

BACKGROUND

- Perinatal transmission rates are currently less than 1% with a growing population of HIV-exposed but uninfected (HEU) infants.
- HEU infants are at increased risk for hospitalization and have worse outcomes with infections.
- Maternal vaccination is an effective strategy to improve health outcomes in both mothers and infants.
- Few vaccine studies have been conducted in pregnant women living with HIV (WLWH) and there is a paucity of data on rates of vaccination in WLWH and the benefits of vaccination on infant outcomes.
- Our primary outcome of interest was the number of medically-attended healthcare visits for an ARI in HEU infants during the first six months of life. In a secondary analysis, we examined the association of maternal vaccination with gestational age, birth weight, rates of small for gestational age (SGA) and intrauterine growth restriction (IUGR).

METHODS

We conducted a retrospective cohort study of WLWH who received prenatal care and delivered between January 1, 2011 and June 30, 2018 at Grady Memorial Hospital (GMH), a large, urban, publicly funded healthcare system in Atlanta, Georgia.

We utilized a prospective database of HIV-positive women at GMH to identify eligible women and infants. Sociodemographic and clinical data were collected from electronic medical records. Influenza vaccination was defined as documented receipt of vaccine from 12 months prior to delivery date; tetanus, diphtheria, and pertussis (Tdap) vaccination was defined as documented receipt of vaccine from 9 months prior to delivery date.

All infant healthcare visits in the first 6 months of life were included in analysis if the infant presented with ≥ 1 of the following symptoms: fever, nasal congestion, rhinorrhea, hoarseness, new or increased-from-baseline cough, sputum production, dyspnea, wheezing of less than 7 days duration or an admitting diagnosis suggestive of an acute respiratory infection (ARI). Pregnancies without a known delivery date, delivery prior to 20 weeks gestation, delivery of non-viable fetus, twin pregnancies were excluded. Infants subsequently lost to follow-up were excluded from vaccine efficacy analysis. This study was approved by the IRB at Emory University and the Grady Research Oversight Committee.

RESULTS

Among 236 WLWH who received prenatal care and delivered a live-born infant at GMH- 66 (28%) received only influenza vaccine, 32 (14%) received only Tdap vaccine, and 64 (27%) received both. We did not see significant differences in demographics between women who did and did not receive antepartum vaccines (Table 1). WLWH who had any vaccination were more likely to have a viral load >200 copies/mL during pregnancy (p-value 0.024).

217 HEU infants were included in analysis, with 664 healthcare encounters for an ARI. There was a trend towards decreased risk for healthcare visits for ARI among infants born to mothers who received any vaccine during pregnancy (Table 2). Infants born to vaccinated mothers had a trend towards higher median gestational age (Table 3).

	Total Population (n=236)	Flu vaccine only (n=66)	Tdap vaccine only (n=32)	Both Flu and Tdap (n=64)	No vaccine (n = 74)	P-value
Age at delivery, years						
Median (IQR)	28.5 (25.3-33.2)	30.5 (25.6-33.5)	30.2 (25.3-34.2)	28.2 (24.3-34.5)	28.4 (25.4-31.2)	0.17
Race, n (%)						
Black	201 (85.17)	58 (87.88)	25 (78.12)	52 (81.25)	66 (89.19)	0.80
White	12 (5.08)	4 (6.06)	3 (9.37)	2 (3.12)	3 (4.05)	
Hispanic	14 (5.93)	2 (3.03)	2 (6.25)	6 (9.37)	4 (5.40)	
Asian	5 (2.12)	2 (3.03)	1 (3.12)	1 (1.56)	1 (1.35)	
Not specified	4 (1.69)	0 (0.0)	1 (3.12)	3 (4.69)	0 (0.0)	
Parity						
Median (IQR)	1 (1-3)	1 (0-2)	1 (0.5-3)	1 (1-2.5)	2 (1-3)	0.0014
Chronic medical conditions, n (%)						
HTN	33 (13.98)	12 (18.18)	4 (12.5)	8 (12.5)	9 (12.16)	0.59
DM	2 (0.85)	0 (0.0)	0 (0.0)	1 (1.56)	1 (1.35)	0.53
Tobacco use in pregnancy, n (%)						
Yes	48 (20.34)	15 (22.73)	8 (25.0)	9 (14.06)	16 (21.62)	0.74
Prenatal care						
On ART during pregnancy, n (%)	134 (56.78)	37 (56.06)	17 (53.13)	34 (53.13)	46 (62.16)	0.26
CD4, cells/mm³ (IQR)						
At presenting appt	421 (247-620)	449.5 (189-621)	338.5 (257-541.5)	435 (276-636)	416.5 (251-648)	0.85
At delivery	464.5 (282-616)	434 (229-592)	464.5 (337.5-623)	469.5 (331-637)	455 (266-607)	0.75
Viral Load, copies/mL						
During pregnancy, n (%)						
>200	138 (59.48)	32 (48.48)	16 (50.0)	40 (62.50)	50 (67.57)	0.024
>1000	120 (51.72)	31 (46.97)	14 (43.75)	33 (51.56)	42 (56.76)	0.13
Trimester 3, n (%)						
>200	80 (34.33)	18 (27.27)	10 (31.25)	21 (32.81)	31 (41.89)	0.061
>1000	59 (25.32)	14 (21.21)	10 (31.25)	13 (20.31)	22 (29.73)	0.22

