MINI-REVIEW

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

MMH Khan*, Fumio Sakauchi, Tomoko Sonoda, Masakazu Washio, Mitsuru Mori

Abstract

Only after a decade from 1993, arsenic contamination of groundwater in Bangladesh has been reported as the biggest arsenic catastrophe in the world. It is a burning public health issue in this country. More than 50 percent of the total population is estimated at risk of contamination. Already thousands of people have been affected by the disease arsenicosis. Many more may be on the way to manifest lesions in future. We conducted a review of previous studies and published articles including MEDLINE database on this issue. We found that 59 districts out of 64 have been already affected by arsenic in underground drinking water, where this particular source of drinking water is the main source for 97 percent of the rural people. The water is unfortunately now a great threat for the human being due to high level of arsenic. Continuous arsenic exposure can lead people to develop arsenicosis, which in turn elevates the risk of cancer. Skin lesions are the most common manifestations in arsenicosis patients. Relatively poor rural people and other socio-economically disadvantaged groups are more affected by this exposure. Until now cancer patients have been relatively limited in Bangladesh. One of the reasons may be that several years are needed to show cancer manifestations from the beginning of arsenic exposure. But it is suspected that after some years a large number of patients will appear with cancer in different sites for arsenic exposure in drinking water. Various studies have been conducted in arsenic affected countries - notably in Argentina, Chile, China, Japan, and Taiwan - to find the potential of arsenic exposure to cause development of cancer. Among the arsenic related cancers, liver, lung, skin, bladder and kidney cancers are reported to be prevalent in these countries. Unfortunately no scientific study has yet been conducted in Bangladesh to find the relationship between arsenic exposure and cancers in different sites of the body. So our aim is to conduct an ecological as well as a case-control study in the country in the future.


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Introduction

Bangladesh, an alluvial and deltaic land of 147,570 square km, is prone to various natural disasters such as cyclones, floods, and droughts (Ahmad et al., 2001). The total population is about 130 million. The people of this country are still overburdened with various infectious diseases and ailments due to malnutrition. Unfortunately one more environmental hazard from geological sources – arsenic contamination of groundwater above the World Health Organization (WHO) permissible level - has been added to these problems and has simply worsened further the existing situation by intensifying natural disasters (Kabir et al., 2001), as well as by creating a devastating public health crisis in Bangladesh (Rahman et al., 1998; Rahman et al., 1999; Tondel et al., 1999). For Bangladesh the current permissible limit of arsenic in drinking water set by WHO is 0.05 milligrams/litre (mg/l) or 50 micrograms/litre (µg/l). Arsenicosis, the outcome of groundwater arsenic poisoning, has been increasing in an alarming way since its
detection in 1993. For its gravity and magnitude it has appeared as the burning issue of public health sectors presently in Bangladesh. Both international and national organizations related to public health sectors have already come forward and given proper priorities for research to save millions of people from its vicious consequences and now they are relentlessly trying to draw considerable attentions and interests from the public health scientists including other national as well as internationals researchers in this field for finding appropriate strategies in this regard.

**Arsenic Contamination Trend in Bangladesh:**

The history of excessive level of arsenic contamination of groundwater in Bangladesh is only about one decade old. It was first detected in Nawabgonj district in 1993. Only 8 patients were identified in 1994 who had been suffering from manifestations of arsenic toxicity. Initially 8 bordering districts (out of 64 districts) of Bangladesh were identified as affected by arsenic in groundwater where 10 million people were estimated at risk. Table-1 reveals that this contamination has spread beyond imagine all over the country very quickly and consequently by January 1998, 44 districts have been identified as arsenic affected where about 35 million people were estimated at risk. About 3,000 arsenicosis patients were also diagnosed in 26 districts during that time (Khan & Elias et al., 2002). By 1998 about 6,000 arsenicosis patients were identified so far in Bangladesh (Ahmad et al., 1998). This particular problem has become wider next. The Department of Public Health and Engineering (DPHE) of Bangladesh indicated that about 75 million people belonging to 59 districts out of the country’s 64 districts are estimated to be clinically and sub-clinically arsenicosis victims (Jakariya, 2000; Bridge and Husain, 1999). The recent data for 2002 is not available but the trend in Table-1 indicates that the present situation may be more badly in terms of arsenicosis patients in the affected areas. Only few districts located in the terraced and hilly areas of Bangladesh are less contaminated (Ahmad et al., 2001). There may be some geological reasons behind this exception but this is our beyond interest. DPHE (2000) analyzed 3,534 boreholes data for measuring arsenic levels and found some districts are severely affected. They also found variation of arsenic concentration even in the same district. For example, the median level of arsenic in Kachua Thana (also called police station) under Chandpur district was 177 µg/l whereas it was 465 µg/l in Chandpur Sadar Thana in the same district (Table-6). The maximum concentration of arsenic detected was 2.97 mg/l in Nawabganj district. The depth of contaminated tube-wells ranged from 50-200 feet commonly (Ahmad et al., 1998).

