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BRIEF REPORT

Respiratory Pathogens in Children 1 Month to 5 Years of Age Presenting With Undifferentiated Acute Respiratory Distress in 2 District-Level Hospitals in Ghana

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Ghanaian children (2176) aged <5 years who presented with undifferentiated acute respiratory distress were tested for respiratory pathogens using a BioFire FilmArray polymerase chain reaction assay. Rhinovirus and/or enterovirus was detected in 36% of the assays, respiratory syncytial virus in 11%, and parainfluenza in 7%. Respiratory syncytial virus and metapneumovirus were detected more frequently in the rainy season than in the dry season.

Keywords: pediatrics; *Picornaviridae* infections; pneumonia; respiratory tract infections; viral diseases.

Despite significant improvements in the survival rates of children younger than 5 years around the world, pneumonia remains a leading killer of children globally [1]. A majority of the 1 million pneumonia deaths per year in children <5 years old occur in low- and middle-income countries; most of them are clustered in Africa [1]. Laboratory diagnostics, such as bacterial cultures and respiratory viral testing, are often lacking in these resource-poor settings [2], which contributes to the dearth of accurate epidemiological data and an unnecessary use of antibiotics, especially outside of tertiary care hospitals. A broad-scope assay that provides an unbiased description of a wide array of respiratory pathogens in children in developing countries is needed.

A recently conducted prospective randomized controlled trial at 2 district-level hospitals in Ghana revealed that the use of continuous positive airway pressure (CPAP) reduces the all-cause mortality rate in children <1 year old who presented with undifferentiated acute respiratory distress [3]. In that study, nasopharyngeal swabs were collected from the children at the time of presentation and tested for common pediatric respiratory pathogens; the goal was to decrease the knowledge gap regarding the incidence of respiratory pathogens that affect children <5 years of age in low- and middle-income countries.

METHODS

Study Sites

The study sites were Mampong District Hospital and Kintampo Municipal Hospital in Ghana; each hospital serves as a catchment area of almost 100 000 people. Both hospitals have limited access to plain radiography, and neither of them can perform bacterial cultures, respiratory virus panels, or blood gas studies or measure C-reactive protein levels. The bimodal rainy season in Ghana runs from approximately April to July as the major season and September to November as the minor season; a long dry season lasts from December through March.

Study Design

Our observational study was part of the prospective CPAP Survival Study [3]. The aims of this observational study are to determine the percentage of children whose nasopharyngeal swab detected a common respiratory pathogen, describe the epidemiology of the pathogens detected, and report the characteristics of patients with and of those without a detectable respiratory pathogen.

The study protocol was approved by and procedures were followed in accordance with the ethical standards of the Columbia University Medical Center Institutional Review Board and local institutional review boards at the Kwame Nkrumah University of Science and Technology and the Ghana Health Services (this study is registered at ClinicalTrials.gov under identifier NCT01839474). The Ghana Food and Drug Authority provided regulatory oversight for the trial.

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Participants

All children who presented to 1 of the 2 hospital emergency departments with a rapid respiratory rate were screened for study eligibility according to the CPAP Survival Study protocol [3]. Specific inclusion criteria were an age of 1 month to 5 years, a respiratory rate of more than 50 breaths per minute in children aged 1 to 12 months or more than 40 breaths per minute in children older than 12 months, and use of accessory muscles or nasal flaring. Patients were excluded if they had a contraindication to the use of nasal CPAP. Written documentation of informed consent was obtained.

Specimen Collection, Storage, and Transport

For the collection of nasopharyngeal swabs, a sterile cotton-tipped swab was inserted gently into 1 nostril, rolled gently in the posterior nasopharynx, and then withdrawn slowly. The swab was placed immediately into a MicroTest M4RT vial containing transport and storage medium (Remel, Lenexa, Kansas). Specimens were placed immediately in a −20°C freezer at each study site. Approximately once per week the frozen specimens were collected and transported by land in an insulated cooler with frozen icepacks to a −80°C freezer at the Kwame Nkrumah University of Science and Technology in Kumasi, Ghana. Every 6 months, the specimens were transported by commercial airline on dry ice to Columbia University, where they were stored at −80°C until the time of testing.

