

In-utero Heavy Metals Exposure, Role of Selenium Mediation and Newborn Telomere Length: A Birth-cohort Study in Ayeyarwaddy Region, Myanmar

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INTRODUCTION

Telomeres are repetitive DNA sequences (TTAGGG), located at the end of chromosomes. Telomere length (TL) shortening is considered as a biomarker of cellular aging and is associated with increased risks age-related health diseases including cardiovascular diseases, malignancy and overall mortality. TL in later life is mainly determined by the TL at birth and in earlier age. However, Limited information about the factors affecting TL at birth. Thus, the objectives of this study are

- 1) to evaluate the effect of *in-utero* exposure of arsenic (As), cadmium (Cd) and lead (Pb) on TL;
- 2) to examine the mediation effect of selenium (Se) on heavy metals induced TL shortening.

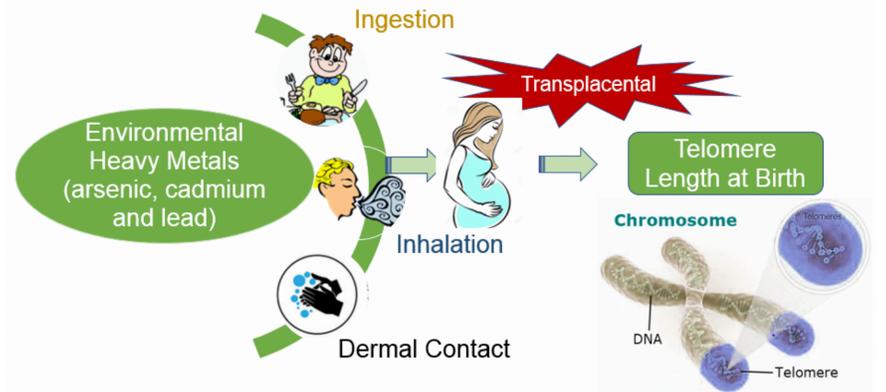
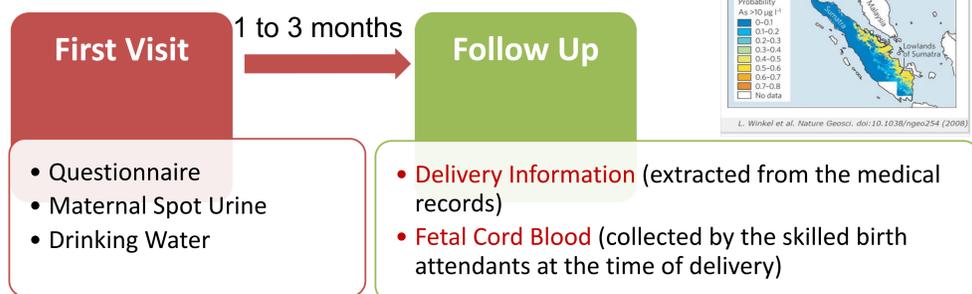
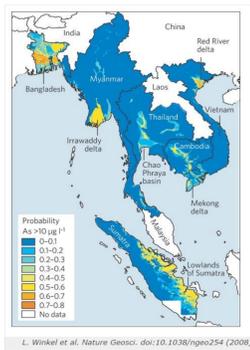


Figure 1: Graphical Abstract, Wai et al., 2018.

