IN UTERO EXPOSURE TO ARSENIC IS ASSOCIATED WITH ALTERED DNA METHYLATION IN UMBILICAL CORD BLOOD LEUKOCYTES

Molly L. Kile, *Harvard School of Public Health, 665 Huntington Avenue, Boston, USA*
Andrea Baccarelli, *Harvard School of Public Health, 665 Huntington Avenue, Boston, USA*
Elaine Hoffman, *Harvard School of Public Health, 665 Huntington Avenue, Boston, USA*
Letizia Tarantini, *Department of Environmental and Occupational Health, Universitá degli Studi di Milano & IRCCS Ca', Granda Policlinico Maggiore Hospital Foundation, Milan, Italy*
Quazi Quamruzzaman, *Dhaka Community Hospital, 190/1 Baro Moghbazar, Wireless Railgate, 1217, Dhaka, Bangladesh*
Mahmuder Rahman, *Dhaka Community Hospital, 190/1 Baro Moghbazar, Wireless Railgate, 1217, Dhaka, Bangladesh*
Golam Mahiuddin, *Dhaka Community Hospital, 190/1 Baro Moghbazar, Wireless Railgate, 1217, Dhaka, Bangladesh*
Robert Wright, *Harvard School of Public Health, 665 Huntington Avenue, Boston, USA*
David C. Christiani, *Harvard School of Public Health, 665 Huntington Avenue, Boston, USA*

Background: Arsenic (As) can cross the placenta and is a suspected epigenetic toxicant.
Objectives: Investigate the effect of prenatal As exposure at *LINE-1, Alu, p16* and *p53* using data from a prospective birth cohort recruited in Bangladesh.
Methods: Women whose gestational age was ≤28 weeks were recruited. At enrollment, water samples were collected from the tubewell the participant identified as her primary source of drinking water and analyzed for As using inductively-coupled plasma mass spectrometry (ICP-MS). DNA was extracted from fresh whole umbilical cord blood (N=114). DNA methylation was quantified using pyrosequencing at *LINE-1, Alu,* and seven and four CpG positions in the promoter region of *p16* and *p53*, respectively.
Results: Infants were categorized as exposed (53.1%) or unexposed (46.9%) using maternal water As concentrations. General linear regression models were used to compare DNA methylation between exposed (As ≥ 1 µg/L) versus unexposed (As < 1 µg/L) infants. In adjusted models, DNA methylation in exposed infants was significantly higher at *LINE-1* (81.5% vs 80.6%, p-value=0.01) and at *p16* position 2 (3.1% vs 2.4%, p-value=0.009) position 5 (2.3% vs 1.9%, p-value=0.01) position 6 (1.4% vs 1.1%, p-value=0.02) and position 7 (2.6% vs 2.1%, p-value 0.02) compared to unexposed infants. No difference was observed at *Alu* or *p53.*
Conclusions: These results suggest that *in utero* exposure to As was associated with DNA hypermethylation in umbilical cord leukocytes at both global and loci specific markers. Additional studies are needed to confirm these results and determine whether changes in DNA methylation of umbilical cord leukocytes are associated with health outcomes.