Specimen Testing

Nasopharyngeal specimens were tested using the FilmArray assay (BioFire, Salt Lake City) [4]. The assay can detect adenovirus, coronavirus strains 229E, HKU1, OC43, and NL63, metapneumovirus (MPV), rhinovirus and/or enterovirus (RV/ENT), influenza types A, A/H1, A/H1-2009, A/H3, and B, parainfluenza types 1, 2, 3, and 4, respiratory syncytial virus (RSV), *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*.

Statistical Analysis

Data were analyzed using GraphPad Prism 7.00 for Windows (GraphPad Software, La Jolla, California). Figures were constructed in Microsoft Excel. Descriptive statistics were used to present the data; the t test was used to compare means, analysis of variance for multiple comparisons of means, and the χ^2 test to compare proportions.

RESULTS

A total of 2486 children were assessed for eligibility, 2200 children were enrolled, and 2176 (99%) nasopharyngeal specimens were collected, transported, and tested for respiratory pathogens. Of the 2176 specimens tested, 1 or more pathogens were detected in 1276 (59%). Most patients (71%) with a positive polymerase chain reaction (PCR) assay result were younger than 2 years. Fifty-six percent of the patients were male; the median weight was 9.0 kg, and the median presenting respiratory rate, heart rate, pulse oxygen saturation on room air, and temperature were 56 breaths per minute, 152 beats per minute, 98%, and 37.5°C, respectively. Patients with a positive PCR result (n = 1276) were younger, weighed less, presented with a higher respiratory rate, had a higher hemoglobin level and white blood cell count, had malaria detected less often, and received less antimalarial therapy but more antibiotics than those whose PCR result was negative ($P < .001$).

The most commonly detected organisms were RV/ENT (n = 776 [36%]), RSV (n = 248 [11%]), parainfluenza viruses (n = 154 [7%]), coronaviruses (n = 102 [5%]), MPV (n = 81 [4%]), adenovirus (n = 79 [4%]), influenza A (n = 39 [2%]), and influenza B (n = 18 [1%]). The presence of bacteria was identified in 8 patients with *Chlamydophila* sp infection, 5 with pertussis, and 3 with *Mycoplasma* sp infection (Figure 1A). The distributions of organisms detected among the 2 study sites were similar. Only 1 respiratory pathogen was detected in 1064 (83.4%) specimens, 2 pathogens in 190 (14.9%) specimens, 3 pathogens in 19 (1.5%) specimens, and 4 pathogens in 3 (0.2%) specimens. Children with RSV were younger, weighed less, had a higher respiratory rate, a higher hemoglobin concentration, a lower oxygen saturation, and a lower rate of malaria than the children in whom another virus was detected ($P < .0001$, analysis of variance).

Forty-six of the patients with a positive PCR result died. RV/ENT (89%), RSV (6.5%), coronaviruses (6.5%), and parainfluenza viruses (4%) were the most common organisms detected in this group.

RSV and MPV were detected more often between the months of July and December in both years of the study period, whereas parainfluenza and adenovirus were detected more often between January and June (Figure 1B). RV/ENT was detected equally throughout both years.

DISCUSSION

In this report, we describe the respiratory pathogens detected in children aged 1 month to 5 years who presented to 1 of 2 district-level hospitals in Ghana with undifferentiated acute respiratory distress. We found a significant burden of respiratory viruses that might have been contributing to their clinical presentation and need for medical care. A viral pathogen, most commonly RV/ENT, was detected in the majority of the study participants.

