Case Report

Increased household exposure to respiratory pathogens in HIV exposed uninfected children due to maternal HIV

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Abstract

Little is known about household exposures to respiratory pathogens in HIV-exposed uninfected children (HEU) in Indian families. This case series investigates the nasopharyngeal carriage of *Streptococcus pneumoniae*, *Staphylococcus aureus*, and respiratory viruses at multiple points in three mother child pairs: (1) an HIV-infected child and mother, (2) an HEU child and HIV-infected mother, and (3) an HIV-unexposed uninfected (HUU) child and mother. Nasopharyngeal carriage densities of *Streptococcus pneumoniae* and *Staphylococcus aureus* were higher in mothers and children living in HIV-affected households, regardless of the child's HIV status. Maternal HIV and ART status impact these household exposures.

Keywords: Antiretroviral therapy, HIV-exposed uninfected children; household exposure, maternal HIV, respiratory microbes

Introduction

Compared with unexposed children, HEU children are at 70% increased risk of all-cause mortality, specifically from lower respiratory tract infections. Respiratory pathogen exposures of HEU children living in HIV-affected Indian households are unknown. This case series is unique in presenting carriage information across time in three households: (1) an HIV-infected child and his mother (2) an HEU child and his mother, and (3) an HIV-uninfected child and his mother from rural India.

Case History

We present a case series of three families with similar socioeconomic backgrounds who participated in a vaccine study on the impact of *Haemophilus influenzae* type b (Hib) and pneumococcal conjugate vaccines (PCV) on nasopharyngeal carriage in children and parents affected by HIV in West Bengal, India.[1] Case 1 is a child living with HIV (CLH); case 2 is an HEU child; and case 3 is an HUU child. We determined nasopharyngeal carriage of *Streptococcus pneumoniae*, *Staphylococcus aureus*, and respiratory viruses by culture and PCR in children and their mothers at multiple points between February 2012 and October 2014.

Case 1: HIV infected child and mother

A 4-year-old boy with perinatal HIV was enrolled in March, 2012, with a baseline CD4 count of 889 cells/mm^3 and viral load of 5560 copies/mL. He was on trimethoprim/sulfamethoxazole (TMP/SMX) but not on ART. He lived with his mother who was HIV infected, four adults, and six children, in a four-room mud house. They used pond water for bathing, tap water for drinking, and cow dung for cooking. He attended school. Their family income was INR 3000--5000/month. His father had died of HIV and tuberculosis (TB). His mother, treated for TB in the past, was on ART. This child had never had TB prophylaxis or

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treatment. He had received BCG, DPT1-4, OPV1-4, and measles vaccines. His baseline weight-for-age Z-score (WAZ) was −4.6 and height-for-age was Z-scores (HAZ) −2.5. Pneumococcus was isolated three times, the highest carriage density was 3.77×10^8 copies/ml, *S. aureus* twice, and Hib once [Table 1]. Both he and his mother had dual colonization with pneumococcus and *S. aureus*. His mother had *S. aureus* carriage at two other times. The highest carriage density for pneumococcus for mother was 5.56×10^3 copies/mL. Pneumococcal isolates were resistant to tetracycline, ofloxacin, azithromycin, and TMP/SMX. No respiratory virus was detected.

Case 2: HEU child and HIV-infected mother

A 3.75-year-old boy born to HIV-infected parents by normal home delivery was enrolled in April, 2012, and misclassified as HIV positive. His CD4 count was 748 cells/mm^3. He was on TMP/SMX. He lived with his parents who were both HIV infected, his father was on ART, but his mother was not. He was breastfed till 8 months.

At study entry, HIV plasma viral load showed undetectable HIV and a repeat serologic HIV test confirmed that he was indeed HIV uninfected. He had gotten BCG, DPT1-5, OPV1-4, measles1, and hepatitis B1-3. He lived with four adults in a two-room brick house. Tube well was used for drinking and bathing and coal and wood for cooking. He attended school. Their medium income was INR 3000--5000/month. His baseline WAZ was −0.86 and HAZ was −0.97.

Pneumococcus was isolated at baseline with carriage density of 1.1×10^{10} copies/mL [Table 1]. He had dual colonization of pneumococcus and *S. aureus* twice. In four of six visits, he had rhinorrhoea and cough. Rhinovirus, adenovirus, and parainfluenza 4 virus were isolated at different times.

His mother had pneumococcal carriage at five of six visits with carriage density of 1.43×10^{10} copies/mL and had dual colonization with *S. aureus* in three [Table 1]. Pneumococcal isolates were resistant to tetracycline, erythromycin, ofloxacin, and TMP/SMX.

Case 3: HUU child and mother

A 3-year-old boy born to HIV-uninfected parents by normal institutional delivery was enrolled in October, 2013. He was breastfed till 3. He attended school. He had received BCG, DPT1-4, OPV1-4, measles1, hepatitis B-1, and Japanese encephalitis. He lived with his parents, two adults, and two children. They used well water for bathing and drinking, cow dung as cooking fuel, and lived in a mud house. His baseline WAZ was −1.25 and HAZ was −0.62. The family's income was INR 3000--5000/month.

He had one time pneumococcal carriage at 2.90×10^5 copies/mL [Table 1]. His mother had respiratory syncytial virus isolated once.

