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Arsenic levels in drinking water and the prevalence of skin lesions in West Bengal, India

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Background A cross-sectional survey was conducted between April 1995 and March 1996 to investigate arsenic-associated skin lesions of keratosis and hyperpigmentation in West Bengal, India, and to determine their relationship to arsenic water levels.

Methods In all, 7683 participants were examined and interviewed, and the arsenic levels in their drinking water measured.

Results Although water concentrations ranged up to 3400 μg/l of arsenic, over 80% of participants were consuming water containing <500 μg/l. The age-adjusted prevalence of keratosis was strongly related to water arsenic levels, rising from zero in the lowest exposure level (<50 μg/l) to 8.3 per 100 for females drinking water containing >800 μg/l, and increasing from 0.2 per 100 in the lowest exposure category to 10.7 per 100 for males in the highest exposure level (⩾800 μg/l). However, 12 cases with keratosis (2 females and 10 males) were drinking water containing <100 μg/l of arsenic. Findings were similar for hyperpigmentation, with strong dose-response relationships. Among those with hyperpigmentation, 29 cases were exposed to drinking water containing <100 μg/l. Calculation by dose per body weight showed that men had roughly two to three times the prevalence of both keratosis and hyperpigmentation compared to women apparently ingesting the same dose of arsenic from drinking water. Subjects who were below 80% of the standard body weight for their age and sex had a 1.6 fold increase in the prevalence of keratoses, suggesting that malnutrition may play a small role in increasing susceptibility.

Conclusion The surprising finding of cases who had arsenic-associated skin lesions with apparently low exposure to arsenic in drinking water needs to be confirmed in studies with more detailed exposure assessment. Further research is also needed concerning susceptibility factors which might be present in the exposed population.

Keywords Arsenic, keratosis, hyperpigmentation, India, cross-sectional study, drinking water

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An environmental tragedy is developing in West Bengal, India where a large population is drinking arsenic-contaminated water, and an alarming number of toxicity cases associated with ingestion of arsenic-contaminated drinking water have been reported. The source of the contamination is geological; arsenic in groundwater has been found above 50 μg/l (the current drinking water standard in much of the world) in seven of the 16 districts of West Bengal.[1] The seven affected districts of West Bengal have a population of over 34 million, and an area of 37 493 km^2.[1] Investigators in West Bengal suspect that at least 800 000 people have been consuming arsenic-contaminated water.[2,3] New regions of contamination are being discovered, with a potentially exposed population of over 1 million.[4]

The duration of arsenic exposure in India is uncertain, but it is thought that the problem began in the late 1960s when digging of tubewells commenced as part of a state-wide irrigation plan.[4,5] Because groundwater was cleaner than water from tanks, ponds and the polluted Ganges River, many inhabitants

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switched to using tubewell water. The contamination of groundwater with arsenic was first detected in 1978, and the first arsenic poisoning cases were reported in the early 1980s.[5–7] Most of the affected villages are located along the western side of the Ganges River. A survey conducted by Das *et al.*[8] which was limited to regions with levels >50 μg/l, indicated that the arsenic concentration was generally between 50 to 500 μg/l in the drinking water supplies. However, concentrations have reached nearly 3000 μg/l in some villages.

Although limited epidemiological data exist, the reported clinical manifestations resulting from ingestion of arsenic-contaminated drinking water include weakness, conjunctival congestion, hyperpigmentation, keratosis, hepatomegaly, portal hypertension, respiratory system effects, polyneuropathy, solid oedema of limbs, and malignant neoplasms.[7,9] Skin abnormalities such as pigmentation change and keratosis have long been known to be hallmark signs of chronic arsenic exposure. Pigmentation changes and keratotic lesions were the most common health effect found in populations exposed to arsenic-contaminated drinking water in Taiwan,[10,11] Chile,[12] and Argentina.[13,14] Hyperpigmentation and keratoses caused by arsenic are quite distinctive. The hyperpigmentation is marked by raindrop-shaped discolored spots, diffuse dark brown spots, or diffuse darkening of the skin on the limbs and trunk.[7] Simple keratosis usually appears as bilateral thickening of the palms and soles, while in nodular keratosis, small protrusions appear on the palms and soles, with or without nodules on the dorsum of the hands, feet, or the legs. Skin lesions pose an important public health problem in India because advanced forms of keratosis are painful, and the consequent disfigurement can lead to social isolation in the villages.[3] In contrast to cancers which take decades to develop, these skin lesions are generally observed 5–10 years after exposure commences.

