REPRODUCTIVE HEALTH IMPACTS OF ARSENIC CONTAMINATION IN DRINKING WATER IN SELECTED AREA OF BANGLADESH

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Dedicated to my Father

Late Nefazuddin Seikh

This Thesis is submitted to the faculty of Postgraduate Medical Sciences and Research, University of Dhaka, in conformity with the requirement of the "Doctor of Philosophy" (Ph.D) course.

10-07-06
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m.a.hasan

Date; 10-07-06 Dr. Md. Aminul Hasan

Declaration

This to certify that Dr. Md. Aminul Hasan has completed the thesis work entitled "Reproductive Health Impacts of Arsenic Contamination in Drinking Water in Selected Area of Bangladesh" under my supervision for the fulfillment of the degree of Doctor of Philosophy (Ph.D) in the faculty of Post Graduate Medical Science & Research from the university of Dhaka.

The work of any part thereof has not been submitted anywhere for any other degree.

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ACRONYM

AAS-HG	Atomic Absorption Spectrophotometer with Hydride Generation
AIDS	Acquired immune deficiency syndrome
AlAso4	Arsenate of Al
As	Arsenic
ASIII	Arsenates-(Trivalent form)
ASV	Arsenate (Pentavalent form)
BAMWSP	Bangladesh Arsenic Mitigation and Water Supply project
BFD	Black foot diseases
CAP	Chronic Arsenic Poisoning
DCH	Dhaka Community Hospital
DCHT	Dhaka Community Hospital trust
DMA	Dim ethyl Arsenic Acid
DNA	Deoxyribonucleic Acid
DGHS	Directorate General of Health Services
DPHE	Department of Public Health Engineering
FeAsS	Arsenopyrite
FeAso4	Arsenate of Fe
GBM	Ganga Brahamaputra Meghna Basin
GO	Government Organization
ICDDRB	International centre for Diarrheal Diseases and Research, Bangladesh
MMA	Monomethyl Arsenic Acid
NGO	Non Government Organization
NOAEL	No observed adverse effect level.
RNA	Ribonucleic Acid
RTI	Respiratory tract Infection
SOES	School of Environmental studies (Jadavpur, Kolkata)
SPSS	Statistical Package for social studies
TMASO	Trim ethyl Arsine oxide
UMIS	Unified Management Information System.
WHO	World Heath Organization

ABSTRACT

This study has been carried out as a case comparative cross sectional study among the arsenic affected married women (15-49 years) of Bera and Sujanagar Upazillas and arsenic free women of Santhia Upazilla of Pabna. The main purpose of the study was to assess the association between arsenic contamination in drinking water with Spontaneous abortion, Stillbirth, and Neonatal death.

According to this study, 500 women were interviewed in exposed group and 500 in the non exposed group. Information on socio-demographic characteristics, drinking water used, and adverse pregnancy outcomes were observed through a structured pre-tested interview schedule. The total households in the exposed group were 425 and non exposed group were 416, and Respondents reported used of a total of 174 tube wells in the exposed area and 181 tube well in the non exposed area. Water samples were taken and tested by using an Atomic Absorption Spectrophotometer with Hydride Generation (AAS-HG) and flow injection system including a continuous flow of hydride generation atomic absorption spectroscopy system.

It is found from this study, that those women who were taking highly arsenic contaminated water (> 200ug/l) having more black spot (56%) and keratosis (22.6%) than those who were taking less concentrated arsenic water (< 200ug/L) . The association of black spot (Hyperpigmentation) and high level of arsenic in tube well water is statistically significant (P<.001) where odd ratio is

6.84, CI= 4.38, 10.07. And also the association of Keratosis (thickening of the skin) and high level of arsenic in tube well water is statistically significant (P<. 001) odd ratio 3.05, CI= 1.75, 5.34.

The study revealed the excess risks for Spontaneous abortion, Stillbirth and Neonatal death among the respondents who were chronically exposed to higher concentrations of arsenic in drinking water after adjusting height, weight, history of hypertension and diabetes. Comparing exposure to arsenic concentration of the exposed with non exposed, the odds ratio is 2, (1.31, 3.07), P<.001 for Spontaneous abortion, odd ratio is 1.77 (1.07, 2.95), P<.05, for Stillbirth, and odd ratio is 2.07 (1.32, 3.27), P<.001 for Neonatal death.

The rate of Spontaneous abortion , Still birth, Neonatal death were also high in that group those who had black spot and keratosis (Thickening of sole , palm) in comparison to the group had no black spot and keratosis and the association is statistically significant (p<.05). In this study it is proved that women with Arsenicosis had more spontaneous abortion than the group of women took arsenic contaminated water but no arsenicosis. Again it is reaveled that the group had more Spontaneous abortion, Still birth & Neonatal death were taking high concentration of Arsenic contaminated tube well water (> 200 ug/l) in comparison to less concentration <200 ug/l, which is also statistically significant (p <.01 , odd ratio 3.62, confidence interval; 2.12, 6.19).

It has been observed that chronic arsenic contamination in drinking water has the potential impact on reproductive health of women.

According to that the study findings suggest that chronic arsenic contamination in drinking water might lead to the risk of Spontaneous abortion, Stillbirth and Neonatal death.

1. INTRODUCTION & BACKGROUND

1.1. Safe Water & its importance

Access to a safe water supply is one of the most important determinants of health and socioeconomic development. This recognition of the importance of safe water supplies has led to an emphasis on the provision of appropriate facilities in developing countries. In the 1970s, it was realized that Bangladesh's population density and lack of access to adequate sanitation had led to severe microbiological contamination of surface water, resulting in high levels of morbidity and mortality. Bangladesh's government and population, supported by international agencies, have since then installed about 4 million tube wells to tap better quality groundwater sources. Water intended for human consumption should be both safe and wholesome. This has been defined as water that is free from pathogenic agents, free from harmful chemical substances, pleasant to taste, i.e. free from color and odour, and usable for domestic purposes. Without ample safe drinking water, communities cannot be healthy.(42)

The health benefits from reducing water-related disease can in some circumstances be transmuted into a greater work capacity, which may contribute to increase production and hence to overall economic development.

Access to safe water will also depend on non-material factors, such as basic hygiene knowledge, social position and water quality. Basic hygiene knowledge and high water quality support/facilitate access to safe water. It is said that these factors alter the efficiency of the household as a safe water producer. Social factors affecting access to water supply sources will also determine the ability of the household to produce safe water. Lower caste households may not have access to high quality water supply sources due to cultural norms which embrace principles of social exclusion. Conversely, higher caste households, may be unwilling to share high quality water supply sources with lower caste households, and instead may choose alternative sources of lower quality water. In other social contexts, the effects on higher castes may be adverse, if they are socially excluded from water sources used by lower castes. (11)

1.2. Arsenic- An emerging challenge:

The provision of clean, wholesome water is a fundamental requirement for a healthy life. Unfortunately, in many countries this is a major problem because of varieties of reasons, be they chemical or bacteriological. In many countries, to avoid health problems from water borne bacteria, tube wells have been sunk to aquifers containing water free from such microbiological contaminants. In some instances, these aquifers have been found to contain water with high arsenic levels. This arsenic contamination invariably arises from natural geological and environmental conditions. Arsenic arises in many ores and minerals and is frequently present in combination with iron and manganese oxides; under various natural conditions it can be rendered soluble and released into the groundwater<28>. This problem is experienced in widespread regions across the globe: Argentina, Bangladesh, Hungary, India (West Bengal), Mongolia, Northern China, Thailand, UK, USA (Arizona, Illinois, New Hampshire, New Mexico, Southern California). The problem is especially acute in the Ganges delta region, where the arsenic is believed to be associated with the iron and manganese oxides in the alluvial sediments. In Bangladesh and West Bengal some 35 million people drink water from wells where the arsenic level in the water exceeds the Bangladesh/Indian standard (0.05mg/l). If the proposed new World Health Organization guideline (0.01mg/l) were adopted then a further 20-25 million people are likely to be included. The scale of the disaster in Bangladesh is greater even than the accidents in Bhopal and Chernobyl (13)

