1496. Aspergillosis Complicating Severe Respiratory Syncytial Virus (RSV) in ICU Patients: A Retrospective Cohort Study

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Session: P-68. Respiratory Infections - Viral

Background. There are recent reports that identify severe influenza pneumonia as an independent risk factor for the development of invasive pulmonary aspergillosis (IPA), even in patients without immunocompromise. We aimed to understand the incidence of IPA as well as other coinfections over multiple seasons in patients with RSV pneumonia in the intensive care unit (ICU).

Methods. A retrospective cohort study was conducted in a single center in Chicago. Data was collected over 9 seasons (January 2009-March 2018) from adult patients admitted to the ICU at a large urban tertiary care center with severe RSV pneumonia. Patients were included if they had a positive RSV PCR test, older than 18 years, admitted to the ICU with acute respiratory failure, and had pulmonary infiltrates on imaging. IPA was defined per both the EORTC/MSG criteria as well as the revised AspICU criteria (Schauwvlieghe et al). Descriptive statistics were calculated. In univariable analysis, we compared categorical variables by Fisher's exact test and Chi-square test, continuous variables by Wilcoxon Rank Sum where appropriate.

Results. Of 224 patients admitted to the ICU with RSV (median ICU LoS 10.5 d), IPA was diagnosed in 8 (3.5%). Patients diagnosed with IPA had an increased LoS in the hospital (23.7 days vs. 11.6 days, p=0.01). Although the mortality was numerically higher (3, 37.5% vs 26, 17.9%) this was statistically not significant). History of hematological malignancy, stem cell transplant, and neutropenia were significant factors in the development of IPA. Those with lung disease had significantly lower rates of IPA. All patients with IPA were treated with voriconazole. Other coinfections among RSV-infected ICU patients included bacterial (21, 13.7%), viral (10, 6.5%), and non-IPA fungal (13, 8.5%) pathogens.

Baseline Characteristics and Mortality/Morbidity

Table 1. Baseline Characteristics and Mortality/Morbidity

Baseline characteristics	All patients with RSV (N=153)	With invasive pulmonary aspergillosis (N=8)	Without invasive pulmonary aspergillosis (N=145)	*p-value*
Median age, years (IQR)	63 (52, 74)	63 (52, 74)	56 (48, 73.5)	0.481
Male sex	67 (43.8)	7 (87.5)	60 (41.4)	0.022
Median LOS (IQR)	11.6 (7.8, 18.8)	23.7 (13.9, 38.1)	11.6 (7.1, 18.3)	0.014
Median ICU LOS (IQR)	3.1 (1.5, 6.8)	4.8 (1.7, 8.1)	3.1 (1.5, 6.8)	0.468
BMI over 30	58 (37.9)	1 (12.5)	57 (39.3)	0.123
Lung disease	86 (56.2)	1 (12.5)	85 (58.6)	0.022
Heart disease	68 (44.4)	2 (25.0)	66 (45.5)	0.223
Diabetes	47 (30.7)	2 (25.0)	45 (31.0)	0.532
Liver cirrhosis	11 (7.2)	1 (12.5)	10 (6.9)	0.457
Chronic kidney disease	37 (24.2)	3 (37.5)	34 (23.5)	0.401
Rheumatologic Disease	30 (19.6)	28 (19.3)	2 (25.0)	0.439
Known risk factors				
Hematological malignancy	30 (19.6)	7 (87.5)	23 (15.9)	0.000
Stem Cell Transplant	19 (12.4)	4 (50.0)	15 (10.3)	0.009
GVHD	5 (3.3)	0 (0.00)	5 (3.45)	0.762
Solid Organ Transplant	11 (7.2)	1 (12.5)	10 (6.9)	0.457
Immune Suppression not due to transplant	36 (23.5)	2 (25.0)	34 (23.5)	0.601
Solid organ malignancy	15 (9.8)	0 (0.00)	15 (10.34)	0.429
Neutropenia	6 (3.9)	2 (25.0)	4 (2.76)	0.032
Lymphopenia	68 (44.4)	6 (75.0)	62 (42.8)	0.078
Mortality/Morbidity				
Mechanical ventilation	61 (39.9)	2 (25.0)	59 (40.7)	0.313
Renal replacement therapy	19 (12.4)	2 (25.0)	17 (11.7)	0.260
ECMO	0 (0.00)	0 (0.00)	0 (0.00)	n/a
Death within 30 days	22 (14.4)	2 (25.0)	20 (13.8)	0.323
Death within 90 days	26 (16.9)	3 (37.5)	23 (15.9)	0.136
Death within 1 year	29 (18.9)	3 (37.5)	26 (17.9)	0.176
RSV				
RSV A	76 (49.7)	3 (37.5)	73 (50.3)	0.710
RSV B	76 (49.7)	5 (62.5)	71 (48.9)	0.495
RSV treatment with ribavirin	6 (3.9)	1 (12.5)	5 (3.5)	0.279
RSV treatment with IVIG	13 (8.5)	5 (62.5)	8 (5.5)	0.000