To determine the prevalence of the various health effects associated with arsenic, a cross-sectional study was conducted in one of the most affected districts of West Bengal, the South 24 Parganas between April 1995 through March 1996. The South 24 Parganas was a suitable location for this survey because of the heterogeneity in exposure, which enabled the investigators to collect exposure-response data. The drinking water arsenic levels in this district ranged from non-detectable to 3400 μg/l. The most prevalent health effects found in the study population were keratosis and hyperpigmentation, and are the focus of this paper.

Methods

Study area and population

Two particular areas within this district were targeted for the survey. The first area was selected because high levels of arsenic were detected in some, but not all, of the shallow tubewells as determined in a prior study.[1,7] The second area included the remaining part of the district where people used shallow tubewell water for drinking purposes. Our survey was the first of its kind in this area; thus, no reports of elevated arsenic levels were available before the survey. The two areas combined contain a total population of 150 457. A total of 7818 individuals participated in the drinking water study. Water-arsenic levels were obtained for 7683 of the participants (4093 females and 3590 males), who constitute the study subjects for this paper.

The high exposure region included 25 villages. Convenience sampling was used for this study which involved remote rural areas. The study team went to the centre of each village and selected the most convenient hamlet (group of houses) to commence sampling. Each member of the household present at the time of the interview was invited to participate. An interview was administered and a brief medical examination was conducted. Sampling continued house-to-house in a village until 50 to 150 participants were recruited.

The low exposure region included 32 villages within 16 administrative blocks. Sampling in this region was restricted to villages with more than 100 houses. One or more villages were selected at random from each of the 16 blocks depending on the population size. Only one village was selected for sampling from a small block, but two or three villages were selected if the block was larger. Again, the study team went to the centre of each village and selected the most convenient hamlet to commence sampling; but, this time residents of every fourth house were invited to participate.

Interview and medical examination

Each participant was questioned briefly about his or her sources of drinking water, current diet and water intake, medical symptoms, height and weight and other variables. A general medical examination was given, including a careful inspection for arsenic skin lesions.

The criteria for classifying keratoses and hyperpigmentation as arsenic-caused were as follows. Keratoses had to involve diffuse bilateral thickening of palms and/or soles with or without nodules of various shapes and sizes. Hyperpigmentation was identified if there were areas of mottled dark brown pigmentation bilaterally distributed on the trunk. Hyperpigmentation was frequently present also on the limbs, and sometimes alongside spots of depigmentation, but these characteristics were not regarded as essential for the diagnosis. All patients were examined in the field by one of two physicians who have had about 10 years experience each in diagnosing arsenic-caused skin lesions in West Bengal, including examining patients regularly in the Arsenic Clinic in the hospital linked with the Postgraduate Medical Institute in Calcutta.

The field work was designed to minimize subjectivity in examining for skin lesions. Field workers inevitably knew if a village they were working in was located in the high exposure area or the low exposure area, but they did not know the tubewell arsenic concentrations at the time of the survey. Each participant was first interviewed by a trained field worker concerning their drinking water consumption and tubewell used, and then examined by one of the two physicians. Water samples were obtained from the tubewell on the same day as the interview and medical examinations, but results of analyses for arsenic were not known until months later. Thus, the physical examinations for skin lesions were conducted blind as to water arsenic concentrations which varied widely, with contaminated wells scattered irregularly throughout the study region.

Water sampling and arsenic measurement

Water samples were collected from private and public tubewells used for drinking and cooking purposes by each recruited household. Arsenic levels were measured by flow-injection hydride generation atomic absorption spectrophotometry. Daily dose per

Table 1 Age, sex, and arsenic water level (μg/l) distribution of the study population

	Arsenic level (μ/l)								
Age group	<50	50–99	100–149	150–199	200–349	350–499	500–799	⩾800	Total
Females									
⩽9	194	31	53	23	84	50	75	26	536
10–19	400	74	58	54	117	57	65	26	851
20–29	577	102	99	74	135	63	83	24	1157
30–39	308	79	48	46	79	40	44	15	659
40–49	175	33	23	27	36	21	28	10	353
50–59	157	38	23	18	27	18	30	11	322
⩾60	97	29	9	17	27	20	10	6	215
All ages	1908	386	313	259	505	269	335	118	4093
Males									
⩽9	220	64	65	27	77	51	81	28	613
10–19	330	73	49	56	96	51	64	29	748
20–29	356	79	56	52	79	43	59	25	749
30–39	246	63	38	40	75	44	53	18	577
40–49	160	43	29	24	53	22	25	12	368
50–59	121	34	20	21	27	16	15	6	265
⩾60	126	34	20	21	27	16	15	6	265
All ages	1559	385	274	235	442	246	320	129	3590

body weight was computed by multiplying the water-arsenic concentration by estimated daily water intake, and then dividing by body weight.