RVs and ENTs are among the most frequent infectious agents globally [5]. Because of the similarities of these 2 viruses, our assay was unable to differentiate them from each other. Because almost half of the patients in whom RV was detected were asymptomatic in other studies [6], the role of RV as a lower

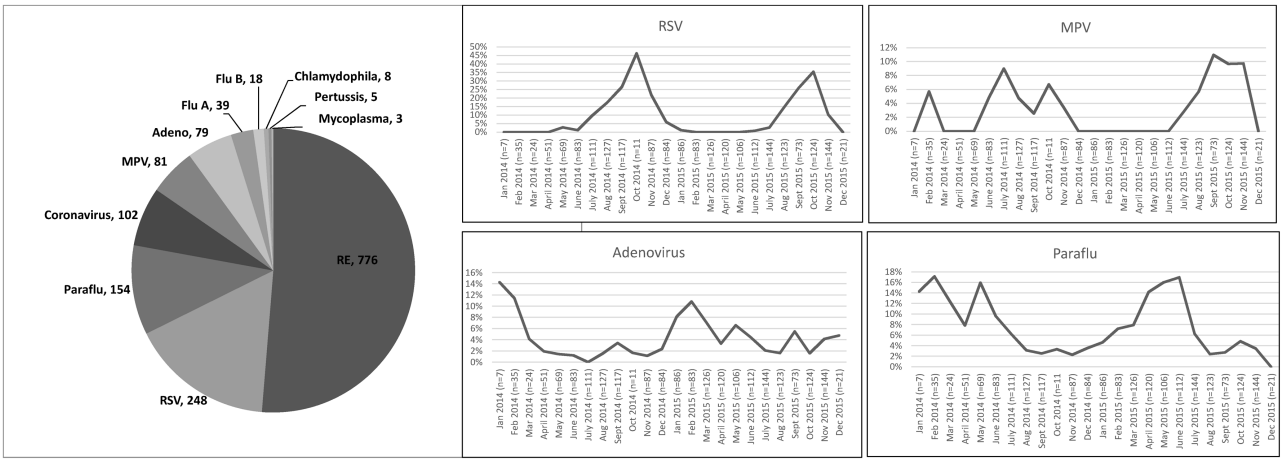

Figure 1. (A) Frequency of organisms detected among the 1276 children with a positive PCR result; 1513 pathogens were detected. (B) Percentages of participants with a specific pathogen detected each month of the 2-year study period. n = number of participants enrolled during each month. Abbreviations: adeno, adenovirus; MPV, metapneumovirus; paraflu, parainfluenza; RE, rhinovirus and/or enterovirus; RSV, respiratory syncytial virus.

respiratory tract pathogen remains uncertain. However, current advances in molecular diagnostic techniques have revealed the presence of RV in the lower respiratory tract, and its role in lower airway diseases is increasingly being reported [5, 7]. As in other studies [8, 9], RSV was detected in a significant proportion of children in our study. Children with RSV were found to be younger and to have more severe respiratory symptoms than children with a different viral infection, which is consistent with previous reports in the literature [9, 10]. Influenza was detected in fewer than 3% of the participants, and we found no apparent seasonal peak in this 2-year study. Because tropical climates usually lack identifiable fall, winter, spring, and summer seasons, the incidence of viral respiratory pathogens might not be similar to those in temperate climates. In Ghana, we found a clear increase in the incidence of RSV and MPV during the rainy months and a marked decrease in the dry season, which might be an effect of more crowding during the rainy season, because it is often seen during the winter months in other settings.

There were several limitations to this study. Because this study was part of another study, children were excluded if they did not meet the criteria for safe use of nasal bubble CPAP. No chest imaging was available, and bacterial cultures were not performed. Testing on specimens obtained from the upper airway was performed and might not represent a true infection of the lower airway. Also, the human immunodeficiency virus status of the study participants was not known, but other literature suggests that its incidence in Ghana is low [11].

Despite the limitations of this study, our results show that viral respiratory pathogens were frequent among children aged 1 month to 5 years who presented with acute respiratory distress to 1 of 2 district-level hospitals in Ghana. RV/ENT was detected most often, but additional studies are needed to determine the role that these viruses play in moderate-to-severe respiratory illness in children who live in a low-income country. RSV and MPV were detected more frequently in the rainy season than in the dry season, and additional studies are needed to elucidate the exact mechanism of the observed seasonal variation.

Notes

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