

Nonmalignant Health Effects of Arsenic Exposure.

av

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Akademisk Avhandling

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Abstract

This thesis comprises a series of studies concerning occupational and environmental exposure to arsenic and some novel chronic health effects of this element, namely diabetes mellitus and hypertension. Substantial prevalence of the well-known skin manifestations of arsenic ingestion was also found to occur as a result of environmental exposure through drinking water.

Two case-control studies on diabetes mellitus and occupational exposure to arsenic included individuals employed at a copper smelting industry (Paper I) and in art glassworks (Paper II) in Sweden. Although the number of smelter workers involved was small (12 cases and 31 controls), a significant exposure-response trend was obtained ($p = 0.03$). The assessment of arsenic exposure among 888 glass workers was less detailed, nonetheless it revealed an approximately doubled risk (MH-OR = 2.1; 95% confidence interval 1.2-3.7) for the workers with occupational titles that suggested exposure. Overall, the results of these studies provide evidence that occupational arsenic exposure may play a role in the development of diabetes mellitus. Four cross-sectional studies were carried out in Bangladesh, where a fairly large part of the population is exposed to inorganic arsenic in drinking water. In the first study (Paper III), the prevalence of diabetes mellitus among subjects with keratosis ($n = 163$) was compared with unexposed subjects ($n = 854$); keratosis was considered to be a definite sign of exposure. A dose-response relationship was found between categories of time-weighted arsenic exposure (mg/L in drinking water) and the prevalence of diabetes mellitus ($p < 0.001$), and the crude overall prevalence ratio amounted to 4.4. Despite the lack of detailed individual exposure data and information on potential confounders other than age, sex, and body mass index (BMI), the association seems strong enough to support a causal relationship, because the adjusted overall prevalence ratio was 5.9 (95% confidence interval 2.9-11.6).

One of the other studies performed in Bangladesh (Paper V; 1481 exposed individuals, 430 exhibiting keratosis) showed a somewhat higher prevalence rate of skin lesions in males (31%) than females (26%) due to chronic arsenic toxicity. The crude overall prevalence was 29% in the studied villages, and there was a distinct dose-response

relationship between arsenic concentrations in drinking water and skin lesions ($p < 0.01$). A clear dose-response relationship was also observed (Paper VI) between arsenic exposure and glucosuria for subjects both with and without skin lesions ($p < 0.01$). The possibility of using the skin lesions for initial screening for glucosuria was considered. However, the appearance of dermatological signs of chronic arsenic toxicity proved to be a poor marker in this respect, because glucosuria also occurred in the absence of skin lesions.

A third Bangladeshi study (Paper IV) indicated a significantly increased risk of hypertension in connection with exposure to inorganic arsenic in drinking water (1481 exposed and 114 unexposed subjects). The overall crude prevalence ratio of hypertension amounted to 1.7, and the adjusted (for age, sex, and BMI) ratio was 1.9 (95% confidence interval 1.0-3.6). A significant trend in risk ($p \ll 0.001$) was observed between an approximate time-weighted mean exposure to arsenic, considered in milligrams per liter or milligram-years per liter, which strengthens the possibility of a causal association.

Key word: arsenic, case-control study, cross-sectional study, diabetes mellitus, drinking water, epidemiology, exposure, keratosis, public health, hypertension, risk factors.

The thesis is based on the following papers

- I. Rahman M, Axelson O. Diabetes mellitus and arsenic exposure: a second look at case control data from a Swedish copper smelter. *Occup Environ Med* 1995; 52: 773-4.
- II. Rahman M, Wingren G, Axelson O. Diabetes mellitus among Swedish art glass workers – an effect of arsenic exposure? *Scand J Work Environ Health* 1996; 22: 146-9.
- III. Rahman M, Tondel M, Ahmad SA, Axelson O. Diabetes mellitus associated with arsenic exposure in Bangladesh. *Am J Epidemiol* 1998; 148: 189-203.
- IV. Rahman M, Tondel M, Chowdhury IA, Faruquee MH, Ahmad SA, Axelson O. Hypertension and arsenic exposure in Bangladesh. *Hypertension* 1999; 33: 74-8.
- V. Tondel M, Rahman M, Magnuson A, Chowdhury IA, Faruquee MH, Ahmad SA. The relationship of arsenic levels in drinking water and the prevalence rate of skin lesions in Bangladesh. *Environ Health Perspect* 1999; 107: 727-729.
- VI. Rahman M, Tondel M, Chowdhury IA, Axelson O. Relation between arsenic exposure, skin lesions and glucosuria. *Occup Environ Med* 1999; 56: 277-281.

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