Impact of Multiplex Polymerase Chain Reaction Testing for Respiratory Pathogens on Healthcare Resource Utilization for Pediatric Inpatients

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Objective To assess whether multiplex polymerase chain reaction (mPCR) vs non-mPCR testing impacts the use of antibiotics, chest radiographs, and isolation precautions.

Study design We retrospectively compared use of antibiotics, chest radiographs, and isolation precautions for patients <18 years old (excluding neonates) hospitalized at a tertiary referral center tested for respiratory pathogens in the emergency department or during the first 2 hospital days, during 2 periods: June 2010-June 2012 (non-mPCR group) vs October 2012-May 2014 (mPCR group).

Results Subjects (n = 2430) in the mPCR group were older, had more complex chronic conditions, and were admitted to the pediatric intensive care unit more often compared with the non-mPCR (n = 2349) group. Subjects in the mPCR group had more positive tests (42.4% vs 14.4%, $P < .01$), received fewer days of antibiotics (4 vs 5 median antibiotic days, $P < .01$), fewer chest radiographs performed, (59% vs 78%, $P < .01$), and were placed in isolation longer (20 vs 0 median isolation-hours, $P < .01$) compared with the non-mPCR group. In multivariable regression, patients tested with mPCR were less likely to receive antibiotics for ≥2 days (OR 0.5, 95% CI 0.5-0.6), chest radiographs at admission (OR 0.4, 95% CI 0.3-0.4), and more likely to be in isolation for ≥2 days (OR 2.4, 95% CI 2.1-2.8) compared with the non-mPCR group.

Conclusions Use of mPCR testing for respiratory viruses among hospitalized patients was significantly associated with decreased healthcare resource utilization, including decreased use of antibiotics and chest radiographs, and increased use of isolation precautions. *(J Pediatr 2016;173:196-201)*.

Multiplex polymerase chain reaction (mPCR) for diagnosis of respiratory pathogens is increasingly used in pediatric inpatient facilities.[1,2] Food and Drug Administration-approved mPCR assays now enable detection of a broader array of viruses with higher specificity, sensitivity, and faster turnaround time than previous testing using immunoassays or cultures.[3,4] Although rapid identification of a viral etiology for clinical illness could affect healthcare resource utilization, this has not been established conclusively in hospitalized children.[5] Previous work assessing the impact of mPCR testing on clinical outcomes such as duration of antibiotic therapy or length of stay in pediatric clinical settings has shown inconsistent results.[2,6] These studies assessed mPCR use in the emergency department[7] or in an ambulatory care setting,[2] limited subjects to those tested with mPCR[6] or those with specific diagnoses,[8] and did not adjust for seasonal trends.[4]

From July to September 2012, New York-Presbyterian Morgan Stanley Children's Hospital transitioned from the use of non-mPCR testing methods to the use of mPCR testing to identify respiratory pathogens. The objectives of this study were to compare the impact of using mPCR vs non-mPCR testing for respiratory pathogens at hospital admission on the utilization of healthcare resources for pediatric inpatients as measured by duration of inpatient antibiotic therapy, chest radiograph use on admission, and duration of isolation precautions. We hypothesized that using mPCR testing at admission would decrease use of antibiotics and chest radiographs, and increase the use of isolation precautions compared with these outcomes when using non-mPCR testing.

Methods

We conducted a retrospective cohort study of children hospitalized at New York-Presbyterian Morgan Stanley Children's Hospital, a 200-bed tertiary

CUMC	Columbia University Medical Center
EMR	Electronic medical record
ICD-9	*International Classification of Diseases, Ninth Revision*
mPCR	Multiplex polymerase chain reaction
PCR	Polymerase chain reaction
PHIS	Pediatric Health Information System
PICU	Pediatric intensive care unit
RSV	Respiratory syncytial virus

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referral children's hospital located in New York City, who underwent testing for a respiratory pathogen either in the emergency department prior to admission or within the first 2 days of hospitalization. The Columbia University Medical Center (CUMC) Institutional Review Board approved this study with a waiver of consent.

Study subjects eligible for inclusion were hospitalized infants, children, and adolescents under 18 years of age, who were tested for respiratory pathogens in the emergency department prior to admission, in inpatient units, or in the pediatric intensive care unit (PICU) within the first 2 calendar days of hospitalization. Children tested after the first 2 calendar days of hospitalization were not included to restrict the sample to patients with community-acquired illnesses. Newborns admitted to the well-baby nursery and neonatal intensive care unit patients were excluded. All other neonates and infants (hospitalized in units other than well-baby nursery and neonatal intensive care unit), were included in the study population, regardless of age.

