Etiology Unknown: Are Less Recognized Respiratory Pathogens Associated with a Milder Course of Illness?

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Background
- The use of multiplex diagnostic platforms has greatly improved rates of etiologic determination among patients with influenza-like illness (ILI).
- A viral respiratory pathogen was identified in >90% of otherwise healthy individuals enrolled in our observational study of ILI. Herein we describe the characteristics and clinical severity of illness among those for whom a viral pathogen was not identified.

Methods
- Since 2009, 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 (Figure 1).
- 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, shortness of breath, or chest pain. Patients with underlying medical conditions were excluded.
- Clinical and demographic information, and a nasopharyngeal swab was collected at baseline (day 0). Participants returned for follow-up visits on days 3, 7, and 10 after onset of symptoms. The study was approved by the Institutional Review Board at the Uniformed Services University of the Health Sciences.

Results
- From 2010-2014, a sample of 898 cases with ILI were tested for viral and bacterial respiratory pathogens using DiaMetr TEM-PCR.
- A viral pathogen was detected in 64.9% (583/898) of cases and was associated with negative detection of viral pathogens in the multivariable logistic regression model (2 table 1 and Figure 2).
- From 2009-2013, a sample of 898 cases with ILI were tested for viral and bacterial respiratory pathogens using DiaMetr TEM-PCR.
- A viral pathogen was detected in 64.9% (583/898) of cases and was associated with negative detection of viral pathogens in the multivariable logistic regression model (Table 1). The composite severity scores reported by adults with viral detection were significantly higher than pan-negative cases.

Conclusions
- Cases with no detectable viral pathogens (pan-negative) tended to be older and had milder clinical symptoms. It is possible that patients with milder clinical symptoms had lower levels of viral shedding (i.e., below the lower limit of detection).
- Pan-negative adults had higher detection of bacterial respiratory pathogens. No such difference was found in children. The role of bacterial pathogens to ILI warrants further study and may affect management strategies for these patients.

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Figure 2. Distribution of number of viral pathogens detected among 898 ARIC patients using DiaMetr TEM-PCR Respiratory Panel, by age

Table 1. Characteristics of 898 ILI patients tested by DiaMetr TEM-PCR Respiratory Panel, by viral detection status

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Figure 3. Clinical severity and outcomes between adults with and without viral detection (all P<0.05)

Figure 4. Composite severity scores between adults with and without viral detection

Similarity between adolescents and children: ILI severity and outcomes between adults with and without viral detection (all P<0.05)