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Serum aflatoxin B₁-lysine adduct concentrations are associated with both length and length for age Z-score **at 2 years of life**

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COLLABORATORS AND TEAM

- Child Health Division, Department of Health Services, MOHP
- Nepal Health Research Council (NHRC) and Tufts IRB
- Patan Academy of Health Sciences (PAHS)
- Helen Keller International (HKI), Nepal
- Purdue University
- University of Georgia, FTF Innovation Lab on Peanuts and Mycotoxins
- USAID Bureau of Food Security and USAID Nepal
- Tufts University
- Banke District Public Health Office
- Banke VDC and Ward Health Posts, FCHVs
- Nepalgunj Medical College
- AflaCohort Field team and participants





BACKGROUND

- Several observational studies have documented an association between aflatoxin and poor child growth.
- One study in Nepal has found no association between length-for-age Z-score and aflatoxins at 36 months of age (1).
- Midline results from a randomized control trial in Kenya showed aflatoxins might affect growth at younger ages; however, the effect disappears at the endline (2).

1. Mitchell NJ, Hsu HH, Chandyo RK, et al. Aflatoxin exposure during the first 36 months of life was not associated with impaired growth in Nepalese children: An extension of the MAL-ED study. *PLoS One*. 2017;12(2):1-12. doi:10.1371/journal.pone.0172124

2. Hoffmann V, Jones K, Leroy JL. The impact of reducing dietary aflatoxin exposure on child linear growth: A cluster randomised controlled trial in Kenya. *BMJ Glob Heal*. 2018;3(6):1-8. doi:10.1136/bmjgh-2018-000983





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AFLACOHORT STUDY

- Observational Birth Cohort Study
- Location: 17 Village Development Committees in the Banke District of Nepal
- n=1,675 mother-infant dyads
- Primary objective: Understand the relationship between past and current mycotoxin exposure (maternal and infant), birth outcomes and linear growth in Nepali children



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AFLATOXIN BIOMARKER

- Serum AFB1-lysine adduct concentration
- Collected samples from pregnant women and from their infants at 3, 6, 12, 18-22 months of age
- HPLC-fluorescence detection method (University of Georgia)





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AflaCohort Study, Banke, Nepal (2015-2019)

Phase I (2015-2018)

Phase II (2018-2019)

Launch
7/2015

Completion
3/2019

Prenatal

Child
3 months

Child
9 months

Child
18-22
months

Child
24-26
months

Birth

Child
6 months

Child
12 months

Urine - L:M,
DON + FB1
Serum - OTA

n=1675 mother-infant dyads; L:M: lactulose:mannitol; DON: Deoxynivalenol; FB1: Fumonisin B1; OTA: Ochratoxin A



METHODS

- AFBI-lysine adduct data were not normally distributed and were therefore log-transformed for statistical analyses
- Anthropometric measurements were converted to z-scores (length-for-age (LAZ) and weight-for length (WLZ)) using the WHO growth reference-2006
- Average 10% undetectable in infants
 - Undetectable serum AFBI values were set to half the LOD (i.e. 0.2 pg/mg AFBI-lysine adduct)
 - Dummy variable created for detectable versus undetectable





STATISTICAL ANALYSIS

- Multivariable fixed-effects regression model
- Association between length (cm) or LAZ and contemporaneous serum AFBI-lysine adduct concentrations
- Contemporaneous model both serum aflatoxin and LAZ reflect past exposure
 - Serum aflatoxin – half life of 90 days

