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Disease burden caused by respiratory syncytial virus compared with influenza among adults: a retrospective cohort study from Eastern Finland in 2017–2018

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ABSTRACT

Objectives Respiratory syncytial virus (RSV) is one of the most important causes of lower respiratory tract illnesses. In this study, we examined the number and severity of RSV infections among adult patients. The underlying diseases and background information of patients with RSV were examined and compared with the patients with influenza.

Design Retrospective cohort study.

Setting Patients receiving tertiary care services in Kuopio University Hospital (KUH) district in Eastern Finland.

Participants 725 patients (152 with RSV infection and 573 with influenza) treated in KUH between November 2017 and May 2018.

Primary and secondary outcome measures Hospitalisation and mortality.

Results Compared with influenza, RSV caused a more serious disease in terms of hospitalisation (84.2% vs 66.0%, p<0.001), incidence of pneumonia (37.5% vs 23.2%, p<0.001), need for antibiotics (67.1% vs 47.3%, p<0.001) and supplemental oxygen (50.7% vs 31.2%, p<0.001). The all-cause mortality during hospitalisation and 30 days after discharge was higher among the RSV-infected patients (8.6% vs 3.5%, p=0.010). Solid malignancies (23.1% vs 5.0%, p=0.042) and chronic kidney disease (30.8% vs 5.8%, p=0.011) were more common among the RSV-infected non-survivors compared with survivors. RSV was an independent risk factor for hospitalisation (adjusted OR (aOR) 2.035; 95% CI 1.17 to 3.55) and mortality (aOR 2.288; 95% CI 1.09 to 4.81) compared with influenza.

Conclusions Among all the screened patients, those with RSV infection were older and had more underlying conditions than patients with influenza. They had increased likelihood of hospitalisation and mortality when compared with influenza. Solid malignancies and chronic kidney disease seemed to be independent risk factors for death among RSV-infected patients. During RSV and influenza epidemics, it is important to test patients with respiratory symptoms for RSV and influenza to prevent the spread of the infections among elderly and chronically ill patients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Respiratory syncytial virus (RSV) is one of the most important causes of lower respiratory tract illnesses.
⇒ RSV has been discovered to cause mortality equal or close to the mortality related to influenza among elderly patients.
⇒ This retrospective cohort study compares the effects of multiple background factors on clinical outcomes in RSV-infected and influenza-infected adult patients.
⇒ The major limitation of the study was that there was no possibility to gather information about patient recovery from primary care facilities.
⇒ During the study, there was a major RSV epidemic in Finland explaining the high number of RSV infections compared with influenza.

INTRODUCTION

Respiratory syncytial virus (RSV) is one of the most important causes of lower respiratory tract illnesses.[1] RSV bronchitis or pneumonia can lead to hospitalisation and even death, especially in elderly people with underlying conditions.[2] A major RSV epidemic is observed in Finland every other winter, often starting in November–December. In addition, minor epidemics occur between the major ones.[3 4]

In adults ≥50 years of age, RSV is responsible for 1%–10% of acute respiratory tract infections.[5] RSV hospitalisation rates in adults ≥65 years of age are estimated to be 1/1000 and 0.3/1000 person-years in industrialised and developing countries, respectively.[6] The mortality rate among the elderly patients treated in hospital due to RSV infection varies between 1.1% and 15.9%[7–12] and the 30-day all-cause mortality rate varies between 3.2% and 13.7%.[9 10 12–14]

Among elderly patients living in long-term care facilities, RSV is estimated to cause 7.2%–11.4% of the hospitalisation among patients with chronic pulmonary diseases.[2] The hospitalised patients with RSV infection and influenza-like symptoms have often immunosuppressive medication, haematological

malignancy or other malignancies.[15 16] In immunocompromised patients, RSV is reported to account for 2.8%–10.3% of all acute respiratory tract infections, and 8.6%–20.0% of all respiratory viral infections.[5] Thirty per cent to 70% of the patients admitted to hospital because of RSV have cardiovascular disease.[7 9 14 15] During hospitalisation, 14%–25% of the patients with RSV infection experience a cardiovascular complication such as worsening heart failure, myocardial infarction or stroke.[7 8 13] Adults who are obese are more likely to be hospitalised from RSV infection and influenza than normal-weight adults.[17] Smoking is associated with higher risk of hospital admissions after influenza infection.[18]

