札幌医学雑誌　75（4 － 6）51 ～ 61（2006）

ORIGINAL

Case-control study of arsenicosis in some arsenic contaminated villages of Bangladesh

MMH KHAN[1, 2], Khandoker AKLIMUNNESSA[1],
Nazmul AHSAN[3], M KABIR[2], Mitsuru MORI[1]

[1] Department of Public Health, Sapporo Medical University School of Medicine, Japan (Chief: Prof. M. Mori)

[2] Department of Statistics, Jahangirnagar University, Savar, Dhaka, Bangladesh

[3] Department of Genetic Engineering and Biotechnology, Dhaka University, Dhaka, Bangladesh.

ABSTRACT

This study compared the arsenicosis cases and frequency matched controls in Bangladesh by some selected socio-demographic characteristics, drinking water related characteristics, perceived health problems, and blood chemicals. From four arsenic contaminated villages of a district in Bangladesh, 117 cases (male=55, female=62) and 120 controls (male=56, female=64) based on age and sex are selected for analyses. Arsenicosis cases were selected using the criterion of having either melanosis or keratosis at the time of survey. Various information relating to above-mentioned characteristics were collected from both cases and controls including aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin, total bilirubin and random blood sugar. We approached 138 cases and 142 controls for blood collection, of which 117 (84.8%) and 120 (83.3%) gave complete information. The mean age (± standard deviation) of the cases and controls was 46.0 (± 16.2) and 45.2 (± 13.9) years respectively. Among the cases, rate of having melanosis and keratosis were 93.2% and 73.5% respectively. Cases reported significantly: less education, higher single marital status, higher mud based floor material, less TV ownership, less TV watching daily, worse perceived health status, higher dissatisfaction by daily activities, higher abnormal result of the arsenic test and red painting (arsenic contaminated) status of the tubewell than controls. Cases also reported significantly higher health problems such as conjunctivitis, losing hair, chronic cough, problem in the eye and ear, weakness, weight loss, loss of appetite and depression than controls. Mean total bilirubin and AST were significantly higher among cases than controls. The logistic regression model- adjusted for age, sex, body mass index (BMI), marital status, education, occupation, smoking status, watching TV daily and perceived health status- showed that arsenicosis was positively associated with the highest quartile of bilirubin (OR=4.84; 95% confidence interval (CI)=1.51-15.52) and AST (OR=2.94; 95% CI= 1.15-7.52). Results suggest that arsenicosis cases are associated with poor socio-economic and health status as well as with liver dysfunction. However, these findings should be validated by further studies with large number of subjects.

(Received November 16, 2006 and accepted December 13, 2006)

Key words: Arsenicosis, Case-control study, Socio-economic characteristics, Liver dysfunction, Bangladesh

1 INTRODUCTION

Chronic arsenic poisoning in the general population is a worldwide public health issue as it has been widely reported in many areas of the world[1]. Although many countries such as Argentina, Bangladesh, Chile, China, India, Mexico and Taiwan have been notably affected by arsenic contamination in drinking water[2-4], unfortunately Bangladesh is the most affected country in the world[3, 5, 6]. Most human are exposed to arsenic through drinking water containing high amount of inorganic arsenic[1]. Arsenicosis has caused a serious public health problem in Bangladesh especially in rural areas where more than 95% people are drinking water from tubewell[3, 7, 8].

The overall situation of Bangladesh is so severe that around 50% of the Bangladeshi population[3, 5], living in 61 districts out of 64, is at risk of arsenic poisoning from naturally occurring arsenic in well water where the maximum permissible level of arsenic in water is 0.05 mg/l[6]. Although arsenic contamination in groundwater was first detected in 1993[3], already thousands of chronic arsenicosis patients are identified in Bangladesh, e. g., about 100,000 by Smith et al[9], mainly manifested by skin lesions such as melanosis and

keratosis[3]. According to the Bangladesh Arsenic Mitigation Water Supply Project (BAMWSP), 38,430 arsenicosis patients have been identified by a survey on 66 million people, living in 270 arsenic contaminated Upzilas (i. e., a sub-district)(please see the link for Map: http://www.bwspp.org/BAMWSPContents/Maps/UnionWiseAsConc.jpg). In these areas, overall 29% of the 4.9 million tubewells were found arsenic contaminated by the field test. The cumulative number (percentage) of Upzilas with arsenic contaminated tubewells of ≧ 90%, ≧ 80%, ≧ 60%, ≧ 40% and ≧ 20% were 11 (4.1%), 23 (8.5%), 61 (22.6%), 88 (32.6%) and 137 (50.7%) respectively[10]. Some other large-scale studies also reported almost similar overall rate of contaminated tubewells. For instance, 25% of the tubewells were found arsenic contaminated by British Geological Survey[11] and around 30% by Chowdhury[2]. Various studies have speculated that if no action is taken now for discontinuing people to drink arsenic contaminated water, this situation would be more alarming in future and as a consequence, substantial proportion of the population will develop arsenic-related diseases called arsenicosis[3, 9, 12].

Review of literatures indicate that arsenicosis diseases are associated with numerous health problems such as dermatitis (e. g., melanosis, leukomelanosis, keratosis, hyperkeratosis, Bowen's disease-carcinoma in situ, skin cancer), cardiovascular (e. g., hypertension, myocardial infarction, thickening of blood vessels, gangrene), respiratory (e. g., bronchitis, shortness of breath), gastrointestinal (e. g., nausea, abdominal pain, diarrhea, anorexia, weight loss), hematological (e. g., anemia, bone marrow depression), hepatic (e. g., jaundice, cirrhosis, enlarged liver, fatty infiltration and degeneration, mitochondrial damage, elevated level of liver enzymes), renal (e. g., hematuria, proteinuria, renal failure, cortical necrosis, kidney cancer), neurological (e. g., headache, lethargy, mental confusion, hallucination, muscle weakness, numbness), reproductive (e. g. low birth weight, spontaneous abortions, still-birth, pre-eclampsia), mutagenetic (e. g. chromosomal aberrations, DNA damage, inhibited DNA repair), and malignancies (e. g. lung, skin, bladder, kidney, liver)[1, 4]. It is also associated with social uncertainty, social injustice, social isolation and problematic family issues[13].

