Supplemental Material

In utero arsenic exposure and infant infection in a United States cohort: A prospective study and systematic review

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Table S1. Published epidemiological studies of arsenic exposure with immune function and infection outcomes in children.

	Author	Population/ Study Group	Study Design	Sample Size	Exposure Assessment	Exposure Level	Outcomes	Findings
Immune function outcomes at the molecular and cellular levels	Soto-Pena, et al., 2006	Zimapan, Hidalgo, Mexico	Cross-sectional (6-10yrs, randomly selected)	N=90	Urine As	Low: <50μg/L High: ≥50μg/L (86% in ≥50μg/L group)	T-cell proliferation, cytokine production, PBMC subpopulation levels	Increased [UA] correlated with decreased T-cell populations, IL-2 levels, proliferative response, and IFNγ secretion and increased GM-CSF secretion in response to LPS stimulation
	Fry, et al., 2007	Bangkok and Ron Pibul Districts, Thailand	Prospective birth cohort (enrolled during pregnancy)	N=32	Maternal toenail As	Unexposed: <50μg/g toenail Exposed: ≥50μg/g toenail Range: 0.1-68.63μg/g toenail	Whole genome microarray analysis of infant cord blood, transcription factor binding site analysis	447 genes were differentially expressed between infants of exposed and unexposed mothers; identified a highly predictive 11 gene signature that correlates with As exposure and 3 As-transcriptionally regulated sub-networks that control inflammation (IL-1β/ NFκB), stress responses (HIF-1α/STAT1, IL-8), and the cell cycle (EGR1, FOS, JUN)
	Luna, et al., 2010	Zimapan, Hidalgo, Mexico	Cross-sectional (6-10yrs, randomly selected)	N=87	Urine As	Mean: 194.6 μg/g creatinine Range: 12.3-1411 μg/g creatinine	Nitric oxide/ oxygen superoxide anion determination, and hemoglobin quantification in PBMCs	As exposure increased basal levels of nitric oxide and oxygen superoxide anion in PBMCs and monocytes and levels of oxygen superoxide anion in activated monocytes, indicative of oxidative stress
	Rocha-Amador, et al., 2011	Durango (D) and San Luis Potosí (SLP), Mexico	Cross-sectional (6-10yrs, randomly selected children)	N=40 (20 per study area)	Urine As	SLP Mean: 14.2 μg/g creatinine SLP Range: 4.2-42.9 μg/g D Mean: 46.3 μg/g D Range: 9.98-101.7 μg/g	Proportion of apoptotic PBMCs	Higher levels of PBMC apoptosis were detected in children of Durango that were exposed to both As and F; both As and F were individually correlated with increased PBMC apoptosis
					Urine F	SLP Mean: 1.94 μg/g creatinine SLP Range: 0.9-4.9 μg/g D Mean: 5.7 μg/g D Range: 1.9-15.6 μg/g		
					Drinking water As	SLP Mean: 6.7 μg/L SLP Range: 4.75-8.8 μg/L D Mean: 157.9 μg/L D Range: 0.98-245.1 μg/L		
					Drinking water F	SLP Mean: 0.67 ug/L SLP Range: 0.34-1.01 ug/L D Mean: 8.19 ug/L D Range: 1.35-11.10 ug/L		

Table S1. Published Epidemiological Studies of Arsenic Exposure with Immune Function and Infection Outcomes in Children (con't).

Infection and clinical outcomes	Raqib, et al., 2009	Matlab, Bangladesh	Prospective birth cohort (enrolled at GW6-10)	N=140	Maternal urine As, GW 6-10	Mean: 68.5 µg/L Range: 1-2020 µg/L	Birth weight and height, infant TI, IL-7 and Ltf in breast milk, maternal and infant morbidity	[UA] was negatively correlated with levels of IL-7 and lactoferrin in breast milk and positively associated with both fever and diarrhea during pregnancy and ARI in male infants; In utero As exposure impaired infant thymic development and enhanced morbidity
					Maternal urine As, GW 30	Mean: 64.7 µg/L Range: 4-1126 µg/L		
	Moore, et al., 2009	Matlab, Bangladesh	Prospective birth cohort (enrolled at GW8)	N=2094	Mean maternal urine As, GW8 and GW 30	Mean: 102 µg/L Range: 5.5-1150 µg/L	Infant TI measured at weeks 0, 8, 24 and 52	TI was negatively associated with maternal arsenic exposure during pregnancy. Infant TI was positively associated with infant weight and month of measurement.
	Rahman, et al., 2011	Matlab, Bangladesh	Prospective birth cohort (enrolled at GW8)	N= 1552	Maternal urine As, GW8	Mean: 152 µg/L Range: 1-1211 µg/L	Infant LRTI, infant diarrhea	Infants born to mothers with high [UA] had an elevated risk of LRTI, severe LRTI and diarrhea, relative to those with lower exposure levels; As exposure during pregnancy is associated with significantly increased morbidity.
					Maternal urine As, GW 30	Mean: 166 µg/L Range: 2-1440 µg/L		
	Ahmed, et al., 2011	Matlab, Bangladesh	Prospective birth cohort (enrolled at GW8)	N=130	Maternal urine As, GW8	Mean: 136 µg/L SD: 167 µg/L	Immune and inflammatory markers in cord blood and placental tissue	As exposure increased placental inflammatory markers, likely by increasing oxidative stress; As exposure decreases placental T-cells and alters cytokine profile
					Maternal urine As, GW 30	Mean: 143 µg/L SD: 164 µg/L		
	Ahmed, et al., 2012	Matlab, Bangladesh	Prospective birth cohort (enrolled at GW6-13)	N=130	Maternal urine As, GW8 or 14	Median: 69 µg/L 5-95 percentiles: 19-441 µg/L	Infant TI and thymic function assessed by sjTREC quantification, oxidative stress, apoptotic and inflammatory markers in cord blood and placental tissue	Maternal arsenic exposure reduced the levels of sjTRECs in cord blood CD4+ and CD8+ cells, a measure of thymic function and lymphocyte maturation. High levels of As exposure were related to differential regulation of multiple oxidative stress and apoptosis related genes in cord blood, as increases in oxidative stress markers 8-oxoG and 8-OHdG, in placenta and cord blood.
					Maternal urine As, GW 30	Median: 85 µg/L 5-95 percentiles: 20-508 µg/L		
					Maternal blood As, GW 14	Median: 4.7 µg/kg 5-95 percentiles: 1.4- 22.2 µg/kg		

GW: gestational week, UA: urinary arsenic, PBMCs: peripheral blood mononuclear cells, TI: thymic index, ARI: acute respiratory infection, LRTI: lower respiratory tract infection, sjTREC: signal-joint T cell receptor excision circles, Ltf: lactoferrin.