Among adult patients hospitalised because of RSV infection, hypoxaemia is reported in 53%–68% and pneumonia in 31%–80% of the patients.[7 8 11 13–16] Empirical antibiotics are used on 76%–95% of the patients,[7 8 10] and blood cultures are positive in 4% of the patients.[8] Ten per cent to 25% of the RSV-infected hospitalised adults require treatment in intensive care unit (ICU)[10 11 16] and mechanical ventilation is needed for 10%–36% of the patients.[7 8 10] The average duration of hospitalisation has been reported to range from 4 to 9 days.[8 10 12 13 16]

When compared with the prevalence of influenza, the prevalence of RSV has been estimated to be up to twice as high among patients at risk and over 65 years.[2] In Finland, seasonal influenza has been estimated to cause 500–1000 excess deaths annually.[19] The patients hospitalised due to RSV are older, have more chronic diseases and are more likely living in long-term care compared with influenza.[8 14 15 20] Among elderly patients aged over 65 years, the in-hospital mortality related to RSV has been estimated to be equal or close to the mortality related to influenza.[5 15] However, the 30-day mortality rate has been estimated to be higher among RSV-infected patients.[14] The patients with RSV infection have more often underlying lung diseases, need more often supplemental oxygen and ventilatory support and develop more complications, such as pneumonia, than the patients with influenza.[8 13–15]

OBJECTIVES

The aim of the study was to examine the number and severity of RSV infections among adult patients in Kuopio University Hospital (KUH) district in Eastern Finland during the RSV epidemic. We also examined the underlying diseases and background information of patients with RSV. The results were compared with patients with influenza. The population in the study area has more underlying diseases than the average Finnish population, and therefore we focused on the disease burden in the outcomes of patients with RSV.[21]

METHODS

Study subjects

This retrospective cohort study was carried out in KUH. KUH is one of Finland's five university hospitals. The hospital is a 600-bed teaching hospital that provides tertiary care services to approximately 800 000 citizens in Central and Eastern Finland. Patients treated in KUH due to influenza and RSV were identified retrospectively from the information management system of Eastern Finland Laboratory Centre (ISLAB) between November 2017 and May 2018. During the study time, there was a major RSV epidemic in Finland.[3] Patients under 18 years of age and patients with mixed infections (influenza and RSV) were excluded from the study. Also, patients from regional hospitals were excluded if there was a lack of availability of electronic medical records.

Data collection

We collected clinical data by using electronic medical records. For general characteristics and background information, we observed age, body mass index (BMI, kg/m^2), gender, smoking status, type of housing and underlying conditions. All underlying conditions were classified according to the 2021 ICD-10-CM (International Classification of Diseases, Tenth Revision, Clinical Modification) codes: hypertension (ICD-10-CM I10–I15), ischaemic heart disease (ICD-10-CM I20–I25), heart failure (ICD-10-CM I50), cerebrovascular disease (ICD-10-CM I60–70), chronic obstructive pulmonary disease (ICD-10-CM J44), asthma (ICD-10-CM J45), solid malignancy (ICD-10-CM C00–C80), haematological malignancy (ICD-10-CM C81–C96), diabetes (ICD-10-CM E08–E13), chronic kidney disease (ICD-10-CM N18) and dementia (ICD-10-CM F00–F03). In addition, the patients with immunosuppressive medication due to other diseases were identified. Type of housing was divided into living independently and living with daily support (nursing homes, home care). Patients with BMI greater than or equal to 30 kg/m^2 were defined as obese and patients with BMI under 18.5 kg/m^2 were defined as underweight.[22] Smoking status was divided into smokers and non-smokers. The requirement and duration of hospitalisation, requirement of supplemental oxygen and non-invasive ventilation support (bilevel positive airway pressure, continuous positive airway pressure or nasal high flow), requirement of treatment in ICU and duration of ICU care, requirement of invasive ventilation, blood culture sample results, use of antibiotics, prevalence of pneumonia, all-cause mortality during hospitalisation and during the following 30 days after discharge were documented. The diagnosis of pneumonia was made by treating physicians based on clinical status, laboratory tests and X-rays.