Patient Characteristics in Invasive Pulmonary Aspergillosis

Table 2. Patient characteristics in Invasive Pulmonary Aspergillosis

	Number of patients in the RSV cohort with invasive pulmonary aspergillosis (N=8)
BAL culture positive	2 (25.0%)
BAL galactomannan test positive	4 (50.0%)
Serum galactomannan test positive	2 (25.0%)
EORTC/MSG criteria	
Proven	0 (0%)
Probable	7 (87.5%)
Possible	1 (12.5%)
***AspICU* criteria**	
Proven	0 (0%)
Putative	2 (25.0%)
Colonization	5 (67.5.0%)
Not classifiable	1 (12.5%)
Initial Treatment	
Voriconazole	8 (100%)
Echinocandins	4 (50.0%)
Isavuconazole	0 (0%)
Posaconazole	0 (0%)
Liposomal amphotericin B	2 (25.0%)
Combination	4 (50.0%)
No treatment	0 (0%)

Conclusion: Although IPA is relatively uncommon in patients admitted to the ICU with severe RSV pneumonia, patients with IPA had significant increased LOS and tended to have underlying host factors. Other coinfections with bacterial, viral, and non-IPA fungal pathogens are common in those with severe RSV pneumonia.

Disclosures. Michael G. Ison, MD MS, AlloVir (Consultant)

1497. Epidemiology of RSV infection in Japan: A nationwide claims database analysis

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Session: P-68. Respiratory Infections - Viral

Background. Respiratory syncytial virus (RSV) is the major global cause of hospitalization for bronchiolitis and pneumonia in infancy around the globe. In Japan, the occurrence of RSV infection is monitored under the national pediatric sentinel surveillance system. However, this system does not provide detailed information about patient distribution by month of birth and clinical features. We aimed to describe the national epidemiology and clinical features of RSV infection in children < 24 months of age utilizing a nationwide healthcare claims database in Japan.

Methods. We retrospectively analysed anonymized claims data from the Japan Medical Data Center (JMDC) of medical insurance beneficiaries who had at least one confirmed RSV-related diagnosis by ICD10 codes between January 2017 and December 2018. In children < 24 months of age, the number of patients by age in Japan was estimated using the prevalence of patients in the database and national population data by age.

Results. In the JMDC database, 9,711 and 8,509 children < 24 months of age had an RSV-related diagnosis in 2017 and 2018, respectively. Of which, 2,473 (25%) and 2,083 (24%) were hospitalized. When extrapolated to the entire Japanese population, an estimated 138,059 and 119,205 RSV-related diagnoses and 33,355 and 27,339 RSV-associated hospitalizations occurred in Japan in 2017 and 2018, respectively. Infants < 6 months of age accounted for between 39% and 42% of total hospitalisations for

RSV. A peak in RSV hospitalization was observed at age 2 months. Only 10% of all children < 24 months of age who were hospitalised with an RSV infection had a specific underlying medical condition (preterm infant, bronchopulmonary dysplasia, Down syndrome, chronic heart disease, immunodeficiency). The estimated rate of RSV-associated hospitalization was 35.4 per 1000 population per year among infants < 6 months of age.

