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The Impact of Maternal Human Immunodeficiency Virus Infection on the Burden of Respiratory Syncytial Virus Among Pregnant Women and Their Infants, Western Kenya

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Background. Respiratory syncytial virus (RSV) is an important cause of respiratory illness worldwide; however, burden data on mother–infant pairs remain sparse in sub-Saharan Africa, where human immunodeficiency virus (HIV) is prevalent. We evaluated the impact of maternal HIV infection on the burden of RSV among mothers and their infants in western Kenya.

Methods. We enrolled pregnant women (≤20 weeks' gestation) and followed them and their newborns weekly for up to 3–6 months postpartum, to document cases of acute respiratory illness (ARI). Nasal/oropharyngeal swabs were collected and tested for RSV using polymerase chain reaction. Analyses were stratified by maternal HIV status and incidence was computed per 1000 person-months.

Results. Compared to RSV-negative ARI cases, RSV-positive cases were associated with cough, apnea, and hospitalization among infants. RSV incidence per 1000 person-months among mothers was 4.0 (95% confidence interval [CI], 3.2–4.4), and was twice that among the HIV-infected mothers (8.4 [95% CI, 5.7–12.0]) compared to the HIV-uninfected mothers (3.1 [95% CI, 2.3–4.0]). Among infants, incidence per 1000 person-months was 15.4 (95% CI, 12.5–18.8); incidence did not differ by HIV exposure or prematurity.

Conclusions. HIV infection may increase the risk of RSV illness among pregnant women. Future maternal RSV vaccines may have added benefit in areas with high HIV prevalence.

Keywords. respiratory syncytial virus; human immunodeficiency virus; pregnant women; infants; incidence.

Respiratory syncytial virus (RSV) is the most common cause of viral pneumonia and bronchiolitis in infants and young children worldwide [1, 2]. Globally, RSV-associated hospitalizations and deaths are estimated at 2.7–3.8 million and 48 000–74 500, respectively, among children <5 years of age, with approximately half of the hospital admissions and in-hospital deaths affecting children <6 months [3]. In Kenya, RSV has been identified as a leading cause of acute lower respiratory tract infections (ALRTIs) in infants and is associated with hospitalizations in young children [4–7]. Furthermore, RSV is a common cause of respiratory illness among pregnant women [8], which may increase morbidity and mortality in mothers and their infants [9, 10].

Vaccines, improved monoclonal antibodies, and/or antivirals against RSV may be available in the next few years [11, 12]. Additional evidence on the burden of RSV infections during pregnancy and early infancy would be important, especially in low- and middle-income countries (LMICs), to guide decisions about the introduction of preventive and/or therapeutic tools targeting these populations. Identification of risk groups that could benefit the most from interventions can further help in prioritizing resources where stakeholders deal with competing health priorities. This study sought to evaluate the burden of laboratory-confirmed RSV illness and assess the potential impact of human immunodeficiency virus (HIV) infection among pregnant women and their infants in rural western Kenya.

METHODS

Study Population and Design

From February 2015 through January 2019, we enrolled pregnant women at ≤20 weeks' gestation (gestation determined by fundal height, first date of the last menstrual period, or

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ultrasound) from 2 clinics (Bondo sub-County and Siaya County Referral Hospitals) in Siaya County, Kenya, where the population is culturally homogenous and HIV and malaria infections are prevalent [13, 14]. We followed them weekly through phone calls or home visits until delivery to assess any signs or symptoms of acute respiratory illness (ARI). After delivery, we continued weekly follow-ups among mother–infant pairs for up to 12 weeks, until January 2018. Thereafter, the follow-up period was extended to 24 weeks. If study staff identified any mothers or infants with ARI, they invited them to the study clinic for evaluation, collection of respiratory specimens for RSV testing, and management per routine care. We defined ARI as any of cough, sore throat, or runny nose for mothers; and as any of cough, difficulty breathing, runny nose, or attending clinician's diagnosis of respiratory illness for the infants. We used structured questionnaires to collect demographic and clinical data from patients at enrollment, delivery, and during each sick visit or hospitalization. Medical record reviews were conducted for those hospitalized. Mothers had their HIV status assessed as per the Kenyan Ministry of Health guidelines, which required that, as part of routine antenatal care services, all pregnant women be tested for HIV [15] and prophylaxis be provided when indicated. Although these guidelines require periodic testing for viral load among HIV-positive individuals, our study did not have access to those data. Similarly, we had no access to HIV testing data for infants; we therefore stratified our analysis by HIV exposure for the infants.