Testing for respiratory pathogens for the study period was ordered by the treating clinicians as part of routine care. Though there were no official guidelines, testing was recommended year round for all patients with respiratory symptoms and for febrile infants less than 2 months of age.

Subjects hospitalized between June 2010 and June 2012 were tested with non-mPCR methods. Non-mPCR testing included enzyme immunoassay for influenza and respiratory syncytial virus (RSV), direct fluorescent antigen for parainfluenza and adenovirus, and polymerase chain reaction (PCR) for influenza and RSV, and/or viral cultures, with a turnaround time of 2-5 days. These assays often were performed sequentially (eg, PCR testing was performed first followed by direct fluorescent antigen and/or culture if PCR results were negative). *Mycoplasma* (serology and PCR sent to a commercial laboratory) and *Bordetella pertussis* (culture and PCR sent to a commercial laboratory) testing were offered in the non-mPCR period but were not included in this analysis because results usually were not available within 48 hours and, hence, would less likely influence clinical decisions made during this period. Subjects hospitalized between October 2012 and May 2014 were tested with mPCR methods. Testing used the Food and Drug Administration-approved mPCR Film Array Respiratory panel (BioFire Diagnostics, Inc, Salt Lake City, Utah),[9] which identifies adenovirus, coronavirus (strains HKU1, NL63, 229E, OC43); human metapneumovirus, rhinovirus/enterovirus; influenza (strains A, A/H1, A/H3, A/H1-2009, B); parainfluenza virus (strains 1, 2, 3, 4); and RSV as well as the bacterial respiratory pathogens *Mycoplasma*, *B pertussis*, and *Chlamydophilia*. This panel has high sensitivity (85%-100%), specificity (95%-100%), and at our institution a turnaround time of approximately 3 hours from order entry to results being viewed by providers.[9,10] Hospitalizations from July to September 2012 were excluded to allow providers to become familiar with mPCR testing.

Clinical, laboratory, and demographic data for study subjects were obtained from the CUMC clinical data warehouse and linked with CUMC data from the Pediatric Health Information System (PHIS) database.[11] The CUMC clinical data warehouse includes patient data from the electronic medical record (EMR) and PHIS is a validated administrative database that contains inpatient data from hospitals affiliated with Children's Hospital Association (Overland Park, Kansas). PHIS contains demographic data, *International Classification of Diseases, Ninth Revision* (ICD-9) diagnostic codes, charge data for medications, and laboratory and radiology utilization.[11] Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Demographic data included age, sex, and insurance status. Race/ethnicity data were not included in the final analysis because these data were unreliable and incomplete. Hospitalization data included dates of admission and discharge, dates/times of transfer to and discharge from the inpatient unit and/or PICU, length of hospital stay, and principal ICD-9 diagnosis. Principal ICD-9 diagnoses were categorized as either respiratory or nonrespiratory by study investigators (**Table I**; available at www.jpeds.com). Patients with complex chronic conditions were also identified using ICD-9 diagnoses.[12] The date and results of respiratory pathogen testing were also collected.

Outcome Variables: Antibiotic and Chest Radiograph Utilization, Duration of Isolation Precautions

To measure the duration of antibiotic therapy, contiguous days of antibiotics commonly used to treat community-acquired respiratory illnesses ordered in the emergency department or within the first 2 calendar days of hospitalization were extracted (**Table II**; available at www.jpeds.com). Contiguous days of antibiotics could include different agents to account for narrowing or broadening therapy during a single antibiotic course. To determine utilization of imaging, chest radiographs ordered in the emergency department or within the first 2 calendar days of hospitalization were included to reflect those obtained to manage community-acquired illness. To measure the duration of isolation, the hours of contact isolation, droplet isolation, and/or contact/droplet isolation were calculated using the date/time for initiation and for discontinuation of isolation orders.

Statistical Analyses

Demographic and clinical characteristics of the subjects in the non-mPCR vs the mPCR group were compared using parametric (Student *t* test) and nonparametric (Wilcoxon rank sum test) tests for continuous variables, and the χ^2 test for categorical variables. As PCR was used to detect RSV and influenza in both the non-mPCR and mPCR groups, rates of positivity for these 2 pathogens were compared to assess for testing patterns over time. Bivariate analysis determined the association between the use of mPCR testing and the 3 outcome variables: duration of antibiotic therapy, performance of chest radiograph, and duration of isolation precautions. We compared overall antibiotic and isolation utilization rates for mPCR and