Statistical analysis

Participants were stratified by age, and the prevalence of keratosis and hyperpigmentation were calculated for each sex separately. To allow comparison without distortion by age, the prevalences were directly standardized to the age distribution of all participants of the same sex in the study population. Skin effects were examined by water arsenic levels which were categorized as follows: <50, 50–99, 100–149, 150–199, 200–349, 350–499, 500–799, and ⩾800 μg/l. Tests for trends in proportions were based on the χ^2 distribution using the mid-points of each grouping of arsenic-water levels.[15] Since age adjustments had little impact on non-adjusted prevalence estimates, the tests for trends were conducted on the unadjusted data. In view of a clear one-directional *a priori* hypotheses, one tailed *P*-values are presented.

The prevalence of skin lesions was also examined by tertiles of daily arsenic dose per body weight (μg/kg/day). Using all subjects, the cut points for the tertiles were: 3.2 and 14.9. The highest dose per body weight found was 73.9 μg/kg/day. Tests for trend in proportions were conducted using the mid-points of each dose tertile (1.6, 9.1, and 44.4 μg/kg/day).

To obtain an approximate indication of nutritional status, we examined individual body weight in relation to standard weight values. Each subject's weight was compared to a table of average values for Indian males and females based on height, age and sex.[16] These standards were compiled from an extensive database of weights, heights and ages of Indian females and males obtained from a life insurance company, and are widely used by insurance companies in India. The cutoff for categorizing subjects into those who might be of poor nutritional status and those with adequate nutrition was 80% of the standard weight; i.e. those with weights 20% or more below the standard for their age, sex, and height were considered likely to have poor nutrition, while those above this cutoff were considered likely to have adequate nutrition. Because of small numbers in the age-specific categories with low body weight, indirect age standardization was conducted. Using those who had adequate nutritional status as a reference group, standardized morbidity ratios (observed cases with skin lesions divided by expected cases) were calculated for each tertile of dose per body weight. Statistical tests of significance were based on the Poisson distribution and 95% confidence intervals (CI) were calculated using exact methods.[17]

Results

Tubewell water concentration

The age, sex and water-arsenic level distribution of the study population is presented in Table 1. The tubewell arsenic concentrations ranged from non-detectable to 3400 μg/l. Altogether, measurements were made on 644 tubewells used by the study participants; 282 of these tubewells had arsenic concentrations >50 μg/l. Keratosis prevalence was examined by arsenic-water levels. Of the 4093 female participants, 48 had keratotic skin lesions (Table 2). A clear relationship was apparent between water levels of arsenic and the prevalence of keratosis. The test for trend yielded a *P*-value <0.001. Similar findings were found for males (Table 2) and for hyperpigmentation in both males and females (Table 3 and Figure 1).

Dose per body weight

The prevalence of skin lesions was also examined by daily dose per body weight (μg/kg/day). The age-adjusted prevalence of keratosis in females rose from 0.8 per 100 in the lowest tertile

Table 2 Keratosis prevalence per 100 by age groups and arsenic exposure level (μg/l) among females with number of cases in parentheses

	Arsenic level (μ/l)								
Age group	<50	50–99	100–149	150–199	200–349	350–499	500–799	⩾800	Total
Females									
⩽9	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.0 (1)	0.0 (0)	0.0 (0)	0.2 (1)
10–19	0.0 (0)	0.0 (0)	0.0 (0)	1.9 (1)	2.6 (3)	0.0 (0)	3.1 (2)	11.5 (3)	1.0 (9)
20–29	0.0 (0)	0.0 (0)	1.0 (1)	1.4 (1)	1.5 (2)	3.2 (2)	0.0 (0)	4.2 (1)	0.6 (7)
30–39	0.0 (0)	2.5 (2)	0.0 (0)	2.2 (1)	2.5 (2)	2.5 (1)	4.6 (2)	0.0 (0)	1.2 (8)
40–49	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	5.6 (2)	9.5 (2)	10.7 (3)	10.0 (1)	2.3 (8)
50–59	0.0 (0)	0.0 (0)	4.4 (1)	11.1 (2)	0.0 (0)	0.0 (0)	10.0 (3)	27.3 (3)	2.8 (9)
⩾60	0.0 (0)	0.0 (0)	11.1 (1)	5.9 (1)	3.7 (1)	5.0 (1)	0.0 (0)	33.3 (2)	2.8 (6)
All ages	0.0 (0)	0.5 (2)	1.0 (3)	2.3 (6)	2.0 (10)	2.6 (7)	3.0 (10)	8.5 (10)	1.2 (48)
Age-adjusted	0.0	0.4	1.2	2.3	2.0	2.7	3.1	8.3	1.2
Males									
⩽9	0.0 (0)	0.0 (0)	0.0 (0)	3.7 (1)	1.3 (1)	2.0 (1)	0.0 (0)	0.0 (0)	0.5 (3)
10–19	0.3 (1)	0.0 (0)	0.0 (0)	1.8 (1)	5.2 (5)	3.9 (2)	3.1 (2)	6.9 (2)	1.7 (13)
20–29	0.0 (0)	0.0 (0)	1.8 (1)	3.8 (2)	5.1 (4)	7.0 (3)	10.2 (6)	20.0 (5)	2.8 (21)
30–39	0.4 (1)	3.7 (2)	2.6 (1)	7.5 (3)	6.7 (5)	15.9 (7)	18.9 (10)	22.2 (4)	5.7 (33)
40–49	0.0 (0)	4.7 (2)	0.0 (0)	8.3 (2)	5.7 (3)	27.3 (6)	12.0 (3)	8.3 (1)	4.6 (17)
50–59	0.8 (1)	6.9 (2)	5.9 (1)	6.7 (1)	8.6 (3)	15.8 (3)	13.0 (3)	9.1 (1)	5.6 (15)
⩾60	0.8 (1)	0.0 (0)	5.0 (1)	4.8 (1)	3.7 (1)	0.0 (0)	13.3 (2)	0.0 (0)	2.3 (6)
All ages	0.3 (4)	1.6 (6)	1.5 (4)	4.7 (11)	5.0 (22)	8.9 (22)	8.1 (26)	10.1 (13)	3.0 (108)
Age-adjusted	0.2	1.5	1.6	4.7	4.9	9.0	8.9	10.7	3.0

