Risk Factors for Small for Gestational Age and Microcephaly among HIV-Exposed Infants in Montreal, Quebec, Canada

Laura-Kim Tremblay, Suzanne Taillefer, Silvie Valois, Christian Renaud, Marc Boucher, Valérie Lamarre, Hugo Soudeyns, Isabelle Boucoiran, Fatima Kakkar

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Background

- HIV Exposed-Uninfected (HEU) children are at risk of growth disorders and increased mortality and morbidity compared to children who are HIV unexposed and uninfected (HUU).
- Potential risk factors include aberrant *in utero* growth due to maternal HIV infection and exposure to antiretroviral agents (ARV).

SMALL FOR GESTATIONAL AGE (SGA)

Birth Weight and Preterm Delivery Outcomes of HIV positive vs HIV negative pregnant women from SMARRT Study and IMPAACT P1025 Protocol (N=2692)

- No association between maternal HIV positive status and preterm delivery (HIV status n=32 (12%) vs non-HIV status n= 265 (11%); P = 0.72) or small for gestational age (SGA) (HIV status n= 41 (15%) vs non-HIV status n=388 (16%); P = 0.69)

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MICROCEPHALY

Head Circumference in SMARTT Cohort Study (n=3055)

Cumulative incidence of microcephaly for a median 5,1 years of follow-up (IQR 3·0-7·2)

- N= 159 (5,2%, 95% CI 4,4-6,1) by Nellhaus criteria
- N=70 (2,3%, 1,8-2,9) by SMARTT criteria

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OBJECTIVES:

- **Primary objective**:

Determine the incidence of small for gestational age (SGA), microcephaly and macrocephaly among HEU newborns

- **Secondary objective:**

To identify specific risk factors among aberrant growth

METHODS:

- Retrospective study of HEU children enrolled in the **Centre Maternel et Infantile sur le SIDA (CMIS) Cohort**
- CMIS: Established in 1988 to follow all HEU children with many visits in their first two years of age, annual visits until the age of 5, and visits every two years thereafter until the age of 18.
- Newborn birth weight (BW), length, and head circumference (HC) were assessed for children born to women living with HIV from the CMIS cohort (1988-2017), for whom linkage to the provincial health administrative databases could be done

Analysis

- Data were analyzed using published Intergrowth 21 standards, with reported Z scores and percentiles adjusted for gestational age (GA) and sex.
- Risk factors for extremes of growth were determined from among: ethnicity, immigration status, age, maternal CD4 and viral load at delivery, maternal ARV regimen during pregnancy (none or any) and type of treatment, infant ARV prophylaxis

RESULTS

- 724 newborns, exposed to HIV but uninfected, were included in the analysis.
- No infants with micro or macrocephaly were born to mothers treated with efavirenz or dolutegravir during pregnancy

		Z-score			
	N	**Mean**	**Standard Deviation**	**Median**	**Interquartile Range (IQR)**
Birth Weight (kg)	669	0.17	1.09	0.21	-0.50-0.90
Head Circumference (cm)	597	0.73	1.20	0.84	-0.01-1.56
Length (cm)	536	0.93	1.33	1.02	-0.01-1.88

	n (%)
Preterm Delivery (GA < 37 weeks); N=724	99 (13.7%)
Small for Gestational Age (BW < 10th percentile); N=669	76 (11.4%)
Microcephaly (HC < 3rd percentile); N=597	14 (2.3%)
Macrocephaly (HC > 97th percentile; N =597	95 (15.9%)

Predictors of Small Gestational Age

- **Not significant**: Maternal age, treatment type and delivery viral load (dVL)
- **Significant:** Maternal dCD4 (Beta: -0.01, p=0.01) and race (Beta: -4.5, p=0.02), both of which remained significant after adjusting for maternal age, treatment type and dVL.

Predictors of Length

- **Significant:** Infants born to mothers of African origin had significantly higher birth Z-scores than those of Haitian origin (0.274 vs. -0.037, p<0.002).

Predictors of Head Circumference

- **Significant:** Maternal dCD4 count was the only relevant predictor of HC at birth (Beta: -0.01, p=0.016)

Summary, Interpretation and Conclusions

SMALL FOR GESTATIONAL AGE

- The rate of SGA in our CMIS cohort corresponds to 11.4%, similar to the expected rate of SGA in the general American population which is 10%.

MICROCEPHALY

- 2.3% of microcephaly overall rate. The mother's dCD4 is a risk factor of microcephaly. This concept will require further development in future research as well as the identification of other potential risk factors.

MACROCEPHALY

- 15.9% of macrocephaly overall rate. Such a high rate of macrocephaly makes us wonder about the benign nature of this phenomenon or its possible association with genetic syndromes or developmental delays. Certainly, this result will have to be investigated further in the future.

PRETERM DELIVERY

- 13.7% is higher than the rate reported for all preterm deliveries in Canada (8%) and the United States (7.7%).
- Similar to our rate, several other studies among HIV positive pregnant women reported rates of preterm delivery who were ranging from 3% to 17%.

In the coming years, it will be important to assess the impact on long-term growth (birth to adolescence) of these factors over the HEU children.

For any questions about this presentation: laurakim.tremblay@gmail.com