Specimen Collection and Processing

We collected nasal and oropharyngeal swabs from consenting patients meeting the ARI case definition during sick visits, combined the 2 into a single vial containing viral transport media, and transported the specimens to the Kenya Medical Research Institute (KEMRI) laboratories in Kisian, Kisumu at 2°C–8°C where they were stored at –80°C until testing. Nucleic acids were extracted from the specimens using the MagMax viral RNA kit on the Kingfisher mL platform (Life Technologies, New York). The extracted material was then tested for RSV in a 1-step real-time reverse-transcription polymerase chain reaction (RT-PCR) assay, using the AgPath-ID 1-step RT-PCR kit (Applied Biosystems, Foster City, California) as per the Centers for Disease Control and Prevention (CDC, Atlanta, Georgia) protocol using CDC's primers and fluorescence-labeled hydrolysis probes. The assay was considered positive for RSV when exponential fluorescence curves crossed the assigned threshold at a cycle threshold value of <40.0.

Data Analysis

We described demographic and clinical characteristics of the patients, stratified by HIV status of the mothers, and compared variables using χ^2 or Fisher exact tests and Student *t* test or Mann–Whitney tests. We considered any 2 RSV detections within a span of 2 weeks in the same participant to represent the same illness episode. One infant, born to a HIV-positive mother, tested positive for RSV 3 times in a span of a month; we treated this as the same episode with prolonged viral shedding. We calculated the rates, per 1000 person-months, as the number of laboratory-confirmed RSV illness cases divided by the person-time at risk in months. We further adjusted for those who were not tested for RSV by dividing the crude rates by the proportion of those who had ARI and had a specimen collected and tested. The 95% uncertainty levels, elsewhere referred to as 95% confidence intervals (CIs), were estimated by running 1000 iterations, each time allowing the proportions of RSV-positive and ARI cases that were tested to randomly vary within a binomial distribution defined by the actual observed proportions and the number of experimental events (RSV tests or ARI cases). The 2.5th and 97.5th values were used to estimate the lower and upper limits of the 95% CI. For pregnant women, person-time at risk was considered as the time from enrollment to a pregnancy outcome (miscarriage or delivery), loss to follow-up (the last day the participant was in contact with the study), or censoring (at last study date, ie, 31 January 2019). For the maternal postpartum period and the infants, person-time at risk was calculated from time of delivery/birth to the last study contact (completion of the 12 or 24 weeks of follow-up, loss to follow-up, or death) or censoring (at last study date, ie, 31 January 2019). We stratified the analysis by trimester of pregnancy, infant age group (monthly), and prematurity (<37 weeks' gestation). We defined the first trimester as 0–13 weeks' gestation, second trimester as 14–27 weeks' gestation, and third trimester as ≥28 weeks' gestation [16] and defined underlying comorbidity as any one of tuberculosis, asthma, chronic obstructive pulmonary disease, diabetes, hypertension, or epilepsy. Analyses were performed using Stata version 13.0 (StataCorp, College Station, Texas).

Ethical Considerations

The study protocol was reviewed and approved by the KEMRI scientific ethics review unit (SSC number 2880) and CDC's institutional review board (CDC IRB number 6709). Written informed consent was obtained from all participants during enrollment.

RESULTS

Characteristics of the Pregnant Women and Their Infants

From February 2015 through January 2019, we enrolled and actively followed 2877 mothers. Of these, 517 (18.0%) were HIV positive and 2233 (77.6%) had delivered by the end of the study period. Four percent of the enrolled mothers had underlying comorbidities—23 (4.5%) and 88 (3.7%) among HIV-positive and HIV-negative mothers, respectively (P = .44). There were 2181 infants born alive and included in this analysis (Figure 1). Of these, 403 (18.5%) were born

to HIV-positive mothers (ie, HIV exposed). Approximately half (1113/2181) of infants were male, and 377 (17.3%) were born preterm (<37 weeks). There was no association between HIV status of the mother and prematurity (P = .44). During the study period, 22 (1.0%) infants died: 6 (1.5%) among the 403 HIV-exposed infants and 16 (.9%) among the 1778 HIV-nonexposed infants; no significant difference was seen in the distribution of infant deaths by maternal HIV status (Table 1). Three stillbirths occurred within 14 days of non-RSV ARI onset.

