Comorbidity Score. However, hospital mortality increased significantly from pre-COVID-19 versus during COVID-19 (7.5% vs 12.1% respectively, 95% CI for difference: 3.0% to 6.3%), a 61% relative increase, coincident with increases in ICU admission (18.3% vs 25.5%, respectively, 95% CI for difference: 5.0% to 9.5%) p<0.001, 39% relative increase) and ventilation (12.7% vs 17.5%, respectively, 95% CI for difference: 2.8% to 6.7%) p<0.001, 38% relative increase). Results remained the same after regression adjustment for age, sex and Charlson score. CAP hospital admissions decreased 27% from pre-COVID-19 (n=1349 and 1433, 2018/2019 and 2019/2020, respectively) versus the first COVID-19 pandemic year (n=1047 in 2020/2021) then rose to prepandemic number (n=1390 in 2021/2022). During prepandemic years, CAP admissions peaked in winter; during COVID-19, the CAP admissions peaked every 6 months.

Conclusions and relevance This is the first study to show that the COVID-19 pandemic was associated with increases in hospital mortality, ICU admission and invasive mechanical ventilation rates of non-COVID-19 CAP and a transient, 1-year frequency decrease. There was no winter seasonality of CAP during the COVID-19 pandemic era. These novel findings could be used to guide future pandemic planning for CAP hospital care.

INTRODUCTION
The COVID-19 pandemic could have impacted non-COVID-19 community-acquired pneumonia (CAP herein)1. CAP is the most common lethal infection affecting >1% of the population causing 17–23 deaths per 100,000 population in Canada in 2016–2020.2 In the USA, deaths due to ‘influenza and pneumonia’ increased from 49,783 pre-COVID-19 (2019) to 53,495 during COVID-19 (2020).3

During the COVID-19 pandemic, several factors could decrease CAP frequency and mortality while other opposing factors could increase CAP frequency and mortality.

CAP frequency could decrease because of outpatient interventions that might decrease numbers of patients requiring hospitalisation (eg, vaccines (eg, influenza,4 pneumococcal), social measures (eg, hand-washing and social distancing5)0), by optimal treatment of underlying comorbidities,6 and early initiation of antimicrobials). COVID-19 could also decrease frequency of CAP because of decreased frequency of influenza, a common cause of CAP.7 Pneumococcal CAP decreased by 30% in the UK during COVID-19.8

Hospital mortality of CAP can be decreased by optimising hospital management, including early diagnosis and antimicrobial treatment,9 more complex respiratory support (more use of continuous positive airway pressure and awake prone positioning that were associated with decreased mortality and need for intubation in wave 2 compared with wave 1 in a UK
study\textsuperscript{9}, oxygen supplementation, and in the critically ill, mechanical ventilation, vasopressors, corticosteroids\textsuperscript{10,11} for vasopressor-resistant septic shock, and renal support for acute kidney injury.\textsuperscript{6,12} Plasma cytokine profiles of hospitalised COVID-19 patients with acute respiratory distress syndrome indicate that higher cytokine levels are associated with increased risk of needing invasive ventilation and tailored glucocorticoids treatment could provide better control of inflammation and patient outcome.\textsuperscript{13} Very recently, hydrocortisone was shown to decrease mortality of critically ill CAP patients.\textsuperscript{14}

The COVID-19 pandemic could increase CAP frequency and/or mortality because of inadequate treatment of comorbidities that increase risk of CAP,\textsuperscript{15–18} increased alcohol\textsuperscript{19} and drug\textsuperscript{20} use, decreased use of pneumococcal vaccine,\textsuperscript{21} avoidance of clinic, emergency department (ED)\textsuperscript{22,23} (down by 50\% at COVID-19 peak\textsuperscript{24}) and hospital admissions because of fear of contracting COVID-19, increased use of virtual medicine (eg, from 1\% to 25\% in Ontario\textsuperscript{25,26}), delays in hospital admission and treatment due to hospital overcrowding, and inadequate adherence to CAP treatment guidelines\textsuperscript{6} because of shortages of staff and caregiver fatigue and shortages.

