

Low incidence of non-COVID-19 community respiratory viral infections amongst adults with haematological malignancies during the COVID-19 pandemic

Dear Editor,

Community acquired respiratory viral infections (CA-RVIs) are a significant cause of morbidity and mortality in patients with haematological malignancies [1,2]. They are usually self-limiting in the immunocompetent individual but can be life threatening in the immunocompromised host [3,4]. In addition, RVIs may impact the clinical course of haematological malignancies through delays in administration of chemotherapy [5]. Thus, measures to reduce CA-RVIs in this vulnerable group may have significant benefit. During the COVID-19 pandemic, public health measures were implemented sequentially from February 2020 onwards to mitigate community transmission of SARS-CoV-2. In Singapore, these included campaigns advocating respiratory and hand hygiene, alongside the legal enforcement of social distancing measures through closure of public spaces and the restriction of non-essential activities. A nationwide lockdown was implemented from April to June 2020, with mass masking made mandatory since April 2020. Since then studies have reported a significant reduction in non-COVID-19 CA-RVIs in vulnerable patient populations, such as those with pre-existing respiratory diseases. [6]. In this study, we describe the potential impact of these measures on reducing hospitalisation for CA-RVIs amongst patients with haematological malignancies at a large tertiary hospital in Singapore.

We defined CA-RVI as the detection of a non-COVID-19 respiratory virus on a 16-target multiplex PCR assay within 72 h of admission to our institution. The 16-target multiplex PCR assay (respiratory syncytial virus A/B, influenza A/B, parainfluenza viruses 1–4, metapneumovirus, rhinovirus A/B/C, human coronavirus OC43/229E/NL63, adenovirus, human enterovirus, human bocavirus 1–4) was performed

on respiratory specimens of haematological patients who presented with a clinical syndrome consistent with a respiratory tract infection. Discharge diagnosis codes from our hospital's epidemiology database were used to identify patients who had a diagnosis of leukemia/lymphoma. The total number of patients who underwent respiratory viral swabs and the number of patients who had a positive non-COVID-19 CA-RVI result from January 2018 were tabulated. Of note, in this epidemiologic study, only aggregated and de-identified data were used. Two-sample *t*-test with unequal variances was used to determine whether the mean number of CA-RVI differed between a pre-pandemic period (January 2018–January 2020) and post-pandemic period (February 2020–March 2021). Fisher's exact test was used to determine whether the incidence rates of CA-RVI differed between a 12-month period pre- (February 2019–January 2020) and post- (February 2020–January 2021) introduction of public health measures during the COVID-19 pandemic. Waiver from our institution's Institutional Review Board was sought and obtained as the study was based on anonymised data collected by our infection prevention and epidemiology department for epidemiological purposes.

The time period following introduction of COVID-19 public health measures was associated with a significant decrease in community acquired PCR-positive RVIs, influenza and non-influenza, amongst patients with haematological malignancies (Fig. 1). Pre-pandemic, our institution saw an average of 91 (SD = 32) CA-RVI cases per month compared to 17 (SD = 18) per month during the pandemic period. This difference was significant, $p < 0.001$. The incidence of PCR-positive CA-RVI pre-pandemic was 62.7 cases per 1000 person-years. This fell to 11.6 cases per 1000 person-years after the introduction of public