Analysis for linear trend in proportions using unadjusted data: $P < 0.0001$ for each sex.

Table 3 Hyperpigmentation prevalence per 100 by age groups and arsenic exposure level (μg/l) among females with number of cases in parentheses

	Arsenic level (μ/l)								
Age group	<50	50–99	100–149	150–199	200–349	350–499	500–799	⩾800	Total
Females									
⩽9	0.0 (0)	0.0 (0)	1.9 (1)	0. 0 (0)	2.4 (2)	12.0 (6)	0.0 (0)	0.0 (0)	1.7 (9)
10–19	0.0 (0)	0.0 (0)	1.7 (1)	5.6 (3)	7.7 (9)	1.8 (1)	3.1 (2)	11.5 (3)	2.2 (19)
20–29	0.0 (0)	0.0 (0)	1.0 (1)	4.0 (3)	4.4 (6)	11.1 (7)	6.0 (5)	8.3 (2)	2.1 (24)
30–39	0.0 (0)	1.3 (1)	12.5 (6)	6.5 (3)	8.9 (7)	12.5 (5)	0.0 (0)	6.7 (1)	3.5 (23)
40–49	1.4 (2)	0.0 (0)	13.0 (3)	3.7 (1)	16.7 (6)	14.3 (3)	17.9 (5)	20.0 (2)	6.2 (22)
50–59	1.9 (3)	2.6 (1)	13.0 (3)	11.1 (2)	0.0 (0)	5.6 (1)	16.7 (5)	27.3 (3)	5.6 (18)
⩾60	0.0 (0)	6.9 (2)	11.1 (1)	11.8 (2)	7.4 (2)	15.0 (3)	0.0 (0)	33.3 (2)	5.6 (12)
All ages	0.3 (5)	1.0 (4)	5.1 (16)	5.4 (14)	6.3 (32)	9.7 (26)	5.1 (17)	11.0 (13)	3.1 (127)
Age-adjusted	0.3	0.8	5.7	5.1	6.5	9.5	5.3	11.5	3.1
Males									
⩽9	0.0 (0)	0.0 (0)	4.6 (3)	3.7 (1)	3.9 (3)	5.9 (3)	0.0 (0)	7.1 (2)	2.0 (12)
10–19	0.0 (0)	2.7 (2)	2.0 (1)	3.6 (2)	9.4 (9)	11.8 (6)	3.1 (2)	13.8 (4)	3.5 (26)
20–29	0.8 (3)	1.3 (1)	12.5 (7)	11.5 (6)	17.7 (14)	14.0 (6)	13.6 (8)	36.0 (9)	7.2 (54)
30–39	0.4 (1)	3.2 (2)	15.8 (6)	12.5 (5)	13.3 (10)	22.7 (10)	22.6 (12)	33.3 (6)	9.0 (52)
40–49	0.0 (0)	11.6 (5)	10.3 (3)	8.3 (2)	13.2 (7)	40.9 (9)	16.0 (4)	25.0 (3)	9.0 (33)
50–59	2.5 (3)	6.9 (2)	5.9 (1)	6.7 (1)	28.6 (10)	15.8 (3)	39.1 (9)	45.5 (5)	12.6 (34)
⩾60	0.0 (0)	2.9 (1)	45.0 (9)	9.5 (2)	18.5 (5)	6.3 (1)	33.3 (5)	0.0 (0)	8.7 (23)
All ages	0.5 (7)	3.4 (13)	11.0 (30)	8.1 (19)	13.2 (58)	15.5 (38)	12.5 (40)	22.5 (29)	6.5 (234)
Age-adjusted	0.4	3.2	11.0	7.8	13.1	15.7	13.8	22.7	6.4

Analysis for linear trend in proportions using unadjusted data: $P < 0.0001$ for both sexes.