This paragraph reports some of the findings associated with arsenic exposure through drinking water in Bangladesh. Compared with drinking water containing <8.1 μg/l of arsenic, drinking water containing 8.1-40.0, 40.1-91.0, 91.1-175.0 and 175.1-864.0 μg/l of arsenic was associated with adjusted prevalence odds ratios of skin lesions of 1.91 (95% CI=1.26-2.89), 3.03 (95% CI=2.05-4.50), 3.71 (95% CI=2.53-5.44), and 5.39 (95% CI=3.69-7.86), respectively[14]. The prevalence ratios for hypertension adjusted for age, sex, and BMI were 2.2 (95% CI=1.1-4.3) and 2.5 (95% CI=1.2-4.9) for those exposed to arsenic by 0.5-1.0 mg/l and >1.0 mg/l respectively compared with subjects not exposed to arsenic[15]. The prevalence ratio for glucosuria in exposed subjects with skin lesions amounted to 1.9 (95% CI=1.5-2.4) compared with subjects not exposed[16]. The multivariate adjusted odds ratios were 2.5 (95% CI=1.5-4.3) for spontaneous abortion, 2.5 (95% CI=1.3-4.9) for still birth, and 1.8 (95% CI=0.9-3.5) for neonatal death for them who exposed to arsenic concentration of greater than 0.05 mg/l compared with 50 mg/l or less[17]. The overall crude prevalence ratios for chronic cough and chronic bronchitis among the subjects with skin lesions and exposed to arsenic drinking water were 3.0 (95% CI=1.6-5.3) and 2.9 (95% CI=1.5-5.3) respectively as compared to control population[18]. Chen and Ahsan[19] estimated at least a doubling of lifetime mortality risk from liver, bladder, and lung cancers. According to Lokuge et al[20], in Bangladesh arsenic related disease results in 9,136 deaths and 174,174 disability-adjusted life years lost per year in those exposed to arsenic concentration.

One of our previous studies based on arsenicosis patients in Bangladesh reported that longer duration of arsenicosis disease (>3 years) is significantly associated with elevated level (3rd tertile) of AST (P for trend=0.027) and blood glucose (P for trend=0.029), although no significant association was found for ALT, total bilirubin and hemoglobin. The major limitation of this study was that there was no control (arsenicosis free) group to compare their blood chemicals[7]. Considering this limitation in mind, we conducted the present case-control study in some arsenic contaminated rural villages of Bangladesh. This study initially compared the arsenicosis cases and frequency matched controls with respect to socio-demographic and water related characteristics. Self reported health problems were also compared by cases and controls. Finally the association of arsenicosis disease with AST, ALT, bilirubin, hemoglobin, and random blood sugar were studied through logistic regression analysis.

2 METHODS

2.1 Study area

This study has been conducted in four rural villages of two Upazilas in Narsingdi district, Bangladesh.

According to the information of British Geological Survey[11], this district is moderately affected where about 27% (26.8%) tested tubewells were found arsenic contaminated by Bangladesh standard (>0.05 mg/l) with a mean concentration of 0.041 μg/l for all tested tubewells. The mean concentration was below Bangladesh standard as majority (73%) of the tubewells was not contaminated. This district consists of 6 Upazilas: Belabo, Monohardi, Shibpur, Raipura, Palash and Narsingdi Sadar. Because of close geographical proximity, still Belabo and Monohardi Upazilas are under the same constituency in Bangladesh. There are 7 and 11 Unions in Belabo and Monohardi Upzila respectively, of which 2 Unions (Binyabaid Union from Belabo Upazila and Char Mandalia Union from Monohardi Upazila) are selected for this study, based on the available information of arsenic contamination level in tubewell water provided by the BAMWSP, affiliated with the Department of Public Health Engineering (DPHE) of Bangladesh government. Three closely located villages (namely Birkanda, Char Kashimnagar and Chhayan) from Binyabaid Union and 1 village (namely Khalia Baid) from Char Mandalia Union are selected for selecting arsenicosis cases and controls.

Verbal consent was obtained from all the subjects by explaining the objectives and importance of the study. Written consent was not taken because of high illiteracy rate among study population. Before conducting the survey, we explained our objectives to the local Chairman (administrative head of the Union Parisad) and elected Members of the Union Parisad residing in the study areas. With the help of the some other elite people, we first visited the selected villages to motivate the people, mainly the arsenicosis patients, to participate into this study. Within two or three days after getting the consent of participation by most of the subjects, our survey including blood collection was started by a trained team composed of principal researcher, two laboratory technicians and four other expert members from the study areas who had experience of identifying arsenicosis patients.

2.2 Arsenic contamination level in the selected villages

According to the information from BAMWSP[10], arsenic contaminated tubewells were 53.7% (out of 177 tubewells tested), 53.2% (out of 280), 24.2% (out of 652), and 11.7% (out of 240) with arsenicosis cases of 51 (out of 1878 population), 32 (out of 2727), 47 (out of 5853) and 0 (out of 1221) in Birkanda, Chhayan, Char Kashimnagar, and Khalia Baid villages respectively.

Our survey team identified 138 arsenicosis cases (131 from three villages of Binyabaid Union and 7 from Khalia Baid of Charmandalia Union) during July-August 2006, of which 117 (male=55, female=62) gave complete information including blood. The cases of the present study were selected using the criterion of having either melanosis or keratosis at the time of survey. Some of the arsenicosis cases were found common in the list provided by the BAMWSP. This list had information of arsenicosis cases such as name of the patient, age, sex, father's name, village, Union, Upazila and district. We excluded some as cases who were listed by the BAMWSP but not fulfilled the above-mentioned criteria at the time of our survey. One hundred twenty frequency matched controls (male=56, female=64) from the study areas, based on age and sex, are considered in this study. Briefly we approached 138 cases and 142 controls for blood collection, of which 117 (84.8%) and 120 (83.3%) gave blood.

Information was collected through trained interviewers from both cases and controls including socio-demographic; body height and weight to calculate body mass index (BMI); water related characteristics such as duration and quantity of drinking water from tubewell, contamination status of water; knowledge and attitudes toward arsenic; food habits and smoking; and self reported health problems; symptoms (melanosis and keratosis) including duration of arsenicosis (for cases only). Expert technicians (working in pathological laboratory) collected the samples of blood (about 5 ml each) by using the sterile disposable syringe and transferred into a clean and dry centrifuge tube. The blood samples, taken into centrifuge tube, are allowed to clot reaction and later centrifuged for 10-15 minutes at 4000 rpm. The serum samples storage in deep freeze are used mainly to measure the AST, ALT, hemoglobin, billirubin, and random blood sugar.