Table 2. Relative Risk for Infant Healthcare visit for ARI, any vaccinated vs unvaccinated mother

	RR (95% CI)	P-value	aRR (95% CI)	P-value
Clinic visit (n = 221)	0.75 (0.27, 2.20)	0.62	--	--
ED/urgent care visit (n = 222)	0.79 (0.53, 1.19)	0.26	0.78 (0.51, 1.20)	0.25
Hospitalization (n = 221)	1.56 (0.45, 5.41)	0.48	--	--
ANY Visit (n = 301)	0.86 (0.59, 1.26)	0.44	0.78 (0.53, 1.16)	0.22

[†]Adjusted for year of delivery, mother's delivery age, race, new diagnosis of HIV during pregnancy, parity, ART pre-pregnancy and CD4 count at presentation; n = 217

Table 3: Preterm delivery, birth weight, SGA, IUGR in HEU infants of vaccinated vs unvaccinated mothers

	Total Population [†] (N = 236)	Flu vaccine only (n = 66)	Tdap vaccine only (n = 32)	Both Flu and Tdap (n = 64)	P-value [‡]	No vaccine (n = 74)	P-value
Gestational Age, wks							
Median (IQR)	38.6 (37.6-39.4)	38.5 (38.0-39.1)	38.5 (38.0-40.0)	39.0 (37.5-40.0)	0.46	38.1 (37.1-39.1)	0.06
Birth weight, g							
Median (IQR)	3012 (2708-3360)	2975 (2710-3290)	3020 (2860-3230)	3122.5 (2738-3458)	0.47	2970 (2550-3320)	0.19
SGA, n (%)[§]	14 (6.01)	5 (35.7)	0 (0.0)	4 (28.6) [¶]	0.3277	5 (35.7)	
IUGR, n (%)[§]	8 (3.43)	4 (50.0)	0 (0.0)	4 (50.0) [¶]	0.4133	0 (0.0)	

[†]Percentages derived from the overall column total, N = 236

[‡]P-value is excluding those designated as 'no vaccine' and across all three remaining groups for continuous/categorical, N = 162; chi-squared or Fisher's exact test used when data is skewed

[§]Three missing observations, n = 233

[¶]One missing observation, n = 63

|| Two missing observations, n = 72

CONCLUSIONS

- Receipt of intrapartum Tdap and influenza vaccine confers some degree of protection against ARI in HEU infants during the first six months of life, a time when they are vulnerable to severe infections and reliant on maternal antibodies for protection
- Even if mothers received only Tdap or influenza vaccine and not both during pregnancy there was a trend towards decreased risk for hospitalization (data not shown)
- Overall vaccine uptake in pregnant WLWH is low. During the 2017-2018 influenza season, 49.1% of pregnant women received influenza vaccine, 54.4% received Tdap and 32.8% received both vaccines. In our population, 28% received influenza, 14% received only Tdap and 27% received both. Further efforts are needed to optimize vaccine uptake.
- Our study was limited by the retrospective nature and small sample size from a single-institution
- A strength of our study was the high retention in care with few infants lost to follow-up. Larger prospective studies are needed to verify these findings.