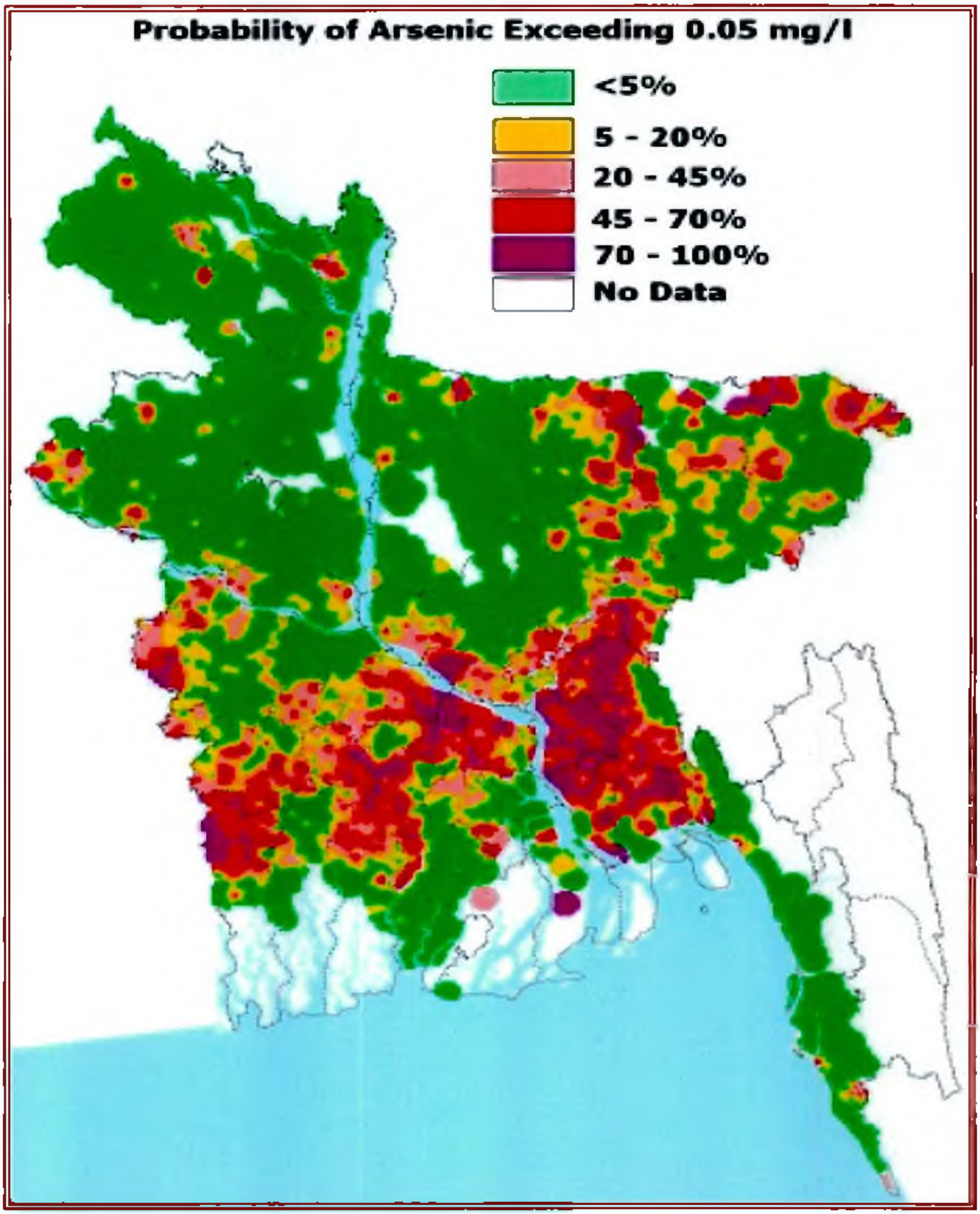
"Bangladesh is grappling with the largest mass poisoning of a population in history because groundwater used for drinking has been contaminated with naturally occurring inorganic arsenic", the monthly bulletin of the United Nations World Health Organization (WHO) reports in September 2000.

The research by Allan H. Smith, professor of epidemiology at the University of California at Berkeley, said that between 33 and 77 million of Bangladesh's 125 million populations were at risk. "The scale of this environmental disaster is greater than any seen before", wrote Smith. "It is beyond the accidents at Bhopal, India, in 1984 and Chernobyl, Ukraine, in 1986."(42)

The study was based on visits to Bangladesh by Smith in 1997 and 1998 and adds to the warnings by the UN Children's Fund, the US government and other agencies.

In the past three decades, the Bangladesh government has dug approximately 5 million wells to provide drinking water and save millions of people from cholera, diarrhea and other water-borne diseases. But the naturally occurring arsenic poison in the ground water now threatens to overturn these health benefits. (13)

1.3. Event of arsenicosis in Bangladesh



1.3.1. Sedimentary History of Bengal Basin

The geological history of this region suggests that the delta was formed since the beginning of the Himalayan mountain range. By the mid –Tertiary period, sediments originating from the eastern part of the peninsula comprising the Chotonagpur and Assam plateau were deposited in the fore deep of South Bengal. By the end of the mid-Tertiary period, the uplifts of the former plateau were over and the magnitude of after movement was much reduced. In the Pleistocene period, the Garo-Rajmahal gap was formed and sediments from the northern rivers were deposited to form the delta.(55)

The major part of the country is covered with Holocene and recent fluvial and deltaic deposits from the eastern Himalayans rivers. The rivers have eroded and dissected the majority of the sediments older than 18000 years, the time when the last glaciations took place. As glacier melted, the sea level rose and subsequently re-deposition occurred in the eroded channels. Due to many reversals and relatively rapid changes in sea level, further erosion, re-deposition, and shifting of the river channels took place. All such events have resulted in a complex subsurface strati-graphy. Moreover, the area is seriously active, faulting and its uplift are still occurring. (14)

1.3.2. Hydro geological activity

The average annual rainfall in Bangladesh varies between 5000 mm in the northeast to 1200 mm in the west, while in most of the areas it ranges between

1500 to 2500 mm. Under natural conditions a large proportion of the precipitation enters surface water as runoff, while only a small fraction is lost as evapo-transpiration. The annual discharge of GBM river system is about 1174 km3 of water, about 80 % of which occurs in monsoon, between June and October a total average runoff of 128.14 Mham flows annually through Bangladesh and empties in to the Bay of Bengal. The river lose water to the aquifer during the wet season and gain water during the dry season. In most parts of Bangladesh the ground water levels within five feet of the surface during the wet season. However, it varies considerably depending on the proximity to surface water sources, depth and type of aquifer, extent of withdrawal due to irrigation and other uses, and other factors. Since the 1970 s growing use of ground water for irrigation has, in general in lowering of aquifer levels during the dry season.(55)

Anthropogenic emissions of arsenic arise from fuel consumption, mining, smelting of ores and the use of arsenic in fertilizers and pesticides. For instance, acidic mine waters could have dissolved arsenic content as high as 250 mg/l. These possibilities do exist in West Bengal, and high arsenic content could be an artifact of mining and smelting activities during the last couple of centuries. However, there is no reason to believe that these emission rates could have been higher in the past than now. If the present and past emission rates are assumed to remain the same, surface soil should have at least as much arsenic contamination as in the lower region of the aquifer <65>. However, arsenic contamination in the Ganges delta is seldom reported at depths less than 15 m. This would imply that sediments at the depth from which drinking water is being presently drawn (>30 m), could not have acquired its arsenic content from man-made sources. It is, therefore, quite justifiable to attribute the arsenic content in the groundwater of the Ganges delta to natural sources.