Laboratory methods

The nasopharyngeal samples of influenza and RSV were taken from the patients during hospital visits. The samples were stored in Copan UTM-RT tubes for transport. The fresh samples were analysed with multiplex PCR assay for detecting influenza A and B virus and RSV nucleic acids in respiratory tract specimens (Xpert Xpress influenza/RSV test, Cepheid) according to the manufacturer's instructions in the clinical microbiology laboratory of

KUH (Eastern Finland Laboratory Centre Joint Authority Enterprise, ISLAB).

Analyses

Data were collected from electronic medical records into an SPSS file and the data analysis was completed using SPSS V.25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows). Mean, median and IQR (25th–75th percentile) were summarised using descriptive statistics. The statistical analyses between categorical variables were done by using the $\chi 2$ test. The Fisher's exact test was used instead of $\chi 2$ test when analysing categorical variables, if any cells had low (<5) minimum expected count. Mann-Whitney U test was used for the comparison between continuous variables. Univariate and multivariable logistic regression analyses were used to calculate the crude ORs and adjusted ORs (aORs) of the factors associated with hospitalisation and all-cause mortality during hospitalisation and 30 days after discharge. In the multivariable model, only the variables with a p value of <0.100 at univariate analysis were included, and the final model was built using a stepwise forward procedure to calculate the aORs. The Hosmer-Lemeshow test was used for goodness of fit for logistic regression models. The results with a p value lower than 0.05 were counted statistically significant.

Patient and public involvement

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

RESULTS

Study population

In total, 2484 patients with positive screening test results for influenza and RSV were identified at ISLAB between November 2017 and May 2018. Patients under 18 years of age, patients without electronic medical record available and patients with mixed infections (influenza and RSV, n=6) were excluded from the study. After this, a total of 725 patients (152 with RSV infection and 573 with influenza infection) were included in the study. BMI was available on 99 (65.1%) of the RSV-infected patients and on 396 (69.1%) of the influenza-infected patients. Smoking status was available on 115 (75.7%) of the RSV-infected patients and on 412 (71.9%) of the influenza-infected patients. Other characteristics and all hospital events were available on all patients in the electronic medical record.

Characteristics

The characteristics of the study population are presented in table 1. The RSV-infected patients were significantly older than the influenza-infected patients (mean 73.3 vs 68.1, median 73 vs 71 years, p=0.002). They were also more likely to have diagnoses of hypertension (60.5% vs 45.5%, p=0.001) and heart failure (17.8% vs 10.5%, p=0.014) than the patients with influenza infection. There were no significant differences in gender, smoking status, housing status or other underlying conditions between patients with influenza and RSV infections, but the patients with RSV infection had more underlying conditions (mean 2.32 vs 1.93, median 2 vs 2 underlying conditions, p=0.003) than those with influenza infection.

Hospitalisation

The hospital events of the study population are presented in table 2. The patients with RSV infection were hospitalised more often than those with influenza (84.2% vs 66.0%, p<0.001). During hospitalisation, the RSV-infected patients needed supplemental oxygen (50.7% vs 31.2%, p<0.001) and developed pneumonia (37.5% vs 23.2%, p<0.001) more often than patients with influenza. There was no difference in ICU admission between the groups, but the duration of the treatment in the ICU was longer in influenza-infected patients than those with RSV (mean 5.3 vs 2.5, median 4 vs 3 days, p=0.016). Blood culture positivity was detected more often (4.6% vs 1.7%, p=0.045) and antibiotics were used more often (67.1% vs 47.3%, p<0.001) among patients with RSV than those with influenza. The all-cause mortality during hospitalisation and 30 days after discharge was higher among RSV-infected patients than among those infected by influenza (8.6% vs 3.5%, p=0.010). There was no significant difference in the in-hospital all-cause mortality between the two groups.

In blood cultures of patients with RSV, *Streptococcus pneumoniae* was found among two patients. *Klebsiella pneumoniae*, *Prevotella oralis*, *Staphylococcus epidermidis*, *Escherichia coli* and *S. viridans* were found in the blood cultures of one patient each. In the blood cultures of influenza-infected patients, *S. aureus* was found among three patients, and *S. pneumoniae* in two patients. Positive blood cultures for *S. epidermidis*, *Pseudomonas aeruginosa*, *S. dysgalactiae* subsp *equisimilis* and *Proteus mirabilis* were detected each in one patient. In one patient with influenza, blood cultures were positive, but the pathogen remained unknown.