RSV in Pregnancy and Postpartum

We detected 52 PCR-confirmed RSV cases in 52 of the 2877 (1.8%) pregnant women. In the postpartum period, RSV was detected in 19 specimens from 18 of 2181 (.8%) mothers (Table 1). Of 52 mothers with RSV during pregnancy and 18 mothers with RSV detected in the postpartum period, 19 (36.5%) and 7 (38.9%), respectively, were HIV positive. RSV detection was more common among the HIV-positive women compared to the HIV-negative women during pregnancy (3.7% vs 1.4%, respectively; P < .001) and in the postpartum period (1.7% vs .6%, respectively; P = .03). No difference in RSV-related signs and symptoms was observed among HIV-positive mothers compared with the HIV-negative mothers (Table 2). There were no ARI-associated maternal deaths.

Mothers were followed for 13 989 person-months of pregnancy (median follow-up period for pregnant women: 0 [range, 0–2.3] months in the first trimester, 2.8 [range, 0–3.2] months in the second, and 2.4 [range, 0–4.0] months in the third) and 6344 person-months after delivery. The overall adjusted incidence of RSV and incidence during pregnancy and the postpartum period per 1000 person-months was 4.0 (95% CI, 3.2–5.0), 4.3 (95% CI, 3.1–5.5), and 3.5 (95% CI, 2.1–5.2), respectively (Table 3). The incidence of RSV per 1000 person-months was significantly higher in the HIV-positive group compared to the HIV-negative group (incidence rate ratio [IRR], 2.8 [95% CI, 1.7–4.4]; P < .001). During the pregnancy and postpartum periods, the IRR was 2.7 (95% CI, 1.5–4.6; P = .001) and 3.0 (95% CI, 1.1–7.6; P = .02), respectively. The overall incidence of RSV illness was similar by trimester (Supplementary Table 1). However, incidence was higher among the HIV-positive mothers compared to HIV-negative mothers in all trimesters.

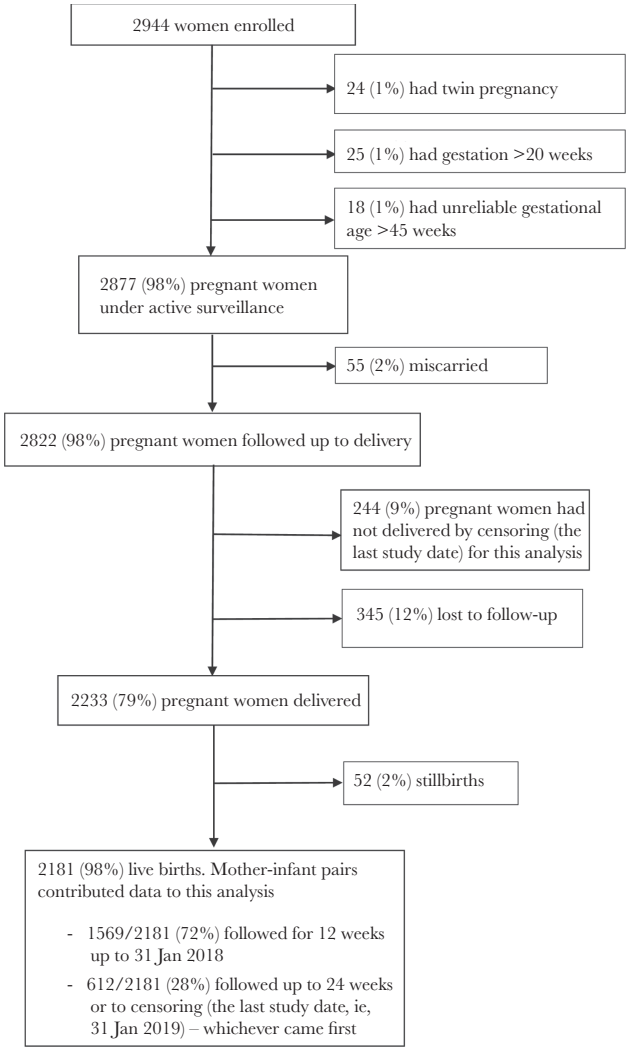

Figure 1. Flowchart of recruitment and follow-up of study participants.