The arsenic-affected areas, as initially recognized in West Bengal and Bangladesh, are mostly confined to the lower flood-delta plains of the Ganges River, downstream of the Rajmahal Hills. The Gangetic alluvial tract upstream of the Rajmahal Hills, in the states of Bihar and Uttar Pradesh (UP), is generally free of arsenic toxicity. However, the adjacent part of the Ganges delta in Bangladesh is equally affected. It was further recognized that arsenic toxicity in Bangladesh extends also to the Sylhet basin and flood-delta plains of the River Meghna in eastern and southern Bangladesh.

The wide expanse and regional extent of the arsenic-toxic zone in the Ganges delta in West Bengal and Bangladesh, as well as, those in the Meghna River floodplain and in the Sylhet basin, in Bangladesh, which all have different catchments areas, indicates multiple natural sources of arsenic contamination. In contrast, the Brahmaputra-Jamuna, and old Brahmaputra floodplains in Bangladesh, is so far unaffected, although these areas are subjected to similar levels of groundwater extraction compared with other areas that are found to contain arsenic.

Likely sources for arsenic in the Ganges delta may include the following. (13)

(i) the Gondwana coal seams in Rajmahal basin contain up to 200 ppm of arsenic,

(ii) the arsenic mineral lollingite and pyrite, which occur sporadically in association with pegmatite's in the mica-belt of Bihar, have an arsenic content in mineralized rocks that ranges from0.12-0.08%,

(iii) pyrite bearing shale from the Proterozoic Vindhyan range, with its Amjhore mine,contains0.26%As, (iv) the gold belt of the Son Valley has an arsenic content in the bedrock at locally reaches 2.8% to 1000ppm,

(v) Isolated outcrops of sulphides contain up to 0.8% of arsenic in the Darjeeling Himalayas.The copper belt of Bihar, and the Damodar valley Gondwana coal basins contain local concentrations of arsenic in pockets that are drained by rivers that flow far to the south of the Ganges tributary system, and thus these cannot be potential sources as postulated by some researchers. Further, the Damodar alluvial fan that flanks the arsenic-affected Bhagirathi delta is free of arsenic problems. The ongoing mineralogical studies indicate that arsenic-rich pyrite and separate arsenic minerals are absent or rare in the sediments of the Ganges delta of West Bengal. However, arsenic appears to be adsorbed to iron-hydroxide-coated sand grains and to clay minerals. The rare presence of pyrite has been recognized from the Ghetughachi area and is also reported from Bangladesh. Sparse occurrence of arsenic-bearing minerals cannot explain the large-scale arsenic contamination in the deltaic plane. Thus, it is likely that arsenic was co-precipitated with or scavenged by iron (III) and manganese (IV) in the sedimentary environment. The presence of arsenopyrite or the pyrite-bearing layers or zones in the aquifer, as has been postulated by some researchers, is doubtful. Instead it is likely that decomposition of pyrite and arsenic bearing sediments in the source area released arsenic in the soluble form, and this was sorbed by secondary iron oxy-hydroxide. Arsenic in solution possibly became more easily entrapped in the fine-grained organic-matter-rich sediments that were preferentially deposited under low energy conditions in the Ganges delta. (11)

1.3.4. Why Arsenic is found in Groundwater in the Bengal Delta

The Himalayan rocks are rich in pyrites, a naturally occurring mineral. It is hypothesized that the Holocene deposits of the Ganges were also rich in arsenopyrites (FeAsS) the most abundant mineral which is enriched by arsenic. Potential sources of arsenic bearing minerals were also identified in the Meghna and Bramaputra river basins. Analysis of hindered of soil sediment samples from aquifers and aquitards in West Bengal , India revealed that arsenic was present in high concentrations, up to 122.5 mg / Kg. analysis of opaque mineral (magnetite, hematite, quartz, pyrite) revealed that the samples contain approximately 400 mg / kg arsenic. Das et al (11) found that approximately 1.3 % of the opaque mineral contains iron, sulpher and arsenic. The above mentioned findings from the same deltaic plain on the other side of the border clearly suggest that the source of arsenic in the sub surface soil is arsenopyrite rich sulphide mineral.

The sediments from the Bengal basin contain high concentration of arsenic relative to the average earth crust. The concentration of arsenic in sediment samples collected in West Bengal from 6 to 211 meters of depth ranged from 14.9 to 122 mg / Kg (11).

While the average concentration of the same in the earth crust is 1.8 mg / kg. (11). Sulphide mineral such as arseno pyrite tend to be relatively insoluble and therefore it is expected that it should not release significant amount of arsenic in ground water. Under favorable redox condition, however, the relatively insoluble arsenic-laden sulphides could transform in to soluble acids.

As mentioned earlier, a large volume of ground water currently is drawn from sub surface and deep aquifer across the country for irrigation and collection of drinking water. When ground water is abstracted from tube well and pumps, the left over interstitial space get exposed to ambient air and or oxygenated water. In such an oxidizing condition, arsenopyrite mineral are oxidized. Sulphide on the other hand plays an important role in retaining and remobilizing arsenic from contaminated sediments. Exposure of the sediments to oxygen provides condition suitable for chemolithotrophic bacteria to oxidize the sulphides. Under oxidizing condition, most of the arsenic is found in pentavalent form and solubility is low. Under reducing conditions, pentavalent arsenic is transformed in to trivalent arsenic, the latter being much more toxic relatively easily solubulised.

During each dry season, due to abstraction of ground water the interstitial pores get exposed to air and oxygenated water. At the end of the dry season the interstitial space are recharged with water and the newly formed arsenate and arsenites get solubilised in it. The same process presumably has continued for the last three decades. The ground water table has thus become contaminated with arsenic. Any amount of water drawn from such contaminated aquifers should contain arsenic, and that is what we are getting now.

There have been other postulates concerning possible sources of arsenic in tube well water samples. The release of anthropogenic arsenic from treated wooden electric poles leading to wide scale contamination of ground water with arsenic was disregarded by an analysis conducted by ICDDR,B. Some thought that pesticide and chemical fertilizer could have caused the problem. It was also disregarded due to the fact that, it was the cause, it could have contaminated the surface water which it did not.

The government is committed to enhance agricultural production through maximum use of its groundwater resource potential. Under such circumstances, it is obvious that the ground water table will be further drawn down and each year the problems regarding arsenic contamination will aggravate further.

From the above discussion it appears logical that, in each successive year more interstitial pores will be filled with air , which will lead to more dissolution of arsenopyrites, and subsequently the concentration of dissolved arsenic will gradually rise

1.4. Arsenic Contamination Worldwide: (17)

Arsenic poisoning episodes have been reported all over the world. Exposure to arsenic may come from natural sources, from industrial sources, or from food and beverages. So, arsenic episodes all over the world are divided into three categories:

1. Natural groundwater arsenic contamination.
2. Arsenic contamination from industrial source.
3. Arsenic contamination from food and beverage.