Altogether, 27 different antibiotics and 591 courses of antibiotics were used during the hospitalisation. In the RSV and influenza-infected patients, 47 (30.9%) vs 154 (26.9%) received a single antibiotic, 44 (28.9%) vs 87 (15.2%) received two different antibiotics, 8 (5.3%) vs 24 (4.2%) received three different antibiotics and 2 (1.3%) vs 6 (1.0%) patients received four different antibiotics. One (0.2%) patient with influenza infection received five different antibiotics during hospitalisation.

Factors associated with hospitalisation and mortality

Cross-tabulation of the baseline characteristics affecting all-cause mortality during hospitalisation and 30 days after discharge is presented in table 3. Non-surviving RSV-infected patients had significantly more often solid malignancies (23.1% vs 5.0%, p=0.042) and chronic kidney disease (30.8% vs 5.8%, p=0.011) than the survivors. In patients with influenza, underlying heart failure was more common among the non-survivors than the

Table 1 Characteristics of the study population

	RSV n=152, n (%)	Influenza n=573, n (%)	P value
Male	75 (49.3)	262 (45.7)	0.427
Age (years)			
Range	23–96	18–100	
Mean (SD)	73.3 (15.1)	68.1 (18.4)	0.002
Median (IQR)	73 (65–86)	71 (59–82)	
BMI (kg/m^2)			
Range	15.4–43.2	14.9–51.2	
Mean (SD)	27.0 (5.7)	27.3 (5.7)	0.297
Median (IQR)	25.6 (22.9–29.2)	27.0 (23.4–30.8)	
Smoking status			
Smoking	26 (17.1)	89 (15.5)	0.454
Non-smoker	89 (58.6)	323 (56.4)	
Housing status			
Independent	102 (67.1)	418 (72.9)	0.155
Supported	50 (32.9)	155 (27.1)	
Number of underlying conditions			
Range	0–6	0–7	
Mean (SD)	2.32 (1.4)	1.93 (1.5)	0.003
Median (IQR)	2 (1–3)	2 (1–3)	
Hypertension	92 (60.5)	261 (45.5)	0.001
Ischaemic heart disease	51 (33.6)	154 (26.9)	0.104
Heart failure	27 (17.8)	60 (10.5)	0.014
Cerebrovascular disease	28 (18.4)	77 (13.4)	0.121
COPD	20 (13.2)	57 (9.9)	0.253
Asthma	39 (25.7)	135 (23.6)	0.590
Solid malignancy	10 (6.6)	47 (8.2)	0.509
Haematological malignancy	7 (4.6)	16 (2.8)	0.257*
Diabetes	34 (22.4)	122 (21.3)	0.774
Chronic kidney disease	12 (7.9)	43 (7.5)	0.872
Dementia	22 (14.5)	71 (12.4)	0.495
Immunosuppressive medication	11 (7.2)	65 (11.3)	0.142

Continuous variables (age, BMI, number of underlying conditions) are presented as mean and SD and median and IQR (25th–75th percentile); categorical variables are presented as number (n) and per cent (%). P values were calculated with Mann-Whitney U test for continuous variables and with $\chi 2$ test and Fisher's exact test for categorical variables.
*Calculated with Fisher's exact test.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; RSV, respiratory syncytial virus.

survivors (30.0% vs 9.8%, p=0.012). The non-survivors were also significantly older (mean 83.6 vs 67.5, median 83 vs 70 years, p<0.001) and lived in supported housing more often than the survivors (55.0% vs 26.0%, p=0.004).

In multivariable logistic regression analyses among all study patients, RSV infection (p=0.012), age (p=0.003), smoking (p=0.001) and number of underlying conditions (p<0.001) were positively associated with the likelihood of hospitalisation (table 4). RSV infection (p=0.029), age (p<0.001) and solid malignancies (p=0.042) were positively associated with the all-cause mortality during hospitalisation and 30 days after discharge (table 5).

