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Arsenic in drinking water and the prevalence of respiratory effects in West Bengal, India

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Background A large population in West Bengal, India has been exposed to naturally occurring inorganic arsenic through their drinking water. A cross-sectional survey involving 7683 participants of all ages was conducted in an arsenic-affected region between April 1995 and March 1996. The main focus of the study was skin keratoses and pigmentation alterations, two characteristic signs of ingested inorganic arsenic. Strong exposure-response gradients were found for these skin lesions. The study also collected limited information concerning respiratory system signs and symptoms, which we report here because increasing evidence suggests that arsenic ingestion also causes pulmonary effects.

Methods Participants were clinically examined and interviewed, and the arsenic content in their current primary drinking water source was measured. There were few smokers and analyses were confined to non-smokers (N = 6864 participants).

Results Among both males and females, the prevalence of cough, shortness of breath, and chest sounds (crepitations and/or rhonchi) in the lungs rose with increasing arsenic concentrations in drinking water. These respiratory effects were most pronounced in individuals with high arsenic water concentrations who also had skin lesions. Prevalence odds ratio (POR) estimates were markedly increased for participants with arsenic-induced skin lesions who also had high levels of arsenic in their current drinking water source ($\geq$500 μg/l) compared with individuals who had normal skin and were exposed to low levels of arsenic ($<$50 μg/l). In participants with skin lesions, the age-adjusted POR estimates for cough were 7.8 for females (95% CI : 3.1–19.5) and 5.0 for males (95% CI : 2.6–9.9); for chest sounds POR for females was 9.6 (95% CI : 4.0–22.9) and for males 6.9 (95% CI : 3.1–15.0). The POR for shortness of breath in females was 23.2 (95% CI : 5.8–92.8) and in males 3.7 (95% CI : 1.3–10.6).

Conclusion These results add to evidence that long-term ingestion of inorganic arsenic can cause respiratory effects.

Keywords Arsenic, respiratory disease, keratoses, hyperpigmentation, cross-sectional study, drinking water, India

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Arsenic-contaminated groundwater has been found in the US, Taiwan,[1] Mexico,[2] Chile[3,4] and Argentina,[5] but the largest reported population exposed to inorganic arsenic is in West Bengal, India and neighbouring Bangladesh.[6] By 1994, investigators estimated that over 800 000 people in West Bengal were exposed to elevated inorganic arsenic levels through drinking water retrieved from tubewells installed in the late 1960s.[7,8] Since the tubewell water was cleaner than surface water from ponds and the Ganges River, many inhabitants switched to using well water. The arsenic source is geological, but controversy exists as to the mechanism whereby inorganic arsenic mobilizes and becomes transported into the groundwater from the bedrock of the Gangetic delta.

Hallmark signs of chronic arsenic toxicity include skin keratoses of the palms and soles, and hyperpigmentation of the torso and upper limbs. These skin lesions generally develop 5–10 years after exposure commences, although shorter latencies are possible. Chronic ingestion of inorganic arsenic causes

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non-melanoma skin cancer, and is also associated with increased risks of cancer of the internal organs.[9] Emerging evidence shows that ingestion of inorganic arsenic may also lead to non-malignant respiratory effects.

Respiratory effects in West Bengal were first noted in 1995 when 57% of the 156 patients who lived in arsenic-affected villages reported having cough.[10] Moreover, epidemiological studies in Chile have previously suggested an association between arsenic and non-malignant respiratory effects. From survey data collected between 1968 and 1972 in Antofagasta, Chile, Zaldivar and Ghai[11] reported that the prevalence of cough among 398 children correlated with mean drinking water arsenic concentrations. In addition, the prevalence of reported cough declined from 38% to 7% after an arsenic removal plant was installed in Antofagasta ($P < 0.001$). Zaldivar[12] also reported that the prevalence of bronchiectasis was 23-fold greater among children with arsenic-induced skin lesions living in Antofagasta compared to children living in the rest of Chile. Rosenberg[13] conducted autopsies on five children who died between 1968 and 1969 in Antofagasta. All five children possessed characteristic signs of chronic arsenic poisoning, including hyperpigmentation and/or keratoses. Lung tissue was examined in four of these children, with abnormalities found in all four. Interstitial fibrosis was detected in two of the cases. A 1976 cross-sectional survey in Antofagasta examined 144 schoolchildren with arsenic-induced skin lesions, and bronchopulmonary disease occurred 2.5 times more often in these children (15.9%) compared with children with normal skin (6.9%).[3] In a recent study, Smith *et al.* [4] found high relative rates for chronic obstructive pulmonary disease (COPD) mortality among young men and women living in the same arsenic-exposed region in Chile which includes Antofagasta. In those aged 30–39 there were four deaths from COPD among males (0.8 expected) and six among women (0.1 expected, SMR [men and women combined] = 11.1, 95% CI : 5.3–20.4, $P < 0.001$). Since COPD mortality was not increased in older age groups, the authors suggested that exposures during childhood were important and led to the increased COPD mortality rates in young adults.

