

Arsenic-related Health Problems among Hospital Patients in Southern Bangladesh

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ABSTRACT

To assess the health effects of arsenic poisoning and to determine the relationship among duration and severity of skin lesions, exposure dose of arsenic, and nutritional status of people, 150 patients attending the Dermatology Outpatients Department of Sher-e-Bangla Medical College Hospital, Barisal, Bangladesh, were included in this cross-sectional study. The study was conducted during January-December 2000. Records of patients were collected prospectively using a pre-tested questionnaire, which included information on demography, sources of water for drinking and cooking, duration and amount of drinking-water obtained from shallow tubewells, clinical presentations, complications, and physical and laboratory findings. Water samples from tubewells currently being used by individual patients were examined. Nine percent of the patients were unaware that arsenic-contaminated water causes diseases. Due to lack of alternative water supplies, 25% of the subjects were still drinking water from contaminated tubewells. About 18% did not complain of any clinical symptoms, except that their skin lesions were ugly-looking, and 82% had moderate or severe skin lesions. Thirty-one percent of the water samples had arsenic concentrations 10-fold higher than the permissible limit of 0.05 mg/L in Bangladesh and 50-fold higher than the WHO guideline value of 0.01 mg/L. The mean arsenic concentration in water was significantly associated with the severity of disease. Body mass index correlated inversely ($r=-0.298$, $p=0.013$) with the duration of disease after controlling for age. The findings suggest the need to enhance public awareness on negative health effects of arsenic poisoning in rural Bangladesh. From a public-health perspective, effective intervention strategies need to be developed to curb the exposure, strengthen rapid diagnostic facilities, establish effective treatment facilities in rural areas, and improve the nutritional status of people.

Key words: Arsenic; Arsenic poisoning; Water supply; Nutritional status; Cross-sectional studies; Bangladesh

INTRODUCTION

Almost half of 129 million people in Bangladesh are at risk of arsenic poisoning (1). In Bangladesh, arsenic contamination was first reported in early 1996 from Bagerhat, Satkhira, and Kushtia—all three are

southwestern districts bordering India (2). By now, the scourge has affected 52 of 64 districts of the country, creating a devastating public-health problem (3). High concentrations of arsenic in groundwater have also been reported from several other countries, including Argentina, Chile, India, Japan, Mexico, Mongolia, Poland, Taiwan, and some parts of the United States (4-9).

Initial theories were that arsenic contamination occurs either due to an excessive use of insecticides and pesticides or due to toxic effluents of industries. Results of studies carried out in West Bengal, India, suggest the

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theory of excessive extraction of groundwater as a causal factor for the contamination (10). As the water table falls, pyrites—a mineral that holds the arsenic—begin to oxidize and leach poison, contaminating thousands of shallow tubewells. Evidence also suggests that sulphate reduction rather than sulphide oxidation is associated with arsenic release to groundwater (11).

Arsenic contamination increases the risk of health hazards, including cancer, melanosis (hyperpigmentation or dark spots and hypopigmentation or white spots), hyperkeratosis (hardened skin), restrictive pulmonary disease, peripheral vascular disease (blackfoot disease), gangrene, hypertension, non-cirrhotic portal fibrosis, ischaemic heart disease, and diabetes mellitus (8,12-21). Despite the fact that Bangladesh's problem of groundwater contamination by arsenic is the largest natural calamity of a population in history, little is known about people's awareness of the problem. Health reports on arsenic-related diseases are also scarce in the country (2,19,20,22).

This study was undertaken to: (i) identify awareness of patients about arsenic-related health problems; (ii) assess clinical features and complications of arsenic poisoning in subjects attending a hospital in southern Bangladesh; and (iii) determine the relationship among arsenic dose, nutritional status, and severity and duration of disease in a group of patients.

MATERIALS AND METHODS

The study was conducted at the Sher-e-Bangla Medical College Hospital in Barisal district of Bangladesh during January-December 2000. Barisal is one of the high-risk areas, where more than 60% of tubewells were found to be contaminated with arsenic, in an amount greater than the maximum permissible limit of 0.05 mg/L in Bangladesh (23,24). The patients who attended the Dermatology Outpatients Department of the hospital were eligible for the study. Informed consent was taken from all adult patients and from legal guardians of children.

Records of patients were collected prospectively using a pre-tested questionnaire, which included information on demography, sources of water for drinking and cooking, duration and amount of drinking-water obtained from shallow tubewells, clinical presentations, complications, and physical and laboratory findings. Water samples from tubewells currently being used by patients were examined. If there had been a change in water source, the one that was

being used for a longer time before attending the hospital was examined for arsenic level. The samples were analyzed at the laboratory of the Public Health Engineering Department at Khulna using atomic absorption spectrometric techniques (25). Anthropometric measurements, such as body weight and height, were recorded, and body mass index (BMI) was calculated in a sub-sample of the study subjects ($n=72$) using the formula: $BMI = [\text{weight (kg)}] / [\text{height (m)}]^2$. The sub-sample for anthropometric analysis was selected as alternative patients who had information on age, sex, weight, and height.

