The Relationship of Arsenic Levels in Drinking Water and the Prevalence Rate of Skin Lesions in Bangladesh

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To determine the relationship of arsenic-associated skin lesions and degree of arsenic exposure, a cross-sectional study was conducted in Bangladesh, where a large part of the population is exposed through drinking water. Four villages in Bangladesh were identified as mainly dependent on wells contaminated with arsenic. We interviewed and examined 1,481 subjects ≥ 30 years of age in these villages. A total of 430 subjects had skin lesions (keratosis, hyperpigmentation, or hypopigmentation). Individual exposure assessment could only be estimated by present levels and in terms of a dose index, i.e., arsenic levels divided by individual body weight. Arsenic water concentrations ranged from 10 to 2,040 µg/L, and the crude overall prevalence rate for skin lesions was 29/100. After age adjustment to the world population the prevalence rate was 30.1/100 and 26.5/100 for males and females, respectively. There was a significant trend for the prevalence rate both in relation to exposure levels and to dose index ($p < 0.05$), regardless of sex. This study shows a higher prevalence rate of arsenic skin lesions in males than females, with clear dose–response relationship. The overall high prevalence rate in the studied villages is an alarming sign of arsenic exposure and requires an urgent remedy. *Key words*: cross-sectional study, ecology, environment, epidemiology, exposure, keratosis, public health. *Environ Health Perspect* 107:727–729 (1999). [Online 29 July 1999]
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Arsenic contamination of well water in Argentina (*1*), Chile (*2,3*), India (*4–7*), Taiwan (*8,9*) and Thailand (*10*) has caused cutaneous skin lesions such as keratosis, hyperpigmentation, or hypopigmentation. Characteristic skin lesions of arsenic toxicity may be used as an indicator of high exposure and are distinctive in contrast to other clinical manifestations of arsenic intoxication including weakness, conjunctival congestion, edema, portal hypertension, bronchitis, and hepatomegaly (*6,7*).

In a previous study on arsenic and diabetes mellitus from a limited area in Bangladesh, a considerable number of patients suffered from arsenical skin lesions (*11*). Bangladesh seems to be one of the largest examples of mass arsenic poisoning: 30–70 million people in 41 of 64 districts may have been consuming arsenic-polluted water containing > 50 µg/L arsenic (the current drinking water standard in many countries of the world) for a long period (*12*).

Until the early 1970s, more than 100 million inhabitants of Bangladesh and the neighboring Indian province of West Bengal drank from shallow hand-dug wells, rivers, and ponds, but pollution was causing epidemics of cholera. Many inhabitants switched to tap tube well water when tube wells came into use as part of a broad irrigation plan. Because the groundwater was cleaner than the previous sources, the epidemics of cholera could be stopped. Arsenic water pollution now poses a public health problem in Bangladesh and is most prominent in terms of skin lesions. Subjective symptoms are usually mild, but patients with obvious palmoplantar keratosis may have pain while walking and/or working. Advanced keratosis with consequent disfigurement can lead to social isolation.

Arsenic is a known carcinogen that causes skin cancer and various internal cancers (*13*). In contrast to cancers, which take decades to develop, characteristic arsenical skin lesions are generally observed 5–10 years after commencement of exposure. The aim of this study was to evaluate the prevalence rate of skin lesions associated with arsenic exposure. The study was conducted as a cross-sectional study in four villages in Bangladesh.

Materials and Methods

Study area. Four villages in four districts in Bangladesh (Faridpur, Jessore, Narayongong, and Nawabgong districts) were selected for the study on the basis of existing survey reports of arsenic measurements in drinking water. These study villages were typical villages and were selected because of a contrast of exposure from low to high levels of arsenic in the drinking water within the villages, i.e., from nondetectable to 2,040 µg/L.

Method of study. The study was cross-sectional and was performed by door-to-door visits to interview families with known arsenic concentrations in their wells. Eligible subjects included those who had lived in the study areas throughout their lifetimes and who had used the same well as long as it had existed. A total of 1,794 subjects ≥ 30 years of age were identified. A total of 1,481 individuals had histories of arsenic exposure, were further interviewed by questionnaire, and were examined for identification of skin lesions according to the description given by Yeh (*14*). The remaining subjects included 114 unexposed subjects who had used water from wells that had nondetectable arsenic levels and another 199 subjects who were not available at the time of the visit to the villages. Participation was voluntary, but there were no refusals. The medical examination was carried out by two experienced physicians from the National Institute of Preventive and Social Medicine (MH Faruquee and SA Ahmad; Dhaka, Bangladesh), who both had long experience in diagnosing arsenical skin lesions.

A total of 430 individuals had signs of skin lesions. Arsenical skin lesions were diagnosed in the presence of one or more of the following criteria: pigmentation changes of unexposed body surfaces and/or keratosis, especially on the palms of the hands and the soles of the feet. Pigmentation changes include hyperpigmentation, which may occur anywhere on the body and often shows raindroplike pigmentation or diffuse dappling of dark brown. Hyperpigmentation is especially marked in nonexposed parts of the body. Hypopigmentation follows the same distribution and may be present even in the absence of hyperpigmentation. Keratosis is an area of small cornlike elevations, usually 0.4–1 cm in diameter and nodular, found on the lateral borders of palms and fingers and on the soles, heels, and toes. Diffuse keratosis on the palms

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and soles may also be present. No case of skin cancer was found in the clinical examination. Body weights were measured with the subjects wearing light clothes and not wearing shoes.