A few occupational studies conducted in the 1950s in Sweden have also reported non-malignant respiratory effects in copper smelter workers exposed to airborne arsenic. In one clinical study of 1459 copper smelter workers cited by Gerhard *et al*., a syndrome characterized by chronic rhino-pharyngeo-tracheobronchitis, lesions of the mucous membranes of the upper respiratory system, emphysema and decreased pulmonary function was described.[14] Information on smoking habits was not presented, which might have contributed to the reported signs and symptoms.

With the exception of the study in Chile, respiratory effects of ingestion of inorganic arsenic has not been reported elsewhere. The cross-sectional survey included over 7000 individuals, one of the largest arsenic-affected populations known to date, living in the 24 South Parganas, West Bengal. The aim of the survey, which was conducted between April 1995 and March 1996, was to determine the prevalence of various health effects associated with arsenic. The most common arsenic-related health effects found were keratoses and hyperpigmentation and a clear exposure-response trend was identified according to arsenic concentrations in drinking water.[15] In this paper, we focus on the prevalence of respiratory signs and symptoms assessed in the survey, including cough, chest sounds, and shortness of breath.

Methods

Study area and population

A survey of one of the arsenic-affected districts south of Calcutta, the 24 South Parganas, was conducted. Two areas in this district were targeted; the first included 25 villages and was selected because high levels of arsenic were reported in some of the tubewells. In this high exposure area which included remote rural areas, a convenience sampling strategy was used. The field team went to the centre of each village, and selected the most convenient hamlet (group of houses) to begin sampling. Every member of the household who was present at the time of interview was invited to participate. Details concerning the participation rate were not recorded, but the response rate from those invited to participate was excellent with negligible refusals. An interview and a brief medical exam were conducted on each participant. Sampling continued house-to-house until 50 to 150 participants were recruited.

The second area included the remaining part of the district (32 villages in 16 administrative blocks), where people were drinking from shallow tubewells. Sampling in this area was limited to villages with more than 100 households. One or more villages were randomly selected from each of the 16 blocks, depending on the population size. One village was targeted for sampling in a small block, but two or three villages were selected if the block was larger. In this area, the field team went to the centre of the village and commenced sampling in the most convenient hamlet; but this time, residents of every fourth house were invited to participate. These two areas combined have a population of 150 457.

In all 7818 individuals participated in the survey. Arsenic levels in the drinking water sources were measured for 7683 individuals (4093 females and 3590 males). There were few smokers and they were excluded from the analyses presented here; thus 6864 participants (4042 females and 2822 males) comprise the study population for consideration of respiratory signs and symptoms.

Interview and clinical exam

Participants were briefly questioned about their sources of drinking water and socio-demographic characteristics. Participants were then asked to volunteer any health problems. If the participant did not volunteer any information concerning the presence of respiratory problems, they were then specifically asked by a physician interviewer the following questions: 'Do you have problems with coughing? Do you have problems with shortness of breath?' Chest sounds were determined by auscultation and included crepitations and/or rhonchi. In view of the potential relationship between reported shortness of breath and general weakness, the present analysis also included responses to the question, 'Are you troubled with feeling weak?' A general medical examination was also performed, including a careful examination for skin lesions. A detailed explanation of the criteria used for diagnosing keratoses and hyperpigmentation appears elsewhere.[15] Physician interviewers who were blind to the arsenic content in the drinking water diagnosed the skin lesions. Arsenic-induced skin lesions are

distinctive. Diffuse keratoses appear as bilateral thickening of the palms and soles. Nodular keratoses occur as small protrusions on the palms and soles, with or without nodules on the dorsum of the hands, feet or legs. Raindrop-shaped discoloured spots, diffuse dark spots, or diffuse darkening of the skin on the limbs and trunk mark changes in pigmentation due to arsenic.