RSV in Early Infancy

We detected 96 laboratory-confirmed RSV illness episodes among 92 of the 2181 infants. Of the 96 episodes, 22 (22.9%) occurred in HIV-exposed infants. Cough and apnea were associated with RSV illness and infants with RSV-associated ARI were more likely to be hospitalized (5/96 [5.2%]) than those with non-RSV ARI (5/1256 [.4%]) (P < .001; Supplementary Table 2). Presenting signs and symptoms were similar among HIV-exposed and unexposed infants. There were no infant deaths associated with RSV. The median length of hospitalization was 6 (range, 3–8) days. One infant required oxygen therapy. Frequency of antibiotic prescription was similar among infants by RSV status as well as by HIV exposure.

Infants were followed for a total of 6344 person-months, with median follow-up of 2.8 months (range, .0–6.0 months). Adjusted incidence of RSV among all infants was 15.5 (95% CI, 12.9–18.8) cases per 1000 person-months, and 19.5 (95% CI, 12.4–27.6) among HIV-exposed infants and 14.6 (95% CI, 11.7–18.1) among HIV-unexposed infants (Table 3). There was no difference in the incidence of RSV among infants by HIV exposure (IRR, 1.3 [95% CI, .8–2.2]; P = .23). The adjusted incidence rate of RSV per 1000 person-months for premature vs term infants was 17.9 (95% CI, 11.8–26.9) vs 15.0 (95% CI, 11.8–18.4), respectively, with an IRR of 1.2 (95% CI, .7–2.0; P = .43) (Supplementary Table 1).

Table 1. Characteristics of Pregnant Women, Pregnancy Outcomes, and Infant Characteristics by Maternal HIV Status, February 2015–January 2019, Western Kenya

Characteristic	All (N = 2877)	HIV^{+} (n = 517)	HIV^{-} (n = 2360)	*P* Value[a]
Pregnant women				
Age at enrollment, y, median (IQR)	24.3 (20.9–29.0)	28.5 (24.4–32.1)	23.6 (20.5–27.8)	<.001
<25 y	1557 (54.1)	139 (26.9)	1418 (60.1)	<.001
≥25 y	1320 (45.9)	378 (73.1)	942 (39.9)	
Education level				
High school and above	1247 (43.3)	132 (25.5)	1115 (47.3)	<.001
Lower than high school	1630 (56.7)	385 (74.5)	1245 (52.8)	
Gestational age at enrollment, wk, median (IQR)	16 (13–18)	16 (12–18)	16 (13–18)	.42
Prior pregnancy	2064 (71.7)	477 (92.3)	1587 (67.3)	<.001
Underlying comorbidity[b]	111 (3.9)	23 (4.5)	88 (3.7)	.44
RSV illness during pregnancy	52 (1.8)	19 (3.7)	33 (1.4)	<.001
Pregnancy outcome				
Miscarriage	55 (1.9)	17 (3.3)	38 (1.6)	.01
Delivery	2233 (77.6)	416 (80.5)	1817 (77.0)	.09
Stillbirth	52 (2.3)	13 (3.1)	39 (2.2)	.23
Survived to discharge	2181 (97.7)	403 (96.9)	1778 (97.9)	
RSV illness in postpartum[c] mothers	18 (0.8)	7 (1.7)	11 (0.6)	.03
Infant characteristics	n = 2181	n = 403	n = 1778	
Male sex	1113 (51.0)	201 (49.9)	912 (51.3)	.61
Prematurity (<37 wk)	377 (17.3)	75 (18.6)	302 (17.0)	.44
Infant death	22 (1.0)	6 (1.5)	16 (0.9)	.27
RSV illness	96 (4.4)	22 (5.4)	74 (4.1)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: HIV^{-}, laboratory-confirmed human immunodeficiency virus negative; HIV^{+}, laboratory-confirmed human immunodeficiency virus positive; IQR, interquartile range; RSV, respiratory syncytial virus.

[a]*P* values estimated using χ^2 or Fisher exact test for categorical variables and Mann–Whitney test for comparison of medians.