Our hypothesis was that changes in frequency, patient mix, treatment and organ dysfunction cascaded together to increase mortality of CAP during COVID-19 compared with pre-COVID-19. We sought to compare CAP frequency, baseline characteristics, comorbidities, treatment including ICU admission and ventilation use and hospital mortality rates 2 years immediately pre-COVID-19 pandemic versus the first 2 years of the pandemic. Using adjusted analyses, we aimed to determine whether any changes in hospital mortality of CAP patients in pre-COVID-19 versus during COVID-19 pandemic were explained by the differences in baseline characteristics.

METHODS

Study design and participants

This study was a single hospital in-patient electronic medical record Cerner database retrospective cohort study, reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist.\textsuperscript{27}

We reviewed the St. Paul’s Hospital (Vancouver, Canada) Cerner electronic medical records of CAP admissions during four fiscal years between 1 April 2018 and 31 March 2022. Non-COVID-19 CAP was defined by ICD10 codes for viral, bacterial and aspiration CAP (online supplemental table 1). We excluded ED only admission, CAP readmissions, and patients who were SARS-CoV-2 positive at admission.

At admission we recorded, age, sex, Charlson Comorbidity Score, mean, systolic and diastolic arterial pressures, heart and respiratory rates, arterial pulse oximetry and temperature. Vital signs were only available on Cerner electronic medical records for patients admitted after 15 November 2019.

The primary outcome was hospital mortality; secondary outcomes were ICU admission, use of mechanical ventilation (ventilation means invasive ventilation throughout), time to death and duration of hospital length of stay. We also examined the seasonality of frequency, hospital mortality, ICU admission and use of invasive mechanical ventilation by fiscal year quarters.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analyses

Patients’ age, sex, comorbidities (Charlson score), admission day vital signs (available for patients admitted after 15 November 2019), dates of admission and discharge or death were compared for the two pre-COVID-19 pandemic years to the first two COVID-19 pandemic years (2018/2019 and 2019/2020 vs 2020/2021 and 2021/2022). Age, sex, comorbidities and vital signs were compared pre-pandemic versus during pandemic by analysis of variance, Kruskal-Wallis test or \( \chi^2 \) test as appropriate, as were for binary and continuous outcomes. Kaplan-Meier curves and log rank test were used to compare time to death. Patients discharged alive were censored at the time of hospital discharge. Analysis adjusted for age, sex and Charlson score was performed by logistic or Cox regression as appropriate. Results were expressed as OR and HR with 95\% CI.

RESULTS

In 5219 CAP admissions, patients in prepandemic versus during pandemic had higher admission mean arterial pressure (median: 90 vs 88 mm Hg (95\% CI for difference: 0.2 to 3.8) \( p=0.015 \)), higher systolic blood pressure (127 vs 124 mm Hg, (95\% CI for difference: 0.5 to 5.5) \( p=0.047 \)), higher arterial oxygen saturation (96 vs 95 (95\% CI for difference: 0.7 to 1.3), \( p=0.009 \)) and faster heart rate (98 vs 95 beat/minute, (95\% CI for difference: 0.1 to 5.9) \( p=0.002 \)) (table 1), but no differences in comorbidities, gender, age or admission respiratory rate, diastolic blood pressure, or temperature prepandemic versus during pandemic (table 1).

CAP hospital admission frequency decreased 27\% during the first fiscal year of the pandemic (1047 in 2020/2021 vs 1349 and 1433 in 2018/2019 and 2019/2020, respectively) then returned to prepandemic levels (1390 in 2021/2022) (figure 1).

