More Severe Disease in Hospitalized HIV Exposed Uninfected vs HIV Unexposed Neonates

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BACKGROUND

- Children HIV exposed and uninfected (CHEU) may have an increased risk of adverse birth outcomes, morbidity and hospitalization compared to children HIV unexposed and uninfected (CHUU).
- There are few insights into patterns of morbidity during the neonatal period.

METHODS

- We followed a prospective cohort of HIV+ and HIV- pregnant women recruited from a large antenatal clinic in Cape Town, South Africa ("B positive" cohort).
- 52% of HIV+ pregnant women were on ART at conception, 20% 'resumed' ART during pregnancy and 28% initiated ART during pregnancy .
- Their infants (CHEU=457; CHUU=475; HIV+ neonates=2 excluded) were followed up from birth.
- Medical records were reviewed to investigate all hospitalizations during the neonatal period (day 0 – 28).
- Infants who were in hospital for routine post-delivery observation were excluded.
- Standardized tools were used to classify diagnoses.

RESULTS

- Similar rates of neonatal hospitalization between CHEU and CHUU: 13% (59/457) vs 16% (75/475); p=0.210).
- Infectious causes were identified in 37% CHEU vs 35% CHUU (p=0.099); bloodstream infections (definite/probable) accounted for most infectious hospitalizations (34/48; 71%).
- Neonatal respiratory distress was the most common cause of non-infectious hospitalization and did not differ between CHEU and CHUU (32% vs 35% of non-infectious admissions; p=0.20).

CHEU were 2-3 times more likely to experience very LBW (<1500g) and very preterm birth (<32w), and twice as likely to require ICU admission.

Table comparing characteristics of all hospitalized neonates:

	CHEU	CHUU	Total	p-value
Hospitalization duration (days): median (IQR)	9 (5-28)	7 (5-17)	8 (5-22)	0.171
Hospitalized directly after birth	52/59 (88%)	64/75 (85%)	116/134 (87%)	0.637
C-section delivery	38/59 (64%)	43/75 (57%)	81/134 (60%)	0.406
ICU admission	**32/59 (54%)**	**21/75 (28%)**	**53/134 (40%)**	**0.002**
Low birthweight (<2500g)	33/59 (56%)	40/75 (53%)	73/134 (55%)	0.764
Very low birthweight (<1500g)	**21/59 (36%)**	**12/75 (16%)**	**33/134 (25%)**	**0.009**
Preterm birth (gestational age <37 weeks)	36/59 (61%)	40/75 (53%)	76/134 (57%)	0.373
Very preterm birth (gestational age <32 weeks)	**16/59 (27%)**	**7/75 (9%)**	**23/134 (17%)**	**0.007**
Diagnosis of infection⅄	22/59 (37%)	26/75 (35%)	48/134 (36%)	0.099
Congenital abnormalities#	8/59 (14%)	6/75 (8%)	14/134 (10%)	0.296
Death during hospitalization	4/59 (7%)	6/75 (8%)	10/134 (8%)	-

***Hospitalized CHEU vs CHUU:**

Very preterm birth	RR=2.64	(95% CI 1.15-6.08)
Very low birthweight	RR=2.04	(95% CI 1.05-3.99)
ICU admission	RR=1.95	(95% CI 1.41-2.70)
ICU adjusted for VPT birth	RR=1.65	(95% CI 1.05-2.60)

**excluding 9 second-born twins and 3 neonates with life-threatening congenital anomalies*



Table comparing characteristics of "B positive" cohort:

Maternal HIV status	**HIV+**	**HIV-**	**Total**	**p**
Number of pregnant women	479	512	991	-
Terminations & ectopics	4 (<1%)	3 (<1%)	7	-
Miscarriage (<20 weeks GA)	7 (1%)	12 (2%)	19 (2%)	0.311
Stillbirth (≥20 weeks GA)	10 (2%)	14 (3%)	24 (2%)	0.508
Lost to follow up	13 (3%)	15 (3%)	28 (3%)	0.838
Multiple pregnancy	14 (3%)	7 (1%)	21 (2%)	0.089
	CHEU	**CHUU**	**Total**	**p**
HIV uninfected infants	457	475	932	-
Female	243 (53%)	238 (50%)	481	0.349
Birthweight(g) (mean; 95% CI)	3023 (2966-3081)	3119 (3061-3176)	3072 (3031-3113)	0.021
Low birthweight (<2500g)	68 (15%)	59 (12%)	127 (14%)	0.274
Very low birthweight (<1500g)	21 (5%)	12 (3%)	33 (4%)	0.087
GA <37 weeks (preterm)	75 (16%)	59 (12%)	134 (14%)	0.083
GA <32 weeks (very preterm)	16 (4%)	7 (1%)	23 (2%)	0.046
C-section delivery	149 (33%)	153 (32%)	302 (32%)	0.898
Neonatal ICU admission	32 (7%)	21 (4%)	53 (5%)	0.089
Neonatal hospitalization	59 (13%)	75 (16%)	134 (14%)	0.210

CONCLUSIONS

- No significant differences in overall hospitalization rates or frequency of infectious events during the neonatal period between CHEU and CHUU.
- However, hospitalized CHEU had increased risk of very preterm birth and very LBW, indicating increased severity of adverse birth outcomes.
- In addition, and independent of very preterm birth, hospitalized CHEU had higher risk of ICU admission, indicating increased disease severity during the neonatal period.

ADDITIONAL INFORMATION

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⅄ *Includes: bloodstream infection, respiratory infection, meningitis, congenital syphilis, congenital tuberculosis, acute diarrhoea/dysentery, urinary tract infection, bacterial skin infection*

\# *Includes: hypospadias, G6PD deficiency, intestinal atresia, bilateral talipes equinovarus, Cornelia de Lange Syndrome, thoracic scoliosis, bilateral undescended testes, Klinefelter Syndrome, VACTERL association, polydactyly, cleft palate, myelomeningocoele, Trisomy 21*