1.4.1 Arsenic contamination in ground water and coal and population at risk around the world

Country/ Area	Population at risk	Ground water concentration (µg As 1~!)	Guidelines (µg As 1~1)	Discovery date
Argentina	2000000	100-1000	50	1981
Bangladesh	50000000	<1-4700	50	1980s
Bolivia	20000		50	1997
Chile	437000	900-1040	50	1971
China, Guizhou	20000	100-10000	8 mg kg-1	1950s
China, Inner Mongolia	600000	1-2400	50	1990s
China, Xingjian province	100000	1-8000	50	1980s
Hungary	220000	110-176	10	1974
India West Bengal	1000000	<10-3900	50	1980s
Mexico	400000	10-4100	50	1983
Nepal	Unknown	up to 456	50	2002
Peru	250000	500	50	1984
Romania	36000	10-176	10	2001
Taiwan	200000	10-176	10	2001
Thailand	1000	1-5000	50	1980s
USA	Unknown	10-48000	10	1988
Vietnam	Millions	1-3050	10	2001

Taiwan incident

The arsenic contamination incident in well water on the south-west coast of Taiwan (1961– 1985) is well known [17]. The population of endemic area is about 140,000. In the villages surveyed, the arsenic content of the well water examined, ranges from 0.01 to 1.82 mg l/l. Most of the well water in the endemic area has arsenic content around 0.4–0.6 mg l-1. The predominant arsenic species in the well waters is IAsIII with an average iAsIII to iAsV ratio of 2.6.

Antofagasta, Chile incident

About 130,000 inhabitants of the city has been drinking supplied water with high content of arsenic (0.8 mg l/l) for 12 years from 1959 to 1970 . The source of the high arsenic content in water is the Tocance River, of which water comes from the Andes Mountain at an altitude of 3000 m and is brought 300 km to Antofagasta. At the beginning of 1960s, the first dermatological manifestation was noted, especially in children (5]. Peripheral vascular manifestations in these children included Raynaud's syndrome, ischemia of the tongue, and hemiplegia with partial occlusion of the carotid artery, mesenteric arterial thrombosis and myocardial ischemia.

Mexico incident

Chronic arsenic exposure via drinking water is reported in six areas of Region Lagunera, situated in the central part of North Mexico with a population of 200,000 during 1963–1983 . The range of total arsenic concentrations is 0.008–0.624 mg /l and concentrations greater than 0.05 mg l/l are found in 50% of them. Most of the arsenic is in inorganic form and pentavalent arsenic is the predominant species in 93% of the samples.

Argentina incident

Similar incident of arsenic contamination in groundwater is also reported in Monte Quemado of Cordoba province, north of Argentina. The occurrence of endemic arsenical skin disease and cancer is first recognized in 1955. Total population of the endemic area is about 10,000. From the observations in the Cordoba, it is concluded that the regular intake of drinking water containing more than 0.1 mg l-1 of arsenic leads to clearly recognizable signs of intoxication and ultimately might develop into skin cancer. (17)

New Hampshire, USA incident

Arsenic concentrations are measured in 992 drinking water samples collected from New Hampshire households.Samples from drilled bedrock wells have the highest arsenic concentrations, while samples from surficial wells have the lowest arsenic concentrations.

Nova Scotia, Canada incident

In 1976, several wells in Halifax County, Nova Scotia are contaminated with arsenic with concentration greater than 3 mg/l. More than 50 families have been affected due to arsenic poisoning. Recently, It is reports also occurrences of elevated arsenic concentrations in bedrock groundwater's used for individual and municipal water supplies in the mainland coast of southern British Columbia, Canada.

Hungary incident

In Hungary also similar arsenic contamination in the well water is observed in the years 1941–1983. The amount of arsenic present in the well water is in the range of 0.06–4.00 mg /l.

New Zealand incident

In 1939, Grimmet and McIntosh described arsenic contamination of groundwater and the resulting effects on the health of livestock. Later on in 1961, high levels of arsenic were found in water from areas of thermal activity. Thermal waters in New Zealand contain up to 8.5 mg As l-1.

China incident

During the 1980s, the endemic arsenicosis was found successiveiy in many areas on mainland China such as Xingjian Uygur A. R., Inner Mongolia, Shanxi, Liaoning, Jilin, Ningxia, Qinghai, and Henan provinces. The arsenic concentration in the groundwater in these affected areas is in the range of 220–2000 _g/l with the highest level at 4440 _g/l. Consequently, a large sector of the rural population has been exposed to chronic arsenic poisoning (CAP) resulting from consuming well water with naturally occurring high levels of arsenic during the past decades. At present, the population exposed to high amounts of arsenic is estimated to be over 2 million and more than 20,000 arsenicosis patients are confirmed

Vietnam incident

This is the first publication on arsenic contamination of the Red alluvial tract (Mekong delta region) in the city of Hanoi and in the surrounding rural districts. The contamination levels vary from 1 to 3050 _g l-1 in rural groundwater samples from private small-scale tube-wells with an average arsenic concentration of 159 _g l-1. In a highly affected rural area, the groundwater used directly as drinking water has an average concentration of 430 _g /l.

Northern Sweden incident

At the Ronnskar smelter in northern Sweden, ores with a high arsenic content were handled. Women employed in the plant as well as those who lived nearby deliver babies having significantly lower weight than those delivered by women who are not so exposed . Among those same women, the frequency of spontaneous abortion is generally higher with closer proximity of residence to the smelter. Although residential proximity to the Ronnskar smelter has no effect on the incidence of congenital malformations, pregnancies during which the mother had worked at the smelter are significantly more apt to babies with single or multiple malformations, particularly uro-genital malformations or hip-joint dislocation.

1.5. The situation in South East Asia region

In the South-East Asia Region, arsenic contamination of groundwater has been reported in Bangladesh, India, and Thailand and to a limited extent in Nepal and Myanmar. In India and Bangladesh, and possibly Nepal and Thailand, arsenic is of geological nature originating from the natural aquifers. However, in Thailand, the contamination is anthropogenic in nature, being due to mining activities. Irrespective of the origin of arsenic, in Bangladesh, India and Thailand, the concentrations in several groundwater samples range from 0.06 mg/L to 1.86 mg/L, a value that is in excess of the WHO Drinking Water Guideline Value of 0.01 mg/L.

Studies from West Bengal in India show that approximately 5 million persons are consuming groundwater containing arsenic exceeding 0.05 mg/L that is their national standard. Recent unconfirmed reports point to the presence of arsenic in Tamil Nadu and other states of India, implying industrial contamination of groundwater. In India, it is estimated that 220 000 of the 5 million exposed subjects are showing signs of arsenicosis.<28>

The arsenic problem in the amphoe of Ronphibun, Thailand originates from tin mining containing arsenite and arsenate. Tin ore mining activities were practiced for over 50 years. At present these mining sites have become water ponds and with natural rainfall, they sediment downstream, contaminating shallow wells used by villages for their water supply.