DISCUSSION

We examined the number and severity of RSV and influenza infections among adult patients in KUH district in Eastern Finland during the 2017–2018 RSV epidemic season. The majority of the patients in both groups were elderly and had several underlying conditions, but most of

Table 2 Outcomes and hospital events of the study population

	RSV n=152, n (%)	Influenza n=573, n (%)	P value
Hospitalised	128 (84.2)	378 (66.0)	<0.001
Discharged from ER	24 (15.8)	195 (34.0)	
Hospital treatment (days)			
Range	1–40	1–66	
Mean (SD)	4.5 (4.5)	4.1 (5.7)	0.425
Median (IQR)	5 (3–6)	5 (3–7)	
Need of supplemental oxygen	77 (50.7)	179 (31.2)	<0.001
Non-invasive ventilation	17 (11.2)	50 (8.7)	0.352
ICU admission	6 (3.9)	23 (4.0)	0.970
ICU treatment duration (days)			
Range	1–3	1–21	
Mean (SD)	2.5 (0.8)	5.3 (4.3)	0.016
Median (IQR)	3 (2–3)	4 (3–6)	
Invasive ventilation	2 (1.3)	4 (0.7)	0.383*
Pneumonia	57 (37.5)	133 (23.2)	<0.001
Positive blood cultures	7 (4.6)	10 (1.7)	0.045*
Antibiotic used	102 (67.1)	272 (47.3)	<0.001
Hospital all-cause mortality	5 (3.3)	15 (2.6)	0.413
All-cause mortality during hospitalisation and 30 days after discharge	13 (8.6)	20 (3.5)	0.010
Time from hospitalisation to death (days)			
Range	3–40	1–51	
Mean (SD)	13.4 (15.3)	8.1 (12.4)	0.266
Median (IQR)	6 (4–27)	4 (2–9)	

Continuous variables (hospital treatment duration, ICU treatment duration, time from hospitalisation to death) are presented as mean and SD and median and IQR (25th–75th percentile); categorical variables are presented as number (n) and per cent (%). P values were calculated with Mann-Whitney U test for continuous variables and with $\chi 2$ test and Fisher's exact test for categorical variables.
*Calculated with Fisher's exact test.
ER, emergency room; ICU, intensive care unit; RSV, respiratory syncytial virus.

them were living independently. However, because of the high general morbidity in population of Eastern Finland, the impact of epidemic RSV and influenza is considerable.[21] Although there was high general morbidity in the population studied, patients with RSV in our study did not have an exceptionally high rate of comorbidities compared with previous similar studies.[7 9 14 15]

Consistent with previous studies, the patients with RSV were older and had significantly more underlying conditions than those with influenza,[8 14 15 20] especially high blood pressure and heart failure. Compared with influenza, RSV caused a more serious disease in terms of hospitalisation, secondary pneumonia, blood culture positivity, need for antibiotics and supplemental oxygen. In addition, the all-cause mortality during hospitalisation and 30 days after discharge was higher among the RSV-infected patients than those with influenza (8.6% vs 3.5%) as found in earlier studies.[8 14 15 20] In multivariate analyses, RSV remained as a significant independent risk factor to hospitalisation (aOR 2.0, p=0.012) and mortality (aOR 2.3, p=0.029) compared with influenza. However, though patients with RSV had more serious disease compared with influenza in many terms, the duration of the treatment in the ICU was longer in influenza-infected patients than those with RSV. The majority of the deaths due to influenza infection occurred during hospitalisation, whereas the majority of the deaths due to RSV infection occurred within 30 days after discharge. RSV-infected patients in our study were generally older and their burden of diseases was heavier compared with patients with influenza. This may reflect the limited ability of many elderly patients to recover from serious illness and therefore explain the high mortality after discharge from hospital.