AST and ALT were determined according to the recommendations of the Expert Panel of the International Federation of Clinical Chemistry. Photometric Colorimetric tests for the determination of hemoglobin in blood (also called Cyanmethemoglobin method) and for the determination of total serum bilirubin (known as DCA method) were used. Random blood sugar was determined using Enzymatic Colorimetric Test for Glucose method without Deproteinisation (also called GOD-PAP method). The temperature in the assayed room was 37^{o}C (Human Gesellschaft fur Biochemica und Diagnostica mBH, Wiesbaden, Germany).

2.3 Statistical analysis

First we compared socio-demographic information,

Table 1 Basic characteristics of the arsenicosis cases and frequency matched controls in some arsenic contaminated villages in Bangladesh.

Characteristics	Cases (N=117)	Controls (N=120)	P-value
Sex:			
Male (number)	55	56	
Female (number)	62	64	
Mean age (± SD)	46.0 (± 16.2)	45.2 (± 13.9)	0.678
Mean BMI (± SD)	19.2 (± 2.0)	19.2 (± 2.6)	0.978
Mean per capita (in decimal) land owned (± SD)	14.0 (± 21.9)	14.6 (± 22.3)	0.841
Agriculture as occupation (%)	52.1	42.5	0.328
Educational years ≧ 6 (%)	13.7	25.0	0.044
Single marital status (%)	10.3	1.7	0.005
Mud floor material (%)	96.6	85.8	0.004
Number of room ≧ 2 (%)	21.4	26.7	0.364
Family members ≧ 9 (%)	17.1	9.2	0.117
Living with other in the same room (%)	30.8	28.3	0.919
Having electricity (%)	42.7	47.5	0.461
Having radio (%)	19.7	26.7	0.201
Having TV (%)	3.4	20.0	<0.001
Watching TV daily (%)	7.7	19.2	0.010
Current tobacco consumption: smoking or chewing (%)	70.9	64.2	0.408
Better perceived health status compared with last year (%)	7.7	36.7	<0.001
Satisfied or highly satisfied by daily activities (%)	50.7	64.8	0.017
Having sufficient food (%)	32.5	42.5	0.111

SD=Standard deviation

Table 2 Drinking water related characteristics for the arsenicosis cases and frequency matched controls in some arsenic contaminated villages in Bangladesh.

Characteristics	Categories	Cases N(%)	Controls N (%)	P-value
Drinking tubewell water:	Yes	117 (100.0)	120 (100.0)	
	No	0 (0.0)	0 (0.0)	
Having own tubewell:	Yes	108 (92.3)	114 (95.0)	0.395
	No	9 (7.7)	6 (5.0)	
Age (in year) of the tubewell for tubewell owner	≦ 10	50 (46.3)	54 (47.4)	0.752
	11-20	41 (38.0)	46 (40.4)	
	≧ 21	17 (15.7)	14 (12.3)	
Depth (in feet) of the tubewell:	≦ 75	68 (63.0)	76 (66.7)	0.563
	≧ 76	40 (37.0)	38 (33.3)	
Water was tested for arsenic:	Yes	97 (89.8)	109 (95.6)	0.095
	No	11 (10.2)	5 (4.4)	
Result of the last test for arsenic in water:	Contaminated	80 (82.5)	19 (17.4)	<0.001
	Not contaminated	17 (17.5)	90 (82.6)	
Still drinking contaminated water even knowing that the water is arsenic contaminated:	Yes	68 (85.0)	14 (73.7)	0.240
	No	12 (15.0)	5 (26.3)	
Amount of drinking water by number of glass:	3-9	72 (61.5)	66 (55.0)	0.466
	10-12	35 (29.9)	45 (37.5)	
	≧ 13	10 (8.5)	9 (7.5)	
Distance (in yard) of the nearest tubewell:	≦ 15	49 (41.9)	44 (36.7)	0.077
	16-30	45 (38.5)	62 (51.7)	
	≧ 31	23 (19.7)	14 (11.7)	
Present status/marking of the nearest tubewell:	Painted green (safe)	31 (26.5)	85 (70.8)	<0.001
	Painted red (unsafe)	62 (53.0)	14 (11.7)	
	Painted nothing	24 (20.5)	21 (17.5)	
Changed previous tubewell for arsenic contamination:	Yes	20 (17.1)	12 (10.0)	0.110
	No	97 (82.9)	108 (90.0)	

Table 3 Perceived health problems reported by cases and frequency matched controls in some arsenic contaminated villages in Bangladesh

Characteristics	Cases (N=117)	Controls (N=120)	P-value
	% yes	% yes	
Itching	61.5	29.2	<0.001
Pain during urination	22.2	20.0	0.675
Nail problem	13.7	5.0	0.021
Constipation	51.3	36.7	0.023
Conjunctivitis	23.1	11.7	0.020
Hair loss (alopecia)	50.4	31.7	0.003
Joint pain	51.3	40.0	0.081
Chest pain	57.3	43.3	0.032
Breathing problem	35.0	29.2	0.333
Swollen joint	34.2	20.0	0.014
Chronic bronchitis	41.0	26.7	0.019
Diarrhea (frequent)	12.0	5.8	0.097
Headache	49.6	41.7	0.222
Problem in the eye and ear	48.7	31.7	0.007
Anemia	43.6	27.5	0.010
Weakness	87.2	75.0	0.017
Weight loss	70.9	38.3	<0.001
Loss of appetite	67.5	34.2	<0.001
Restlessness	50.4	40.8	0.138
Insufficient sleep	53.0	35.8	0.008
Drowsiness	63.2	36.8	0.001
Vomiting tendency	35.9	19.2	0.004
Depression	60.7	44.2	0.011
Burning hand and leg	57.3	26.7	<0.001

Table 4 Results of the blood test for some selected indicators by cases and frequency matched controls in some arsenic contaminated villages in Bangladesh

Characteristics	Cases(N=117)	Controls(N=120)	P-value
	mean ± SD	mean ± SD	
Hemoglobin (g/dl)	10.70 ± 1.36	11.94 ± 1.38	0.184
Billirubin (mg/dl)	0.58 ± 0.15	0.53 ± 0.17	0.017
AST (U/L)	35.89 ± 11.81	31.88 ± 9.27	0.004
ALT (U/L)	22.77 ± 7.01	21.50 ± 6.38	0.147
Random blood sugar (mmol/l)	6.38 ± 1.06	6.13 ± 1.10	0.078

SD=Standard deviation

Table 5 Adjusted odds ratio (OR) for having arsenicosis by quartiles of different blood chemicals

