

GENETIC SUSCEPTIBILITY TO ARSENIC EXPOSURE AND PREVALENT SKIN LESIONS IN BANGLADESH

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ABSTRACT

Background and Aims: Elevated concentrations of arsenic in groundwater pose a public health threat to millions of people worldwide. While arsenic is an established human carcinogen, a mode of action has yet to be determined for arsenic carcinogenesis. However, the oxidative stress and DNA repair pathways have been implicated in arsenic toxicity and have been hypothesized to underlie arsenic carcinogenesis.

Methods: Utilizing cross-sectional data from the 2000-2002 survey of the Health Effects of Arsenic Longitudinal Study (HEALS) for 610 prevalent arsenical skin lesion cases and 1,079 randomly selected controls, we evaluated the associations of single nucleotide polymorphisms (SNPs) in genes encoding antioxidant enzymes and DNA repair enzymes on skin lesion prevalence based on logistic regression and Hierarchical Bayes modeling. We also evaluated potential SNP-SNP interactions as well as SNP-environment and higher-order interactions in determining skin lesion prevalence through a multi-analytic approach by MDR, CART, and logistic regression models.

Results: There were no statistically significant associations between individual SNPs and skin lesion prevalence. However, there was marginal evidence that skin lesion prevalence was increased among individuals who carried 4 or more risk alleles compared to individuals carrying 0-2 risk alleles in antioxidant enzyme SNPs. Additionally, there was a significant departure from additivity for the risk allele score and primary methylation index (i.e., ratio of MMA to inorganic arsenic) on skin lesion prevalence. Additionally, we observed a significant inverse association of total fruit and vegetable consumption with skin lesion prevalence and, there was a significant interaction on the additive scale between fruit and vegetable intake with the polymorphism in ERCC5 in relation to skin lesion prevalence.

Conclusions: The results of this study provide evidence of genetic and gene-environment effects in relation to arsenic-related skin lesion prevalence.

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