Conclusion. In conclusion, 3 to 4 out of every 100 Japanese children aged < 6 months were hospitalized for RSV. Ninety percent of children < 24 months of age hospitalised with RSV infection did not have a recognised underlying medical condition. The peak of hospitalization for RSV infection occurred at 2 months of age. Thus, broad-based prevention strategies targeting young infants are needed.

Disclosures. Yasuhiro Kobayashi, MS, Pfizer (Employee, Shareholder) Kanae Togo, PhD, Pfizer (Employee) Yasmeen Agosti, MD, Pfizer (Employee, Shareholder) John M. McLaughlin, PhD, Pfizer (Employee, Shareholder)

1498. Etiology of Community-acquired Pneumonia in Adults: A Systematic Review

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Session: P-68. Respiratory Infections - Viral

***Background. Background*:** Recent guidelines recommend immediate empiric antibiotic treatment for patients (pts) with community-acquired pneumonia (CAP). Concerns about treatment recommendations and antibiotic stewardship motivated a systematic literature review of the etiology of CAP.

Methods. We reviewed English-language literature using PRISMA guidelines. Data were stratified into diagnostic categories according to the microbiologic studies that were done (Table1).

Fig.1. Flowchart of systematic literature review and study selection

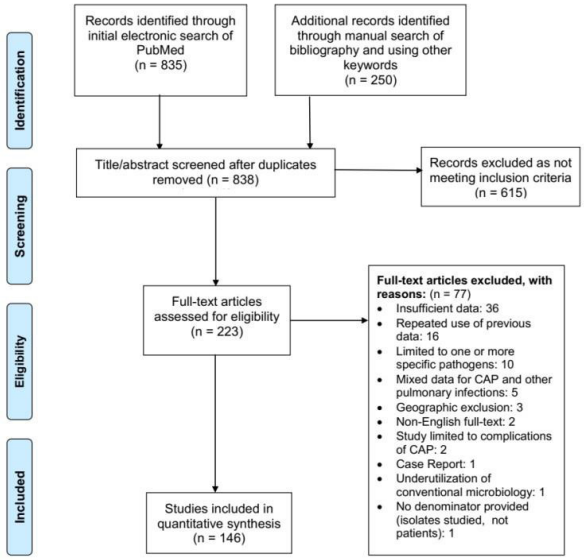

Fig.1. Flowchart of systematic literature review and study selection

Table 1. Characteristics of studies reporting the etiology of community-acquired pneumonia

Table1. Characteristics of studies reporting the etiology of community acquired pneumonia (CAP)

Nature of the microbiologic studies	Bacteriology only	Bacteria & 'atypicals' *	Bacteria, 'atypicals' & viruses	Modern Studies: Bacteria and:		
				PCR for 'atypicals'	PCR for viruses	PCR for 'atypicals' and viruses
Number of studies	25	37	46	16	10	12
Publication years	1945 – 2010	1984 – 2020	1967 – 2017	1999 - 2020	2008 - 2019	2005 - 2019
Study setting						
Inpatient only	8,653	14,281	23,555	6,790	6,260	4,399
Inpatient/outpatient	118	3,786	3,512	1,069	5,295	2,752
Outpatient only	610	1,368	226	0	0	0
Number of CAP patients	9,381	19,435	27,293	7,859	11,555	7,151
Antibiotic exposure prior to microbiologic testing	687 (7.3 %)	3,104 (16 %)	4,203 (15.4 %)	1,074 (13.7 %)	2,085 (18 %)	966 (13.5 %)
Number of patients with no etiology determined	6,293 (67.1 %)	11,663 (60.0%)	13,704 (50.2%)	4,484 (57.1%)	5,823 (50.4%)	4,380 (61.3%)

* "Atypicals" is a term used loosely in publications to refer to *Mycoplasma, Chlamydophila, Legionella* and/or *Coxiella*