[b]Any one of tuberculosis, asthma, chronic obstructive pulmonary disease, diabetes, hypertension, or epilepsy.

[c]Postpartum period was for 12 weeks until January 2018, then we extended the follow-up period to 24 weeks until January 2019.

RSV Illness in Mother–Infant Pairs

Of the 18 mothers who had RSV illness in the postpartum period, 7 (38.9%) of their infants had concurrent RSV illness. Five of the 7 pairs were swabbed on the same day; 3 mothers had an earlier onset than the infants and 2 pairs had the same onset. In 1 of these pairs, the mother had RSV detected first, and 5 days later in her infant. In the last pair, RSV was detected in the infant first and a week later detected in the mother.

Only 1 of 19 (5.3%) children born to an HIV-positive mother who had RSV illness during pregnancy developed RSV in early infancy. In this case, RSV was detected in the mother during the last week of pregnancy, and 2 weeks after birth in her infant. There was no RSV illness among infants born to HIV-negative mothers with RSV illness in pregnancy.

ARI and RSV Seasonality

Acute respiratory illnesses occurred throughout the year, varying in frequency by month without any clear distribution pattern (Figure 2). The frequency of RSV positivity, however, followed a seasonal pattern, with an increase in detections during the months of April through July, coinciding with the rainy season in western Kenya. The peak of infection was in May–June for mothers and their infants alike, and the intensity of the seasons varied with the highest overall percentage of RSV positivity observed in 2017 and 2018 (23.8% and 34.0%, respectively), whereas the overall (mothers and infants) peak percentage RSV detections in the 2 previous years were <15%. Furthermore, we observed a higher RSV incidence per 1000 person-months within the first 3–6 months of life among infants born in March, April, and May (51.2 [95% CI, 40.4–64.1]) compared with those born in the other months of the year (4.7 [95% CI, 3.0–7.1]; Figure 3) (IRR, 10.8 [95% CI, 6.7–18.1]; $P < .001$).

DISCUSSION

We found that the incidence of RSV among HIV-positive mothers during pregnancy and the postpartum period was more than twice that of the HIV-negative mothers overall (8.5 vs 3.1 per 1000 person-months). If HIV infection increases the likelihood of RSV illness in pregnant women, they would be at risk of ALRTIs that could affect them and their pregnancy. Moreover, RSV illness in the mother during the postpartum period could lead to infection of the infant at a time when severe RSV-associated complications are likely. In our cohort, 5% of RSV-positive infants were hospitalized, reinforcing the importance of preventing RSV infection in early life.

Table 2. Clinical Characteristics Associated With Respiratory Syncytial Virus Illness During Pregnancy by HIV Status, February 2015–January 2019, Western Kenya

Clinical Characteristics	RSV in HIV$^+$ (n = 27)	RSV in HIV$^-$ (n = 44)	*P* Value[a]
Signs and symptoms			
Cough	27 (100.0)	43 (97.7)	1.00
Runny nose	16 (59.3)	29 (65.9)	.57
Headache	11 (40.7)	15(34.1)	.57
Reported fever in the last 48 h	7 (25.9)	8 (18.2)	.44
Temperature ≥38°C	0 (0.0)	1 (2.3)	1.00
Shortness of breath	2 (7.4)	0 (0.0)	.14
Chest pain while breathing	2 (7.4)	3 (6.8)	1.00
Muscle/joint pain	2 (7.4)	3 (6.8)	1.00
Nausea/vomiting	1 (3.7)	1 (2.3)	1.00
Abnormal vaginal pain with urination	1 (3.7)	1 (2.3)	1.00
Sore throat	0 (0.0)	6 (13.6)	.08
Diarrhea	0 (0.0)	1 (2.3)	1.00
Care seeking from onset			
≤2 d	20 (74.1)	21 (47.7)	.03
>2 d	7 (25.9)	23 (52.3)	
Hospitalization	0 (0.0)	0 (0.0)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: HIV$^-$, laboratory-confirmed human immunodeficiency virus negative; HIV$^+$, laboratory-confirmed human immunodeficiency virus positive; RSV, respiratory syncytial virus.

[a] *P* values estimated using χ^2 or Fisher exact test.