Participants were also asked if they smoked currently or had smoked in the past. In rural India, small hand-rolled cigarettes (*biris*) are most frequently consumed. *Biris* are usually filterless and are about an inch and half in length. The 819 participants (768 males and 51 females) who reported they had smoked regularly or often, either currently or in the past, were excluded from consideration because of relatively small numbers and potential confounding.

Arsenic measurements in drinking water

Water samples were obtained from the main private or public tubewells used for drinking by each household. Arsenic concentration was measured by flow-injection hydride generation atomic absorption spectrophotometry. The detection limit determined at the 90% confidence level was 3 μg/l.[16]

Statistical analyses

The outcomes analysed included participant-reported cough, shortness of breath, and weakness, and the presence of chest sounds recorded by the examining physician. To allow for direct comparisons without the distorting effects of age, the prevalence of each outcome was directly standardized to the age distribution of all study participants of the same sex. Each outcome was examined according to arsenic levels in the tubewell drinking water source used by each participant. The tubewells were categorized according to arsenic concentrations as follows: <50, 50–199, 200–499, 500–799 and ⩾800 μg/l.

Tests for trend in proportions using the midpoints of the exposure categories were based on the χ^2 distribution.[17] In view of unidirectional *a priori* hypotheses, one-sided *P*-values are presented for the test of trend.

Prevalence odds ratios (POR) were also calculated for each outcome comparing those with very high exposure to arsenic in drinking water (⩾500 μg/l) with those with the lowest exposures (<50 μg/l). The Mantel-Haenszel method was used to adjust for age. Data were also stratified by the presence or absence of arsenic-caused lesions.

Results

Trends by arsenic concentrations in drinking water

Table 1 presents the age and sex distribution of all non-smoking participants by arsenic levels in drinking water. The arsenic concentration in the tubewell water samples ranged from <3 μg/l to 3400 μg/l.

Tables 2–4 present findings for cough, chest sounds and shortness of breath. Among females, the overall age-adjusted prevalence for each respiratory outcome (cough, chest sounds and shortness of breath) was close to 2.5 per 100. Clear trends of increasing prevalence by arsenic water concentration can be seen for cough (Table 2, test for trend $P < 0.0001$) and chest sounds (Table 3, test for trend $P = 0.002$). However, the prevalence of shortness of breath showed a markedly non-linear relationship ($P < 0.0001$) peaking in the third exposure category (200–499 μg/l), but declining sharply thereafter to almost baseline levels.

Among males, the overall age-adjusted prevalence of cough (5.2 per 100) and chest sounds (4.4 per 100) was nearly twice

Table 1 Distribution of non-smoking participants by age, sex and arsenic level in drinking water (μg/l)

	Arsenic level (μg/l)					
Age group	<50	50–199	200–499	500–799	⩾800	Total
Females						
⩽9	194	107	134	75	26	536
10–19	399	186	173	65	26	849
20–29	572	275	197	83	23	1150
30–39	304	172	119	44	15	654
40–49	168	78	55	28	9	338
50–59	156	74	43	29	11	313
⩾60	94	52	41	9	6	202
All ages	1887	944	762	333	116	4042
Males						
⩽9	220	156	128	81	28	613
10–19	313	166	144	62	29	714
20–29	292	140	96	50	20	598
30–39	147	84	79	38	15	363
40–49	78	58	45	14	5	200
50–59	65	31	35	18	8	157
⩾60	82	48	31	12	4	177
All ages	1197	683	558	275	109	2822

Table 2 Prevalence of cough per 100 by age group and arsenic level (μg/l) among non-smokers, with number of cases in parentheses