Characteristics	Case/Control n	OR (95% CI)
Hemoglobin (g/dl):		
1st quartile (≦ 10.90)	37/31	1.00
2nd quartile (10.91-12.00)	28/26	0.96 (0.40-2.28)
3rd quartile (12.01-12.60)	27/31	0.80 (0.31-2.05)
4th quartile (≧ 12.61)	25/32	0.81 (0.31-2.13)
		P for trend=0.622
Billirubin (mg/dl):		
1st quartile (≦ 0.40)	23/43	1.00
2nd quartile (0.41-0.60)	58/51	1.80 (0.82-3.96)
3rd quartile (0.61-0.70)	17/14	2.06 (0.70-6.05)
4th quartile (≧ 0.71)	19/12	4.84 (1.51-15.52)**
		P for trend=0.010
AST (U/L):		
1st quartile (≦ 27.45)	25/35	1.00
2nd quartile (27.46-32.00)	34/25	2.09 (0.83-5.24)
3rd quartile (32.01-38.00)	21/40	1.19 (0.48-3.00)
4th quartile (≧ 38.01)	37/20	2.94 (1.15-7.52)*
		P for trend=0.074
ALT (U/L):		1.00
1st quartile (≦ 18.00)	30/30	1.03 (0.43-2.49)
2nd quartile (18.01-20.00)	26/34	1.17 (0.50-2.73)
3rd quartile (20.01-25.00)	28/29	1.77 (0.71-4.41)
4th quartile (≧ 25.01)	33/27	*P for trend=0.238*
Random blood sugar (mmol/l):		
1st quartile (≦ 5.50)	29/40	1.00
2nd quartile (5.51-6.30)	27/29	1.55 (0.63-3.85)
3rd quartile (6.31-6.80)	28/33	1.33 (0.54-3.28)
4th quartile (≧ 6.81)	33/18	2.17 (0.82-5.72)
		P for trend=0.176

***P<00.01, *P<0.05; CI=Confidence Interval*
Adjusted for age, BMI, sex, marital status, education, occupation, smoking status, watching TV daily and perceived health status

water related characteristics, self-reported health problems and blood related variables by cases and control. P-values based on χ^2 test and t-test are also presented. Later blood chemicals were categorized using quartile technique and the odds ratio of having arsenicosis (adjusted for age, BMI, sex, marital status, education, occupation, smoking status, watching TV daily, and perceived health status) by quartiles, estimated by logistic regression analysis, are calculated. All the analyses were performed using SPSS. Significant level was set at P<0.05.

3 RESULTS

Among arsenicosis cases, having melanosis and keratosis were 93.2% and 73.5% respectively. The average duration of arsenicosis disease was 61.2 months with a standard deviation (SD) of 30.2 months (not shown). Table 1 presents some of the basic characteristics of the arsenicosis cases and frequency matched controls. The average age (± SD) of the cases and controls were 46.0 (± 16.2) and 45.2 (± 13.9) years respectively. The rate of education by 6 years and above was found to be significantly lower among cases (13.7%) than controls (25.0%). Remained single (unmarried) was significantly higher among cases than controls. Mud based floor of the house was significantly higher among cases than controls. Having TV as well as watching TV daily was significant-

ly lower among cases than controls. Perceived health status and satisfaction about daily activities differed significantly between cases and control. However, several characteristics such as age, BMI, per capital land owned, occupation, number of room, family members, household having radio and electricity, smoking/chewing tobacco, and food sufficiency in the whole year differed insignificantly between cases and controls.

Drinking water related characteristics by cases and controls are shown in Table 2. This table also revealed that all the cases and controls (i. e. 100%) were drinking tubewell water, although 92.3% cases and 95% controls owned own tubewell (P=0.395). Only two characteristics namely result of the last test for arsenic in water (contaminated versus not contaminated) and painting status of the tubewell (painted green means safe, painted red means unsafe, painted nothing) differed significantly (P<0.001) by cases and controls.

Table 3 shows that itching (P<0.001 based on χ^2 test), nail problem (P=0.021), constipation (P=0.023), conjunctivitis (P=0.020), losing hair (P=0.003), chest pain (P=0.032), swollen joint (P=0.014), chronic cough (P=0.019), problem in the eye and ear (P=0.007), anemia (P=0.010), weakness (P=0.017), weight loss (P<0.001), loss of appetite (P<0.001), insufficient sleep (P=0.008), drowsiness (P=0.001), vomiting tendency (P=0.004), depression (P=0.011) and burning hand and leg (P<0.001) were significantly higher among cases than controls.

Table 4 indicates that mean level of some blood chemicals namely serum bilirubin (P=0.017) and AST (P=0.004) were significantly associated with arsenicosis. Hemoglobin (P=0.184), ALT (P=0.147) and random blood sugar (P=0.078) were insignificantly associated with arsenicosis.

The logistic model adjusted for age, BMI, sex, marital status, education, occupation, smoking/chewing tobacco, watching TV daily and perceived health status (Table 5) indicates that arsenicosis cases were positively associated with the highest quartile of bilirubin (OR=4.84; 95% CI=1.51-15.52, P<0.01) and AST (OR=2.94; 95% CI= 1.15-7.52, P<0.05) level. Hemoglobin, ALT and random blood sugar were found to be insignificantly associated with arsenicosis.

4 DISCUSSION

Among cases of the present study, percentage of having melanosis and keratosis were 93.2% and 73.5% respectively. This is consistent with the findings of some other studies in Bangladesh[21-23]. For instance, melanosis and keratosis were reported 97.0% and 68.7% by Hossain et al[21], 100% and 80.9% by Milton et al[23], and 94.4% and 65.3% by Guha Mazumder[22].

Various socio-economic factors (Table 1) revealed that arsenicosis cases are relatively poorer than controls, which is consistent with the findings of other studies[5, 24-30]. Some possible explanations could be given in this regard. Firstly, a large percentage (20-70%) of the arsenicosis patients, most of which are extremely poor, remains untreated due to financial crisis. The status of being untreated further deteriorates the condition of arsenic victims. In case of getting treatment for arsenicosis, the spending money diminishes household income and increases the economic burden of the poor victims and their family. Poverty could also be aggravated as the untreated poor victims are incapable of doing hard labor and associated with social discriminations such as losing jobs, barrier to access new jobs and social rejections[24].