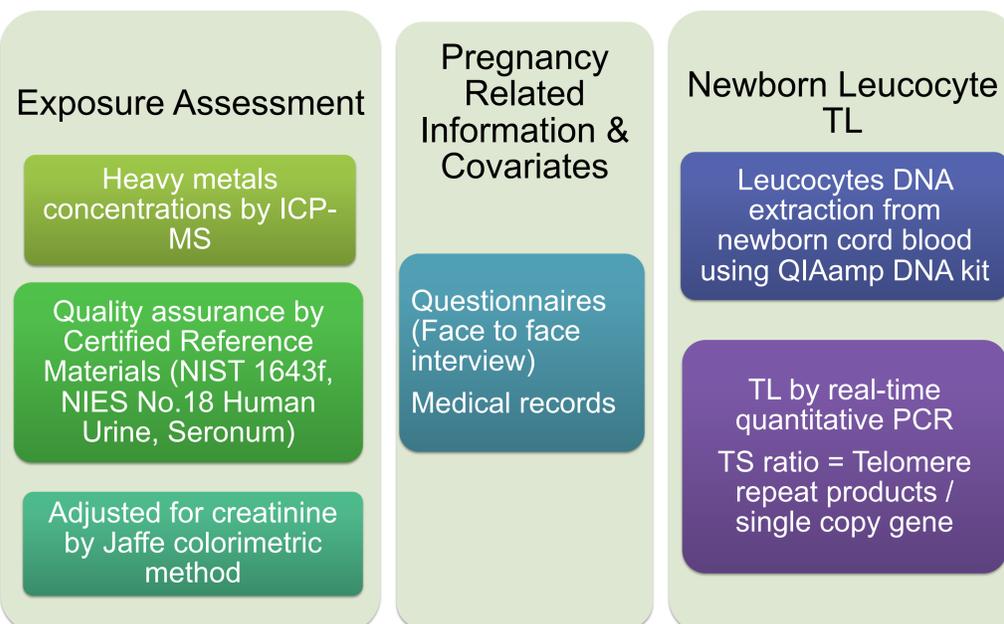
METHODS

Study Setting

- Design: A birth-cohort study
- Subjects: 408 mother-newborns pairs
- Area: Ayeyarwady Region, Myanmar



Measurements and Statistical Analysis



- To evaluate the mediation effect of Se, the molar ratios of As-Se, Cd-Se and Pb-Se were calculated accordingly.
- Bivariate analysis was performed to examine the associations between each heavy metal and TL, individually and after Se mediation.
- Later, multivariable linear regression models were applied for adjusting the potential confounders.

RESULTS

Table 1. Maternal Urinary Heavy Metals Concentration and Molar Ratios (n=408)

Concentration (µg/g creatinine)	Median	IQR	Detection Limit
As	74.0	45.6-126.4	0.239
Cd	0.8	0.5-1.4	0.002
Pb	1.7	1.0-3.2	0.843
Se	22.6	17.7-29.5	0.362
As-Se ratio	5.7	3.5-8.8	
Cd-Se ratio	0.04	0.02-0.1	
Pb-Se ratio	0.05	0.03-0.08	

Table 2. Associations between *in-utero* Heavy Metals Exposure and Newborn TL and Effects of Se Mediation (n=408)

Variables	Relative TL	
	Unadjusted Coefficient (95% CI)	Adjusted Coefficient (95% CI)
As (log-transformed)	-0.21 (-0.31, -0.11) ***	-0.22 (-0.32, -0.12) ***
Cd (log-transformed)	-0.18 (-0.27, -0.10) ***	-0.19 (-0.29, -0.10) ***
Pb (log-transformed)	-0.10 (-0.18, -0.02) *	-0.10 (-0.18, -0.01) *
As-Se ratio	-0.15 (-0.25, -0.04) **	-0.16 (-0.26, -0.06) **
Cd-Se ratio	-0.16 (-0.26, -0.06) **	-0.17 (-0.27, -0.06) **
Pb-Se ratio	-0.05 (-0.14, -0.03)	-0.06 (-0.14, 0.03)

Adjusted for maternal age, education, smoking, parity, gestational age at birth, birth weight, and baby's sex.

*p < 0.05, ** p < 0.01, ***p < 0.001

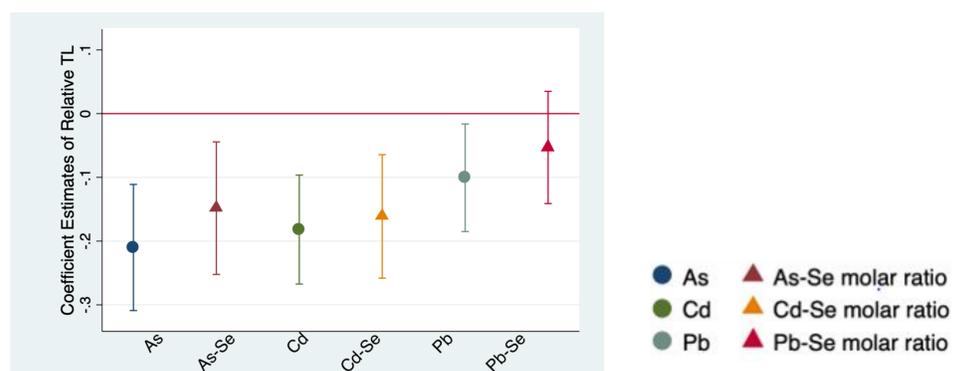


Figure 2. A regression plot of the coefficient estimates of newborn relative TL with 95% coefficient intervals in response to prenatal heavy metals exposure (n=408). The differences in the response were depicted by the individual metal effect and selenium mediation effect.

CONCLUSION

- *In-utero* exposure of As, Cd and Pb was significantly, negatively associated with newborn TL.
- Effect size was lower with Se mediation compared to individual metal exposure.
- This suggests that the mediation effect of Se does exist; and future studies are recommended to consider the role of Se species and other essential metals/micronutrients in the protection of heavy metals-induced TL shortening.

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