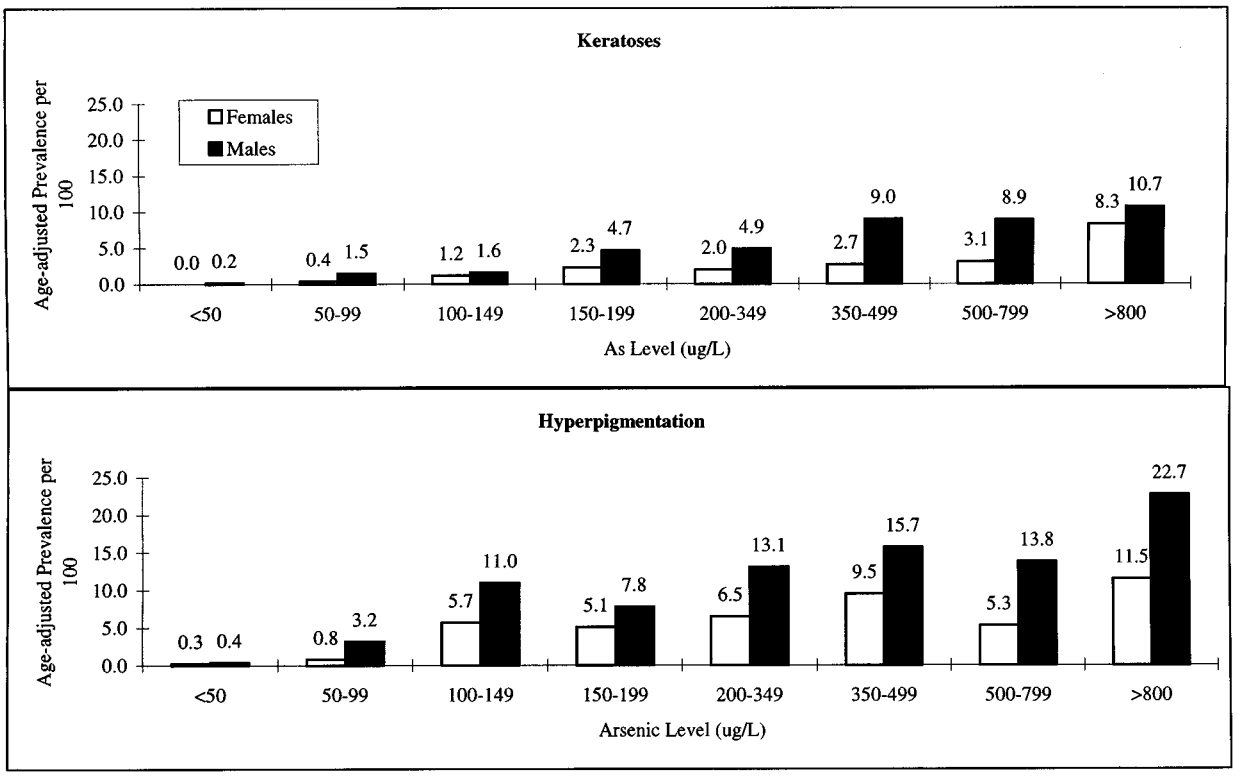

Figure 1 Prevalence of keratoses and hyperpigmentation per 100 for females and males in West Bengal, India, 1995–1996

(<3.2 µg/kg/day) to 3.5 per 100 in the highest tertile (>14.9 µg/kg/day) (Table 4). Using the unadjusted data, the one-tailed *P*-value test for trend for females was 0.03. A steeper pattern was apparent with males ($P < 0.001$, Table 4). In the lowest tertile, the age-adjusted prevalence of keratosis was 0.8 per 100 among males; in the highest tertile, the prevalence reached 11.0 per 100. The findings for hyperpigmentation paralleled those for keratosis (Table 4), with males again showing higher prevalence based on estimation of dose per body weight.

Findings among those with low body weights

Of the 2320 females with known body weights, 690 (30%) were below the standard weight by ⩾20%. Of the 2123 males with known values, 808 (38%) were below the standard weight by ⩾20%.