Secondly, poorer families are more likely to depend on arsenic contaminated tubewell than socio-economically better families because of limited alternatives of safe water[24, 31] including inability to install a new tubewell. Rich people generally have the ability to take advantage of safe alternative water sources[31]. Our data (not shown in Table) support both the above-mentioned explanations. For instance, 85 arsenicosis cases (out of 117) and 15 controls (out of 120) were continuing to dink arsenic contaminated water even after knowing that the water was arsenic contaminated by a previous test. Each of them was asked to mention the main reason of drinking such contaminated water. In response, 55 arsenicosis cases out of 85 (i. e., 68.6%) mentioned that scarcity of money including inability to install a new tubewell was the main reason, whereas this figure was 7 out of 15 (i. e., 46.7%) among controls.

Thirdly, various studies reported that socio-economically poor people are significantly less likely to be aware about arsenic and related problems[25, 27]. Fourthly, poor nutritional status, highly correlated with poor socio-economic status, is found to be associated with high arsenic toxicity[22, 29, 31, 32]. For instance, the prevalence of keratosis was found significantly higher among the people of poor nutritional status than adequately nourished people[22]. Mitra et al[29] also reported that the majority of the arsenicosis patients came from very socioeconomic class with severely malnutrition. It is reported that poor nutritional status or dietary deficiency, associated with lower intake of the antioxidants, folate, and/or dietary proteins[33, 34],

diminishes the ability of metabolism and detoxification of arsenic in the body and hence increases an individual's susceptibility of chronic arsenic toxicity[31-35]. In short, high protein containing diet possibly helps in clearance of inorganic arsenic by increased methylation[22]. Unfortunately most of the poor people can not afford the cost of buying nutritious foods against arsenic toxicity[24].

Our study also showed significantly higher perceived health problems among cases than controls related to arsenic toxicity (Table 3). These findings are supported by many other studies[21, 28-30]. For instance, loss of appetite (anorexia), nausea (vomiting tendency), diarrhea, anemia, neuropathy, hepatomegaly, lung disease, and weakness are frequently reported by the arsenicosis patients[22, 30]. Mahmood and Ball[5] reported that patients with chronic arsenicosis in Bangladesh often present with weakness, conjunctivitis, aching, anorexia, nausea, vomiting, pain in abdomen, constipation, diarrhea, and weight loss. According to Milton et al[23], the predominant features of arsenicosis cases are cough, redness of eye, conjunctivitis, chronic bronchitis. Hossain et al[21] found significant association conjunctivitis, bronchitis, loss of appetite and wasting with keratosis. Mitra et al[29] reported that majority of the patients had multiple symptoms namely weakness, chronic cough, joint pain, itching, abdominal pain, chest pain, loss of appetite, insomnia, shortness of breathing, and burning in urination.

AST and ALT are used as indicators of hepatocellular injury[36]. Present study showed that AST level was significantly higher among cases than controls. Although elevated level of ALT was found among cases, it was statistically insignificant. These findings are consistent with the findings of some other studies[22, 30, 37-39]. For instance, increased activities of AST or ALT or both were reported among the individuals exposed to arsenic via drinking water[37, 39]. An epidemiological study showed the evidence of hepatomegaly in 62 (92.5%) of 67 members who drank arsenic contaminated water (ranging from 0.2-2 mg/l). In contrast, only 6 (6.3%) of 96 persons from the same area who drank safe water (arsenic level, <0.05 mg/l) had non-specific hepatomegaly[30]. According to Sinha et al[38] the reduced urinary excretion of arsenic observed in the arsenic affected patients may be related to liver dysfunction. Studies reported that inorganic arsenic is quickly absorbed into the blood stream[40] and mostly transported to the liver[40-43] and alters the hepatic functions or increases the liver enzyme activity indicating hepatocellular injury[36, 43]. The hepatic arsenic, weight of the liver, AST and ALT were increased significantly, after 6 or 12 months of arsenic contaminated water consumption, among arsenic-fed groups (mice) than controls[41].

Although hepatic damages caused by chronic exposure to arsenic has been reported by many studies[30, 36, 37, 41], little is known about the arsenic-induced liver toxicity[44]. Particularly the mechanism by which arsenic causes liver damage remains elusive[36]. However, it is reported that liver is the main site of inorganic arsenic methylation[4, 42] and associated with the process of liver dysfunction/carcinogenesis. Some possible of carcinogenesis due to arsenic toxicity may include: DNA hypomethylation due to continuous methyl depletion facilitating aberrant gene expressions and abnormality in cell proliferation[44-48], decreased DNA repair[49], excessive formation of oxygen free radicals (oxidative stress) in plasma and reducing antioxidant capacity[40, 47, 50, 51], hypomethylation of the estrogen receptor-α gene promoter[45], loss of tumor suppressor genes in the liver (e. g., glucocorticoid receptor (GR)) resulting from increased chromosomal aberrations and sister chromatid exchanges[52, 53], liver deletion of selenium via biliary excretion[54], presence of substantial chromosome damage in lymphocytes in the exposed population[47, 55], and weakening of the antioxidant defense system of the liver and consequent peroxidative damage of the lipid membranes due to the cumulative depletion of hepatic glutathione (GSH)[41, 56].

Present study revealed that serum bilirubin is significantly higher among arsenicosis cases than control (Table 4), which is consistent with the findings of some other studies[36, 37, 57]. Armstrong et al[57] observed increased concentration of total bilirubins in serum samples from seven individuals intoxicated with arsenic via drinking water. Although insignificant, Lu et al[37] reported higher total bilirubin in arsenic affected areas than control area. Hernandez-Zavala et al[36] also found significant correlation between total bilirubin and urinary arsenic concentrations, which suggest that arsenic exposure is strongly related to bilirubin alteration. The increase in bilirubin, a heme degradation product, could be explained by the induction of heme oxygenase (HO), the rate limiting enzyme of heme catabolism, since it has been reported that arsenic induces HO activity in rodents are associated with marked elevations in the biliary excretion of bilirubin[36].

Our study showed elevated glucose level among cases than controls although it was insignificant. Higher concentration of blood glucose can be a sign of variety of diseases such as diabetes mellitus (DM). This finding may be supportive for other studies which reported the

positive associations of DM with both long term arsenic exposure and cumulative arsenic exposure[58-60]. Significantly higher prevalence of DM was observed among the subjects with keratosis compared with subjects who did not have keratosis[59]. The administration of arsenic has been demonstrated to cause hyperglycemia in experimental animals and to affect the functions of insulin receptor and glucose transportation[58]. Arsenic has been found to cause mitochondrial damage, degeneration, and necrosis of β-cells in the islets of mice after intraperitoneal injection or arsenic plus hydroxylamine, with a consequence of transient hyperglycemia[61]. GR mediates blood glucose regulation and disrupting its normal function due to arsenic which could be a part of how arsenic affects diabetes[52, 62].