Though review of literatures indicates some inconsistencies in reporting the number of people at risk and arsenicosis patients, definitely a large portion of the total people of Bangladesh is ingesting arsenic contaminated drinking water. Some authors reported this problem as one of the largest and unparalleled arsenic calamities of the world (Chowdhury et al., 2000; Smith et al., 2000) as compared to other affected countries elsewhere.

Bangladesh is a country with higher mortality as compared to other developing countries. Water-borne communicable diseases (for example diarrhea) were highly responsible for high infant and child mortality in Bangladesh in the near past. To reduce the rate of mortality people were motivated by several programs, taken by both government and non-government organizations (national and international), to use tube-wells water for drinking and cooking purposes considering this underground water as the safeguard against water-borne communicable diseases (Kabir et al., 2001). Fortunately Bangladesh has achieved a remarkable success in this campaign. About 97 percent of rural population has now access to the tube-well water and they are used to use this water. Unfortunately when people have developed the habits of drinking tube-well water (Ahmed, 2002), the wide spread arsenic polluted water has posed a considerable threat to the country’s safe drinking water supply (Bhuiyan and Islam, 2002). A major proportion of the tube-wells in Bangladesh have been contaminated with arsenic above the permissible limit of the WHO (Rahman and Axelson, 2001; Ahmad et al., 1997, 1999; Dhar et al., 1997; Biswas et al., 1998; Rahman et al., 1998, 1999; Tondel et al., 1999; Chowdhury et al., 2000). Of the tube wells examined in the 60 districts, 50% contained arsenic above Bangladesh safe limit 0.05 mg/l (Ahmad et al., 2001). Arsenic level in the water of the affected districts is 25 to 35 times higher than the safety level (0.01 mg/l) set by the WHO for other regions except Bangladesh (Bhuiyan & Islam, 2002).

**Table 1. Trend and Magnitude of Arsenic Contamination of Drinking Water in Bangladesh by Number of Districts.**

<table>
<thead>
<tr>
<th>Year</th>
<th>Affected districts by arsenic (out of 64 districts in Bangladesh)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994 June</td>
<td>8</td>
</tr>
<tr>
<td>1996 December</td>
<td>23</td>
</tr>
<tr>
<td>1997 March</td>
<td>26</td>
</tr>
<tr>
<td>1997 September</td>
<td>42</td>
</tr>
<tr>
<td>1998 January</td>
<td>44</td>
</tr>
<tr>
<td>1998 June</td>
<td>48</td>
</tr>
<tr>
<td>1998 October</td>
<td>50</td>
</tr>
<tr>
<td>2002 April</td>
<td>59</td>
</tr>
</tbody>
</table>

(Sources: Ahmad et al., 1998; Jakariya 2000)