The water monitoring section of PCD conducted a survey in 1993 to establish the extent of arsenic contamination in groundwater in Ronpiboon district of Nakorn Si Thammarat province. During the survey, it was established that arsenic concentration in excess of Thailand standard (0.05mg/L) was detected in more than 90% of shallow wells and there were "hot spots" in the soil with arsenic concentration exceeding 1 000 mg/Kg of soil. A recent survey done in collaboration with JICA has identified that six hot spot areas still remain for targeting pollution control measures. A health survey funded by SEARO in August 2000 estimates that approximately 6 120 of potentially 24 566 exposed subjects were showing symptoms of arsenicosis.<28>

Arsenic testing was undertaken in Nepal, since it shares some geological features with the Gangetic plains of India and Bangladesh. The Department of Water Supply and Sewerage (DWSS) of Nepal, with assistance from WHO, conducted a systematic study in 1999 on possible arsenic contamination of groundwater in Jhapa, Morang and Sunsari districts. The study revealed that most of the contaminated samples were found around the active flood plains of River Koshi. The Nepal Red Cross Society (NRCS), with Japan Red Cross Society (JRCS), jointly tested groundwater samples at their project sites in 17 Terai districts. This study showed that the concentration of arsenic in groundwater is found to be high in the districts of Nawalparasi, Rautahat, Bara and Bardia. The Rural Water Supply & Sanitation Support Project (RWSSSP), FINNIDA has also tested some of the tube wells at their scheme areas. Approximately 3% of the wells tested were found to be positive with arsenic concentration up to 0.17 mg/L. Another survey has found that about 3% of the 1 142 subjects surveyed were showing signs of arsenic diseases in the form of dermal lesions.<14>

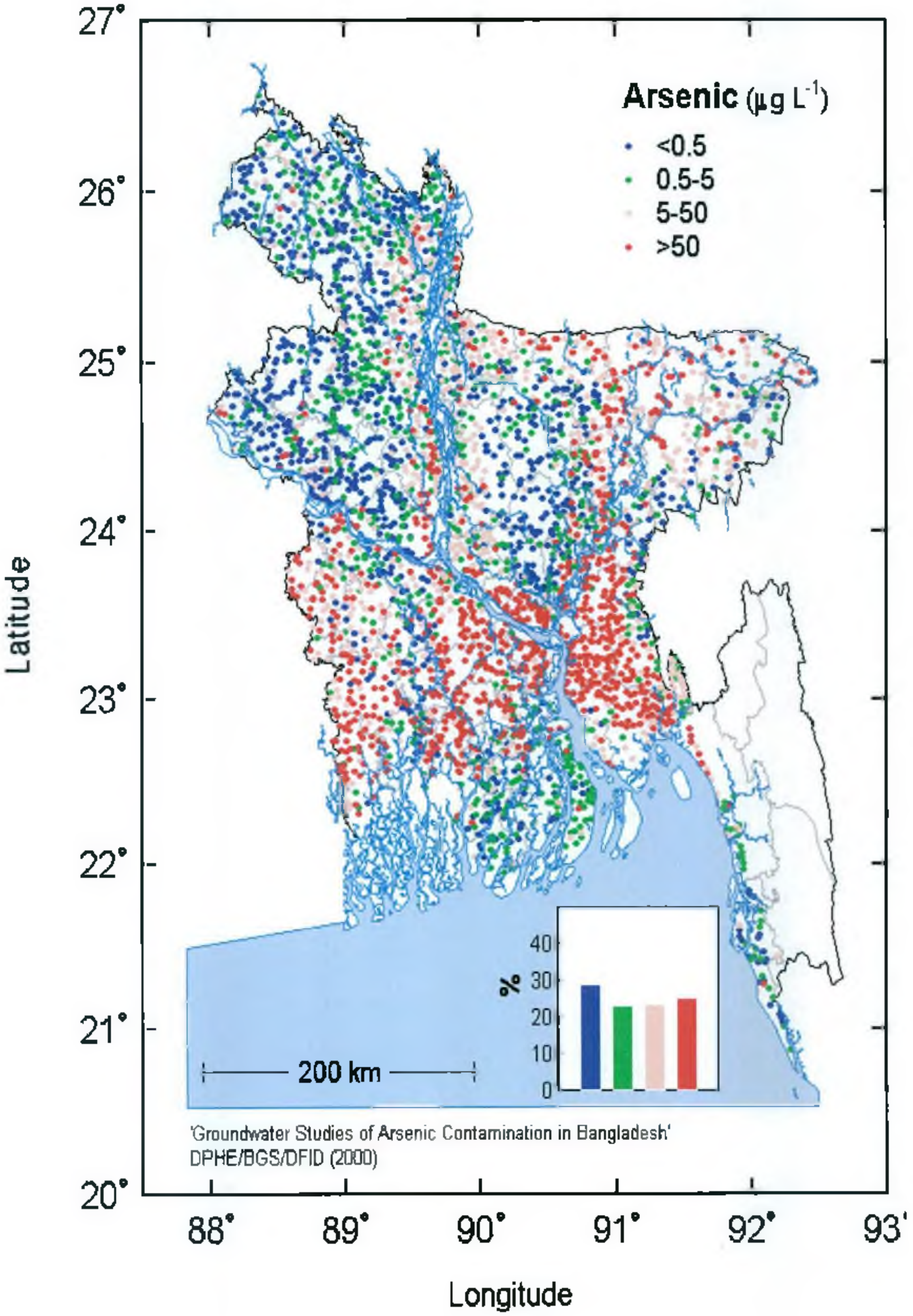
The Water Resources Utilization Department (WRUD) in the Ministry of Agriculture and Irrigation of Myanmar conducted arsenic testing in mid-1999. Samples drawn from Lower Myanmar showed traces of arsenic. A survey conducted by the Save the Children Fund, (UK) in Thabaung, Laymyethan and Hethada townships during March-May 2000 found that 35% of 125 sunken tube wells that were tested showed arsenic concentration in excess of 0.05 mg/L. Currently, the WRUD has conducted a thorough water quality monitoring programme in five selected townships, namely Magway, Sittway, Kawmu, Kyaungkone and Henthada. In these townships, localized random distribution arsenic concentration of varying magnitude was observed.

1.6 Arsenic situation in Bangladesh

In the face of the heavily polluted surface water, the government of Bangladesh and foreign aid agencies took action in the 1970s and '80s in order to provide the masses with safe water. The government and agencies dug over a million public pipe wells to shallow aquifers, providing the population with water that was believed to be clean and safe. A pipe well or tube-well consists of a 5cm diameter tube inserted into the ground and capped with a iron or steel hand pump. The majority of the wells were sunk by the United Nations Children's Fund, UNICEF. Ironically these wells led to the large st arsenic contamination crisis in the world. In later years, privately sunk wells became more prominent, eventually outnumbering public wells. Currently more than 90% of the drinking water in Bangladesh derives from aquifers less than 300m deep, with most aquifers less than 100 meters deep. <13>

The WHO recommended value of arsenic contamination in water is 0.01 mg/l, while the maximum permissible limit for Bangladesh and India has been fixed at 0.05 mg/l. In the DCH-SOES survey, less than 0.01 mg/l arsenic concentration was detected in 46% or 2803 out of 6101 water samples while above the WHO recommended value (0.01 mg/l) was found in the rest 54% or 3298 samples. On the other hand, arsenic concentration at less than the permissible limit (0.05 mg/l) was detected in 62% or 3783 samples, while above the limit was found in the rest 38% or 2318 water samples. <14>

Arsenic contamination at higher level than the WHO recommended value was found in the tube-wells of 52 districts out of the 60 surveyed. Of these, the level of arsenic presence exceeds the maximum permissible limit in the tube-wells water of 41 districts. In 11 districts, the level of arsenic concentration was found


27°
26°
25°
24°
23°
22°
21°
20°
Latitude
Arsenic (µg L-1)
<0.5
0.5-5
5-50
>50
%
40
30
20
10
0
200 km
'Groundwater Studies of Arsenic Contamination in Bangladesh'
DPHE/BGS/DFID (2000)
88°
89°
90°
91°
92°
93°
Longitude

more than the WHO recommended value, but less than the maximum permissible limit. That means, highest 0.05 mg/l exist in the tube-wells water of these districts. These areas may be considered moderately safe. These 11 districts are: Kurigram, Lalmonirhat, Rangpur, Bogra, Dhaka, Joipurhat, Gazipur, Borguna, Bhola, Sylhet, and Habiganj. A total of 695 tube-wells were brought under investigation in these districts. Less than 0.01 mg/l was found in 582 tube-wells (84%). The level of arsenic concentration between 0.01 mg/l and 0.05 mg/l was found in the rest 113 tube-wells (16%). <36>

Besides, after testing the water of 328 tube-wells of 8 districts, the survey did not find alarming level of arsenic. Arsenic was found in less than 0.01 mg/l in these samples. These districts may be considered as completely safe from arsenic pollution. These 8 districts are: Panchagar, Thakugaon, NIlfamari, Dinajpur, Galbandha, Naogoan, Patuakhali and Moulavi Bazar.