The first 2 years of the COVID-19 pandemic was associated with increased absolute numbers of deaths (n=296) compared with the 2 years pre-COVID-19 pandemic (n=209). The absolute number of CAP deaths per year increased from 103, 106 and 120 in fiscal years 2018/2019, 2019/2020 and 2020/2021 to 176 in 2021/2022—the second fiscal year during the COVID-19 pandemic (figure 1).
Hospital mortality increased significantly from pre-pandemic to during pandemic (7.5% vs 12.1%, respectively, (95% CI for difference: 3.0% to 6.3%) p<0.001; 61% relative increase), coincident with significant increases in ICU admission (18.3% vs 25.5%, respectively, (95% CI for difference: 5.0% to 9.5%) p<0.001; 39% relative increase) and invasive ventilation (12.7% vs 17.5%, respectively, (95% CI for difference: 2.8 to 6.7%) p<0.001; 38% relative increase) (table 1). Hospital mortality, ICU admission and invasive mechanical ventilation rates during the pandemic remained significantly higher than pre-pandemic in adjusted regression analyses (table 2).

Survival times during the COVID-19 pandemic decreased significantly compared with prepandemic (figure 2B; HR 1.39 (95% CI 1.17 to 1.66), p<0.001). Notably, the survival curves of prepandemic versus during the pandemic separated at about 12 days and then continued to separate indicating higher mortality after 12 days in CAP patients during the pandemic.

The CAP survivors’ length of stay also increased during the COVID-19 pandemic compared with pre-COVID-19 CAP patients (table 1).

The seasonality of frequency, hospital mortality, ICU admission and invasive mechanical ventilation use was evaluated by examining each of these variables according to fiscal year quarter (figure 3). Seasonality of CAP frequency differed in the pre-COVID-19 pandemic versus during COVID-19 pandemic eras. During the
pre-COVID-19 pandemic years, CAP admissions peaked annually in winter quarters whereas during COVID-19 years, the CAP frequency peaked about every 6 months (figure 3A). There was no seasonality of use of invasive ventilation or hospital mortality rates expressed as percentages. Interestingly, the ICU admission rates (percentages) peaked in the second quarters of each of the 4 years of study, in the prepandemic (Q2 2018 and Q2 2019) and during COVID-19 pandemic years (Q2 2020 and Q2 2021, figure 3B).

DISCUSSION

In 5219 CAP admissions, there was a significant 61% relative increase of hospital mortality during pandemic versus prepandemic and 40% relative increases of ICU admission and invasive ventilation rates. Prepandemic CAP winter seasonality preceded a transient 27% decrease in frequency in the first pandemic year. The COVID-19 pandemic appeared to change the seasonality of CAP; CAP frequency peaked annually in the winter months prepandemic, but then peaked every 6 months during the first two pandemic years.

The fact that ICU admission rates were higher during COVID-19 when mortality rates were also higher likely means that resource constraint was not the cause for the higher mortality but possibly that only more severe non-COVID-19 CAP patients were hospitalised during than before the COVID-19 pandemic.

There were no differences in age, sex or comorbidities to explain increases in CAP outcomes; adjusted analyses yielded the same outcome findings. Small statistically significant differences in admission mean and systolic arterial pressure and heart rate were not clinically relevant, reflecting the large sample size.

There are no publications formally assessing the impact of the COVID-19 pandemic on hospital mortality of CAP. There is some information about overall CAP mortality before versus during COVID-19. COVID-19 mortality was higher than influenza mortality in studies of influenza prepandemic and deaths due to influenza and pneumonia increased in the USA from 49,783 in 2020 compared with 53,495 in 2019.

Although we found that the COVID-19 pandemic had specific effects on CAP that required hospital admission, to date, there are few studies of the effects of the COVID-19 era on overall CAP frequency and incidence. Several other studies suggest that overall outpatient and hospitalised CAP may have decreased during the pandemic in Japan.

