“Association between maternal aflatoxin exposure during pregnancy and adverse birth outcomes in Mukono, Uganda”

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Background and Objective

- Aflatoxins (AFs) are naturally-occurring, toxic secondary metabolites of *Aspergillus* molds, particularly *A. flavus* and *A. parasiticus*.
- AFs are prevalent in many staple foods (ex. maize, sorghum, and groundnuts), particularly in LMICs where poor harvest and storage practices leave food supplies vulnerable to contamination.[1]
- Aflatoxin B1 (AFB1), the most prevalent and toxic type of AF, has been linked to both poor growth and development and impaired immune function in young children.[2-5]
- AFB1 is known to cross the placental barrier, putting the fetus at risk of aflatoxin exposure[6-7] and potentially contributing to the burden of adverse birth outcomes as well.[8-10]
- The objective of this study was to investigate the association between maternal AF exposure during pregnancy and adverse birth outcomes in newborn infants (lower weight and length, smaller head circumference, and shorter gestational age at birth).

Photos: Visible aflatoxin contamination on (i) maize and (ii) groundnuts

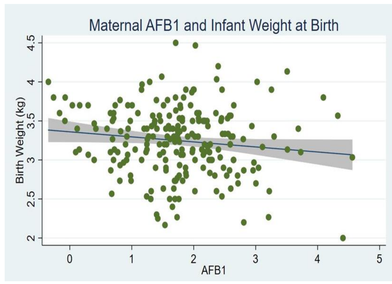
Methods

- We conducted a prospective cohort study in Mukono District, Uganda from February-November 2017. Women who met the inclusion criteria were recruited at their first prenatal visit to Mukono Health Center IV until the desired sample size (n=258) was reached.
- Anthropometry measurements were taken and a blood draw, an obstetric ultrasound exam, and a hemoglobin test were performed at enrollment.
- Covariate data (ex. prior pregnancies, health status, diet, food security, and WASH practices) were obtained from two questionnaires, one at enrollment and one three weeks prior to the participant’s estimated date of delivery.
- Anthropometry and birth outcome variables (sex, gestational age, weight, length, and head circumference) for 220 live infants were obtained within 48 hours of delivery.
- Maternal AF exposure was assessed by measuring the serum concentration of AFB1-lysine (AFB-Lys) adduct using HPLC at the Wang laboratory at UGA.
- Associations between maternal AF exposure and birth outcomes were assessed with STATA 15 software using multivariate linear regression models adjusted for confounding factors.
  - Anthropometry measurements were converted to Z-scores (WAZ, WHZ, LAZ, HCZ) using the World Health Organization standards.
  - Because of their skewed distribution, AFB-Lys levels were natural log-transformed prior to all analyses.

Results

- At the time of enrollment, participants were (mean ± SD) 23.9 ± 4.2 years of age and 17.9 ± 3.4 weeks gestation.
- AFB-Lys levels were detected in 100% of maternal serum samples. Median maternal AFB-Lys level was 5.71 pg/mg albumin (range: 0.71-95.60 pg/mg albumin, IQR: 5.98 pg/mg albumin).
- Infant weight and length at birth were (mean ± SD) 3.3 ± 0.4 kg and 48.7 ± 2.0 cm, respectively. WHZ, WAZ, and LAZ scores were 0.47 ± 1.54, -0.13 ± 0.95, and -0.44 ± 1.07, respectively. HCZ was 0.88 ± 1.19.
- **In adjusted linear regression models, elevated maternal AFB-Lys levels were significantly associated with lower birth weight, lower WAZ, smaller head circumference, and lower HCZ in infants at birth**.

Figures: Correlation between maternal ln AFB-Lys levels and infant (i) birth weight (r=-0.1280; p=0.0586) and (ii) head circumference at birth (r=-0.1309; p=0.0526)



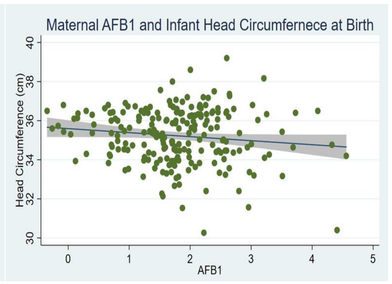


Table: Association between maternal aflatoxin exposure during pregnancy (ln AFB-Lys levels) and birth characteristics

	Unadjusted Model	Adjusted Model
Weight	-0.06 (-0.13, 0.002) p=0.059	**-0.07 (-0.13, -0.002) p=0.045***
Length	-0.09 (-0.42, 0.23) p=0.566	-0.12 (-0.44, 0.21) p=0.476
WAZ	**-0.16 (-0.31, -0.01) p= 0.032***	**-0.16 (-0.30, -0.03) p=0.021***
WHZ	-0.13 (-0.39, 0.12) p=0.301	-0.14 (-0.40, 0.11) p=0.274
LAZ	-0.07 (-0.24, 0.10) p=0.444	-0.08 (-0.25, 0.09) p=0.357
Head circumference	-0.23 (-0.47, 0.003) p=0.053	**-0.27 (-0.51, -0.03) p=0.028***
HCZ	**-0.19 (-0.37, -0.007) p=0.042***	**-0.23 (-0.41, -0.04) p=0.016***
Gestational age	-0.10 (-0.43, 0.23) p=0.561	-0.08 (-0.42, 0.26) p=0.642

Cells present β-coefficient, 95% confidence interval, and p-value; *p < 0.05

Adjusted linear regression model controls for mother’s age, body mass index (BMI), pulse pressure, first pregnancy (y/n), and years of education in all models. Gestational age was controlled for in all models except for when it was an outcome.

Conclusions

- Chronic AFB1 exposure is widespread among pregnant women in Mukono and may be contributing to the burden of adverse birth outcomes, including lower birth weight, lower WAZ, smaller head circumference, and lower HCZ.
- Initiatives to reduce AF exposure, especially targeted at women of reproductive age, *may* result in improved birth outcomes in LMICs.
- More robust studies examining a wider range of mycotoxins (ex. fumonisins) are warranted to better quantify the burden and establish causality.

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