**Symptoms of Arsenosis Patients:**

Arsenosis is a term which includes various types of diseases and manifestations. Due to arsenosis disease, a number of socio-medico and psychological problems have arisen in the country (Bhuiyan and Islam, 2002). Various studies indicated that prolonged consumption of water containing high concentration of arsenic affects health of the people in many ways. The effect on health is more serious...
with increasing length of exposure and with increasing concentration (IARC, 1990; Thornton, 1996; WHO, 1981; Kabir, 2001). Arsenic contaminated drinking water can cause both acute and chronic toxic effects in all the organs and systems of the human body: skin, nervous system, liver, cardiovascular system, endocrine and respiratory system. Acute arsenism may occur in short time but chronic arsenism take longer period and may not become apparent clinically for a decade or more (Maidul et al., 1996). However, minimum duration of drinking arsenic contaminated water and developing manifestation from its toxicity was found to be 8 months. Severity of arsenic toxicity depends on chemical and physical form of arsenic compound, the route by which it enters the body, the dose and duration of exposure, dietary levels of interacting elements, age and sex of the individual (Khan et al., 1997a).

Symptoms of acute toxicity are severe projectile vomiting and watery diarrhea, muscular cramp, facial edema, and cardiac abnormalities (WHO, 1981: Khan et al., 1997a). Chronic arsenic poisoning is associated with brown pigmentation and keratosis of palm, sole and rarely in the body along with other signs like anorexia, lethargy, diarrhea or constipation, anemia, abdominal pain, neuropathy and so on (Hoque et al., 1996; Bakshi, 1968). One of the most common causes of chronic arsenic poisoning is use of ground water containing high concentration of arsenic (Hoque et al., 1996; Chakraborty and Shaha, 1987). The skin manifestations that are predominant among the arsenicosis patients in Bangladesh include melanosis (diffuse and spotted), keratosis of palm and sole (spotted or diffuse), leukomelanosis (rain drop pigmentation), and hyperkeratosis. Melanosis is not always associated with keratosis but keratosis is always associated with melanosis. Chronic arsenicosis has also been associated with elevated risk of skin cancer as well as cancer of the lung, liver, colon, bladder and kidney. The main cause of death due to chronic ingestion of arsenic in drinking is the internal cancer as per studies in other countries (Smith, 1997).

The symptoms of arsenicosis (summarized in Table-2) manifest themselves after several years initially as skin lesions, and progress to localized gangrene and eventually cancers of the skin, lung, bladder and kidneys (Anwar, 2002). Dhar et al. (1997) examined 1,630 people including children, covering 45 villages, and found 57.5% of them with arsenical skin lesions.

Table 2. Clinical Manifestations of Chronic Arsenic Toxicity: Separation into Three Different Stages.

<table>
<thead>
<tr>
<th>Initial stage:</th>
<th>Second stage:</th>
<th>Last stage:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanosis (spotted, diffuse)</td>
<td>Depigmentation (leukomelanosis-rain drop)</td>
<td>Nephropathy (late stage)</td>
</tr>
<tr>
<td>Keratosis (diffuse, spotted)</td>
<td>Hyperkeratosis</td>
<td>Hepatopathy (late stage)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Oedema of legs (non-pitting)</td>
<td>Gangrene</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>Peripheral neuropathy</td>
<td>Cancer (skin, bladder and lung)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>Nephropathy (early stage)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatopathy (early stage)</td>
<td></td>
</tr>
</tbody>
</table>

(Source: Khan et al., 1997a).

Several studies indicate that some manifestations are common among the arsenicosis patients than others. Hoque et al. (1996) have found that melanosis on skin (hyper pigmentation: dark spots on the skin), hypo pigmentation (white spots on the skin), keratosis, anemia and malignancy are the commonest presentation of chronic arsenicosis due to consumption of high concentration of arsenic containing water. This finding is highly comparable with other authors given in Table-3 including Mazumder (1996) and Anwar (2002).

The reliable information about mortality due to arsenic contamination is almost absent in Bangladesh. One report has mentioned that arsenic content of tube-well water in a village of Ishwardi Thana under Pubna district was 0.66 mg/l has caused 11 deaths in 2 years period due to consumption of arsenic contaminated water (Hoque et al., 1996).