Discussion

Nasopharyngeal carriage densities of pneumococcus and *S. aureus* were higher in both mothers and children living in HIV-affected households, regardless of the child's HIV status. Case 2, the HEU child, had more frequent bacterial and viral carriage. The mother of the HEU child, not on ART, was frequently colonized with high densities of pneumococcus and *S. aureus* compared with the mother of case 1 who was on ART.

Maternal HIV has a profound impact on the health outcomes of exposed offspring. HEU children have increased mortality if their mothers have high HIV viral loads and CD4 counts <350 cells/mm^3.[2] In Mozambique, HEU children

Table 1: Comparison of nasopharyngeal colonization of *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae* type b and their density (copies/mL), and viral activity in HIV-infected child and his mother, HIV-exposed uninfected child and his mother, and, HIV-unexposed uninfected child and his mother at different time points (V1--V6) during the entire study period

	CLH*	MCLH	HEU	MHEU	HUU	MHUU
V1	*S. pneumoniae* (3.77×10^8/mL), *S. aureus* (1.07×10^4/mL)	*S. pneumoniae* (5.56×10^3/mL), *S. aureus* (3.95×10^3/mL)	*S. pneumoniae* (1.1×10^{10}/mL), *S. aureus* (2.41×10^9/mL) Hib, Rhinovirus	*S. pneumoniae* (1.43×10^{10}/mL) *S. aureus* (2.10×10^9/mL)	*S. pneumonia* (2.90×10^5/mL)	Negative
V2	Negative	Negative	S. pneumoniae (4.33×10^9/mL), S. aureus (2.62×10^4/mL), Rhino & Adeno virus	*S. pneumoniae* (3.93×10^8/mL), *S. aureus* (5.16×10^7/mL), Rhinovirus	-	-
V3	Hib, *S. pneumoniae*	Negative	*S. aureus* (4.98×10^4/mL)	*S. pneumoniae* (8.12×10^5/mL), S. aureus (2.92×10^3/mL)	Negative	Negative
V4	S. pneumoniae	S. aureus	Rhino, Adenovirus	*S. pneumoniae* (6B)†	-	-
V5	*S. aureus* (5.18×10^6/mL)	Negative	Negative	Negative	Negative	Negative
V6	Negative	*S. aureus* (1.48×10^3/mL)	*S. pneumoniae* (1.4×10^8/mL), Parainfluenza 4 virus	*S. pneumoniae* (5.21×10^7/mL) (6B)†	Negative	RSVA/B‡ virus

*Nasopharyngeal swabs were collected from HIV infected child (CLH) and HIV-exposed uninfected child (HEU) and their respective mothers MCLH, MHEU at 6 scheduled visits while HIV-unexposed uninfected child (HUU) and his mother (MHUU) had nasopharyngeal swabs from 4 visits (V1, V3, V5, V6) as part of the study plan. Nasopharyngeal swabs were subjected to culture for the identification of Streptococcus pneumoniae (S. pneumoniae), *Staphylococcus aureus (S. aureus) and Hemophilus influenzae type B (HiB)*. Swabs were also tested for 21 respiratory viruses and 4 bacteria by quantitative multiplex real time PCR as part of the FTD Respiratory pathogens 21 plus kit (FTD Diagnostics®). Following identification the pneumococcal isolates were serotyped by Quellung method. †Pneumococcal serotype, ‡Respiratory Syncytial Virus A/B

had two times the mortality of HUU children, increased hospitalizations, and higher rates of malnutrition.[3]

HEU children have increased morbidity and mortality from lower respiratory tract infections.[4,5] Maternal HIV impacts lung development and respiratory health in offspring.[6] Exposure to HIV in utero especially in mothers, who are untreated as case 2, leads infants to have increased lymphocyte apoptosis, reduced memory B cells, and immune senescence.[7]

HEU infants have increased risk for invasive pneumococcal disease (IPD) compared with HUU children. We found increased pneumococcal density in HIV-infected mother--child pairs, regardless of the child's HIV status.

PCVs prevent IPD and intercept transmission of pneumococcus by decreasing carriage. PCVs are being introduced in India, and both CLH and HEU children need to be included in national programs, given their increased risk for pneumococcal disease.

HIV infection increases the risk of *S. aureus* infection. We found increased *S. aureus* carriage in HIV-infected mother--child pairs, regardless of the child's HIV status and higher *S. aureus* density in the ART naïve HIV-infected mother.

Viral respiratory infections specifically RSV cause hospitalizations and mortality in CLH and HEU children.[7] The HEU child had frequent URIs with viral--bacterial coinfections.[7]

The HEU child had increased carriage and exposure to respiratory pathogens including pneumococcus. Maternal HIV and ART status impact these household exposures.

Programs for prevention of mother-to-child transmission of HIV have dropped rates of HIV infection in children born to HIV-positive women. As a result, there is a growing population of children who are HIV-exposed and uninfected (HEU). This case series will aid primary care physicians and pediatricians in understanding that the HEU child also falls into the category of children who are at increased risk for infection due to perinatal exposure and continued environmental exposure. This highlights the thrust to consider HEU children in a vulnerable high-risk group by healthcare providers.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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