Characteristic skin lesions, in the absence of other causes, represented a case (18). Skin lesions were graded as: (i) mild—presence of only skin melanosis, typically appearing in a raindrop pattern on trunk or extremities; (ii) moderate—skin melanosis plus hyperkeratosis of palm or sole; and (iii) severe—diffuse skin melanosis plus wart-like nodules, with or without complications. An arsenic exposure dose for each patient was computed by multiplying the arsenic concentration in water with the duration of drinking, assuming that the current levels of arsenic in tubewell-water were also representative of the past.

Statistical methods

Data were analyzed using SPSS Windows version 10.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were computed for demographic information, water use, awareness of people about arsenic-related health problems, clinical features and complications, arsenic concentrations in water, and nutritional status. Statistical tests were done to compare major outcome variables by severity of disease, duration of disease, nutritional status, and gender using Student's *t*-test or Mann-Whitney U-test for continuous variables and chi-square test for categorical variables. Correlation was done between the exposure dose of arsenic (arsenic concentration \times exposure time in year) and the duration of disease, severity of disease (moderate or severe=1, mild=0), and BMI after controlling for age. A probability level of 0.05 was considered statistically significant, using two-tailed tests.

RESULTS

Demographic information and water use

The study enrolled 150 subjects (75 males and 75 females) by convenience sampling. Seventy-two of the patients were young adults, with a median age of 25 years (range:

10-70 years), and 43% were 8-12 grade students. Categories of subjects involved in the study are shown

Variable	No.	%
Categories of subjects		
Student	65	43
Housewife	34	23
Day-labourer or jobless	17	11
Cultivator	15	10
Service	15	10
Others	4	3
Had you consulted any registered doctor earlier for your illness?		
Yes	82	55
No	68	45
Have you been informed that arsenic in drinking-water causes health problems?		
Yes	136	91
No	14	9
If yes, how did you know about it?		
TV/radio/poster	75	55
Doctor/health worker	45	33
Relative/friend/patient	16	12
Total	136	100
If yes, how long did you know about it?		
Less than 1 year	72	53
1-3 year(s)	57	42
4-5 years	7	5
Total	136	100
Was arsenic testing done on water samples from your tubewell?		
Yes	77	51
No/don't know	73	49
Did you drink water from the same tubewell after you knew that it was contaminated?		
Yes	13	25
No	40	75

in Table 1. Two-thirds (66%) of the patients came from poor socioeconomic class with an average monthly income of less than US\$ 60. About 10% did not have any formal education. The social background of the study patients was similar to that usually seen at this hospital.

All except one person in the sample used shallow tubewell as the primary source of drinking-water, and most (95%) used pond or river water for cooking. The amount of drinking-water consumed from a shallow tubewell by an individual varied from 1 to 6 litre(s) per day. Duration of using water obtained from shallow tubewells for drinking purpose varied from 3 to 40 years, with a median duration of 15 years.

Awareness of arsenic-related health problems

Fourteen (9%) patients had never heard that diseases may be caused by arsenic from contaminated drinking-water (Table 1). However, 136 (91%) patients were only recently aware of the adverse health effects of arsenic primarily through mass media. Seventy-three (49%) subjects reported that water samples from their tubewells had never been tested or, if tested, they were not aware of the results. Thirteen (25%) patients were still drinking water from the same contaminated tubewells due to lack of alternative water supplies, even after knowing that their tubewells were contaminated with arsenic. Forty-four (29%) subjects reported that they had other persons in the family with similar skin lesions. The median number of family members suffering from similar illnesses was 1 [range: 0-7 member(s)]. When asked about how many people in the community drank water from the same tubewell and how many of them got sick, the proportion of sick people was reported to be 6 in 100.

Clinical features and complications

All patients presented with raindrop skin pigmentation, and more than 80% had hyperkeratosis with or without nodular skin lesions (Fig. 1). Biopsy specimens from

