Molecular Detection of Human Rhinovirus in Hospitalized Kansas City Children (2009-2012): Demographics, Chest Radiograph Findings and Length of Stay in Relation to Pre-existing Comorbidity

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Abstract

Background: Human rhinovirus (HRV) is the pediatric respiratory virus most often detected by routine molecular diagnostics. The relevance/utility of HRV detection remains unclear. We performed a 40month retrospective review of hospitalized children (Jan 2009May 2012).

Methods: Multiplex PCR testing detected ≥1 virus in 2375 patients (1290 HRV/enterovirus (EV)). Excluding nosocomial HRV, confirmed EV, NICU/immunocompromised patients, and charts with missing data, 617 charts were reviewed. Chest Xrays (CXR) were interpreted by a blinded pediatric radiologist. Admission groups and definition:
1. Bacterial N= 72 (11.7%): confirmed serious bacterial infection (SBI);
2. Equivocal N=37 (5.6%): pneumonia unconfirmed as bacterial or viral;
3. Nonbacterial N=509 (82.6%). Preexisting comorbidities were noted in 154/617.

Results: HRV was the sole virus in 85%. Peak HRV detection was Mar-May and Sept-Nov. Male/female ratio was 329/288; 76% were <3 yrs old. There were 55 PICU stays (15 bacterial and 35 nonbacterial). HRV results were available at Mn 1.54d (08.5) post admit but returned after hospital discharge (D/C) for 177/617. For all 509 nonbacterial admits, the D/C rate by 48hr after HRV results were available was 46% and Mn length of stay (LOS) was 8.1d (range 0-402d, St Dev +27.3). For the N=439 with HRV results available to clinicians before patient D/C, the D/C rate was 57% and LOS 8.2d (0-196, +13.6). The D/C rates at both 24hr and 48hr after HRV results became available were less, p<0.001, for patients with preexisting comorbidity (23.7% and 33%) vs for previously healthy patients (57.4% and 67% respectively). A comorbidity effect on D/C rate and LOS held true for PICU admits (p=0.02). CXR on 386 patients (SBIs excluded) showed 74 normal, 2 atelectasis only, 211 viral pattern, 25 bacterial pattern, and 74 mixed pattern. CXR suggested underlying chronic lung disease in 39 and congenital heart disease in 31.

Conclusion: Almost 90% of non-SBI admits had HRV as the sole detected pathogen (70%of PICU cases). ¾ of HRV occurred in children <3 years old. Molecularly detected HRV was associated with early D/C for previously healthy children. During admission, CXR patterns in almost 2/3 HRV patients were inconsistent with a bacterial process. HRV seems an important pathogen in hospitalized, even previously healthy, children. Our data may allow less antibiotic use and early discharge.

Introduction

Human rhinovirus (HRV) is frequently detected in hospitalized children [(1)] with and without respiratory symptoms in the era of routine molecular multiplex testing. HRV may cause severe disease in children with co-morbidity. [(2)] It is unclear if HRV test results change resource utilization or management. We evaluated 2 respiratory seasons and the interval between, for the impact of chest-ray (CXR) and HRV results on length of stay (LOS) and related to patient risk factors and demographics

Methods

- Retrospective chart review focusing on HRV(+)
- Mid turbinate specimens – flocked swab
- Multiplex PCR tests by Luminex XTAG multiplex respiratory panel
- 40 months: Jan 2009–May 2012
- N = 2375 patients with any respiratory virus
- N = 694 (29.2%) HRV/enterovirus (EV) for whom data collected
- Exclusions: (N=77)
  - Nosocomial HRV (N=52) or confirmed EV (N=22)
  - NICU/immunocompromised patients (N=1)
  - Charts missing key data (N=2)
- **N = 617 patients for whom data analyzed**
- CXR (N=386) interpreted by blinded pediatric radiologist [(3)]
- Stats - X^2 for dichotomous variables
  - Student t test for continuous variables
  - ANOVA for multiple group comparison

Results 1

- **General: All HRV(+) Patients – N=617**
  - Most (76%) HRV found in children <3 years old. **Fig. 1**
  - Peak HRV detection = Mar-May and lesser in Sept-Nov. **Fig, 2**
  - HRV was the sole detected virus in 85%
  - Co-morbidity pre-existing in 159 (26%)
  - PICU admissions: N = 55 (15 bacterial and 35 nonbacterial)
- **Annualized HRV admission rate – Table 1**
  - No difference year-to-year for patients with co-morbidity
  - **Higher rates for previously healthy HRV patients in 2009 & 2011**

Table 1. Annualized HRV rate/1000 admissions

	2009	2010	2011	2012
With co-morbidity	4.45	3.91	4.64	4.01
Previously Healthy	**19.54**	**7.63**	**11.91**	**6.05** (P < 0.05)

- **Overall HRV molecular test results availability:**
  - Overall mean = 1.54d (S.D. ±0.85d)
  - Available before hospital discharge (D/C) in 540 / 617 (71.3%)
- **HRV (+) Groups by Reason for Admission :**