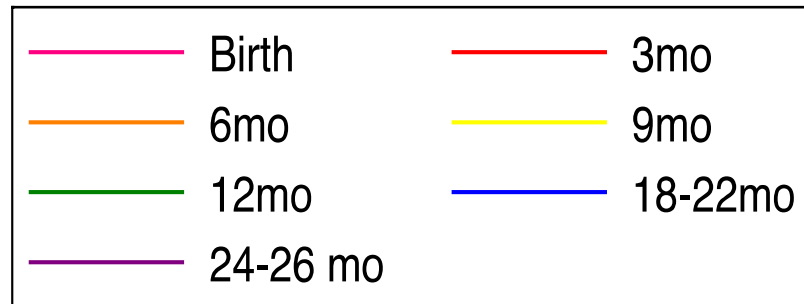
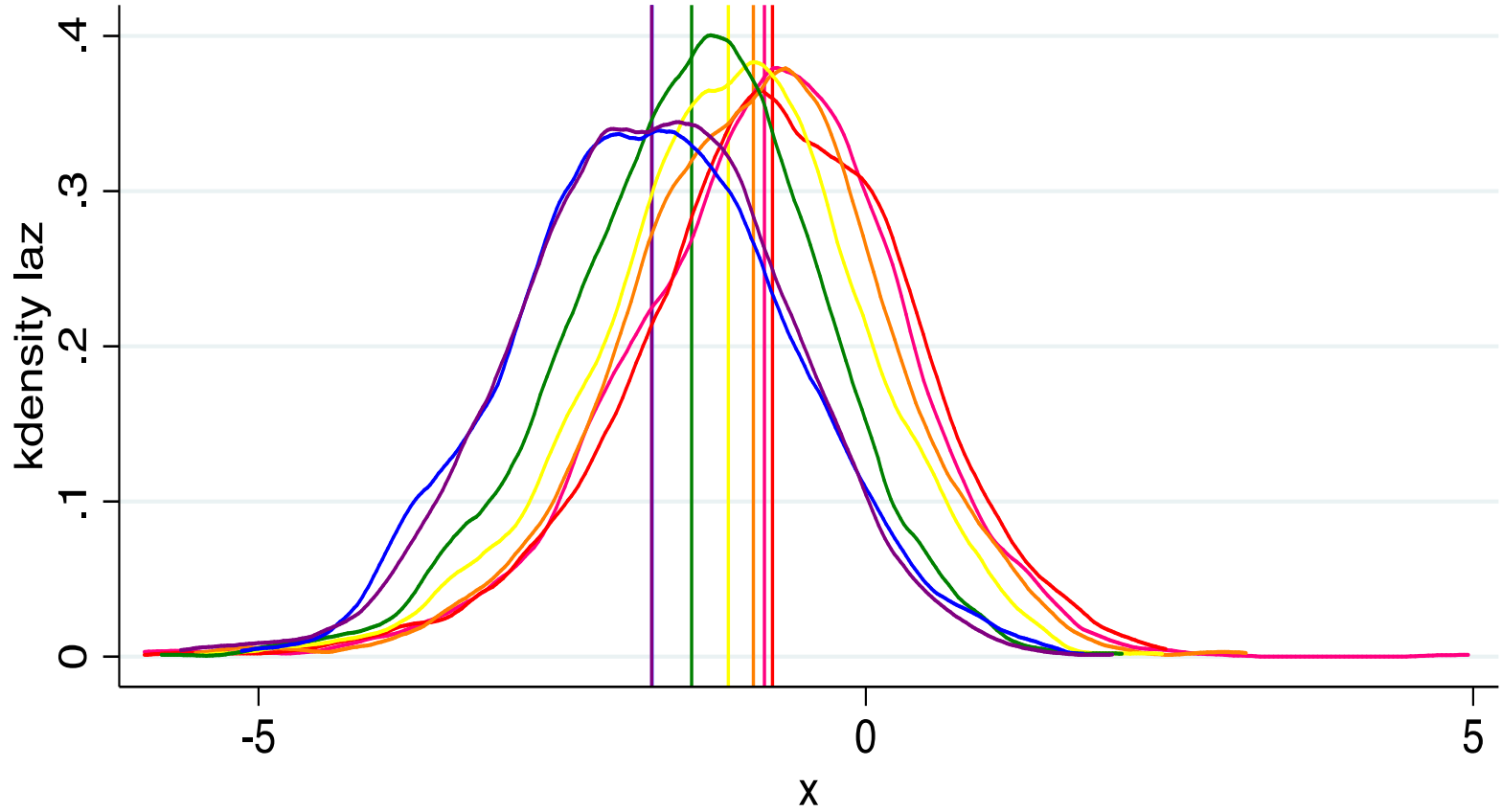
SERUM AFLATOXIN B1 CONCENTRATIONS

	n	Detectable Aflatoxin B1-lysine adduct (%)	Mean ± SD Aflatoxin B1-lysine adduct* (pg/mg alb)	Min	Max
Pregnancy	1652	94.3	3.4 ± 8.5	0.4	147.3
Child 3 months	1363	80.5	1.0 ± 1.1	0.4	24.7
Child 6 months	1294	75.3	1.2 ± 2.1	0.4	41.6
Child 12 months	1329	81.1	2.0 ± 4.6	0.4	84.6
Child 18-22 months	699	85.1	2.4 ± 7.9	0.4	128.1

* Detectable only; alb: albumin; mg: milligrams; min: minimum; mo: months; n: samples size; pg: picograms



LAZ over time



Source: Mycotoxin Birth Cohort Study / Banke, Nepal / 2015-2019

FIXED EFFECTS MODELS CHILDREN 3-22 MONTHS

	Length (cm)	P-value	LAZ	P-value
(Ln) aflatoxin BI-lysine adduct	-0.19	<0.001	-0.05	<0.01
(Ln) aflatoxin BI-lysine adduct/kg weight	-0.25	<0.001	-0.08	<0.001

cm: centimeter; LAZ: length-for-age z-score; Ln: natural log

Covariates: age, weight-for-length z-score, season of measurement, detectable AFB1 concentrations



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CONCLUSIONS

- Significant negative association with length, length for age Z-score when assessing exposure from 3 through 22 months (absolute serum levels and per kg body weight)





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FUTURE WORK

- Measure exposure to other mycotoxins (i.e. fumonisin, DON, OTA) and test cross-sectional associations of co-exposure to these mycotoxins and child growth
- Test associations between aflatoxin, other mycotoxins, inflammation and environmental enteric dysfunction (EED).
- Test associations between aflatoxin exposure and cognitive function
- Test the association between serum aflatoxin levels and long bone growth (i.e. knee-heel length) overtime





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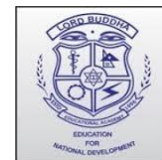
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