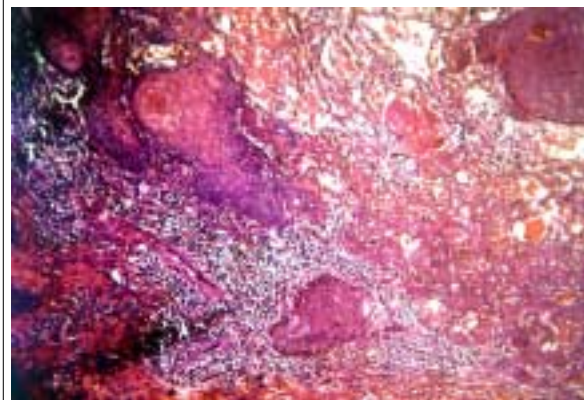
Fig. 1. A 42-year old woman with raindrop skin pigmentation and a nodule on her thigh



skin nodules of one person, aged 42 years, showed squamous cell carcinoma (Fig. 2). About 18% did not complain of any clinical symptoms, except that their skin lesions were ugly-looking. One hundred and twenty-three (82%) patients had moderate or severe skin lesions. Sites of appearance of skin lesions, in order of frequency, were trunk, including chest (38%), hands only (18%), both hands and feet (15%), feet only (13%), and chest

only (11%). One hundred and fifteen (77%) subjects had multiple symptoms, including weakness, chronic cough,

Fig. 2. Dermis is infiltrated with anaplastic squamous epithelial cells in interconnected sheets and islands. Well-defined keratin horn pearls are demonstrated (Haematoxylin-Eosin Stain, x122)



joint pain, itching, abdominal pain, chest pain, loss of appetite, insomnia, shortness of breathing, and frequent urination with burning (Table 2).

Table 2. Clinical presentations of arsenic-related illnesses in 150 patients

Clinical feature	No.	% [*]
Weakness	59	39
Chronic cough	35	23
Joint pain or backache	26	17
Itching	26	17
Abdominal pain	24	16
Chest pain	24	16
Loss of appetite	18	12
Insomnia	15	10
Shortness of breathing	15	10
Frequent urination with burning	15	10
Tingling and numbness	12	8
Headache	12	8
Malaise	8	5
Chronic dysentery	6	4
Blurred vision	4	3
Conjunctivitis	2	1
Palpitation	2	1
Decreased libido	1	1

^{*} Total percentage exceeds 100 because several patients had multiple symptoms and complications

Laboratory tests performed on all patients included complete blood count, haemoglobin, random blood sugar, urine microscopy, chest X-ray, serum alanine aminotransferase, serum aspartate aminotransferase, and

alkaline phosphatase. High blood pressure (systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg) and depression (lowered mood or sadness, loss of interest, and anxiety) were the two most frequent complications, each observed in 20 (13%) subjects. The other important findings included raised serum alanine aminotransferase (n=13), palpable liver (n=8), X-ray features suggestive of pneumonia, interstitial lung disease and lung abscess (n=11), peripheral vascular problems in the form of intermittent claudication, in the absence of history of smoking (n=2), pulmonary tuberculosis (n=2), diabetes (n=1), and decreased libido (n=1). Anaemia (haemoglobin: <135 g/L in males and <120 g/L in females) was a major clinical finding observed in 88 (58%) subjects; 14 had pedal oedema. Ten (7%) patients were admitted to the hospital due to complications or associated major illnesses, including severe anaemia, hepatitis, hepatic cirrhosis, renal failure, lung abscess, interstitial lung disease, intermittent claudication with uncontrolled diabetes, and skin cancer. One of them died due to heart failure from chronic obstructive pulmonary disease and lung abscess.

Arsenic concentration and disease

The median duration of disease (i.e. the time from the first symptom to the time of interview) was four years, ranging from less than one year to 25 years. About 14% of the subjects had symptoms lasting for less than two years. The duration of disease greater than 10 years was six times as common in males than their female counterparts (15% vs 3%; $p=0.02$). There were no significant gender differences in other major outcome variables, including age, BMI, exposure dose, and severity of disease.

Arsenic concentrations in all 150 water samples were greater than 0.05 mg/L. The mean \pm SD arsenic concentration in drinking-water was 0.50 \pm 0.21 mg/L (range: 0.07-1.70 mg/L). Table 3 shows that 47 (31%) of the 150 water samples tested had arsenic concentrations 10-fold higher than the prevailing permissible limit of 0.05 mg/L in Bangladesh and 50-fold higher than the WHO standard value of 0.01 mg/L (26). The mean \pm SD arsenic concentration was significantly higher in water samples from tubewells used by people who had a moderate or severe disease compared to those who had a mild disease (0.52 \pm 0.21 vs 0.43 \pm 0.20; $p=0.023$). The exposure dose of arsenic had a direct significant correlation with the duration of disease ($r=0.182$, $p=0.028$, $n=145$). After controlling for

age, the relationship between the variables was not statistically significant. The duration of disease was significantly higher among those with a moderate or severe disease compared to those with a mild disease (5.9 ± 4.2 years vs 2.2 ± 1.5 years; $p < 0.001$) (Table 3). There was no significant difference between the severity of disease and the arsenic exposure status or nutritional status, when stratified for men and women.

when these patients were examined, 49% of the tubewells were not tested for arsenic levels or, if tested, people were not aware of the results. Even 25% of those who were aware of the positive test results were still consuming water from the contaminated tubewells. All these facts indicate some missed opportunities for increasing public awareness about arsenic-related health problems in a poor community of Bangladesh. After