Estimated Incidence Rate of Skin Cancer in Bangladesh:

WHO in 1993 made a provisional guideline value of 10 µg/l for arsenic in drinking water, which is associated with a lifetime excess skin cancer risk of about 6 per 10,000 population. The Bangladesh standard of 50 µg/l (i.e. 0.05 mg/l) is associated with a higher number of 30 per 10,000 population. Using a multistage model developed by United States Environmental Protection Agency (EPA), the total numbers associated with a lifetime excess skin cancers under different conditions of water supply with unequal concentration of arsenic are estimated for 129.25 million population in Bangladesh and presented in Table-4. The information reveals that the estimated number of excess skin cancer due to arsenic contamination of drinking water in Bangladesh is 415,100 and the estimated excess skin cancer risk is 32.1 per 10,000 population. The estimated number (risks) from drinking water supply in Bangladesh complying with Bangladesh standard and WHO guideline value are 55,200 (4.3 per 10,000 population) and 15,200 (1.2 per 10,000 population) respectively. Although the incidence rates calculated for some Upazilas (some Upazilas make a district) are found one-third of that estimated number by EPA model. In this sense, EPA model may provide overestimated number and risks for Bangladesh population (Ahmed, 2002). Anyway the data indicates a positive relationship between
arsenic concentration in drinking water and estimated number of excess skin cancer.

The information given in the Table-3 and Table-4 show that the cancer manifestations among arsenicosis patients are very low in Bangladesh. One of the reasons for the small number of cases is probably that all the surveys were made after only a relatively short period of exposure to arsenic. Generally speaking, arsenical cancers appear, symptomatically, first on the skin followed by cancers on the internal organs. It is noted that the period from first exposure to death from lung cancer varied from 11 to 35 years, with a mean of 26.7 years (Anwar, 2002).

Numerous studies [Khan et. al., (1997a); Ahmad et al., (2001); Ahmad et al., (1998)] reported that arsenicosis patients may vary from age 4 to 75 years though most of them occur between ages 10 to 40 years. Males are mostly affected than females. Khan et al. (1997a) found that among 1,625 arsenicosis patients 54% were male and 46% were female. However, the findings contradict with the results of another study conducted by Anwar (2002) where male was 41.2% and female was 58.8% among the cases. Majority (90%) of cases were found in rural areas and in the people having poor socio-economic conditions.

Other Countries Affected by Arsenic:

High level of arsenic in groundwater is not only confined to Bangladesh. It has been reported in many other parts of the world notably in China, Taiwan, Thailand, India, Argentina, Chile, Mexico, USA, Hungary, United Kingdom, Russia, Ghana, and New Zealand (Jakariya, 2000; Khan et al., 1997). The Table-5 shows that major arsenic incidents occurred in different parts of the world.

Association between Arsenic in Drinking Water and Cancer in Other Countries:

We utilized the MEDLINE database to search the articles using the key words: arsenic and cancer from 1975 to 2002. Few of them are selected which are found more relevant to this article. Summary findings for different countries are presented below.

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The association between arsenic ingestion and cancer has been documented for more than a century (Guo et al., 2001). Arsenic is a known human carcinogen and ingestion of it induces cancer at multiple sites, including the skin and various other organs (Byrd et al., 1996). It has been indicated as a bladder carcinogen in Argentina, Chile and Taiwan (Johansson & Cohen, 1997). Studies in other countries with long-term exposure indicate that 1 in 10 persons who drink water containing 500 µg/l (i.e. 0.5 mg/l) may ultimately die from arsenic related cancers of the lung, bladder and skin (Rahman, 2002). Bladder cancer standardized mortality ratios (SMRs) are consistently higher in countries with documented arsenic exposure (Hopenhayn-Rich et al., 1996). Though dose-response relationships between arsenic and various health outcomes, both cancer and non-cancer remain elusive, especially at lower levels of exposure (Christiani et
al., 2002). The review shows that investigations had been conducted mostly for Taiwan, Chile, Argentina and China though many others countries have been affected by arsenic contamination in groundwater.