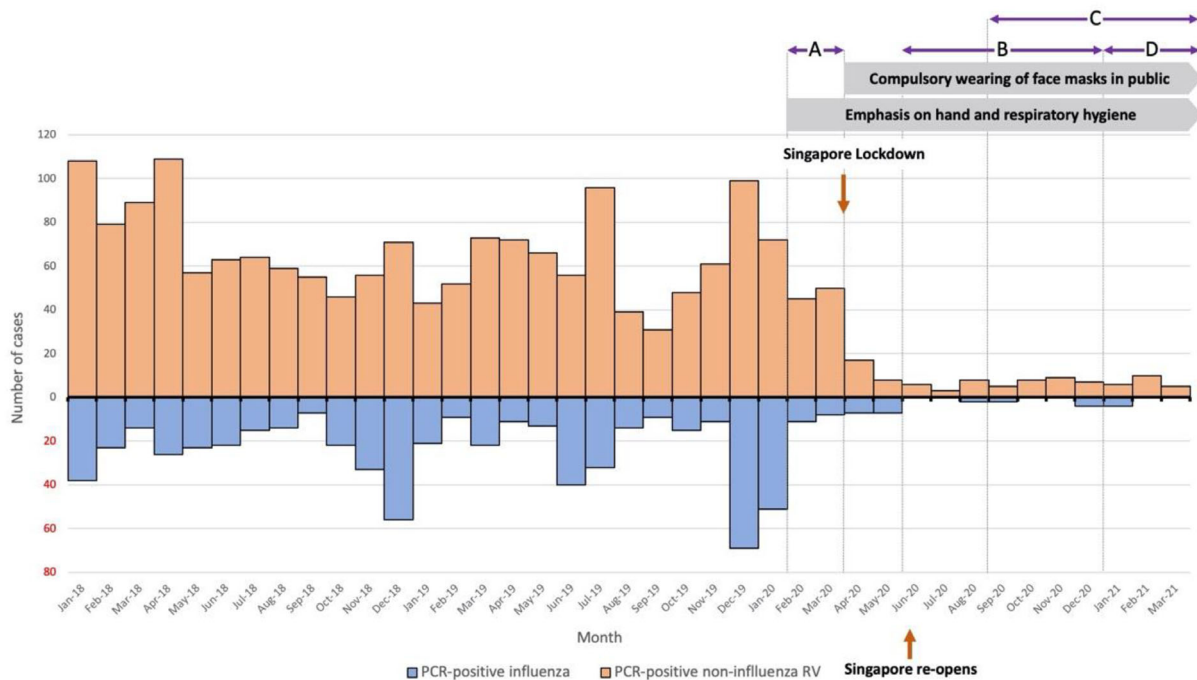


Fig. 1 Trend of PCR-positive RV-16 (influenza and non-influenza) in hospitalized patients with haematological malignancies. Standard respiratory virus multiplex panel (RV-16) at our institution included respiratory syncytial virus A/B, influenza A/B, parainfluenza viruses 1–4, metapneumovirus, rhinovirus A/B/C, human coronavirus OC43/229E/NL63, adenovirus, human enterovirus, human bocavirus 1–4. (A) Enforcement of social distancing and limiting social gatherings. Cancellation of large scale events. Closure of public venues (e.g., religious places and entertainment venues). (B) Social gatherings allowed—limited to five people, more jobs allowed to resume work, dining-in allowed. (C) Resumption of live indoor performances. Religious gatherings allowed with capacity limit. (D) Reversal of most social distancing measures. Social gatherings increased to eight people

health measures during the COVID-19 pandemic. The difference was significant, incidence rate ratio = 0.19, 95% confidence interval = 0.14–0.24, $p < 0.001$. The lowest recorded number of CA-RVI amongst inpatients with haematological malignancies since January 2018 occurred during the period where public health measures were in place.

The observational nature of our study prevented us from establishing causality between enactment of the various public health measures and incidence of CA-RVI amongst patients with haematological malignancies. However, the possible benefit of compulsory masking and hand and respiratory hygiene was demonstrated by the absence of a rebound in CA-RVI after the sequential relaxation of measures from September 2020. Even after the nation exited the lockdown, and social distancing measures were relaxed, Singapore continued to mandate the use of face masks in public and

enforce hand and respiratory hygiene. Our hospital continued to observe a low incidence of CA-RVIs amongst hospitalised patients with haematological malignancies.

A major limitation of our study is the use of aggregated epidemiological data which precludes adjustments for co-variables and hence potential confounders affecting CA-RVI incidence. Seasonal variations in CA-RVI incidence may also account for some degree of variability. However, surveillance was maintained over an entire year during the pandemic period, reducing the likelihood of these observations being due to seasonal variation alone. Our observations suggest that measures such as compulsory masking and judicious hand and respiratory hygiene could be effective in reducing community onset of non-COVID-19 RVIs, and there may be benefit in continuing these measures amongst haematologic patients even after the current pandemic has ended.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Jing Yuan Tan conceived the study, performed statistics and wrote the manuscript. Edwin Philip Conceicao and Liang En Wee assisted with the literature search and data collection and revised the manuscript. Edwin Philip Conceicao cross-checked the statistical calculations. Heng Joo Ng and Indumathi Venkatachalam provided critical input and extensively revised the manuscript. All authors approved the final version of the manuscript.

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