Results. 146 articles with 82,674 CAP pts met criteria for inclusion; 63,938 (77.3%) were inpatients, 16,532 (20.0%) were in- or outpatients, and 2,204 (2.7%) were outpatients. Pneumococcus was the most common cause of CAP without regard to which microbiological techniques were used (33-50% of all cases). The proportion due to this organism declined with time, much more strikingly in the US than in Europe. *Haemophilus influenzae* was the second most common cause (7-16% of cases), followed by *Staphylococcus aureus* and *Enterobacteriaceae* each in 4–10%. *Pseudomonas* (0.8-4.5%) and *Moraxella* (1.2-3.5%) were less common; all other bacteria were isolated far less frequently. *Mycoplasma* caused 4-11% of CAP, *Legionella* 3-8%, *Chlamydophila* 2-7%, and *Coxiella* < 2%; some studies showed a much higher frequency of *Mycoplasma*. With routine use of viral PCR, a virus was identified in 30-40% of pts; bacterial/viral coinfection was found in 25-35% of these cases. In a separate study of CAP pts in whom viral PCR was positive, 40% had bacterial coinfection. Influenza viruses were identified in 6.2-13.7% of cases and rhinoviruses in 4.1-11.5%. RSV and human metapneumovirus were less common (0.4-4.7%), followed more distantly by other viruses. Even with the use of the most sophisticated diagnostic techniques, no etiologic agent for CAP was identified in > 50% of cases.

Trends of identification of S. pneumoniae and H. influenzae as the etiology of CAP (above); and the proportion of S. pneumoniae as the causes of CAP in different geographic regions (below).

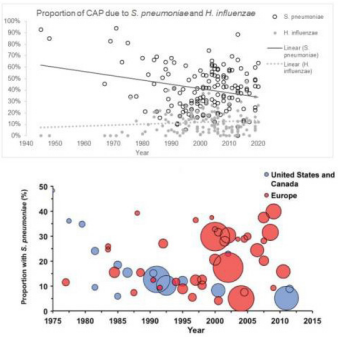

Figure 2. Trends of identification of *S. pneumoniae* and *H. influenzae* as the etiology of CAP (*above*); and the proportion of *S. pneumoniae* as the causes of CAP in different geographic regions (*below*).

Conclusion: Our results justify current guidelines for initial empiric antibiotic treatment of all pts with CAP. With pneumococcus and *Haemophilus* continuing to predominate, efforts at antibiotic stewardship might be enhanced by greater attention to routine use of sputum Gram stain and culture. Because viral/bacterial coinfection is relatively common, the identification of a virus by PCR does not, by itself, permit the non-use of an antibiotic.

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1499. Incidence of Community Acquired Pneumonia by Age and Comorbid Conditions in the Veterans Health Administration (VHA)

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Session: P-68. Respiratory Infections - Viral

Background. Community acquired pneumonia (CAP) remains a major cause of morbidity and mortality. Risk factors for CAP are often grouped as moderate- (e.g., diabetes mellitus, chronic liver, lung, or heart disease) and high-risk (e.g., immunosuppressive) conditions, which in turn influences preventative strategies, notably pneumococcal vaccination. Here, we use the national VHA databases to assess the risk of CAP among adults, expanding on previous work by using administrative data to assess the incidence of CAP among people with > 1 moderate risk condition

Methods. We used the national VHA databases merged with claims summaries from the Centers for Medicare and Medicaid Services (CMS) to identify patients receiving clinical care in the VHA without clinical Medicare claims in 2016-2017. Within this population, we identified CAP cases defined by the presence of a diagnostic code for pneumonia, chest X-ray, and antibiotics as well as the absence of healthcare exposure or antibiotics in prior 90 days. We determined the total patient years at risk and calculated incidence rates by age group and by moderate- and high-risk comorbid conditions.

Results. We identified 37,348 CAP cases in 7.9 million person-years at risk and observed similar annual rates in 2016 and 2017 (468.9 and 472.2 cases/100,000 person-years, respectively). The prevalence of high-risk conditions and incidence of CAP increased with age whereas the prevalence of >1 moderate-risk condition peaked for ages 50-64 and 65-74 years (**Table**). The incidence of CAP among those with > 1 moderate-risk condition exceeded that of patients with high-risk conditions across all age strata (**Figure**).