As arsenic toxicity is more pronounced among poor and malnourished people as compared to rich, arsenic mitigation programs should target the arsenic exposed malnourished population as a priority[32]. People should be urged to take food containing proteins in good quantity either from animal sources or if unable, from vegetable sources like pulses, soybeans, wheat and so on[22]. Health education programs should be targeted to the lower socio-economic society for encouraging the well-switching[25]. Some chief remedy should be available for poor victims. In this regard, taking a potentized homeopathic medicine, called arsenicum albumin-30, may be beneficial at least for sometime where provision of safe arsenic-free drinking water or suitable medical help due to the remoteness of the area or any other more efficient drug is available. A recent randomized controlled trail indicated that taking two doses of 'verum' (arsenicum album-30 soaked globules) daily for 10 consecutive days (when each dose contains eight small globules soaked) is effective in improving the hepatic conditions. The notable changes observed in activities of hepatic functions as well as increased appetite reported by most of the subjects taking 'verum' may ameliorate the arsenic-induced toxicity. As this homeopathic remedy is reasonable (in terms of cost and accessibility) for most the poor people, there is a great potential of the remedy (by its large scale use) to ameliorate the groundwater arsenic toxicity in millions of poor rural people living in remote places[63].

Other mitigation activities or interventions such as (i) identification of a nearby tubewell with water of low arsenic concentration, (ii) installation of community wells where the proportion of safe wells is particularly low and the sharing of tube-wells is consequently not a viable option, (iii) close highly contaminated tubewells where alternative water source is available, (iv) sharing nearby arsenic free tubewells, (v) proper watershed management, treating surface and ground water, (vi) rain water harvesting, (vii) traditional water management such as dug well and surface water with controls of bacterial and other chemical contamination through filtration and chlorination, (viii) increasing public awareness of the arsenic calamity[5, 8, 9, 12, 25, 64] may be useful to address the arsenic problem effectively in Bangladesh. Community education, mobilization, motivation and proper monitoring may be essential for a sustainable solution to the problem[9, 12].

Media particularly TV can be used to deliver more and more messages regarding the consequences of ingesting arsenic as the significant negative association was found between television and drinking arsenic contaminated water. As arsenic level may change over time[8, 65] and mislabeling of tubewells are reported[66], all the tubewells should be checked periodically. Periodic testing by trained persons is necessary because many of the country's people are facing the scarcity of uncontaminated water. Government also may extent the laboratory facilities phase by phase (based on contamination level) for testing the arsenic concentration in drinking water at the district level.

Some potential limitations such as small sample size, the possibility of mislabeling of arsenic contaminated tubewell by previous tests, motivating patients to participate into the study, difficulty in obtaining blood in the field and carrying blood samples from the field to the laboratory for analysis within a reasonable time were important to note. Although significantly higher health problems are reported by cases than control (Table 3), it is not possible to determine whether their perceived health problems appeared before or after their diagnosis of arsenicosis.

In short, arsenicosis cases are socio-economically poorer than controls. Perceived health problems as well as liver dysfunctions are also higher among cases than controls. These findings suggest us to recommend more mitigation activities and interventions for poor segment of the victimized society. The arsenicosis cases should be advised by the available health services to consult with medical practitioners for examining their liver functions to reduce the risk of developing liver cancer. Finally, arsenic poisoning should be on the top of the pubic heath agendas because of its' cascading effects.

Acknowledgments

The authors thank Sapporo Medical University

Foundation for Promotion of Medical Science for funding the study in Bangladesh. We also thank all other persons who supported us and involved in the data collection and blood testing during survey.

References

1. Yoshida T, Yamauchi H, Sun GF. Chronic health effects in people exposed to arsenic via the drinking water: dose-response relationships in review. Toxicol Appl Pharmacol 2004; 198: 243-252.
2. Chowdhury AMR. Arsenic crisis in Bangladesh. Sci Am 2004; 291: 86-91.
3. Khan MMH, Sakauchi F, Sonoda T, Washio M, Mori M. Magnitude of arsenic toxicity in tube-well drinking water in Bangladesh and its adverse effects on human health including cancer: evidence from a review of the literature. Asian Pacific J Cancer Prev 2003; 4: 7-14.
4. Mandal BK, Suzuki KT. Arsenic around the world: a review. Talanta 2002; 58: 201-235.
5. Mahmood SAI, Ball C. Defining and implementing arsenic policies in Bangladesh: possible roles for public and private sector actors. J Health Hum Serv Administration 2004; 27: 158-174.
6. Fazal MA, Kawachi T, Ichion E. Extent and severity of groundwater arsenic contamination in Bangladesh. Water Int 2001; 26: 370-379.
7. Khan MMH, Hossain MK, Kobayashi K, Sakauchi F, Yamashita T, Ahmed MF, Hossain MD, Quamruzzaman Q, Mori M. Levels of blood and urine chemicals associated with longer duration of having arsenicosis in Bangladesh. Int J Environ Health Res 2005; 15: 289-301.
8. Caldwell BK, Calwell JC, Mitra SN, Smith W. Searching for an optimum solution to the Bangladesh arsenic crisis. Soc Sci Med 2003; 56: 2089-2096.
9. Smith AH, Lingas EO, Rahman M. Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. Bull World Health Organ 2000; 78: 1093-1103.
10. Bangladesh Arsenic Mitigation Water Supply Project (BAMWSP). Newsletter and Upzila wise summary results. Dhaka: National Arsenic Mitigation Information Centre (NAMIC), BAMWSP, DPHE, 2005.
11. Kinniburgh DG, Smedley PL editors. Arsenic contamination of groundwater in Bangladesh. In: Vol 1: Summary. Keyworth: British Geological Survey; 2001 (British Geological Survey WC/00/19.)
12. Rahman M. Arsenic and contamination of drinking-water in Bangladesh: a public health perspective. J Health Popul Nutr 2002; 20: 193-197.
13. Hassan MM, Atkins PJ, Dunn CE. Social implications of arsenic poisonning in Bangladesh. Soc Sci Med 2005; 61: 2201-2211.
14. Ahsan H, Chen Y, Parvez F, Zablotska L, Argos M, Hussain I, Momotaj H, Levy D, Cheng Z, Slavkovich V, van Geen A, Howe GR, Graziano JH. Arsenic exposure from drinking water and risk of premalignant skin lesions in Bangladesh: baseline results from the Health Effects of Arsenic Longitudinal Study. Am J Epidemiol 2006; 163: 1138-1148.
15. Rahman M, Tondel M, Ahmad SA, Chowdhury IA, Faruquee MH, Axelson O. Hypertension and arsenic exposure in Bangladesh. Hypertension 1999; 33: 74-78.
16. Rahman M, Tondel M, Chowdhury IA, Axelson O. Relations between exposure to arsenic, skin lesions, and glucosuria. Occup Environ Med 1999; 56: 277-281.
17. Milton AH, Smith W, Rahman B, Hasan Z, Kulsum U, Dear K, Rakibuddin M, Ali A. Chronic arsenic exposure and adverse pregnancy outcomes in Bangladesh. Epidemiology 2005; 16: 82-86.
18. Milton AH, Hasan Z, Rahman A, Rahman M. Chronic arsenic poisoning and respiratory effects in Bangladesh. J Occup Health 2001; 43: 136-140.
19. Chen Y, Ahsan H. Cancer burden from arsenic in drinking water in Bangladesh. Am J Public Health 2004; 94: 741-744.
20. Lokuge KM, Smith W, Caldwell B, Dear K, Milton AH. The effect of arsenic mitigation interventions on disease burden in Bangladesh. Environ Health Perspect 2004; 112: 1172-1177.
21. Hossain MK, Khan MMH, Alam MA, Chowdhury AK, Hossain MD, Ahmed MF, Kobayashi K, Sakauchi F, Mori M. Manifestation of arsenicosis patients and factors determining the duration of arsenic symptoms in Bangladesh. Toxicol Appl Pharmacol 2005; 208: 78-86.
22. Guha Mazumder DN. Chronic arsenic toxicity: clinical features, epidemiology, and treatment: experience in West Bengal. J Environ Sci Health A 2003; A38: 141-163.
23. Milton AH, Hasan Z, Rahman A, Rahman M. Non-cancer effects of chronic arsenicosis in Bangladesh: preliminary results. J Environ Sci Health A 2003; A38: 301-305.
24. Chowdhury MAI, Uddin MT, Ahmed MF, Ali MA, Rasul SMA, Hoque MA, Alam R, Sharmin R, Uddin SM, Islam MS. Collapse of socio-economic base of Bangladesh by arsenic contamination in groundwater. Pakistan J Biol Sci 2006; 9: 1617-1627.
25. Parvez F, Chen Y, Argos M, Hussain AZMI, Momotaj H, Dhar R, van Geen A, Graziano JH, Ahsan H. Prevalence of arsenic exposure from drinking water and awareness of its health risks in a Bangladeshi population: results from a large