We observed higher incidence of RSV illness among pregnant women (4.3 per 1000 person-months) compared to studies done with Nepalese [17] and Mongolian [18] populations (.3 and 1.0 per 1000 person-months, respectively). These differences may be associated with variations in the prevalence of comorbidities or other population factors, study case definitions and laboratory methods used, or due to geographical and temporal variations in RSV circulation. We found maternal RSV illness rates similar to those from a South African study, which reported 1.5–6.5 cases per 1000 person-months [19]. Unlike the South African study, we observed a significant difference in the incidence of RSV illness among HIV-positive pregnant women compared to the HIV-negative women. The South African authors attributed the lack of difference in RSV incidence by HIV status to their small sample size. Data on RSV illness among HIV-positive adults are scarce. However, available evidence suggests that HIV-positive patients may be more susceptible to RSV illness [20, 21], and that these patients are more likely to be hospitalized with RSV and to have more severe presentations [21].

The incidence of RSV was high in infants, about 4 times higher that of their mothers. This finding is expected as it is well established that infants bear the highest burden of RSV [5, 22, 23]. The high incidence among infants in our study (15.5 cases per 1000 person-months) was comparable to findings inw

Table 3. Incidence per 1000 Person-Months of Respiratory Syncytial Virus Among Women and Infants Enrolled in the Cohort, by Maternal HIV Status

Group	RSV: Overall			RSV Among HIV$^+$/Exposed			RSV Among HIV$^-$/Unexposed			Rate Ratio (95% CI)	*P* Value[a]
	No.	IR (95% CI)	aIR (95% CI)	No.	IR (95% CI)	aIR (95% CI)	No.	IR (95% CI)	aIR (95% CI)		
All women	71	3.5 (2.8–4.3)	4.0 (3.2–5.0)	27	7.4 (4.6–10.1)	8.5 (5.2–11.6)	44	2.6 (1.9–3.5)	3.1 (2.2–4.1)	2.8 (1.7–4.4)	<.001
Pregnancy	52	3.7 (2.7–4.8)	4.3 (3.1–5.5)	19	7.6 (4.4–11.3)	8.8 (5.2–12.7)	33	2.9 (1.9–3.9)	3.3 (2.2–4.6)	2.7 (1.5–4.6)	.001
Postpartum	19	3.0 (1.7–4.4)	3.5 (2.1–5.2)	8	6.7 (2.5–11.8)	8.0 (3.0–13.8)	11	2.1 (1.0–3.5)	2.5 (1.1–4.0)	3.0 (1.1–7.6)	.02
All infants	96	15.1 (12.6–18.3)	15.5 (12.9–18.8)	22	18.6 (11.8–26.1)	19.5 (12.4–27.6)	74	14.2 (11.4–17.6)	14.6 (11.7–18.1)	1.3 (.8–2.2)	.23

Abbreviations: aIR, adjusted incidence rate; CI, confidence interval; HIV$^-$, laboratory-confirmed human immunodeficiency virus negative; HIV$^+$, laboratory-confirmed human immunodeficiency virus positive; IR, incidence rate; RSV, respiratory syncytial virus.

[a] Compares RSV illness among HIV$^+$ to HIV$^-$ mothers or HIV-exposed infants to unexposed infants.