Dangerous level (above 0.05 mg/l) of arsenic was found in the water of 41 districts. These are: Nawabganj, Rajshahi, Pabna, Kushtia, Meherpur, Chuadanga, Jhenida, Jessore, Satkhira, Khulna, Bagerhat, Pirojpur, Narayanganj, Faridpur, Rajbari, Magura, Chandpur, Noakhali, Luxmipur, Madaripur, Shariatpur, Narail, Barisal, Jhalakati, Gopalganj, Natore, Comilla, Manikganj, Munshiganj, Feni, Narshlndi, Chittagong, Sherpur, Netrokona, Mymensingh, Jamalpur, Tangail, Kishoreganj, Sunamganj, Sirajganj and Brahmanbaria. (67)

The water of 5036 tube-wells were tested in these 41 districts. Of those 38% or 1983 tube-wells were found having arsenic at less than WHO-recommended value. Arsenic at a level of upto 0.49 mg/l or less than the maximum permissible limit was found in 55% or 2760 samples. And the rest 2286 samples (45%) were found having above 0.05 mg/l.

The survey in these 41 districts revealed a more dangerous fact. That is the presence of high level of arsenic in the polluted water. The detected arsenic level was from 0.10 mg/l to 1.0 mg/l, even more, in 1743 samples. Arsenic concentration more than 1.0 mg/l was found in 75 samples. Such a high concentration was not found even in the worst affected districts of West Bengal.

According to WHO more than 1.0 mg/l arsenic in water may create a disastrous situation. This concentration is 100 times higher than the WHO recommended value and 20 times higher than the maximum permissible limit.

Not only in the water samples, arsenic at high level was found in 89% of the total 1758 hair samples tested in these districts. The normal amount of arsenic in hair is less than 1 mg/kg. 98% of tested 1760 nail samples were detected having arsenic above the normal value. The normal content arsenic in nail is 0.43-1.08 mg/kg.

High level of arsenic presence was also found in 95% urine samples out of the total 830 samples tested. The normal level of arsenic presence in urine is between 0.01 mg/l and 0.05 mg/l. There is no recommended value of arsenic in skin-scales. But while testing 210 skin-samples, the DCH-SOES survey detected on an average 7.41 mg/kg arsenic.

Out of the 41 districts, where arsenic has been found above 0.05 mg/l, the DCH and SOES so far surveyed 22 districts for arsenic patients. In 21 districts they found people suffering from arsenic induced skin lesions like melanosis, leuco-melanosis, keratosis, hyper-keratosis, dorsum, non-petting oedema, gangrene, skin cancer etc. During the preliminary field survey conducted for last one and half year in 96 groundwater arsenic contaminated villages in 44 thanas of 22 districts they found arsenic patients in 93 villages in 21 districts. They examined at random 5664 people including children and out of them, 33.6% were found to have arsenical skin-lesions.

1.7. Survey repot of BAMWSP (January 2005)<67>

Total population surveyed:	(Male): 26865945 (Female) : 23586892
Total population surveyed:	50452837 (50.45)
Total village surveyed:	344999
Total Tube well:	3035964 (3.035 million).
Total Safe Tube well:	2149846
Total number of contaminated tube well:	886118 (0.886 million)
Percentage of contamination:	29.19 %
Total number of house hold :	9439450
Total Male Patient :	13308
Total Female Patient :	16211
Total Patient :	29500.

1.7.1 Factors influencing arsenic content in soil :

The principal factors influencing the concentration of elements in soils are the parent rock and human activities. Factors such as climate, the organic and inorganic components of the soils and redox potential status also affect the level of arsenic in soils. Q model factor analysis, linear discriminate analysis and principal component analysis indicate that the kind of parent rock is a much more important factor affecting soil metal contents than soil type.

1.7.2 Arsenic in soil. Inorganic and organic forms :

Arsenic occurs mainly as inorganic species but also can bind to organic materials in soils. Under oxidizing conditions, in aerobic environments, arsenates (iAsV) are the stable species and are strongly sorbed onto clays, iron and manganese oxides/hydroxides and organic matters. Arsenic precipitates as ferric arsenate in soil horizons rich in iron. Under reducing conditions arsenites (iAsIII) are the predominant arsenic compounds. Inorganic arsenic compounds can be methylated by microorganisms, producing under oxidizing conditions, monomethylarsonic acid (MMA), dimethylarsinic acid (DMA) and trimethylarsine oxide (TMAsO) . Under anaerobic conditions these can be reduced to volatile and easily oxidized methylarsines. The forms of arsenic present in soils depend on the type and amounts of sorbing components of the soil, the pH and the redox potential. Arsenates of Fe and Ai (AlAsO4, FeAsO4) are the dominant phases in acid soils and are less soluble than calcium arsenate (Ca3AsO4), which is the main chemical form in any alkaline and calcareous soils [40]. The adsorbed arsenate fraction in soils is closely related to soil pH and redox potential (Eh). It also varied with soil type under the same pH conditions, increasing in order from sucrose to brown soil to chestnut soil . Arsenic gets biomethylated (i.e. addition of CH3 to arsenic through biological activity) in the soil–water, sediment water interfaces through the activity of bacteria (such as Escherichia coli, Fla_obacteriun sp, Methanobacterium sp) and fungi (such as Aspergillus glaucus, Candida humicola). In the course of biomethylation, iAsIII is oxidized to iAsV and CH3 + is reduced to CH3 - and stable arsenic oxy-species was formed [42].

1.8. Physical properties (68)

Arsenic is often called a metal; however, it is classified as a non-metal or metalloid. The valence states of arsenic are +3, +5, and −3. In the environment, arsenic usually is present in a crystalline form and it has a light gray appearance.

The physical properties of arsenic are as follows:

Atomic Weight (12C = 12.0000)	*74.9216*
Density at 26 8C, kg/m3	*5778*
Latent heat of fusion, J/ (mol.K)a	*27,740*
Latent heat of sublimation, J/ (mol.K)a	*31,974*
Specific heat at 25 8C, μm/(m.8C)	*5.6*
Electrical resistively at 0 8C, μΩ.cm	*26*
Magnetic susceptibility at 20 8C, cgs	*-5.5 x 10-6*
Nuclear adsorption cross section (thermal neutrons 2200 m/s of arsenic mass 75)	*4.3 + 0.2*
Crystal system	*Hexagonal (rhombohedral)*
Lattice constants at 26 8C, nm	*a = 0.376, c = 1.0548*
Hardness, Mohs' scale	*3.5*

1.9. Concentrations of arsenic in groundwater (55)

According to the scientific literature, areas having elevated groundwater concentrations of arsenic,be they naturally occurring or due to human activity, can be found in all the major world regions. For example, in Iowa, Missouri and

Ohio, arsenic, apparently of natural origin, was found in groundwater at concentrations between 34 and 490 ug/L . In Hungary, it was found that arsenic concentrations in deep groundwater ranged from 1 to 174 ug/L, with an average value of 68 ug/L. High arsenic levels originating from arsenic-rich bedrock were found in drilled wells in southwest Finland with concentrations ranging from 17 to 980 ug/L , while in parts of Mexico arsenic concentrations ranged from 8 to 624 ug/L with over 50% of samples in excess of 50 ug/L.