	Arsenic level (μg/l)					
Age group	<50	50–199	200–499	500–799	⩾800	Total
Females						
⩽9	0.5 (1)	0.9 (1)	1.5 (2)	2.7 (2)	0.0 (0)	1.1 (6)
10–19	1.8 (7)	0.5 (1)	1.7 (3)	3.1 (2)	7.7 (2)	1.8 (15)
20–29	1.7 (10)	0.7 (2)	1.5 (3)	3.6 (3)	4.3 (1)	1.7 (19)
30–39	2.6 (8)	2.3 (4)	2.5 (3)	0.0 (0)	6.7 (1)	2.4 (16)
40–49	3.6 (6)	0.0 (0)	3.6 (2)	10.7 (3)	0.0 (0)	3.3 (11)
50–59	5.1 (8)	2.7 (2)	4.7 (2)	17.2 (5)	9.1 (1)	5.8 (18)
⩾60	3.2 (3)	5.8 (3)	9.8 (4)	11.1 (1)	16.7 (1)	5.9 (12)
All ages	2.3 (43)	1.4 (13)	2.5 (19)	4.8 (16)	5.2 (6)	2.4 (97)
Age-adjusted	2.2	1.3	2.6	4.9	5.5	2.4
Males						
⩽9	1.8 (4)	0.6 (1)	0.8 (1)	1.2 (1)	3.6 (1)	1.3 (8)
10–19	1.6 (5)	1.2 (2)	4.2 (6)	1.6 (1)	13.8 (4)	2.5 (18)
20–29	5.5 (16)	5.0 (7)	6.3 (6)	6.0 (3)	15.0 (3)	5.9 (35)
30–39	6.1 (9)	8.3 (7)	8.9 (7)	10.5 (4)	20.0 (3)	8.3 (30)
40–49	10.3 (8)	3.4 (2)	4.4 (2)	0.0 (0)	20.0 (1)	6.5 (13)
50–59	6.2 (4)	3.2 (1)	11.4 (4)	16.7 (3)	0.0 (0)	7.6 (12)
⩾60	11.0 (9)	10.4 (5)	6.5 (2)	8.3 (1)	0.0 (0)	9.6 (17)
All ages	4.6 (55)	3.7 (25)	5.0 (28)	4.7 (13)	11.0 (12)	4.7 (133)
Age-adjusted	5.1	4.1	5.5	5.4	11.9	5.2

Females: Test for trend $P < 0.0001$, test for non-linearity $P = 0.03$.
Males: Test for trend $P = 0.0014$, test for non-linearity $P = 0.24$.

Table 3 Prevalence of chest sounds (crepitations and/or rhonchi) per 100 by age group and arsenic level (μg/l) among non-smokers, with number of cases in parentheses

	Arsenic level (μg/l)					
Age group	<50	50–199	200–499	500–799	⩾800	Total
Females						
⩽9	0.5 (1)	0.9 (1)	3.0 (4)	0.0 (0)	0.0 (0)	1.1 (6)
10–19	1.0 (4)	1.1 (2)	2.3 (4)	1.5 (1)	3.8 (1)	1.4 (12)
20–29	1.4 (8)	0.7 (2)	0.5 (1)	3.6 (3)	4.3 (1)	1.3 (15)
30–39	2.3 (7)	2.3 (4)	3.4 (4)	0.0 (0)	0.0 (0)	2.3 (15)
40–49	5.4 (9)	2.6 (2)	7.3 (4)	10.7 (3)	11.1 (1)	5.6 (19)
50–59	2.6 (4)	8.1 (6)	0.0 (0)	17.2 (5)	9.1 (1)	5.1 (16)
⩾60	5.3 (5)	5.8 (3)	17.1 (7)	11.1 (1)	33.3 (2)	8.9 (18)
All ages	2.0 (38)	2.1 (20)	3.1 (24)	3.9 (13)	5.2 (6)	2.5 (101)
Age-adjusted	2.0	2.1	3.1	4.2	5.4	2.5
Males						
⩽9	0.5 (1)	1.3 (2)	0.8 (1)	2.5 (2)	0.0 (0)	1.0 (6)
10–19	1.3 (4)	0.6 (1)	4.9 (7)	1.6 (1)	3.4 (1)	2.0 (14)
20–29	4.1 (12)	2.9 (4)	2.1 (2)	4.0 (2)	10.0 (2)	3.7 (22)
30–39	0.0 (0)	3.6 (3)	5.1 (4)	7.9 (3)	0.0 (0)	2.8 (10)
40–49	1.3 (1)	1.7 (1)	11.1 (5)	7.1 (1)	20.0 (1)	4.5 (9)
50–59	9.2 (6)	9.7 (3)	22.9 (8)	33.3 (6)	0.0 (0)	14.6 (23)
⩾60	14.6 (12)	14.6 (7)	16.1 (5)	8.3 (1)	25.0 (1)	14.7 (26)
All ages	3.0 (36)	3.1 (21)	5.7 (32)	5.8 (16)	4.6 (5)	3.9 (110)
Age-adjusted	3.1	3.5	6.5	6.8	6.6	4.4

Females: Test for trend $P = 0.002$, test for non-linearity $P = 0.37$.