**Evidence from Taiwan, China, Chile and Argentina:**

A large number of skin cancers have been reported in Taiwan and elsewhere of the world (Smith and Rahman, 2001). Studies in Taiwan have found dose-response relationships between arsenic ingestion from drinking water and cancers of the skin, bladder, lung, kidney and liver (Guo et al., 2001; Morris, 1995). The study conducted by Morales et al. (2000) in 42 villages in an arseniasis-endemic region of Taiwan indicates that the current standard 50 µg/l (i.e. 0.05 mg/l) is associated with a substantial increased risk of cancer and is not sufficiently protective of public health. Kurttio et al. (1999) found some sorts of positive association between bladder cancer and arsenic concentration. A dose-response relationship was observed in Taiwan between the long-term arsenic exposure from drinking artesian well water and the incidence of lung cancer, bladder cancer, and cancers of all sites combined after adjustment for age, sex, and cigarette smoking through Cox’s proportional hazards regression analysis (Chiou et al., 1995).

Smith et al. (1998) conducted their study over 400,000 people in a region of Northern Chile (Region II) and found the association between inorganic arsenic in drinking water and bladder and lung cancer. Ferreccio et al. (2000) investigated the relation between lung cancer and arsenic in drinking water in northern Chile in a case-control study involving patients diagnosed with lung cancer between 1994 and 1996 and frequency-matched hospital controls and found strong association between inorganic arsenic and lung cancer. They found that the more the arsenic in the drinking water, the more the risk of getting lung cancer. In another study, Ferreccio et al. (1998) found the evidence that arsenic exposure is higher among cases with lung cancer.

The risk of death of malignant tumors in the villagers of Heihe village Inne Mongolian Autonomous region who drink water with high arsenic content was 9.38 times to the risk in the inhabitants who do not drink water with high arsenic content. In malignant tumor deaths, cancer for the lung takes the lead, followed by liver cancer and then bladder cancer (Luo et al., 1995).

Hopenhayn-Rich et al (1998) conducted a study in Cordoba, Argentina and found that arsenic ingestion increases the risk of lung and kidney cancer.

**Our Proposed Study in Bangladesh with Justification:**

The review of available literatures indicates that no scientific study has been yet conducted in Bangladesh emphasizing on the association between arsenic in drinking water and cancer (mainly skin cancer) in different sites. But widespread contamination of groundwater by arsenic in Bangladesh makes it important for public health sector. Obviously it needs urgent scientific investigations for making proper policy and strategy. Reviewing information from other countries except Bangladesh, Rahman et al.

### Table 5. List of Countries with Major Arsenic Incidents in the World

<table>
<thead>
<tr>
<th>Name of the countries</th>
<th>Year of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina, Corodobe province</td>
<td>1938</td>
</tr>
<tr>
<td>Chile, Antofegasta</td>
<td>1957</td>
</tr>
<tr>
<td>Mexico, Legunia province</td>
<td>1963</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1968</td>
</tr>
<tr>
<td>India, West Bengal province</td>
<td>1983</td>
</tr>
<tr>
<td>Inner Mongolia, China</td>
<td>1990</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>1993</td>
</tr>
</tbody>
</table>

Sources: Mahiyuddin et al., (2000).

### Table 6. Distribution of Arsenic Level in the Proposed Study Districts by several Tanas

<table>
<thead>
<tr>
<th>Thana (Police station)</th>
<th>Arsenic level (µg/l)</th>
<th>Gazipur district (non-exposed area*)</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gazipur sadar (n=11)</td>
<td>0.68</td>
<td>0.6</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Kaliakair (n=7)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Kaliganj (n=33)</td>
<td>17.1</td>
<td>17.1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Kapasia (n=9)</td>
<td>0.53</td>
<td>0.53</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Sripur (n=8)</td>
<td>1.5</td>
<td>1.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>4.3</td>
<td>Overall</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thana (Police station)</th>
<th>Arsenic level (µg/l)</th>
<th>Chandpur district (exposed area**)</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faridganj (n=10)</td>
<td>357</td>
<td>265</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Haimchar (n=4)</td>
<td>265</td>
<td>263</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Hajiganj (n=8)</td>
<td>413</td>
<td>445</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Shahrast (n=8)</td>
<td>407</td>
<td>336</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Kachua (n=17)</td>
<td>182</td>
<td>177</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Matlab (n=9)</td>
<td>389</td>
<td>407</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>366</td>
<td>Overall</td>
<td>391</td>
<td></td>
</tr>
</tbody>
</table>

Source: DPHE (2000)

Note: * less than 50 µg/l is non-exposed area and
      ** greater than 50 µg/l is exposed area.