Arsenic contamination of groundwater from arsenic-rich sediment has been reported widely in both India and Bangladesh. Chatterjee et al.(9) analysed groundwater from six districts of West Bengal, India. Mean total arsenic levels ranged from 193 to 737 ug/L with a maximum value of 3700 ug/L. Mandal et al. (28) reported that 44% of groundwater samples collected in West Bengal up to January 1996 contained total arsenic levels greater than 50 ug/L. Dhar et al. found that 38% of groundwater samples collected from 27 districts of Bangladesh contained total arsenic levels greater than 50ug/L. During 1990 and 1991 Chatterjee et al. (9) sampled groundwater in the vicinity of a chemical plant in Calcutta, India, which had produced the insecticide Paris-Green (acetocopper arsenite) for 20 years. Groundwater contained total arsenic levels ranging from <0.05 to 58 mg/L; the highest total arsenic level included 75% arsenite. British Geological Survey (1998) found only two out of 280 tube well below 200 m in Bangladesh to be contaminated with high level of Arsenic

1.9.1 Drinking Water:

Concentrations of total arsenic in fresh surface and groundwaters, both potential sources of drinking-water. Although arsenic levels in natural waters are usually low (a few µg/L), drinking waters in some areas in the world contain concentrations of total arsenic well in excess of 100 of µg/L. These elevated arsenic concentrations are generally a result of natural geochemical activity. Arsenate is usually the predominant species; however, some groundwaters have been found to contain up to 50% arsenite. Concentrations of methylated species in natural waters are usually low, that is less than 0.3 µg/L. Unless stated otherwise, monitoring data for drinking water given in this section are reported as total arsenic. A review of water quality monitoring data collected during the period 1976-1993 revealed that concentrations of arsenic in drinking waters in the USA lie between < 2.5 and 28 µg/L in surface waters, and between < 5 to 48 µg/L in groundwater sources. (Detection limits of 2 or 5 µg/L precluded more accurate estimates of the lower limit of these ranges). Based on these data, it was estimated that approximately 2% of the US population is exposed to drinking water containing more than 10 µg/L of arsenic. Areas of especially high arsenic concentrations have been identified by the US EPA in a detailed analysis of 1978 water quality monitoring data. These include parts of California and Neveda, were levels are arsenic in the bedrock are naturally high; mean arsenic concentrations of up to 80 µg/L and maximum levels of more than 1,400 µg/L have been reported.

1.10. METABOLISM

1.10.1 KINETICS AND METABOLISM

Humans are exposed to many different forms of inorganic and organic arsenic species (arsenicais) in food, water and other environmental media. Each of the forms of arsenic has different physicochemical properties and bioavailability and therefore the study of the kinetics and metabolism of arsenicals in animals and humans is a complex matter. Arsenic metabolism is also characterized by large interspecies differences compared with other metals and metalloids.(23)

1.10.2 INORGANIC ARSENIC

The fate of ingested or inhaled inorganic arsenic in the human body is largely dependent on its valence state. The two most common valence states to which humans might be environmentally exposed are the trivalent and pentavalent forms, arsenite (AsIII) and arsenate (AsV). Since arsenicals may change valence state depending on handling and preparation methodologies, studies cited in this review were evaluated with particular attention to the use of appropriate methods to ensure that the inorganic arsenic valence state was maintained.

1.10.3 Placental transfer

Both As(III) and As(V) have been found to cross the placenta of laboratory animals (54). Case reports of arsenic poisoning in pregnant women, in which the fetus died and was subsequently found to have toxic levels of arsenic in its organs and tissues, demonstrate that arsenite (arsenic trioxide) also readily passes through the placenta of humans. This conclusion is substantiated by a more recent study (18) conducted who observed that similar arsenic concentrations were found in cord blood and maternal blood (~9 ug/L) of maternal-infant pairs exposed to high arsenic-containing drinking water (~200 ug/L).

1.10.4 Distribution

1.10.4.1 Fate of inorganic arsenic in blood (60)

Inorganic arsenic is rapidly cleared from the blood of most laboratory animals and humans; for this reason blood arsenic is considered to be a useful bioindicator of recent, relatively high-level exposures.

1.10.4.2 Elimination and excretion (54)

Inorganic arsenic and its metabolites are eliminated primarily via the kidney. Studies in adult human males voluntarily ingesting a known amount of either trivalent or pentavalent arsenic 28 indicate that between 45% and 75% of the dose is excreted in the urine within a few days to a week. Although relatively few studies in volunteers have included measurement of arsenic in both faeces and urine.

Although arsenic is excreted by other routes than via urine and faeces (e.g. in sweat), these routes of excretion are generally minor (54). Since arsenic can accumulate in keratin-containing tissues, skin, hair and nails could also be considered as potentially minor excretory routes. Both older and recent studies indicate that arsenic can be excreted in human milk, although the levels are low.

1.10.5 ORGANIC ARSENIC COMPOUNDS

The kinetics and metabolism of MMA, DMA, trimethylarsine (TMA) and trimethylarsine oxide (TMAO) as well as arsenobetaine and arsenocholine are discussed in this section. In general, relative to inorganic arsenic, organoarsenicals are less extensively metabolised and more rapidly eliminated.

1.10.6 Placental transfer

Older studies have demonstrated that DMA is capable of crossing the placenta of rats (46) and that the organoarsenical feed additive Roxarsone (3-nitro-4-hydroxyphenylarsonic acid) accumulates in eggs . However, more recent human or animal data are not available to substantiate these findings.

1.10.6.1 Elimination and excretion

Humans eliminate orally administered MMA and DMA predominantly in urine. Hood et al.(22) reported that an average of 78.3% and 75.1% of a single oral dose (500 ug as) of MMA and DMA, respectively, were eliminated in urine of human volunteers within a four-day 32 period. Arsenic ingested in seafood (where it is most likely to be present as arsenobetaine) is rapidly eliminated in urine. It is worthy of note that the percentage of the dose eliminated in urine following ingestion of arsenic in seafood is quite similar to that seen in laboratory animals dosed orally with arsenobetaine. No studies were identified that addressed the issue of biliary excretion or other routes of elimination for organoarsenicals in humans.

1.11. BIOMARKERS OF ARSENIC EXPOSURE

The three most commonly employed biomarkers used to identify or quantify arsenic exposure are total arsenic in hair or nails, blood arsenic, and total or speciated metabolites of arsenic in urine.

1.11.1 Arsenic in hair and nails

Because arsenic (as the trivalent form) accumulates in keratin-rich tissues such as skin, hair and nails , arsenic levels in hair and nails have been used as indicators of past arsenic exposure. Hair and nails have the advantage of being readily and non-invasively sampled, but can suffer from problems of external contamination. In the case of hair, sampling from less readily contaminated sites (e.g. the occipital area or the nape of neck) and closer to the scalp can minimize some of these problems.(61)

Several studies have reported hair-As levels in subjects without known exposure to arsenic. In one such study, conducted by Zhuang et al. (64), levels of 0.40 ± 0.22 ug/g were measured in the hair of adult male Chinese subjects who had died as a result of accidents. These authors also reported a significant positive correlation (r=0.75) of hair- arsenic with arsenic levels in kidney33 cortex, but not in lung or liver. Similar studies performed in other parts of the world (USA and Europe) have found lower levels of hair arsenic following acute poisoning, arsenic levels in both hair and nails are elevated within one to a few weeks and return to background levels within a few months (Since the relative rate of hair growth is known (around 1 cm per month), the segmental distribution of arsenic along the hair shaft has been used to distinguish between acute and chronic poisoning, as well as to estimate length of time since a poisoning incident . Arsenic levels in hair and nails can also be influenced by arsenic-induced disease state. Lin et al. (26) have reported that both hair and fingernail arsenic are elevated in patients with black foot disease.