Regarding hospital events in RSV-infected patients, the time in hospital treatment (mean 4.5 vs 4–9 days), incidence of pneumonia (37.5% vs 31%–80%) and positive results in blood cultures (4.6% vs 4%) were in accordance with other studies.[7 8 11–15] However, hypoxaemia and the need of supplemental oxygen (50.7% vs 53%–68%), ICU admission (3.9% vs 10%–25%) and the use of invasive ventilation (1.3% vs 10%–36%) were less common in our study.[7 8 10 11 13] Separate Step Down Units (SDUs) are in active use in our own hospital and this might be one explanation for the low ICU admissions. SDUs provide an intermediate level of care between ICU and the medical wards. One of these SDUs is located in our pulmonary unit, where intensive observation, treatment and oxygen support like high nasal flow oxygen therapy and non-invasive ventilation are available. Fragile patients and patients with treatment limitations, for example, withholding of life-sustaining treatment, are especially treated in SDUs instead of the ICU. Interestingly, a decision not to initiate or escalate a life-sustaining treatment in terminal illness in accordance with expressed wishes of the patient or surrogate is a widespread practice in Finland. These decisions are more common in elderly patients, non-surgical patients and those who have more comorbidities, malignancy and cardiovascular or respiratory insufficiency.[23] This description correlates quite nicely with hospitalised patients with RSV in this paper. The exact number of patients who denied intensive treatment in present study is not known but they also exist. Despite the differences in treatment compared with earlier studies, in-hospital mortality rate (3.3%)

Table 3 Comparison of the characteristics between RSV-infected non-survivors and survivors and influenza-infected non-survivors and survivors during hospitalisation and 30 days after discharge

	RSV non-survivors (n=13), n (%)	RSV survivors (n=139), n (%)	P value	Influenza non-survivors (n=20), n (%)	Influenza survivors (n=553), n (%)	P value
Male	5 (38.5)	70 (50.4)	0.412	9 (45.0)	253 (45.8)	0.947
Female	8 (61.5)	69 (49.6)		11 (55.0)	300 (54.2)	
Age (years)						
Range	39–94	23–96		68–100	18–98	
Mean (SD)	77.5 (15.2)	73.0 (15.1)	0.195	83.6 (10.0)	67.5 (18.4)	<0.001
Median (IQR)	81 (70–90)	73 (64–86)		83 (77–93)	70 (59–82)	
Obesity	2 (15.4)	23 (16.5)	0.648*	2 (10.0)	111 (20.1)	0.308*
Underweight	0 (0)	4 (2.9)	0.708*	0 (0)	20 (3.6)	0.512*
Smoking	2 (15.4)	24 (17.3)	0.598*	0 (0)	89 (16.1)	0.109*
Number of underlying conditions						
Range	1–6	0–6		0–5	0–7	
Mean (SD)	3.2 (1.8)	2.2 (1.3)	0.059	2.2 (1.3)	1.9 (1.5)	0.291
Median (IQR)	3 (2–5)	2 (1–3)		2 (1–3)	2 (1–3)	
Supported housing	6 (46.2)	44 (31.2)	0.222*	11 (55.0)	144 (26.0)	0.004
Hypertension	8 (61.5)	84 (60.4)	0.938	8 (40.0)	253 (45.8)	0.612
Ischaemic heart disease	7 (53.8)	44 (31.7)	0.097*	6 (30.0)	148 (26.8)	0.460
Heart failure	4 (30.8)	23 (16.5)	0.179*	6 (30.0)	54 (9.8)	0.012*
Cerebrovascular disease	5 (38.5)	23 (16.5)	0.065*	4 (20.0)	73 (13.2)	0.276*
COPD	2 (15.4)	18 (12.9)	0.534*	1 (5.0)	56 (10.1)	0.390*
Asthma	1 (7.7)	38 (27.3)	0.106*	6 (30.0)	129 (23.3)	0.323*
Solid malignancy	3 (23.1)	7 (5.0)	0.042*	3 (15.0)	44 (8.0)	0.221*
Haematological malignancy	1 (7.7)	6 (4.3)	0.472*	1 (5.0)	15 (2.7)	0.438*
Diabetes	4 (30.8)	30 (21.6)	0.324*	3 (15.0)	119 (21.5)	0.353*
Chronic kidney disease	4 (30.8)	8 (5.8)	0.011*	1 (5.0)	42 (7.6)	0.548*
Dementia	1 (7.7)	21 (15.1)	0.409*	3 (15.0)	68 (12.3)	0.460*
Immunosuppressive medication	3 (23.1)	8 (5.8)	0.054*	2 (10.0)	63 (11.4)	0.599*

