

Aspergillosis Complicating Severe Respiratory Syncytial Virus in ICU Patients: A Retrospective Cohort Study

Hannah Nam, MD, MSCI¹, Michael G. Ison, MD, MS²

Email : hannahn@hs.uci.edu | Twitter : @HannahNamMD

¹Division of Infectious Diseases, University of California– Irvine ²Divisions of Infectious Diseases and Organ Transplantation, Northwestern University Feinberg School of Medicine

Background

- Severe influenza pneumonia has been identified as an independent risk factor for the development of invasive pulmonary aspergillosis (IPA), even in patients without immunocompromise
- Aim to understand the incidence of IPA as well as other co-infections over multiple seasons in patients with RSV pneumonia in the intensive care unit (ICU)

Methods

- Retrospective cohort study from a single-center in Chicago, IL with data collected across 9 flu seasons (March 2009 – March 2018)
- Included patients \geq age 18 with a positive influenza PCR test who were admitted to ICU with respiratory distress
- IPA defined by both EORTC/MSG and *AspICU* criteria

Results

- 153 ICU patients with RSV during the study period
- IPA incidence was 5.2% (8/153)
- History of male sex, lung disease, hematological malignancy, neutropenia, stem cell transplant, were significant risk factors for development of IPA
- Median ICU LoS was significantly increased in those with development of IPA

Incidence of Non-Aspergillus Coinfections

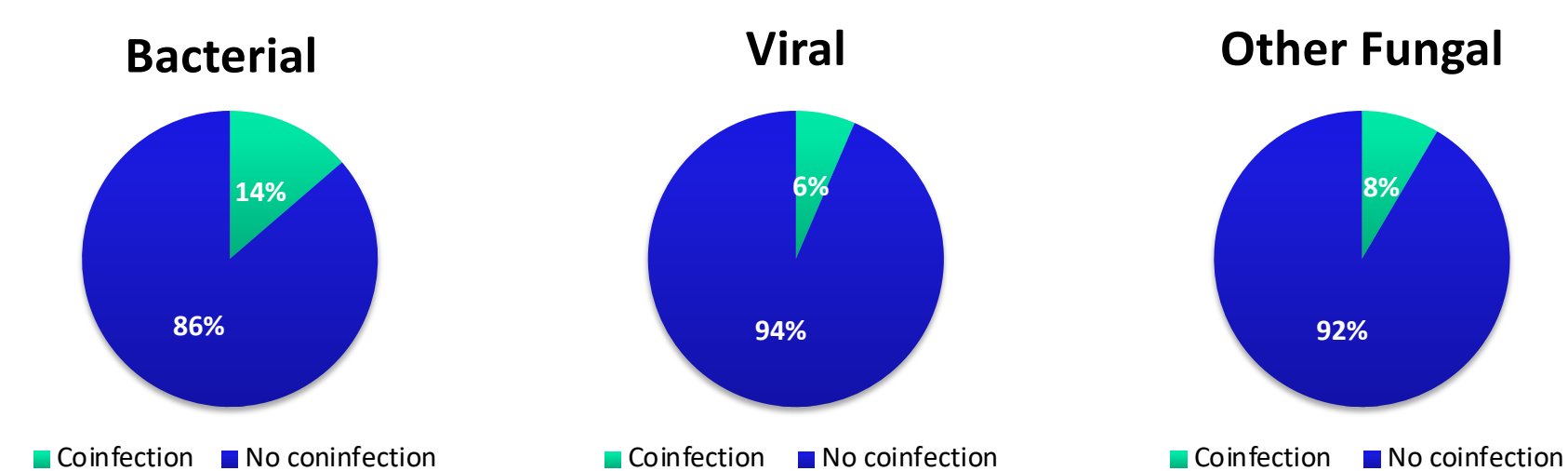


Table 1. Baseline Characteristics and Morbidity/Mortality

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

Table 2. Patient Characteristics in IPA

	Number of patients in the RSV cohort with IPA (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%)
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%)

Conclusions

- Overall incidence of IPA is low at 5.2% in those with severe RSV pneumonia
- All patients who developed IPA had underlying immunocompromise (87.5% with hematological malignancy, 12.5% with SOT)
- History of male sex, hematological malignancy, neutropenia, stem cell transplant, were significant risk factors for development of IPA
- IPA did not clearly predict morbidity and mortality among these critically ill patients

1. Kalil AC, Thomas PG. Influenza virus-related critical illness: pathophysiology and epidemiology. *Crit Care*. 2019;23(1):258.
 2. Juliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *The Lancet*. 2018;391(10127):1285-300.
 3. 4. Crum-Cyffrone NF. Invasive Aspergillosis Associated With Severe Influenza Infections. *Open Forum Infect Dis*. 2016;3(3):ofw171.
 4. Huang L, Zhang N, Huang X, Xiong S, Feng Y, Zhang Y, et al. Invasive pulmonary aspergillosis in patients with influenza infection: A retrospective study and review of the literature. *Clin Respir J*. 2019;13(4):202-11.
 5. Schuurvlieghe AFAD, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Van Tienen C, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. *The Lancet Respiratory Medicine*. 2018;6(10):782-92.
 6. van de Groep K, Verboom DM, van de Veerdonk FL, Haas PA, van der Poll T, Schultz MJ, et al. Detection of invasive aspergillosis in critically ill patients with influenza: the role of plasma galactomannan. *American Journal of Respiratory and Critical Care Medicine*. 2019;200(5):636-8.
 7. van de Veerdonk FL, Kolwijck E, Lestrade PP, Hodiadont CJ, Rijnders BJ, van Paassen J, et al. Influenza-Associated Aspergillosis in Critically Ill Patients. *Am J Respir Crit Care Med*. 2017;196(4):524-7.
 8. Wauers J, Baar I, Meersseman P, Meersseman W, Dams K, De Paep R, et al. Invasive pulmonary aspergillosis is a frequent complication of critically ill H1N1 patients: a retrospective study. *Intensive Care Med*. 2012;38(11):1761-8.