“n” indicates the number of borehole tested for arsenic level
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(2001) mentioned that advanced neglected cases with many years of arsenic exposure presented with cancer of skin and of lung, liver, kidney and bladder. If the findings of other countries are true for Bangladesh, then a large number of arsenicosis patients from those who are at risk may develop cancers gradually in future with high risk of mortality provided, if they are not diagnosed early with proper care and treatment. Most probably they are now in a latency period (the period from arsenic exposure to manifestation) and gradually they are walking to deadly cancer. It should be reminded that it needs several years after arsenic exposure for the manifestations of cancer.

Considering the factors mentioned in this paper we are planning to conduct a scientific epidemiological research study in Bangladesh in near future. This study will: (1) calculate prevalence rates for each manifestation (given in table 2) of arsenic poisoning in the exposed and non-exposed areas, (2) explain variations of prevalence rates by socio-economic, demographic and other important factors from empirical and scientific points of views, (3) measure the strength of association using case-control study design, and (4) compare the results between exposed and non-exposed areas. Hopefully this study will provide us some guidelines to take a proper strategy to tackle the upcoming hazard situation by arsenic manifestation including cancer.

Proposed Study Design:

Considering the objectives of the study both ecological survey as well as case-control study would be employed for data collection. These methods are briefly discussed in the following section.

Ecological Survey:

An ecological survey would mainly provide us the prevalence rates for different manifestations from arsenic poisoning in drinking water. A total of 12 villages (one from each Thana) from two selected districts will be randomly selected for the survey. We will make a list of individuals (with name, age and sex) for each village those who fulfill the criteria of inclusion (given later) for the study through house-to-house visits. The list would be treated as sampling frame for drawing the sample of the study. We will select required number of respondents by simple random sampling from the sampling frame. Then the randomly selected individuals of the villages will be examined thoroughly though proper medical tools to find the manifestations of the arsenic poisoning. All the tube-wells in the villages will be also tested to know the level of arsenic in groundwater. The information about duration and depth of the tube-wells would be collected at the time of interview.

Selection of Exposed and Non-exposed Areas:

Multi-stage sampling is proposed here to find the study areas. At the first stage two districts namely Chandpur and Gazipur have been selected purposively based on available data on arsenic in drinking water released by DPHE in May 2000. According to the overall data presented in Table-6, Gazipur is arsenic free district (both mean and median is less than 10 µg/l) and Chandpur is most severely arsenic affected district (mean and median arsenic level are 366 µg/l and 391 µg/l respectively). This table also shows the mean and median levels of arsenic by different Thanas in each district. Different sample sizes (that indicate number of boreholes) are used to measure arsenic levels and are indicated in the parentheses. The arsenic levels in all Thanas of Chandpur district are higher as compared to other 63 districts in Bangladesh. So this district is obviously is a “hot spot” (which means most vulnerable by arsenic) of the country. One Union from each the selected Thana of the selected districts would be selected randomly at the second stage. From each selected Union one village would be selected randomly at the third stage. Thus a total of 12 villages would comprise finally our study sites for data collection. In our study five Thanas under Gazipur district would be treated as non-exposed area (since the level of arsenic is less than 50 µg/l) and seven Thanas under Chandpur district would be considered as exposed area (since the arsenic level is higher than 50 µg/l). The total sample of the Chandpur district will make exposed group and the total sample of Gazipur district would make non-exposed group. We will compare our results by exposed and non-exposed groups using socio-economic, demographic, cultural, behavioral, medical variables, and so on.

Selection of Study Sample:

After selecting villages we will first conduct a door to door survey for each village by the trained interviewers to make a sampling frame for each sex. This frame would be used for drawing randomly required sample of the study.