Individual exposure assessments. All water samples had been measured by flow-injection hydride generation atomic absorption spectrometry and came from various sources, including our previous study (*11*) and an official (*15*) as well as an unpublished report of water analysis performed by the Bangladesh National Institute of Preventive and Social Medicine (Dhaka, Bangladesh). Exposure was assessed in terms of levels and as a dose index. Exposure levels were taken as the current arsenic concentration in the drinking water in micrograms per liter. The dose index was the present arsenic level divided by individual body weight in micrograms per liter per kilogram (μg/L-kg), which may crudely account for arsenic intake in relation to body size.

Statistical analysis. Participants were stratified by sex and four age categories: 30–39, 40–49, 50–59, and ≥ 60 years. Arsenic levels were categorized as ≤ 150, 151–350, 351–550, 551–1,000, and > 1,000 μg/L. In the analyses, the prevalence rate of skin lesions was considered both in relation to these levels and in relation to the individual body weight in micrograms per liter per kilogram. Cut points for the dose index were ≤ 5, > 5–10, and > 10 μg/L-kg; the highest exposure was 52.3 μg/L-kg.

To allow comparisons without distortion by age, all of the prevalence rates were directly standardized to the world age distribution by the International Agency for Research on Cancer (*16*). Age-adjusted prevalence rates with 95% confidence intervals (CIs) and test for trend were calculated in PEPI version 3 (*17*). A loglinear regression model was used for the arsenic-level dose–response analysis with log as the linkfunction and binomial as the probability distribution (*18*). The model estimated the relative risk per unit and the unit was set to 1,000 μg/L.

Results

The arsenic concentrations in the tube well water used by the study population ranged from 10 to 2,040 μg/L.

Prevalence rate by arsenic levels. Table 1 shows the prevalence rate of skin lesions by arsenic water levels in micrograms per liter. There were skin lesions in 279 of 903 males and in 151 of 578 females. The male to female ratio was 1.2:1. The overall crude prevalence rate was 29/100; males had a higher rate in almost all age groups. A dose–response relationship was apparent, independent of sex, between water levels of arsenic and the prevalence rate of skin lesions ($p < 0.05$). The loglinear regression, with adjustment for age, showed a significant trend for males [relative risk (RR), 1.55 per 1,000 μg/L; CI, 1.23–1.91] and females (RR, 1.42 per 1,000 μg/L; CI, 1.04–1.90).

Prevalence rate and exposure by dose index. When the prevalence rate of skin lesions was considered by dose index, the age-adjusted prevalence rate in females increased from 19.7/100 in the lowest dose index to 30.8/100 in the highest dose index category. In the lowest category, the age-adjusted prevalence rate of skin lesions for men was 19.6/100 and increased to 34.8/100 for the highest dose-index category. For both males and females the trend was significant, $p < 0.001$ (Table 2).

Discussion

The morbidity from skin lesions due to chronic arsenic toxicity included almost one-third of the population in the studied ages of ≥ 30 years. This study clearly indicates a consistent dose–response relationship between arsenic concentration in drinking water and skin lesions for different ways of assessing exposure. The relatively good individual exposure data and the fairly large numbers involved are major strengths of this study. Despite publication of several papers that deal with skin lesions and elevated arsenic levels in drinking water (*3,8,9,19,20*), the majority of those earlier studies lack individual exposure data or have rather small study populations, except for a 1998 study from India (*20*). This study showed a high prevalence rate of hyperpigmentation, 22.7/100 for males and 11.5/100 for females, in the highest exposure category, ≥ 800 μg/L. The arsenic concentration in the drinking water ranged from nondetectable to 3,400 μg/L.

The presence of a stable population in rural villages with different degrees of arsenic exposure enabled us to study the dose–response pattern of skin lesions. There are some limitations, however, such as the

Table 1. Prevalence rate of skin lesions per 100 study subjects by age, sex, and arsenic exposure levels.