Males: Test for trend $P = 0.04$, test for non-linearity $P = 0.018$.

Table 4 Prevalence of shortness of breath per 100 by age group and arsenic level (μg/l) among non-smokers, with number of cases in parentheses

	Arsenic level (μg/l)					
Age group	<50	50–199	200–499	500–799	⩾800	Total
Females						
⩽9	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
10–19	0.0 (0)	3.2 (6)	5.2 (9)	0.0 (0)	0.0 (0)	1.8 (15)
20–29	0.3 (2)	4.0 (11)	10.2 (20)	1.2 (1)	0.0 (0)	3.0 (34)
30–39	0.7 (2)	4.1 (7)	5.9 (7)	4.5 (2)	0.0 (0)	2.8 (18)
40–49	0.6 (1)	5.1 (4)	3.6 (2)	3.6 (1)	0.0 (0)	2.4 (8)
50–59	0.6 (1)	4.1 (3)	16.3 (7)	17.2 (5)	9.1 (1)	5.4 (17)
⩾60	2.1 (2)	5.8 (3)	19.5 (8)	11.1 (1)	0.0 (0)	6.9 (14)
All ages	0.4 (8)	3.6 (34)	7.0 (53)	3.0 (10)	0.9 (1)	2.6 (106)
Age-adjusted	0.4	3.5	7.5	3.3	0.7	2.6
Males						
⩽9	0.0 (0)	0.6 (1)	0.8 (1)	1.2 (1)	0.0 (0)	0.5 (3)
10–19	0.6 (2)	4.8 (8)	4.9 (7)	0.0 (0)	3.4 (1)	2.5 (18)
20–29	2.4 (7)	2.1 (3)	2.1 (2)	2.0 (1)	10.0 (2)	2.5 (15)
30–39	2.7 (4)	3.6 (3)	5.1 (4)	2.6 (1)	0.0 (0)	3.3 (12)
40–49	0.0 (0)	8.6 (5)	11.1 (5)	7.1 (1)	20.0 (1)	6.0 (12)
50–59	4.6 (3)	3.2 (1)	22.9 (8)	5.6 (1)	0.0 (0)	8.3 (13)
⩾60	3.7 (3)	12.5 (6)	16.1 (5)	8.3 (1)	25.0 (1)	9.0 (16)
All ages	1.6 (19)	4.0 (27)	5.7 (32)	2.2 (6)	4.6 (5)	3.2 (89)
Age-adjusted	1.7	4.1	6.5	2.8	6.6	3.6

Females: Test for trend $P = 0.02$, test for non-linearity $P < 0.0001$.

Males: Test for trend $P = 0.04$, test for non-linearity $P = 0.0004$.

Table 5 Prevalence of weakness per 100 by age group and arsenic level (μg/l) among non-smokers, with number of cases in parentheses