Eligible Criteria for Selecting the Respondents of the Study:

- Should live in the villages throughout life time after birth
- Age of the respondent is between 10 - 60 years. Because review of literature shows that most of the arsenicosis patients are found within this age range.
- Should use same well water as drinking purpose after its installation
- Should be available at the time of interview
- Should give consent to participate after explaining the study objectives

The Sample Size (n) has been Calculated Using the Formula Given by Bland (2000):

\[
n = \frac{f (\alpha, P)(p_1(1-p_1) + p_2(1-p_2))}{(p_1^2p_2)^2}
\]
where sample sizes ‘n’ are equal for both the control and the comparison group.

This formula provides us \( n = 219 \) arsenicosis patients for each group when the following information is used:
- Average prevalence rate of arsenicosis patients indicated by \( p_1 \) in an arsenic affected village (exposed area) given by Bhuiyan and Islam (2002) = 7 percent. That is, \( p_1=0.07 \)
- Prevalence rate in non-exposed area (arsenic free area) indicated by \( p_2 \) is unknown. So the prevalence rate \( p_2 = 0.01 \) is taken hypothetically.
- Power of the test statistic \( (P) \) = 90 percent
- Level of significance \( (\alpha) \) = 0.05
- Bland (2000) have shown that \( f(\alpha, P) = 10.5 \) when \( P= 90 \) percent and \( \alpha = 0.05 \)

Since the prevalence rate of arsenicosis patients in the exposed area is 7 percent, to find 219 arsenicosis patients we need to survey 3,120 persons in the arsenic exposed area. However, we will inflate the sample size by an arbitrary figure of 80 as a check against possible dropouts. Thus the required sample is 3,200 persons. Similarly we need to survey 21,900 persons in the area non-exposed area. But because of feasibility of time and cost, we would like to restrict our sample size in the non-exposed area equal to 3,200 also. Thus the total sample to be investigated in the study would be 6,400.

Case-control Study:

After completing the ecological study at the first stage we will conduct case-control (retrospective) study at the second stage. Lilienfeld and Stolley (1994) argued that case-control study is the most appropriate epidemiologic method to study the association between exposure of interest and the outcome of rare diseases. Although we are expecting that a large number of arsenicosis patients will manifest skin cancer in future, still it is not a common disease.

Selection of Cases and Controls:

The following operational definitions would be used in this study for selecting both cases and controls:

**Cases:** Any person from the selected sample during ecological survey diagnosed with any arsenicosis manifestations including cancer will be treated as cases in the study. The ambiguous cases will not be selected. We are expecting about 250 cases (arsenicosis patients) in total from both areas.

**Control:** Any person without having arsenicosis manifestations would be treated as a control. A total of 1000 (4 times of cases) controls will be investigated in the study. All cases and controls would be included in the study after getting the informed consents from them. Gail et al. (1976) mentioned that an increased number of controls – up to 4 per case - may give more power for studying the rare disease. Therefore we would select 4 controls per case in our proposed study and the controls would be selected in an appropriate manner. To ensure comparability of cases and controls we will follow the guidelines of Lilienfeld and Stolley (1994). However, we will restrict the controls to the same locality (village), age, religion, gender, income, education and other important characteristics as the cases. The results are compared at each factor level between cases and controls with the usual statistical tests as proposed by Mantel and Haenszel (1959). SPSS or SAS packages would be used to analyze the data.

The Department of Public Health in Sapporo Medical University will mainly conduct this study in Bangladesh. Some experts from Bangladesh working on arsenic issues will be included in the study to facilitate its success.

References


Bhuiyan RH, Islam N (2002). Coping strategy and health seeking appropriate manner. To ensure comparability of cases and controls we will follow the guidelines of Lilienfeld and Stolley (1994). However, we will restrict the controls to the same locality (village), age, religion, gender, income, education and other important characteristics as the cases. The results are compared at each factor level between cases and controls with the usual statistical tests as proposed by Mantel and Haenszel (1959). SPSS or SAS packages would be used to analyze the data.

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References


