Epidemiologic, clinical, and virologic characteristics of Respiratory Syncytial Virus infection among otherwise healthy adults

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547

Background

- Respiratory Syncytial Virus (RSV) is a well known cause of significant respiratory illness in young infants, geriatric, and chronically-ill adult populations.
- At present, little is known about the clinical characteristics of RSV illness in the healthy adult population.
- In addition, there is a lack of knowledge about the differences in clinical characteristics of RSV illness as compared to other Influenza-like Illnesses (ILI) in healthy adults.
- This is one of the few studies to compare specific symptoms and reveal independent risk factors of RSV illness in healthy adults.

Methods

- From 2009-15, we enrolled otherwise healthy military personnel and beneficiaries into an observational, longitudinal study of influenza-like illness (ILI) at five military treatment facilities across the continental United States.
- Eligibility: Patients presenting for care <72h after the onset of ILI, defined as fever (temperature of 100.4° F or greater at the time of evaluation, or by self-report) and sore throat or one of the following respiratory symptoms: cough, sputum production, shortness of breath, or chest pain. Patients with underlying medical conditions were excluded.
- Clinical and demographic information, and a nasopharyngeal swab were collected at baseline (day 0). Participants returned on days 3±1, 7±2 and 28±7; a daily symptom diary was completed for the first seven days following ILI onset.
- Symptom presence and severity were recorded as: 0 (none); 1 (mild); 2 (moderate); and 3 (severe). Participants were trained by research personnel on the definitions of each score.
- Swabs were tested for influenza by real-time reverse transcription polymerase chain reaction (rtRT-PCR) at the Naval Health Research Center (San Diego, CA). A target-enriched multiplex PCR (TEM-PCR) panel for adenovirus, Coxsackievirus/echovirus, bocavirus, coronavirus, human metapneumovirus, rhinovirus, influenza A/B, parainfluenza and respiratory syncytial virus was also performed by Diatherix Laboratories, LLC. (Huntsville, AL).
- Statistical analyses were performed using SAS (Version 9.3; SAS Institute, Cary, NC) and R Package (version 3.1.3 for Windows). The study was approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences (IDCRP-045).

Results

Table1: Comparing Clinical Outcome/Severity Between Flu-Positive, RSV-Positive and HRV-Positive Adult Cases

	Among Patients tested by Diatherix			
Clinical Measures	*RSV-Positive (N=26)*	*Flu-Positive (N=105)*	*HRV-Positive (N=93)*	*P-value*
Presence of Symptoms				
sneezing	18(69.2%)	57(54.3%)	66(71%)	0.04
nausea	6(23.1%)	45(42.9%)	48(51.6%)	0.03
dizziness	18(69.2%)	42(40%)	34(36.6%)	0.01
Sev/Mod Symptoms				
nose	19(73.1%)	53(50.5%)	60(64.5%)	0.04
sneezing	12(46.2%)	23(21.9%)	29(31.2%)	0.04
sorethroat	19(73.1%)	54(51.4%)	61(65.6%)	0.04
Severe Symptoms				
chills	3(11.5%)	28(26.7%)	10(10.8%)	0.01
muscle	1(3.8%)	33(31.4%)	21(22.6%)	0.01
chest	1(3.8%)	17(16.2%)	6(6.5%)	0.04
Composite Score				
Upper resp.	6.5(4-8)	4(2-7)	6(4-7)	**<0.01**

HRV = Human Rhinovirus

Table 2. Multivariate analysis of factors associated with positive RSV detection (n=898, both children and adults are included in one analysis; Morbid obesity is not included in the analysis due to large proportion of missing data.)

Variables	OR	95% CI
Ethnicity		
White	REF	
African American	1.13	(0.57, 2.23)
Asian	1.94	(0.75, 4.97)
Other	3.29*	(1.72, 6.29)

NOTE *, p<0.05

Table 3: Understanding Demographic Characteristics and Risk Factors Among RSV Detection among Adult ARIC Cases (Univariate Analysis)

	Among Patients tested by Diatherix		
Characteristics	*RSV Positive (N=30)*	*RSV Negative (N=607)*	*P-value*
Currently pregnant(Only adult female <50 yrs)			
Yes	2(12.5%)	14(87.5%)	0.05
No	8(3.1%)	247(96.9%)	
Missing	20	346	

Table 4: Comparing Demographic Characteristics and Risk Factors Among RSV positive cases, Flu positive cases and HRV positive cases among ARIC Cases (Univariate Analysis)

	Among Patients tested by Diatherix			
Characteristics	*RSV Positive (N=26)*	*Flu Positive (N=105)*	*HRV Positive (N=93)*	*P-value*
Smoking status in patients aged 13 and older				
Current Smoker	7(26.9%)	13(12.4%)	30(32.3%)	0.01
Former Smoker	4(15.4%)	20(19%)	16(17.2%)	0.01
Non-Smoker	14(53.8%)	72(68.6%)	46(49.5%)	0.01
Adults with missing status	1(3.8%)	0(0%)	1(1.1%)	0.01
Morbid Obese (BMI>=40)				
Yes	2(8.7%)	1(1.1%)	(0%)	0.01
No	21(91.3%)	93(98.9%)	89(100%)	0.01
Missing	3	11	3	

Discussion

- RSV represented a minority of our ILI cases in healthy adults
- Smoking was significantly more often seen in RSV and HRV illnesses, as compared to Influenza. RSV+ subjects were also more often morbidly obese compared to both Flu+ and HRV+ subjects.
- Non – Caucasian race was also associated with increased risk of detecting RSV.
- Our study also found that pregnancy was a novel, independent risk factor for RSV illness.
- Composite upper respiratory scores were significantly higher in RSV as compared to HRV illness, a well known cause of upper respiratory illness.
- As expected, Influenza positive ILI was associated with more systemic symptoms such as chills, myalgia, and chest pain.

Conclusions

- This is one of few studies to detail the clinical characteristics of RSV illness in healthy adults presenting with ILI.
- We found that RSV is an uncommon, but notable cause of ILI in healthy adults.
- Overall severity of symptoms was generally lower for RSV than ILI caused by rhinovirus and influenza, with the exception of more severe upper respiratory symptoms in RSV cases.
- We also identified novel risk factors for RSV induced ILI: morbid obesity, pregnancy, smoking, and Non-Caucasian race.

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