In categorical variables, men were compared with women, obese (BMI ≥30 kg/m^2) and underweight (BMI <18.5 kg/m^2) patients with patients with BMI greater than or equal to 18.5–29.9 kg/m^2, smokers with non-smokers and patients living in supported housing with patients living independently. The patients with certain underlying condition were compared with those without the underlying condition in question. Continuous variables (age, number of underlying conditions) are presented as mean and SD and median and IQR (25th–75th percentile); categorical variables are presented as number (n) and per cent (%). P values were calculated with Mann-Whitney U test for continuous variables and with $\chi 2$ test and Fisher's exact test for categorical variables.
*Calculated with Fisher's exact test.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; RSV, respiratory syncytial virus.

was generally low and in accordance with earlier studies (1.1%–15.9%).[7 8 10–12]

The use of antibiotics among both RSV-infected (67.1%) and influenza-infected (47.3%) patients was common in our study, but lower than reported earlier among RSV-infected patients (76%–95%).[7 8 10] Among patients with influenza, the proportion of patients treated with prophylactic antibiotics has been reported to be as high as 96.6%.[24] In our study, the proportion of patients with influenza treated with antibiotics was significantly lower. In both groups, the proportion of those who received antibiotics was higher than the amount of actual pneumonia diagnoses. In Finland, the antimicrobial resistance has remained low compared with other countries in European Union due to strict antimicrobial policy.[25] The lower usage of antibiotics in our study did not increase the mortality rate in RSV-infected patients compared with other studies where the use of antibiotics had been studied.[7 8 10]

The number of deceased patients in our study was low, which is in line with previous studies conducted with RSV-infected and influenza-infected patients.[7–14] Solid malignancies and chronic kidney disease were more common among the RSV-infected non-survivors than survivors.

Table 4 Univariable and multivariable logistic regression analyses of factors associated with hospitalisation among all study population (n=725)

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
RSV infection	2.751 (1.721 to 4.398)	<0.001	2.035 (1.167 to 3.546)	0.012
Male gender	0.929 (0.676 to 1.277)	0.650		
Age (years)	1.032 (1.023 to 1.042)	<0.001	1.021 (1.007 to 1.035)	0.003
Obesity	1.419 (0.892 to 2.257)	0.140		
Underweight	1.233 (0.475 to 3.200)	0.667		
Smoking	1.995 (1.189 to 3.346)	0.009	2.621 (1.502 to 4.573)	0.001
Number of underlying conditions	1.611 (1.418 to 1.830)	<0.001	1.433 (1.210 to 1.696)	<0.001
Supported housing	1.546 (1.069 to 2.238)	0.021		
Hypertension	2.864 (2.047 to 4.007)	<0.001		
Ischaemic heart disease	2.445 (1.641 to 3.644)	<0.001		
Heart failure	3.342 (1.738 to 6.425)	<0.001		
Cerebrovascular disease	2.502 (1.449 to 4.317)	0.001		
COPD	3.190 (1.609 to 6.325)	0.001		
Asthma	1.323 (0.901 to 1.942)	0.153		
Solid malignancy	1.891 (0.960 to 3.725)	0.065		
Haematological malignancy	0.806 (0.337 to 1.929)	0.628		
Diabetes	2.310 (1.481 to 3.602)	<0.001		
Chronic kidney disease	1.434 (0.754 to 2.729)	0.272		
Dementia	1.205 (0.739 to 1.964)	0.455		
Immunosuppressive medication	0.814 (0.492 to 1.346)	0.422		

The HL confirmed the goodness of fit for the multivariable model (p=0.138). In categorical variables, men were compared with women, obese (BMI ≥30 kg/m^2) and underweight (BMI <18.5 kg/m^2) patients with patients with BMI greater than or equal to 18.5–29.9 kg/m^2, smokers with non-smokers, patients living in supported housing with patients living independently. The patients with certain underlying condition were compared with those without the underlying condition in question.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; HL, Hosmer-Lemeshow; RSV, respiratory syncytial virus.

Older age and heart failure were more common among non-survivors than survivors in influenza-infected patients, but not in RSV-infected patients. In earlier studies, older age has been reported to be a significant factor predicting mortality in RSV-infected patients.[8 9 12–14] Age and previous haematological disease have been reported to be associated with an increased risk of death during the first 21 days of hospitalisation among both RSV-infected and influenza-infected patients.[12] As far as we know, our finding that solid malignancies and chronic kidney disease are factors predicting mortality in RSV infections has not been reported before.