Figure 1  The absolute numbers of CAP cases in St. Paul’s Hospital, Vancouver, BC, Canada are shown according to the fiscal years pre-COVID-19 pandemic (2018/2019 and 2019/2020) and during the COVID-19 pandemic (2020/2021 and 21021/2022). CAP, community-acquired pneumonia; ICU, Intensive Care Unit.
Canada (significant decreases in incidence of influenza and respiratory syncytial virus during vs before COVID-19), the UK8 and other countries.6 30 31

We found that the number of hospital admissions for CAP decreased in the first year of the pandemic compared with prepandemic, but the reasons are not clear. Factors that could decrease CAP frequency include CAP vaccines such as pneumococcal and influenza vaccines. Unfortunately, we did not have such data. In Japan, pneumococcal vaccine use decreased yet invasive pneumococcal disease in children was lower during versus COVID-19 due to containment measures.21

Pandemic social interventions (eg, mandatory masking, lockdowns and travel restrictions; increased use of virtual medicine; inadequate treatment of chronic conditions) could have decreased the number of CAP admissions. Decreased seasonal respiratory infection during versus before COVID-19 was attributed to social interventions in Canada,7 in a multicountry study (sustained decrease in invasive Streptococcus pneumoniae, Haemophilus influenzae and Neisseria meningitidis), in Maryland USA (mask mandates were associated with decreased ED visits for viral disease, asthma and COPD exacerbations, common risk factors for CAP) and in Scandinavia (decreased frequency of influenza in the first pandemic year).

It would appear that factors that could have increased hospital admissions for CAP during the pandemic might not have been dominant enough to offset the above factors that could have decreased CAP admissions during the first pandemic year. For example, alcohol and drug use are risk factors for CAP that could have altered pandemic versus prepandemic frequency of CAP, but we do not have such information in our cohort. Alcohol and drug use increased in the USA33 34 but varied by country35 during versus before COVID-19 pandemic catalysing CAP36 risk.

We found that hospital mortality increased by 61% relatively in the first two pandemic versus the two immediate prepandemic years. COVID-19 could have increased mortality of hospitalised CAP because of inadequate comorbidity management (eg, heart failure, COPD, chronic kidney disease and diabetes15–17), decreased healthcare visits for fear of contracting COVID-19, increased use of virtual medicine, decreased adherence to treatment guidelines,6 37 decreased hospital and ICU bed availability because of overcrowding.

We found that there was no difference in frequency of comorbidities prepandemic versus during the pandemic and in adjusted analyses, the primary outcome, hospital mortality rate of CAP, remained significantly higher during than prepandemic. Comorbidities that increase

| Table 2 | Outcomes (time to death, in-hospital death, use of mechanical ventilation and ever admitted to ICU during hospital admission) adjusted for age, sex and comorbidities |
|----------------|---------------------------------|------------------|------------------|
| | Unadjusted analysis | Adjusted analysis |
| | HR or OR (95% CI) | P value | HR or OR (95% CI) | P value |
| Time to death | | | |
| 2019/2020 vs 2018/2019 | 1.00 (0.76 to 1.31) | 0.999 | 1.06 (0.81 to 1.40) | 0.659 |
| 2020/2021 vs 2018/2019 | 1.35 (1.04 to 1.76) | 0.024 | 1.39 (1.07 to 1.81) | 0.015 |
| 2021/2022 vs 2018/2019 | 1.42 (1.12 to 1.81) | 0.005 | 1.52 (1.19 to 1.94) | <0.001 |
| During versus prepandemic | 1.39 (1.17 to 1.66) | <0.001 | 1.42 (1.19 to 1.69) | <0.001 |
| In-hospital death | | | |
| 2019/2020 vs 2018/2019 | 0.97 (0.73 to 1.28) | 0.812 | 1.01 (0.75 to 1.35) | 0.959 |
| 2020/2021 vs 2018/2019 | 1.57 (1.19 to 2.07) | 0.001 | 1.59 (1.20 to 2.12) | 0.001 |
| 2021/2022 vs 2018/2019 | 1.75 (1.36 to 2.26) | <0.001 | 1.94 (1.49 to 2.53) | <0.001 |
| During versus prepandemic | 1.70 (1.41 to 2.05) | <0.001 | 1.78 (1.47 to 2.15) | <0.001 |
| Ventilation during hospitalisation | | | |
| 2019/2020 vs 2018/2019 | 0.85 (0.68 to 1.06) | 0.144 | 0.83 (0.66 to 1.04) | 0.104 |
| 2020/2021 vs 2018/2019 | 1.13 (0.90 to 1.43) | 0.284 | 1.12 (0.89 to 1.42) | 0.318 |
| 2021/2022 vs 2018/2019 | 1.51 (1.23 to 1.85) | <0.001 | 1.47 (1.20 to 1.81) | <0.001 |
| During versus prepandemic | 1.46 (1.25 to 1.70) | <0.001 | 1.45 (1.24 to 1.69) | <0.001 |
| Ever admitted to ICU | | | |
| 2019/2020 vs 2018/2019 | 0.80 (0.66 to 0.97) | 0.023 | 0.78 (0.64 to 0.95) | 0.013 |
| 2020/2021 vs 2018/2019 | 1.29 (1.07 to 1.57) | 0.009 | 1.29 (1.06 to 1.56) | 0.012 |
| 2021/2022 vs 2018/2019 | 1.43 (1.19 to 1.71) | <0.001 | 1.39 (1.16 to 1.67) | <0.001 |
| During versus prepandemic | 1.53 (1.34 to 1.75) | <0.001 | 1.52 (1.33 to 1.74) | <0.001 |