	Arsenic levels (μg/L)[a]					
Age	≤ 150	151–350	351–550	551–1,000	> 1,000	Total (μg/L)[a]
Males						
30–39	23.0 (14/61)	29.7 (27/91)	31.2 (30/96)	43.1 (31/72)	27.3 (21/77)	31.0 (123/397)
40–49	20.9 (9/43)	25.4 (16/63)	36.0 (27/75)	46.2 (24/52)	29.7 (11/37)	32.2 (87/270)
50–59	5.3 (1/19)	17.4 (4/23)	40.5 (17/42)	28.9 (11/38)	48.3 (14/29)	31.1 (47/151)
≥ 60	22.2 (4/18)	13.3 (2/15)	25.0 (5/20)	26.3 (5/19)	46.2 (6/13)	25.9 (22/85)
All ages	19.9 (28/141)	25.5 (49/192)	33.9 (79/233)	39.2 (71/181)	33.3 (52/156)	30.9 (279/903)
Age-adj PR	18.6	21.9	32.9	36.8	37.0	30.1
CI	11.8–25.4	15.3–28.5	26.0–39.7	29.3–44.4	27.8–46.1	26.7–33.5
Females						
30–39	13.8 (4/29)	20.0 (13/65)	27.5 (14/51)	37.5 (21/56)	21.4 (12/56)	24.9 (64/257)
40–49	17.6 (3/17)	19.5 (8/41)	35.7 (15/42)	39.0 (16/41)	25.0 (8/32)	28.9 (50/173)
50–59	4.8 (1/21)	23.1 (3/13)	23.8 (5/21)	41.9 (13/31)	19.2 (5/26)	24.1 (27/112)
≥ 60	33.3 (1/3)	20.0 (1/5)	40.0 (2/5)	18.2 (2/11)	33.3 (4/12)	27.8 (10/36)
All ages	12.9 (9/70)	20.2 (25/124)	30.3 (36/119)	37.4 (52/139)	23.0 (29/126)	26.1 (151/578)
Age-adj PR	17.9	20.5	32.1	34.0	24.9	26.5
CI	3.1–32.6	9.7–31.3	19.6–44.6	25.4–42.6	16.0–33.8	21.9–31.2

Abbreviations: adj, adjusted; CI, 95% confidence interval; PR, prevalence rates.
[a]Cases and total number of study subjects in parentheses. Chi-square for trend: $\chi^2 = 12.34$, $p < 0.001$ (males); $\chi^2 = 5.82$, $p < 0.02$ (females).

Table 2. Prevalence rate of skin lesions per 100 study subjects by age, sex, and arsenic dose index.

Sex/age	Dose index 1[a,b] (μg/L-kg)	Dose index 2[a,c] (μg/L-kg)	Dose index 3[a,d] (μg/L-kg)
Males			
30–39	23.7 (28/118)	37.8 (34/90)	32.3 (61/189)
40–49	21.5 (17/79)	41.8 (28/67)	33.9 (42/124)
50–59	10.0 (3/30)	33.3 (10/30)	37.4 (34/91)
≥ 60	20.7 (6/29)	6.7 (1/15)	36.6 (15/41)
Total age	21.1 (54/256)	36.1 (73/202)	34.2 (152/445)
Age-adj PR	19.6	30.2	34.8
CI	14.2–24.9	23.9–36.5	29.7–39.9
Females			
30–39	13.0 (7/54)	26.6 (17/64)	28.8 (40/139)
40–49	16.7 (6/36)	25.0 (10/40)	35.0 (34/97)
50–59	7.7 (2/26)	18.8 (3/16)	31.4 (22/70)
≥ 60	40.0 (2/5)	16.7 (1/6)	28.0 (7/25)
Total age	14.0 (17/121)	24.6 (31/126)	31.1 (103/331)
Age-adj PR	19.7	22.1	30.8
CI	8.0–31.3	12.4–31.7	24.9–36.8

Abbreviations: adj, adjusted; CI, 95% confidence interval; PR, prevalence rates.
[a]Cases and total number of study subjects in parentheses. Chi-square for trend: $\chi^2 = 11.11$; $p < 0.001$ (males); $\chi^2 = 13.37$; $p < 0.001$ (females). [b]≤ 5 μg/L-kg. [c]> 5–10 μg/L-kg. [d]> 10 μg/L-kg.

unsystematic sampling of water supplies in the study areas, the lack of subjects younger than 30 years of age, the lack of information on deaths caused by high exposure to arsenic, and the lack of information on the amount of water consumed by the individuals. On the other hand, each individual had only one main source of drinking water with a known arsenic concentration even if the concentrations might have varied in the same well over time. There is no information in this respect, however, because arsenic analyses had not previously been performed in the villages in the study. In spite of these uncertainties and limitations it is nevertheless reasonable to believe that the available water measurements were proper enough for creating the broad exposure categories used in the analyses. There is a stronger dose response when using a dose index instead of levels to assess exposure. It may be assumed, therefore, that arsenic levels in relation to body weight more accurately reflect the dose of arsenic obtained by the individual rather than just the water concentration.

Chakraborty and Saha have studied the incidence of arsenical dermatosis in 14 villages of West Bengal, India (*21*). According to their study the lowest arsenic concentration in water producing dermatosis was 200 µg/L. The present study has numbers too small in lower level categories to calculate the lowest arsenic concentration producing skin lesions.

An important question is how arsenic concentrations might vary in well water by time. The valence state of arsenic present in the water is also of interest. Convincing epidemiologic evidence indicates that trivalent arsenic is more toxic than pentavalent arsenic, although both valences have been classified as carcinogenic (*13*). A thorough monitoring scheme should better establish the relationships between the degree of exposure, valence state, and the cutaneous lesions in Bangladesh and elsewhere. Government and public health officials in Bangladesh and elsewhere are aware of the devastating arsenic pollution crisis. There is an urgent need for a technical solution on how to provide good quality drinking water to a large population.

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