	Arsenic level (μg/l)					
Age group	<50	50–199	200–499	500–799	⩾800	Total
Females						
⩽9	1.0 (2)	0.9 (1)	0.7 (1)	0.0 (0)	3.8 (1)	0.9 (5)
10–19	0.5 (2)	1.1 (2)	1.2 (2)	6.2 (4)	11.5 (3)	1.5 (13)
20–29	1.4 (8)	2.5 (7)	6.1 (12)	14.5 (12)	4.3 (1)	3.5 (40)
30–39	1.3 (4)	5.2 (9)	5.0 (6)	4.5 (2)	6.7 (1)	3.4 (22)
40–49	4.8 (8)	5.1 (4)	14.5 (8)	14.3 (4)	22.2 (2)	7.7 (26)
50–59	3.2 (5)	10.8 (8)	4.7 (2)	34.5 (10)	27.3 (3)	8.9 (28)
⩾60	3.2 (3)	5.8 (3)	7.3 (3)	11.1 (1)	50.0 (3)	6.4 (13)
All ages	1.7 (32)	3.6 (34)	4.5 (34)	9.9 (33)	12.1 (14)	3.6 (147)
Age-adjusted	1.7	3.5	4.9	10.7	11.9	3.7
Males						
⩽9	0.5 (1)	0.6 (1)	0.8 (1)	1.2 (1)	0.0 (0)	0.7 (4)
10–19	0.3 (1)	1.8 (3)	0.0 (0)	1.6 (1)	6.9 (2)	1.0 (7)
20–29	0.7 (2)	2.9 (4)	6.3 (6)	6.0 (3)	20.0 (4)	3.2 (19)
30–39	1.4 (2)	4.8 (4)	8.9 (7)	5.3 (2)	13.3 (2)	4.7 (17)
40–49	1.3 (1)	1.7 (1)	6.7 (3)	0.0 (0)	0.0 (0)	2.5 (5)
50–59	1.5 (1)	6.5 (2)	0.0 (0)	11.1 (2)	0.0 (0)	3.2 (5)
⩾60	2.4 (2)	14.6 (7)	12.9 (4)	16.7 (2)	25.0 (1)	9.0 (16)
All ages	0.8 (10)	3.2 (22)	3.8 (21)	4.0 (11)	8.3 (9)	2.6 (73)
Age-adjusted	0.9	3.6	4.4	4.7	9.5	2.9

Females: Test for trend $P < 0.0001$, test for non-linearity $P = 0.0001$.

Males: Test for trend $P < 0.0001$, test for non-linearity $P = 0.01$.

as high as among females, but once again there were trends of increasing prevalence by water arsenic concentration (Tables 2 and 3). The overall age-adjusted prevalence for shortness of breath in males (3.6 per 100, Table 4) was higher than in females (2.6 per 100). As with females, the highest prevalence of shortness of breath occurred in the water concentration range of 200–499 μg/l. The prevalence of both cough and chest sounds increased with increasing water arsenic content in children of both sexes, especially in age range 10–19 (Tables 2 and 3).

The age-adjusted prevalence of weakness increased strongly with arsenic water concentrations in both sexes (from 1.7 per 100 to 11.9 per 100 among women, $P < 0.0001$, and from 0.9 to 9.5 per 100 among men, $P < 0.0001$, Table 5).

Comparisons between the high and low exposure groups

Table 6 gives POR comparing the highest exposure category (⩾500 μg/l) with the lowest exposure category (<50 μg/l). All POR are elevated, but particularly so for shortness of breath among females and weakness in both sexes. Table 6 also presents POR separately for those with and without arsenic-caused skin lesions (keratoses and/or pigmentation changes). Markedly increased POR are seen for each outcome in both males and females with skin lesions. With the exception of shortness of breath among women and weakness in both sexes, there is little to see in the way of effects among participants without skin lesions.

Finally, the joint occurrence of the outcomes of interest was examined. The most frequent combination was cough plus chest sounds. Among those with skin lesions and current drinking

Table 6 Age-adjusted prevalence odds ratios (POR) for respiratory effects in non-smokers comparing those exposed to ⩾500 μg/l to participants exposed to <50 μg/l

	Females			**Males**		
	Cases exposed to ⩾500 μg/l	POR	(95% CI)	Cases exposed to ⩾500 μg/l	POR	(95% CI)
All participants						
Cough	22	2.4	(1.4–4.1)	25	1.6	(1.0–2.7)
Crepitations and/or rhonchi	19	2.5	(1.4–4.4)	21	2.2	(1.3–4.1)
Shortness of breath	11	7.2	(2.8–18.5)	11	2.1	(0.9–4.4)
Weakness	47	7.2	(4.4–11.5)	20	6.9	(3.2–15.0)
With skin lesions						
Cough	7	7.8	(3.1–19.5)	14	5.0	(2.6–9.9)
Crepitations and/or rhonchi	8	9.6	(4.0–22.9)	12	6.9	(3.1–15.0)
Shortness of breath	4	23.2	(5.8–92.8)	5	3.7	(1.3–10.6)
Weakness	10	15.3	(6.5–35.8)	8	14.2	(5.2–38.7)
Without skin lesions						
Cough	15	1.8	(1.0–3.4)	11	0.9	(0.5–1.7)
Crepitations and/or rhonchi	11	1.6	(0.8–3.2)	9	1.2	(0.5–2.6)
Shortness of breath	7	5.2	(1.9–14.8)	6	1.5	(0.6–3.7)
Weakness	37	6.7	(4.1–11.1)	12	5.4	(2.3–12.8)

water containing >500 μg/l, 5 of the 7 females reporting cough were also found to have lung chest sounds, as did 6 of the 14 men reporting problems with coughing.