HR, hazard ratio; OR, odds ratio.
Figure 2  The hospital mortality rates of CAP cases in St. Paul’s Hospital, Vancouver, BC, Canada are shown in (A) according to each of the fiscal years 2018/2019, 2019/2020, 2020/2021 and 2021/2022 and in (B) according to the pooled two fiscal years pre-COVID-19 pandemic (2018/2019 and 2019/2020) versus pooled two fiscal years during the COVID-19 pandemic (2020/2021 and 2021/2022). CAP, community-acquired pneumonia.
Figure 3  Seasonality of CAP frequency, ICU admission, use of mechanical ventilation and hospital mortality of CAP cases in St. Paul’s Hospital, Vancouver, BC, Canada in the pre-COVID-19 and during COVID-19 pandemic years. The absolute numbers of cases, ICU admissions, numbers needing ventilation and numbers of deaths are shown in (A) according to quarter. The ICU admission, ventilation and mortality rates expressed as percentages are shown in (B) according to quarter. CAP, community-acquired pneumonia; ICU, Intensive Care Unit.
risk of CAP include hypertension, asthma, heart failure, COPD, chronic kidney disease and diabetes. Effectivenes
tive chronic condition management mitigates the risk of getting CAP and hospital admission.

Virtual medicine use could have altered CAP frequency in our study. In British Columbia, Canada virtual medicine use increased nearly 400% during the pandemic (28–106 visits/physician April 2019 to March 2021. Virtual medicine dramatically increased in Ontario, Canada in the early pandemic era virtual care increased from 1.6% of outpatient visits (second quarter 2019) to 70.6% (second quarter of 2020).

We were not able to evaluate compliance with CAP treatment guidelines in this hospital database retrospective cohort study. We were also unable to obtain bed availability prepandemic versus during pandemic. During COVID-19 surges, overcrowding of hospitals limited accessibility for patients with CAP. Furthermore, many countries identified lack of ICU beds and ventilators prior to COVID-19. Patients could have feared visiting medical facilities for fear of contracting COVID-19.

We believe this is the first report that the COVID-19 pandemic had clinically relevant effects on hospitalised CAP patients’ mortality, ICU admission and invasive ventilation and frequency. Understanding the effects of the COVID-19 pandemic on CAP could be used for future pandemic preparedness because most pandemics are respiratory infections that cause CAP. There are well-known seasonal variations in CAP due to influenza and common bacterial causes of CAP, both non-COVID-19 CAP and pandemic causes of CAP are altered by prevention (treatment of underlying conditions that are risk factors and vaccines) and non-specific supportive treatment (oxygen, vital organ support and ICU admission) and specific antimicrobials and host response interventions (such as anti-inflammatory agents).