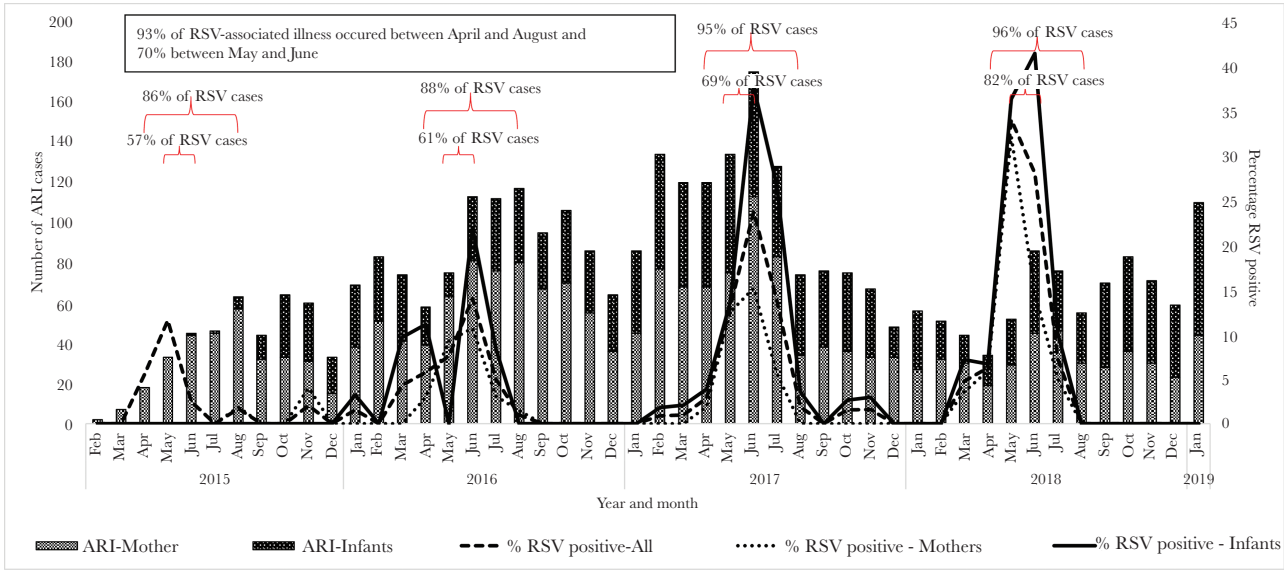

Figure 2. Distribution of acute respiratory illness (ARI) and percentage of laboratory-confirmed respiratory syncytial virus (RSV) among pregnant mothers and their infants by year and month of study, February 2015–January 2019, western Kenya.

Kilifi, Kenya (8.5–17.7 per 1000 person-months among children 0–5 months with ALRTI) [24]. We did not observe any RSV-associated infant deaths. However, those with RSV-associated ARI were more likely to be hospitalized than those with non-RSV-associated ARI, confirming that RSV in infants can lead to severe disease [25, 26] and that RSV infection is associated with high healthcare use and costs [27]. We did not observe a statistically significant difference when we stratified our analysis by HIV exposure. Other studies have found that HIV-exposed infants are at increased risk of acquiring RSV and that they are also at higher risk of severe disease compared to nonexposed infants [28–30]. The difference in our findings and these studies may be attributed to the low RSV case numbers in our study.

Infants whose mothers had RSV during pregnancy did not have RSV during follow-up except for 1 mother–infant pair where the mother had RSV in the last week of pregnancy and the baby was RSV positive within 2 weeks after birth. This observation could suggest a direct infection from the mother to the baby, given that the mother was HIV positive and may have had prolonged viral shedding [19, 31]. Alternatively, it could be that the mother was unable to mount a sufficient immune response against RSV in utero and transfer protective antibody levels to the baby at birth as infection occurred late in pregnancy. This may also suggest that vaccine-induced antibodies from HIV-positive mothers may not afford similar protection to the infants as antibodies transferred by