population-based study. Environ Health Perspect 2006; 114: 355-359.

26. Hadi A, Parveen R. Arsenicosis in Bangladesh: prevalence and socio-economic correlates. Public Health 2004; 118: 559-564.
27. Hadi A. Fighting arsenic at the grassroots: experience of BRAC's community awareness initiative in Bangladesh. Health Policy Plann 2003; 18: 93-100.
28. Dey RK, Hoque MM, Haque MA, Hossain MZ, Cockcroft A. Assessment of risk factors for arsenicosis in a selected Upazila in Bangladesh: Final repot. Dhaka: UNICEF, September 2002.
29. Mitra AK, Bose BK, Kabir H, Das BK, Hussain M. Arsenic-related health problems among hospital patients in southern Bangladesh. J Health Popul Nutr 2002; 20: 198-204.
30. Guha Mazumder DN, Chakraborty AK, Ghose A, Gupta JD, Chakraborty DP, Dey SB, Chattopadhyay N. Chronic arsenic toxicity from drinking tubewell water in rural West Bengal. Bull World Health Organ 1988; 66: 499-506.
31. Hanchett S, Nahar Q, van Agthoven A, Geers C, Rezvi MFJ. Increasing awareness of arsenic in Bangladesh: lessons from a public education programme. Health Policy Plann 2002; 17: 393-401.
32. Milton AH, Hasan Z, Shahidullah SM, Sharmin S, Jakariya MD, Rahman M, Dear K, Smith W. Association between nutritional status and arsenicosis due to chronic arsenic exposure in Bangladesh. Int J Environ Health Res 2004; 14: 99-108.
33. Gamble MV, Liu X, Ahsan H, Pilsner JR, IIievski V, Slavkovich V, Parvez F, Levy D, Factor-Litvak P, Graziano JH. Folate, homocysteine, and arsenic metabolism in arsenic-exposed individuals in Bangladesh. Environ Health Perspect 2005; 113: 1683-1688.
34. Steinmaus C, Carrigan K, Kalman D, Atallah R, Yuan Y, Smith AH. Dietary intake and arsenic methylation in a U. S. population. Environ Health Perspect 2005; 113: 1153-1159.
35. Buchet JP, Geubel A, Pauwels S, mahieu P, Lauwerys R. The influence of liver disease on the methylation of asrenite in humans. Arch Toxicol 1984; 55: 151-154.
36. Hernandez-Zavala A, Del Razo LM, Aguilar C, Garcia-Vargas GG, Borja VH, Cebrian ME. Alteration in bilirubin excretion in individuals chronically exposed to arsenic in Mexico. Toxicol Lett 1998; 99: 79-84.
37. Lu S-N, Chow N-H, Wu W-C, Chang T-T, Huang W-S, Chen S-C, Lin C-H, Carr BI. Characteristics of hepatocellular carcinoma in a high arsenicism area in Taiwan: a case-control study. J Occup Environ Med 2004; 46: 437-441.
38. Sinha SK, Misbahuddin M, Ahmed ANN. Factors involved in the development of chronic arsenic poisoning in Bangladesh. Arch Environ Health 2003; 58: 699-700.
39. Franzblau A, Lilis R. Acute arsenic intoxication from environmental arsenic exposure. Arch Environ Health 1989; 44: 385-390.
40. Chiou H-Y, Hsueh Y-M, Liaw K-F, Horng S-F, Chiang M-H, Pu Y-S, Lin JS-N, Huang C-H, Chen C-J. Incidence of internal cancers and ingested inorganic arsenic: a seven-year follow-up study in Taiwan. Cancer Res 1995; 55: 1296-1300.
41. Santra A, Maiti A, Das S, Lahiri S, Charkaborty SK, Guha Mazumder DN. Hepatic damage caused by chronic arsenic toxicity in experimental animals. Clin Toxicol 2000; 38: 395-405.
42. Benramdane L, Accominotti M, Fanton L, Malicier D, Vallon J-J. Arsenic speciation in human organs following fatal arsenic trioxide poisoning- a case report. Clin Chem 1999; 45: 301-306.
43. Chiou PW-S, Chen K-L, Yu B. Effects of roxarsone on performance, toxicity, tissue accumulation and residue of eggs and excreta in laying hens. J Sci Food Agric 1997; 74: 229-236.
44. Cui X, Li S, Shraim A, Kobayashi Y, Hayakawa T, Kanno S, Yamamoto M, Hirano S. Subchronic exposure to arsenic through drinking water alters expression of cancer-related genes in rat liver. Toxicol Pathol 2004; 32: 64-72.
45. Chen H, Li S, Liu J, Diwan BA, Barrett JC, Waalkes MP. Chronic inorganic arsenic exposure induces hepatic global and individual gene hypomethylation: implications for arsenic hepatocarcinogenesis. Carcinogenesis 2004; 25: 1779-1786.
46. Liu J, Xie Y, Ward JM, Diwan BA, Waalkes MP. Toxicogenomic analysis of aberrant gene expression in liver tumors and nontumorous livers of adult mice exposed in utero to inorganic arsenic. Toxicol Sci 2004; 77: 249-257.
47. Roy P, Saha A. Metabolism and toxicity of arsenic: a human carcinogen. Current Sci 2002; 82: 38-45.
48. Zhao CQ, Young MR, Diwan BA, Coogan TP, Waalkes MP. Association of arsenic-induced malignant transformation with DNA hypomethylation and aberrant gene expression. Proc Natl Acad Sci USA 1997; 94: 10907-10912.
49. Andrew AS, Karagas MR, Hamilton JW. Decreased DNA repair gene expression among individuals exposed to arsenic in United States drinking water. Int J Cancer 2003; 104: 263-268.
50. Pi J, Yamauchi H, Kumagai Y, Sun G, Yoshida T, Aikawa H, Hopenhayn-Rich C, Shimojo N. Evidence for induction of oxidative stress caused by chronic exposure of Chinese residents to arsenic contained in drinking water. Environ Health Perspect 2002; 110: 331-336.