Among all study patients, smoking (aOR 2.621, p=0.001) was positively associated with the increased risk of hospitalisation, but not with mortality. The result is in line with previous studies, where the positive association with likelihood of hospitalisation has been observed, but effect on mortality has been less conclusive.[18] Unlike reported previously,[17] obesity was not associated with the increased risk of hospitalisation among influenza-infected and RSV-infected patients in our study. In current study, 15.8% of the patients with RSV and 19.8% with influenza were obese (BMI greater than or equal to 30 kg/m^2), while on average in Finland 26.1% of men and 27.5% of women over 30 years of age are obese.[26] Still, only 15.4% of the deceased patients with RSV and 10.0% with influenza in our study were obese. When compared with COVID-19, the difference is remarkable, since 28.9% of the deceased patients aged 20 years and older with COVID-19 have been reported to be obese.[27]

The study was carried out in a tertiary care hospital, and there was no possibility to gather information about patient recovery from primary care facilities, which is a limitation. During the study period, there was a major RSV epidemic in Finland, which explains the high number of RSV infections compared with influenza infections. During this time, influenza B was more common than influenza A in Finland and the total number of influenza infections was higher than in previous years explained by the high prevalence of influenza B.[19] However, there was no significant difference in excess mortality compared with previous influenza seasons during the study time.[19]

In our study, RSV infection was associated with increased likelihood of hospitalisation and mortality compared with influenza. The patients with RSV infection were older and had more underlying conditions than the patients with influenza. No difference in BMI or smoking status was found, but solid malignancies and chronic kidney disease

Table 5 Univariable and multivariable logistic regression analyses of factors associated with all-cause mortality during hospitalisation and 30 days after discharge among all study population (n=725)

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
RSV infection	2.586 (1.255 to 5.327)	0.010	2.288 (1.089 to 4.806)	0.029
Male gender	1.188 (0.586 to 2.407)	0.633		
Age (years)	1.065 (1.031 to 1.100)	<0.001	1.063 (1.029 to 1.099)	<0.001
Obesity	0.633 (0.206 to 1.942)	0.424		
Underweight	–	–		
Smoking	0.411 (0.094 to 1.807)	0.239		
Number of underlying conditions	1.290 (1.037 to 1.606)	0.022		
Supported housing	2.848 (1.410 to 5.753)	0.004		
Hypertension	0.991 (0.493 to 1.994)	0.981		
Ischaemic heart disease	1.693 (0.826 to 3.470)	0.151		
Heart failure	3.473 (1.593 to 7.570)	0.002		
Cerebrovascular disease	2.328 (1.050 to 5.160)	0.037		
COPD	0.835 (0.249 to 2.804)	0.771		
Asthma	0.846 (0.361 to 1.985)	0.701		
Solid malignancy	2.793 (1.103 to 7.075)	0.030	2.703 (1.038 to 7.039)	0.042
Haematological malignancy	2.061 (0.463 to 9.187)	0.343		
Diabetes	0.981 (0.418 to 2.305)	0.965		
Chronic kidney disease	2.293 (0.848 to 6.196)	0.102		
Dementia	0.935 (0.321 to 2.721)	0.901		
Immunosuppressive medication	1.562 (0.585 to 4.173)	0.374		

The HL confirmed the goodness of fit for the multivariable model (p=0.607). In categorical variables, men were compared with women, obese (BMI ≥30 kg/m^2) and underweight (BMI <18.5 kg/m^2) patients with patients with BMI greater than or equal to 18.5–29.9 kg/m^2, smokers with non-smokers, patients living in supported housing with patients living independently. The patients with certain underlying condition were compared with those without the underlying condition in question.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; HL, Hosmer-Lemeshow; RSV, respiratory syncytial virus.

were shown to be independent risk factors for death among RSV-infected patients. During RSV and influenza epidemics, it is important to test all hospitalised patients with respiratory symptoms to prevent the spread of infection by using contact and respiratory precautions as well as isolation and cohorting of infected patients. The same practices are important in managing COVID-19-infected patients.

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