Compared to those with adequate nutrition, subjects ⩾20% below the standard weight had a higher age-adjusted prevalence of keratosis (Table 5). The overall SMR for keratosis was 2.1 for females (95% CI : 0.8–4.6, $P = 0.07$) indicating that the age-adjusted keratosis prevalence among females with potentially poor nutrition was approximately twice that of females considered to have adequate nutrition. The overall SMR for males was 1.5 (95% CI : 0.9–2.4, $P = 0.08$). The combined SMR for both sexes was 1.6 (95% CI : 1.0–2.4, $P = 0.02$).

Weaker associations were found for hyperpigmentation. The overall SMR for females was 1.8 (95% CI : 0.8-3.5, $P = 0.09$) (Table 5). Thus, women with poor nutritional status had an age-adjusted hyperpigmentation prevalence nearly twice that of females considered to have adequate nutrition. This increase was less apparent in males, where the increase in the age-adjusted prevalence was only 10% greater among those with poor nutrition (SMR = 1.1, 95% CI : 0.7–1.7, $P = 0.39$). Combining men and women, the overall SMR was 1.2 (95% CI : 0.8–1.8, $P = 0.17$).

Discussion

This is the first population study assessing water levels of arsenic and skin lesions in India in a structured population survey. Clear exposure-response relationships were found between water-arsenic levels and the prevalence of skin effects. The steepest exposure-response relationships were found for males (Figure 1, Tables 2 and 3). This finding is not explained by the fact that males have a greater water consumption because this pattern was also apparent when the prevalence of skin lesions was analysed by tertiles of daily dose per body weight, using identical groupings for each sex (Table 4).

The most striking finding was identifying cases with skin lesions who apparently had low levels of arsenic in their drinking water. It is possible that these individuals were exposed to high levels of arsenic from drinking water sources other than the one measured in the survey; e.g. from their worksite or past residences. We are currently planning a further investigation focusing on participants in this study with low levels of arsenic in their drinking water.

Previous studies conducted in West Bengal have reported numerous cases of skin lesions.[5,7] Chakraborty and Saha[5] conducted a cross-sectional study of five affected regions in West

Table 4 Age-adjusted keratosis and hyperpigmentation prevalence per 100 by dose per body weight for females and males, with numbers of cases in parentheses

Age group	Tertile 1	Tertile 2	Tertile 3	test for trend
Keratosis				
Females				
⩽9	0.0 (0)	0.0 (0)	3.1 (1)	
10–19	0.0 (0)	0.0 (0)	3.5 (2)	
20–29	0.0 (0)	1.5 (1)	2.9 (2)	
30–39	2.1 (1)	2.3 (1)	2.5 (1)	
40–49	0.0 (0)	2.5 (1)	0.0 (0)	
50–59	0.0 (0)	6.3 (1)	10.5 (2)	
⩾60	8.3 (1)	13.3 (2)	6.3 (1)	
All ages	0.7 (2)	2.3 (6)	3.5 (9)	$P = 0.028$
Age-adjusted	0.8	2.2	3.5	
Males				
⩽9	0.0 (0)	0.0 (0)	2.9 (1)	
10–19	0.0 (0)	1.6 (1)	6.6 (4)	
20–29	0.0 (0)	5.9 (3)	11.1 (6)	
30–39	2.5 (1)	10.3 (3)	21.2 (14)	
40–49	0.0 (0)	9.7 (3)	20.0 (6)	
50–59	0.0 (0)	5.0 (1)	20.0 (5)	
⩾60	5.9 (1)	0.0 (0)	0.0 (0)	
All ages	0.8 (2)	4.2 (11)	12.7 (36)	$P < 0.001$
Age-adjusted	0.8	4.6	11.0	
Hyperpigmentation				
Females				
⩽9	0.0 (0)	3.5 (1)	9.4 (3)	
10–19	0.0 (0)	1.9 (1)	3.5 (2)	
20–29	0.0 (0)	2.9 (2)	4.3 (3)	
30–39	0.0 (0)	2.3 (1)	2.5 (1)	
40–49	0.0 (0)	2.5 (1)	4.6 (1)	
50–59	0.0 (0)	0.0 (0)	15.8 (3)	
⩾60	0.0 (0)	13.3 (2)	12.5 (2)	
All ages	0.0 (0)	3.0 (8)	5.9 (15)	$P < 0.001$
Age-adjusted	0.0	2.9	5.9	
Males				
⩽9	0.0 (0)	0.0 (0)	5.7 (2)	
10–19	0.0 (0)	3.2 (2)	9.8 (6)	
20–29	0.0 (0)	13.7 (7)	16.7 (9)	
30–39	0.0 (0)	10.3 (3)	21.2 (14)	
40–49	0.0 (0)	6.5 (2)	30.0 (9)	
50–59	0.0 (0)	5.0 (1)	24.0 (6)	
⩾60	5.9 (1)	10.0 (2)	7.7 (1)	
All ages	0.4 (1)	6.5 (17)	16.6 (47)	$P < 0.001$
Age-adjusted	0.4	6.9	15.2	