51. Wu M-M, Chiou H-Y, Wang T-W, Hsueh Y-M, Wang I-H, Chen C-J, Lee T-C. Association of blood arsenic levels with increased reactive oxidants and decreased antioxidant capacity in a human population of Northeastern Taiwan. Environ Health Perspect 2001; 109: 1011-1017.
52. Kaltreider RC, Davis AM, Lariviere JP, Hamilton JW. Arsenic alters the function of the glucocorticoid receptor as a transcription factor. Environ Health Perspect 2001; 109: 245-251.
53. Chen C-J, Chen CW, Wu M-M, Kuo T-L. Cancer potential in liver, lung, bladder and kidney due to ingested inorganic arsenic in drinking water. Br J Cancer 1992; 66: 888-892.
54. Spallholz JE, Boylan LM, Rahman MM. Environmental hypothesis: is poor dietary selenium intake an underlying factor for arsenicosis and cancer in Bangladesh and West Bengal, India? Sci Total Environ 2004; 323: 21-32.
55. Mahata J, Chaki M, Ghosh P, Das JK, Baidya K, Ray K, Natarajan AT, Giri AK. Chromosomal aberrations in arsenic-exposed human populations: a review with special reference to a comprehensive study in West Bengal, India. Cytogenet Genome Res 2004; 104: 359-364.
56. Guha Mazumder DN. Effect of chronic intake of arsenic-contaminated water on liver. Toxicol Appl Pharmacol 2005; 206: 169-175.
57. Armstrong CW, Stroube RB, Rubio T. Outbreak of fatal arsenic poisoning caused by contaminated drinking water. Arch Environ Health 1984; 39: 276-279.
58. Tseng C-H, Tai T-Y, Chong C-K, Tseng C-P, Lai M-S, Lin BJ, Chiou H-Y, Hsueh Y-M, Hsu K-H, Chen C-J. Long-term arsenic exposure and incidence of non-insulin-dependent diabetes mellitus: a cohort study in arseniasis-hyperendemic villages in Taiwan. Environ Health Perspect 2000; 108: 847-851.
59. Rahman M, Tondel M, Ahmad SK, Axelson O. Diabetes mellitus associated with arsenic exposure in Bangladesh. Am J Epidemiol 1998; 148: 198-203.
60. Lai M-S, Hsueh Y-M, Chen C-J, Shyu M-P, Chen S-Y, Kuo T-L, Wu M-M, Tai T-Y. Ingested inorganic arsenic and prevalence of diabetes mellitus. Am J Epidemiol 1994; 139: 484-492.
61. Boquist L, Boquist S, Ericsson I. Structural β-cell changes and transient hyperglycemia in mice treated with compounds inducing inhibited citric acid cycle enzyme activity. Diabetes 1988; 37: 89-98.
62. Josephson J. Arsenic and endocrines: new study suggests disruption. Environ Health Perspect 2001; 109: A132-A133.
63. Khuda-Bukhsh AR, Pathak S, Guha B, Karmakar SR, Das JK, Banerjee P, Biswas SJ, Mukherjee P, Bhattacharjee N, Choudhury SC, Banerjee A, Bhadra S, Mallick P, Chakrabarti J, Mandal B. Can homeopathic arsenic remedy combat arsenic poisoning in humans exposed to groundwater arsenic contamination?: a preliminary report on first human trial. Evid Based Complement Alternat MED 2005; 2: 537-548.
64. van Geen A, Ahmed KM, Seddique AA, Shamsudduha M. Community wells to mitigate the arsenic crisis in Bangladesh. Bull World Health Organ 2003; 81: 632-638.
65. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ORC Macro. Bangladesh Demographic and Health Survey 2004. Dhaka: NIPORT, Mitra and Associates, and Calverton, MD: ORC Macro, 2005.
66. Rahman MM, Mukherjee D, Sengupta MK, Chowdhury UL, Lodh D, Chanda CR, Roy S, Selim M, Quamruzzaman Q, Milton AH, Shahidullah SM, Rahman MT, Chakraborti D. Effectiveness and reliability of arsenic field testing kits: are the millions dollar screening projects effective or not? Environ Sci Technol 2002; 36: 5385-5394.

Corresponding author:
MMH Khan
Department of Public Health
Sapporo Medical University
Chuo-ku, S 1, W 17
Sapporo 060-8556, Japan
Email: mmhkhan70@yahoo.com or khan@sapmed.ac.jp
Fax: 81-11-641-8101