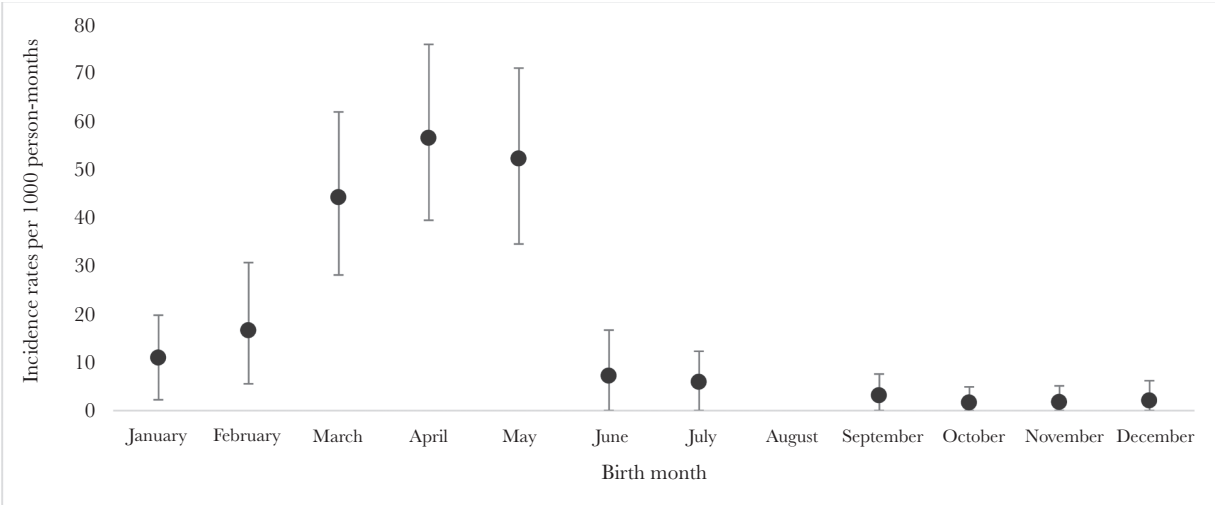

Figure 3. Incidence rate of respiratory syncytial virus infection per 1000 person-months by month of birth, February 2015–January 2019, western Kenya.

HIV-negative mothers [32–34]; therefore, more investigation on RSV-specific vaccine response among HIV-positive patients and their infants, especially the impact of HIV viral load, could guide future vaccine recommendations. Finally, we found that RSV circulation in western Kenya has a clear seasonal pattern, peaking in May–June of most study years and that infants born during March through May had a higher incidence of RSV within the first 3–6 months of life compared to those born in other months. This could be useful should interventions currently in development be ready for the market, as adequate planning on intervention rollout can be timed before the RSV season.

Previous studies by Chu et al in Nepal and Anderson et al in the United States observed an association between prematurity and RSV illness, with the Nepal study finding significantly higher rates of RSV illness in premature infants compared to term infants [35, 36]. In contrast, we found no difference in the incidence of RSV illness by prematurity. Though we did not evaluate the impact of gestational age on RSV infection, it is important to note that previous studies observed a significant decrease in RSV infection with increase in gestational age for premature babies [35, 36]. These data highlight the need for prevention of RSV in high-risk groups including HIV-exposed and premature babies. Maternal vaccination and use of monoclonal antibody therapies currently in different phases of clinical trials may be helpful; however, consideration should be given to cocooning strategies [37], especially in LMICs where monoclonal antibodies may not be affordable.

Our study had some limitations. First, we did not retest HIV-negative pregnant women toward the end of their pregnancy. There could have been some seroconversion in this period, but probably not enough to result in serious misclassification given reductions in HIV incidence in this area [38]. Also, HIV-infected persons have been shown to seek care more than their uninfected counterparts [39]; therefore, caution should be taken while interpreting these findings. Second, we had no access to the HIV viral load and treatment compliance data for the mothers. All of our HIV-positive study participants were on HIV treatment, but we cannot infer the level of suppression provided by the treatment without viral load data. Third, we were unable to access the HIV testing data for the infants and instead relied on their HIV exposure status to assess the possible role of HIV infection on burden of RSV. The findings may be different when actual HIV infection data are used. Last, gestational age was estimated by ultrasound—which is regarded as a gold standard approach in gestational age determination—in 25% of the mothers who delivered. This could lead to misclassification of term and preterm babies, affecting our ability to look at association between RSV and prematurity. This could explain the difference between our study and others that observed difference in RSV incidence by prematurity status.

In conclusion, we found a substantial burden of RSV among mothers and infants in Kenya. The disease burden was higher among HIV-positive mothers who had twice the burden of RSV illness compared to HIV-negative mothers. Maternal RSV vaccine recommendations may have added benefit, especially in high HIV-prevalence areas as in our study. Moreover, prevention measures such as maternal vaccination, cocooning strategies, or monoclonal antibody therapy in early life could potentially reduce the RSV disease burden among infants and could be especially important for HIV-exposed and premature infants. To further inform policy decisions, additional studies on the impact of HIV infection in placental transfer of antibodies may be considered, and the cost-effectiveness of various public health interventions in LMICs should be explored in the context of other competing health priorities.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. B. O. N., N. A. O., and S. S. C. conceived the study. All authors contributed to the study design and implementation. C. O. O., S. L., and J. N. tested the specimens for respiratory syncytial virus. B. O. N. and S. S. C. analyzed and interpreted the data. B. O. N. drafted the manuscript under the supervision of S. S. C. All authors critically reviewed the manuscript for intellectual content and approved the final version.

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