Table 5 Standardized morbidity ratios (SMR) and 95% confidence intervals (CI) for keratosis and hyperpigmentation by tertiles of dose per body weight for subjects below 80% of the standard weight using those above 80% for each sex separately as the referent population

	Tertile 1[a]	Tertile 2[b]	Tertile 3[c]	Overall
Keratosis				
Female				
Observed/Expected	1/0.3	1/0.7	4/1.9	6/2.8
SMR	3.1	1.5	2.2	2.1
95% CI	(0.1–17.4)	(0.04–8.3)	(0.6–5.5)	(0.8–4.6)
P-value	0.27	0.49	0.12	0.07
Male				
Observed/Expected	0/0.6	2/1.2	14/9.0	16/10.8
SMR	0	1.7	1.6	1.5
95% CI	(0–4.7)	(0.2–6.0)	(0.9–2.6)	(0.9–2.4)
P-value	–	0.34	0.07	0.08
Both sexes				
Observed/Expected	1/0.96	3/1.87	18/10.8	22/13.7
SMR	1.0	1.6	1.7	1.6
95% CI	(0.03–5.80)	(0.3–4.7)	(1.0–2.6)	(1.0–2.4)
P-value	0.62	0.29	0.03	0.02
Hyperpigmentation				
Female				
Observed/Expected	0/0	2/0.7	6/3.8	8/4.5
SMR	0	2.8	1.6	1.8
95% CI	–	(0.4–10.3)	(0.6–3.4)	(0.8–3.5)
P-value	–	0.16	0.19	0.09
Male				
Observed/Expected	0/0.4	4/2.6	15/14.5	19/17.1
SMR	0	1.5	1.0	1.1
95% CI	(0–7.1)	(0.4–3.9)	(0.6–1.7)	(0.7–1.7)
P-value	–	0.26	0.49	0.39
Both sexes				
Observed/Expected	0/0.42	6/3.3	21/18.3	27/22.0
SMR	0	1.8	1.1	1.2
95% CI	(0–7.1)	(0.7–4.0)	(0.7–1.8)	(0.8–1.8)
P-value	–	0.12	0.29	0.17

[a] 0–3.2 μg/kg/day.

[b] 3.2–14.9 μg/kg/day.

[c] 14.9–73.9 μg/kg/day.

Bengal. Their study revealed that high amounts of arsenic in the tubewell water were associated with keratoses and hyperpigmentation, the most common health effects in their study population. Of 784 exposed individuals, 197 (25%) were found to have keratosis or hyperpigmentation. The mean drinking-water arsenic concentration among those with skin lesions was 640 μg/l (range 200–2000 μg/l). Among those without any skin lesions, the mean arsenic concentration was 210 μg/l (range 0–740 μg/l).

Studies conducted in other countries have also investigated the prevalence of hyperpigmentation and keratosis in regions with elevated arsenic levels in drinking water; however, the studies either lacked individual exposure data or had small numbers. For instance, arsenic levels in Taiwan were reported by village.[10,11,18] Mean arsenic levels were reported for an entire affected village in Mexico[19] and China,[20] and by towns in Chile.[12] Thus, a major strength of this study is that it is the first large population-based study with individual exposure data, which can provide critical information with which to characterize the exposure-response relationship.

The overall SMR for keratosis suggested that those with poor nutritional status had an age-adjusted prevalence that was 1.6

times greater than those considered to be adequately nourished (SMR = 1.6, 95% CI : 1.0–2.4, $P = 0.02$). The overall SMR for hyperpigmentation for both sexes combined was 1.2 (95% CI : 0.8–1.8, $P = 0.17$). These small differences do not suggest that malnutrition is the reason for the high prevalence of skin lesions in West Bengal. Nevertheless, it is still possible that some dietary factors affect the susceptibility of the whole population, malnourished or not.

Limitations of this cross-sectional study involve the methods that were used for the sampling strategy and estimation of the doses. Because the survey involved remote rural areas, a perfectly random sample could not be obtained. However, no reason exists to believe that the convenience sampling strategy used would have resulted in a non-representative study population. The dose calculations relied upon estimates of daily water consumption. Although this measure is prone to error because of inaccurate recall of water intake, the main determinant of the exposure is the arsenic concentration in water. Therefore, it is unlikely that gross discrepancies in reported water consumption exist which could have led to a major misclassification of dose. Nevertheless, more detailed exposure assessment and measurement of all past and present water arsenic levels may show that those thought to be consuming low arsenic water may actually have been more heavily exposed from other sources.