Discussion

This study provides evidence that ingestion of inorganic arsenic in drinking water results in pulmonary effects manifested by cough, chest sounds in the lungs and shortness of breath. With the exception of shortness of breath among females, the prevalence of each outcome rose with increasing concentrations of arsenic in the primary drinking water sources (Tables 2–4). A possible explanation for findings concerning shortness of breath in women relates to the presence of weakness. Women who are feeling weak might be able to cope during the day without needing to physically exert themselves sufficiently to report feeling short of breath. This might not be true to the same extent for men who mainly work in agriculture, although they also had the highest prevalence of shortness of breath in the mid-exposure category. Although the numbers were small, there was evidence of respiratory effects in children, especially in the age range 10–19.

The results in Table 6 indicate that in this population, the presence of respiratory effects was largely confined to those who had the arsenic-caused skin lesions. Why this should be so is not clear, but could be related to some underlying susceptibility to arsenic effects. In Chile, it was also noted that there were differences in respiratory disease in schoolchildren with skin lesions compared to those without the lesions.[3] Interestingly, this was not true for reported weakness which while dramatically increased in those with skin lesions (Table 6, POR 15.3 and 14.2 for females and males, respectively), was still markedly elevated in those with high current exposures who did not have skin lesions (age-adjusted POR of 6.7 and 5.4). Weakness is a highly subjective symptom which has previously been reported in arsenic-exposed patients.[10] The reason people exposed to high arsenic levels report feeling weak is not clear. While arsenic can cause peripheral neuropathy, it is not known to cause central nervous system effects that could explain general feelings of weakness.

Although information about the relationship between ingested arsenic and non-malignant respiratory effects has so far only been reported from Chile and now India, studies from arsenic-affected regions in Taiwan, Chile and Argentina show marked increases in lung cancer mortality.[1,4,5,18,19] It is of interest to note that many established lung carcinogens, including smoking, asbestos and silica, also cause non-malignant respiratory disease. The surprising characteristic of arsenic is that it seems to increase both malignant and non-malignant respiratory disease following ingestion.

While toxicological mechanisms for pulmonary effects of inorganic arsenic are not known, some reports have demonstrated that arsenic can accumulate in human lung tissue thus enhancing the plausibility that the metal can produce respiratory effects. Figueroa *et al.* noted evidence of lung tissue accumulation in humans.[20] They investigated mummies hundreds of years old that were found in Region II of Chile, an area that has had high arsenic levels in drinking water. Kidney, liver, nail, and lung tissues had some of the highest concentrations of total arsenic, followed by the skin, intestines, hair, ribs, and muscles, respectively. Further, case reports from poisoning deaths have also demonstrated that high levels of arsenic occur in the lungs.[21,22] In the first case, the lung tissue concentration of total arsenic at autopsy of a 3-year-old boy who accidentally ingested a weed killer containing 44% sodium arsenite was 7550 μg/kg. In the second case, a 25-year-old white male ingested 8 g of arsenic trioxide. At autopsy, the largest total arsenic concentration was found in the gastrointestinal tract, but a concentration of 2750 μg/kg was also discovered in the lungs. An autopsy study determined that the mean lung tissue arsenic concentration was sixfold greater in 85 copper smelter workers in Sweden compared to 25 non-exposed controls (35 versus 6 μg/kg wet weight).[14]

The main drawback of the current investigation is that limited time existed for interviewing and carefully assessing each subject involved in the large population survey that included over 7000 participants. Observer bias was possible during interviews and clinical examination of patients with skin lesions. We are therefore planning a more detailed assessment of selected participants with high exposure and skin lesions, including focused interviewing, medical examination and spirometric testing. Nonetheless, the strength of the current findings in terms of trend with water concentration and the very high POR, along with the plausibility of finding non-malignant respiratory effects based on studies in Chile, suggest that non-malignant respiratory effects may indeed result from ingestion of inorganic arsenic.

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