1. Bacterial cause for admission detected* N= 71 (11.7%):
   - Confirmed serious bacterial infection (SBI) or pertussis
   - 19 UTI, **13 pertussi**s, 10 empyema, 11 bacteremia/sepsis, 5 meningitis, 6 cellulitis/abscess, 9 other
2. Equivocally a bacterial cause for admission N=37 (5.6%): Uncomplicated pneumonia, unconfirmed as bacterial or viral
3. No bacterial cause for admission detected **N=509** (82.6%) Not any of above diagnoses

* Concurrent AOM not considered a bacterial admission etiology – N=26)

- **General: Non bacterial admission's - N= 509 analyzed**

  Age = Mean 24.0±35 mos

  Gender = 54.8% male; 279 male/230 female

  Race/ethnicity: 316 White, 80 Black, 49 Hispanic 44 Mixed, 8 not reported, 1 Native American
- Comorbidity = 23.2% (118/509) nonbacterial HRV admissions
  - 44 asthma, 37 congenital heart disease, 28 neuromuscular disease, 9 chronic lung disease/CF

Results 2

Figure 1. Age Distribution of HRV (+) Hospitalized Patients

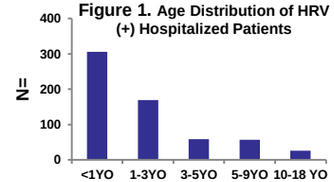
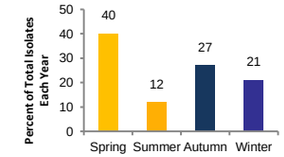


Figure 2. Seasonality of HRV Detection



Hospital Course for Nonbacterial admission Group

Length of stay (LOS) not different whether HRV Results available pre-D/C

- Overall: N= 509 with HRV results available **pre or post** D/C
  - Mn LOS = **8.1d (range 0-402d, SD 27.3)**
  - 46% discharged by 48hr post availability of HRV results
- Subset: N=439 with HRV results available only **pre**-D/C:
  - Mn LOS = **8.2d (range 0-196, SD 13.6**)
  - 57% discharged by 48hr post HRV results availability

Presence of Co-morbidity extended LOS (Table 2; Figure 4)

Table 2. Time to D/C post availability of HRV test

	By 24hr	By 48hr
With Co-morbidity	23.7%	33.0%
Previously healthy	**57.4%**	**67.0%**

p<0.001 for both

Comorbidity also affected D/C rate and LOS in PICU (p=0.02)

- 0/15 (0)% with vs. 10/25 (40%) without co-morbidity had <3 day LOS

Blinded Interpretation of CXR at closest to HRV Testing

Table 3. % D/C Rate at 24 hrs after Admit by CXR Result N=609

CXR Result	Pre-existing Co-morbidity	Otherwise Healthy	P	Overall	P
No CXR	35.7	77.0	0.06	56.3	
Normal	33.3	68.9	0.002	46.1	
Bacterial	33.3	44.4	NS	28.2	0.010
Mixed	22.5	32.1	NS	20.8	0.008
Viral	14.0	57.3	0.002	42.9	

- CXR available for 386 nonbacterial admits: **Figure 5**
- Most common interpretation: Viral pattern – N=211 (55%)
- CXR suggested chronic lung dis (N= 39), congenital heart dis (N= 31)

Results 3

Figure 4. Faster Discharge post HRV Test Result Availability w/o Co-morbidity

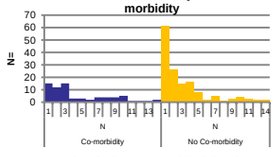
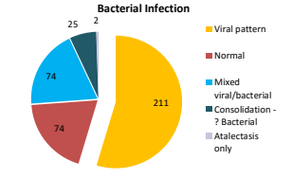


Figure 5. Chest Xray Blinded Interpretation for N=386 HRV Patients with no Known Bacterial Infection



Discussion

Known aspects of HRV infection that we confirmed

- HRV was the only virus detected in 85% of inpatients with HRV
- Modest seasonality (Spring > Fall > Winter > Summer)
- 76% of HRV (+) inpatients < 3 yo [(4)]
- No racial / ethnic differences in HRV (+) inpatients
  - i.e. race/ethnicity paralleled that of our region
- No effect overall on LOS due to availability of HRV results

New aspects of data

1. Possible biannual increase in HRV admits in otherwise healthy children
2. ¼ of HRV(+) inpatients had pre-existing co-morbidities
3. If no patient co-morbidity, HRV result availability on D1 of admit associated with D/C more often at both 24 & 48 hrs thereafter
4. Normal CXR or insufficient respiratory symptoms to warrant CXR predicted early D/C in HRV(+) inpatients
5. HRV (+) inpatients w no co-morbidity BUT w viral pattern CXR
   - D/C at 24hrs not different than those w normal or no CXR

Conclusion:

HRV test result availability plus a CXR without consolidation in otherwise healthy HRV (+) inpatients predicted early D/C.

Prospective studies could confirm the utility of this combination in management pathways aimed at safely reducing resource utilization, e.g. hospital costs and antibiotic use.

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