In conclusion, this study demonstrates clear exposure-response relationships between the prevalence of skin lesions and both arsenic water levels and dose per body weight, with males showing greater prevalence of both keratosis and hyperpigmentation. Based on limited exposure assessment, some cases appear to be occurring at surprisingly low levels of exposure. There is evidence that the risks were somewhat greater for those who might be malnourished. Further studies are needed to confirm the apparent low exposure effects, to determine why males have more skin effects than females at the same doses per body weight, and to identify susceptibility factors which may be present in this population.

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References

[1] Mandal BK, Chowdhury TR, Samanta G *et al.* Arsenic in groundwater in seven districts of West Bengal, India—the biggest arsenic calamity in the world. *Curr Sci* 1996;**70:**976–86.

[2] Chatterjee A, Das D, Mandal BK, Chowdhury TR, Samanta G, Chakraborti D. Arsenic in ground water in six districts of West Bengal, India: the biggest arsenic calamity in the world. Part I. Arsenic species in drinking water and urine of the affected people. *Analyst* 1995; **120:**643–50.

[3] Das D, Chatterjee A, Samanta G *et al.* Arsenic contamination in ground water in six districts of West Bengal, India: the biggest arsenic calamity in the world. *Analyst* 1994;**119:**168N–70N.

[4] Bagla P, Kaiser J. India's spreading health crises draws global arsenic experts. *Science* 1996;**274:**174–75.

[5] Chakraborty AK, Saha KC. Arsenical dermatosis from tubewell water in West Bengal. *Indian J Med Res* 1987;**85:**326–34.

[6] Garai R, Chakraborty AK, Dey SB, Saha KC. Chronic arsenic poisoning from tube-well water. *J Indian Med Assoc* 1984;**82:**32–35.

[7] Guha Mazumder DN, Chakraborty AK, Ghose A *et al.* Chronic arsenic toxicity from drinking tubewell water in rural West Bengal. *Bull World Health Organ* 1988;**66:**499–506.

[8] Das D, Chatterjee A, Mandal BK, Samanta G, Chakraborti D. Arsenic in ground water in six districts of West Bengal, India: the biggest arsenic calamity in the world. Arsenic concentration in drinking water, hair, nails, urine, skin-scale and liver tissue (biopsy) of the affected people. *Analyst* 1995;**120:**917–24.

[9] Guha Mazumder DN, Das Gupta J, Santra A *et al.* Non-cancer effects of chronic arsenicosis with special reference to liver damage. In: Abernathy CO, Calderon RL, Chappell WR (eds). *Arsenic: Exposure and Health Effects*. London: Chapman and Hall, 1997, pp.112–23.

[10] Tseng WP, Chu HM, How SW, Fong JM, Lin CS, Yeh S. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. *J Natl Cancer Inst* 1968;**40:**453–63.

[11] Tseng WP. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. *Environ Health Perspect* 1977;**19:**109–19.

[12] Borgono JM, Vicent P, Venturino H, Infante A. Arsenic in the drinking water of the city of Antofagasta: epidemiological and clinical study before and after the installation of a treatment plant. *Environ Health Perspect* 1977;**19:**103–05.

[13] Zaldivar R. Arsenic contamination of drinking water and food stuffs causing endemic chronic poisoning. *Beitr Path Bd* 1974;**151:**384–400.

[14] Biagini RE. Consideraciones actuales sobre hidroarsenicismo cronico regional endemico (HACRE) *La Semana Medica* 1974;**145:**2171–79.

[15] Breslow NE, Day NE. *Statistical Methods in Cancer Research. Vol. I. The Analysis of Case-Control Studies. IARC Sci Publ.*, 1980.

[16] Antia FP. *Dietetics and Nutrition. Third Edn*. Bombay: Oxford University Press, 1991, pp.418–19.

[17] Breslow NE, Day NE. *Statistical Methods in Cancer Research. Vol. II. The Design and Analysis of Cohort Studies. IARC Sci Publ.*, 1987.

[18] Chen CJ, Chen CW, Wu MM, Kuo TL. Cancer potential in liver, lung, bladder, and kidney due to ingested inorganic arsenic on drinking water. *Br J Cancer* 1992;**66:**888–92.

[19] Cebrian ME, Albores A, Aguilar M, Blakely E. Chronic arsenic poisoning in the north of Mexico. *Hum Toxicol* 1983;**2:**121–33.

[20] Huang YZ, Qian XC, Wang GQ *et al.* Endemic chronic arsenicism in Xinjiang. *Chin Med J (Engl)* 1985;**98:**219–22.