Large scale trials of new interventions were conducted in COVID-19 and give lessons for other conditions such as non-COVID-19 CAP. Surveys of research staff show that patient recruitment was hampered by complex protocols without adaptation to a pandemic, so there is a need to develop and test pandemic-specific protocols.

Strengths of our study are the use of a comprehensive Cerner hospital database to identify and include CAP patients, and to evaluate frequency and outcomes consistently in the two immediate prepandemic years versus the first two pandemic years, and that our primary outcome was robust to adjustment for age, sex and comorbidities.

Limitations of our study include that this is a retrospective single centre cohort study (limiting generalisability); we used ICD10 codes to identify CAP patients (that may not be optimal to accurately identify and select patients); and we did not have data to evaluate possible mechanisms of changes in non-COVID-19 CAP frequency and mortality, for example, information on respiratory severity, effects of societal interventions (lockdowns and travel restrictions could have directly and indirectly altered non-COVID-19 CAP frequency and mortality), vaccine use (could have increased or decreased and altered CAP frequency and outcomes), telemedicine use (likely increased in our region during the pandemic and could explain in part altered CAP frequency and mortality), adherence with CAP treatment guidelines (decreased adherence could have explained increased CAP mortality), or hospital bed availability (that may be less likely because ICU and invasive ventilation rates also increased when non-COVID-19 CAP mortality increased in our study).

In conclusion, to our knowledge, this is the first study to show that hospital mortality, ICU admission and invasive mechanical ventilation rates of non-COVID-19 CAP increased significantly during the COVID-19 pandemic. A transient 1-year decrease of CAP frequency was followed by a monthly rather than winter CAP frequency peaks. These novel findings are thus highly relevant and could be used to guide future pandemic planning for CAP hospital care.

Contributors JAR designed the study, was PI of the supporting grant, organised and made the data request and wrote the first draft of the manuscript. JAR is responsible for overall content and is the guarantor. TL did statistical analyses. All authors contributed to the interpretation of the data and revised it critically for important intellectual content.

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Competing interests KRW has received Foundation Grant from the Canadian Institutes for Health Research, held by UBC. He is the Chair of a DSMB for Northern Therapeutics, unpaid service. KAC received payment from Becton, Dickinson and Company for advisory meeting participation and speaking related to sepsis from October 2022. JAR reports grants owned by the University of British Columbia (UBC) that are related to (1) the use of PCSK9 inhibitors in sepsis, (2) the use of vasopressin in septic shock and (3) a patent owned by Ferring for use of selegluceptin in septic shock. JAR is an inventor on these patents. JAR was a founder, Director and shareholder in Cyon Therapeutics Inc. (now closed) and is a shareholder in Molecular You Corp. JAR is Senior Research Advisor of the British Columbia, Canada Post COVID—Interdisciplinary Clinical Care Network (IC-ICCN). JAR is no longer actively consulting for any industry. JAR reports receiving consulting fees in the last 3 years from: (1) JAR was a funded member of the Data and Safety Monitoring Board (DSMB) of an NIH-sponsored trial of plasma in COVID-19 (PASS-IT-0N) (2020-2021). (2) PAR Pharma (sells prepared bags of vasopressin), JAR has received grants for COVID-19 and for pneumonia research: 4 from the Canadian Institutes of Health Research (CIHR) and 3 from the St. Paul’s Foundation (SPF). JAR was a non-funded Science Advisor and member, Government of Canada COVID-19 Therapeutics Task Force (June 2020–2021).

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and this study was approved by the Providence Health Care and University of British Columbia (UBC) Human Research Committee (Approval number H20-00600) as low risk and no consent was required. This study was approved by the Providence Health Care and University of British Columbia (UBC) Human Research Committee (Approval number H20-00600) as low risk and no consent was required.

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