Table 3. Relationship between arsenic concentration, nutritional status, and skin lesion

Variable	Severity of disease		p value
	Moderate or severe	Mild	
Age (years)	28.7 \pm 12.9 (n=123)	23.6 \pm 11.2 (n=27)	0.02 ^a
Body weight (kg)	39.5 \pm 8.4 (n=59)	40.4 \pm 5.2 (n=13)	0.72 ^b
Height (m)	1.52 \pm 0.09 (n=59)	1.52 \pm 0.08 (n=13)	0.83 ^b
Body mass index	16.8 \pm 2.4 (n=59)	17.6 \pm 2.0 (n=13)	0.26 ^b
Arsenic (mg/L)			
≤0.50	81 (66)	22 (82)	
0.51-0.99	36 (29)	4 (15)	
≥1.00	6 (5)	1 (4)	0.27 ^c
Mean \pm SD	0.52 \pm 0.21 (n=123)	0.43 \pm 0.20 (n=27)	0.02 ^a
Exposure dose (arsenic level x exposure time in year)	8.29 \pm 5.25 (n=123)	7.66 \pm 4.47 (n=27)	0.60 ^a
Duration of disease (year)	5.9 \pm 4.2 (n=123)	2.2 \pm 1.5 (n=25)	<0.001 ^a
Duration of drinking from contaminated source (year)	15.8 \pm 7.2 (n=120)	17.1 \pm 6.0 (n=27)	0.41 ^b
The figures are mean \pm SD or number (%)			
^a Mann-Whitney U-test			
^b Student's <i>t</i> -test			
^c Chi-square=2.59, df=2			

Nutritional status and disease

Poor nutritional status was indicated by the average BMI of 17.0 ± 2.3 (range: 12-23), as measured in a subset of population (n=72). Eighty-nine percent of the patients were underweight, 11% had appropriate weight, and none was overweight or obese. After controlling for age, the duration of disease varied inversely with BMI ($r = -0.298$, $p = 0.013$, $n = 70$). Their body weight, height, and BMI did not differ by the severity of disease.

DISCUSSION

In our study, 91% of the subjects were aware of the adverse health effects of arsenic, but they were all patients with arsenic-induced skin lesions. At the time

obtaining the test results, the authors disseminated the information to the health authorities, local people, and patients and their family members. People were advised not to use the contaminated tubewells after marking these with red paint.

This study identified moderate or severe skin lesions in 82% and other health effects in a number of patients. Several clinical symptoms that were present in our study patients were in conformity with previous reports (19-23,27). Anaemia was a common finding but was not more common than reported from the community. Some late complications of the disease, including cancer, were probably yet to be established in most cases because our study patients were relatively young. Only one patient

had squamous cell carcinoma. The true incidence of cancer and of any arsenic-related symptoms cannot be derived from this study because of possible selection bias since the cases were recruited from the Dermatology Outpatients Department. Arsenic poisoning often takes months or years to become lethal or debilitating, easily resulting in missed diagnosis. An early diagnosis of cases and provision of alternate safe drinking-water to the exposed population may prevent further complications of the disease.

In this study, the arsenic concentrations in shallow tubewells were much higher than the permissible limit in Bangladesh. We found a significant direct relationship between the mean arsenic concentration in water and the severity of clinical disease. A similar dose-effect relationship has been reported between arsenic and patients with skin cancer, blackfoot disease, cardiovascular disease, hypertension, and diabetes (8,19,20,28).

The majority of our study subjects came from very poor socioeconomic class and were severely malnourished. We observed a significant inverse relationship between BMI and the duration of disease. As expected, the duration of disease was directly correlated with the severity of disease. Evidence suggests that poor nutritional status may increase toxicity to arsenic retained in the body, probably by diminished ability to methylate inorganic arsenic (29). Patients with protein-energy malnutrition are particularly deficient in methionine, and studies by Vahter and Marafante found that a low amount of methionine or protein in the diet decreased methylation of inorganic arsenic in the rabbit (30). Deficiency of certain other dietary trace elements, including zinc and selenium, associated with malnutrition, may also contribute to the toxic effects of accumulated levels of arsenic in the body (31). Our study confirmed previous reports of the relationship between malnutrition and increased arsenic toxicity (6,24). We cannot, however, draw a causal inference from the association between the nutritional status and the duration of disease. The possibility is obvious that this may reflect a patient with arsenicosis becoming malnourished. It may also reflect a social confounding because arsenic exposure through drinking-water is more common among poor and malnourished people.

In conclusion, we recommend for measures to: (i) intensify mass-awareness campaigns about arsenic toxicity and related health problems; (ii) curb the

exposure to arsenic through providing safe drinking-water and strengthening early diagnosis and treatment at regional level; and (iii) improve the nutritional status of people.

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