There were also reports of skin effects (i.e. a higher prevalence for hyperkeratosis) in the Lokoshaza area among children exposed to increased arsenic concentrations. The arsenic content of both fingernails and toenails has also been used as a bioindicator of past arsenic exposure. Fingernail arsenic has been reported to be significantly correlated with hair arsenic content (26). Agahian et al. (1990) reported that fingernail arsenic was elevated due to occupational arsenic exposure and correlated significantly (r=0.89) with mean arsenic air concentrations. The use of toenails over fingernails has been recommended in some studies due to the larger amount of sample that can generally be provided. Toenails have the added advantages of slower growth (and so reflect exposures in the more distant past) and fewer external contamination problem.

1.11.2 Blood arsenic

As previously mentioned inorganic arsenic is very quickly cleared from human blood. For this reason blood arsenic is only used only an indicator of very recent and/or relatively 34 high level exposure, for example, in poisoning cases (133) or in cases of chronic stable exposure (i.e from drinking water). Studies have shown that in general blood arsenic does not correlate well with arsenic exposure in drinking water, particularly at low levels. In five Californian communities having average

concentrations of 6, 51, 98, 123 and 393 ug/L arsenic in their drinking water, blood arsenic concentrations (mean ± SD) were 0.49±0.12, 0.51±0.65, 0.29±0.18, 0.42±0.17 and 1.33±1.18 ug/dL, respectively. However, arsenic levels in drinking water were significantly correlated with increased total arsenic in both hair and urine (53).

1.11.3 Arsenic and metabolites in urine

In common with other biomarkers of arsenic exposure, arsenic levels in urine may result from inhalation exposure as well as ingestion from food, water and soils and as such provide a measure of the total absorbed dose. However, since arsenic is rapidly metabolised and excreted into the urine, levels in urine are best suited to indicate recent arsenic exposure. Total arsenic, inorganic arsenic and the sum of arsenic metabolites (inorganic arsenic + MMA + DMA) in urine have all been used as biomarkers of recent arsenic exposure. In many older studies, total urinary arsenic was used as a biomarker of recent arsenic exposure. This approach has become increasingly uncommon because certain organoarsenicals (for example, the practically non-toxic compound arsenobetaine) present in substantial amounts in certain foodstuffs are excreted mainly unchanged in urine (53). Since consumption of seafood (e.g., marine fishes, crustaceans, bivalves, seaweeds) by human volunteers is associated with increased total urinary arsenic excretion, assessment of inorganic arsenic exposure using total urinary arsenic under these conditions would result in overestimation of inorganic arsenic exposure.

To avoid the potential for over-estimation of inorganic arsenic exposure inherent in using total urinary arsenic, most studies now measure speciated metabolites in urine, and use either inorganic arsenic or the sum of arsenic metabolites (inorganic arsenic + MMA + DMA) as an index of arsenic exposure. However, this can give misleading results unless a careful diet history is taken and/or seafood consumption is prohibited for two to three days prior to urine collection. There are two reasons for this. First, some seafoods contain the arsenic metabolites MMA and DMA, particularly DMA, in fairly high amounts. Secondly, arsenosugars present in seaweeds and some bivalves are extensively metabolised to DMA (either by the body itself or the gut microbiota), which is then excreted in urine.

1.12. HEALTH EFFECTS

Arsenic has long been associated with toxic effects, producing marked impacts on health after both oral and inhalation exposure. Effects range from acute lethality to chronic effects, such as cancer and diseases of the vascular system. Studies in laboratory animals have demonstrated that the toxicity of arsenic is dependent on its form and its oxidation state. It is generally recognised that the soluble inorganic arsenicals are more toxic than the organic ones, and the trivaient forms (AsIII) are more toxic than the pentavalent ones (AsV). There are multiple end-points, with several different organ systems being affected, including the skin and the respiratory, cardiovascular, immune, genitourinary, reproductive, and gastrointestinal and nervous systems. Much of the information about the human health effects of arsenic, in particular in relation to its carcinogenicity, comes from evidence obtained through the study of exposed human populations. Unusually, it has been difficult to find any suitable animal model for the study of arsenic carcinogenicity.

1.12.1 Short-term effects

Ingestion of large doses of arsenic usually results in symptoms within 30 to 60 minutes, but may be delayed when taken with food. Acute arsenic poisoning usually starts with a metallic or garlic like taste, burning lips and dysphasia. Violent vomiting may ensue and may eventually lead to hematemesis. These gastrointestinal symptoms are the result of intestinal injury caused by dilatation of splanchnic vessels leading to mucosal vesiculation. These vesicles rupture causing bleeding, diarrhoea, and protein wasting. Gastrointestinal symptoms often result in dehydration and electrolyte imbalance, and may lead to the development of hypotension and hypoxia. After the initial gastrointestinal problems, multiorgan failures may occur, followed by death. Survivors of acute arsenic poisoning have been shown to develop hepatomegaly, melanosis, bone marrow suppression, hemolysis, and polyneuropathy resulting from damage to the peripheral nervous system. Fatal arsenic poisonings have been reported after oral exposure to estimated single doses of 2 g ,8 g and 21 g. Non-fatal outcomes (usually following treatment) have been documented after oral single doses of 1-4 g. In children non-fatal but nevertheless serious acute effects have been observed after exposure to as little as 0.7 mg of As_2O_3 (51).

1.12.2 Chronic arsenic exposure

Chronic exposure to lower levels of arsenic has long since been linked to adverse health effects in human populations. The earliest reports date back to the latter part of the 19th century when the onset of skin effects (including pigmentation changes, hyperkerotosis and skin cancers) were linked to the consumption of arsenic in medicines and drinking water. In the early 1900s, numerous reports of skin disorders in Argentina, Chile, Mexico and Taiwan, which were attributed to arsenic exposure via drinking water, were published (51). In the 1940s the discovery of a case of lung cancer, believed to be the result of exposure to arsenical dust in a British factory, sparked a series of more detailed investigations into the matter. These in turn revealed unexpectedly high lung cancer rates in a number of different occupational exposure situations. Of the earliest reported cases of chronic arsenic poisoning, that of Blackfoot disease (BFD) or Wu Chiao Ping as it is locally known, is perhaps the most notorious. This peripheral vascular disease, which leads to progressive gangrenes of the legs, has been recognised in parts of Taiwan since the 1920s. During the 1950s its prevalence increased markedly, and since the late 1950s it has been the subject of intensive study.

1.12.3 The following diseases occur due to chronic arsenic exposure

- Peripheral vascular diseases
- Cardio and cerebrovascular diseases
- Hypertension
- Cancer of different system
- Genotoxicity
- Diabetes Mellitus

- Neurological effects
- Reproductive effects

1.12.4 Reproductive effects

In addition to the health effects already mentioned, arsenic has also been linked to adverse reproductive outcomes. A number of studies have attempted to investigate this possible connection, the results of which suggest increased fetai, neonatal and postnatal mortalities, and elevations in low birth weights, spontaneous abortions, and stillbirths, pre-eclampsia and congenital malformations.

A series of ecological studies involving workers and their families living in the vicinity of the Ronnskar copper smelter in Sweden, for example, have reported an increase in the prevalence of low birth weight infants , higher rates of spontaneous abortions and elevations in congenital malformations (33) among female employees and in women living close to the smelter relative to women living further field. According to Tabocova & Hunter (49) the frequency of pregnancy complications, mortality rates at birth and low birth weights were significantly higher in 49 maternal-infant pairs living near a Bulgarian copper smelter, relative to country-wide rates. Placental arsenic levels were also found to be higher for the smelter area than for the non-smelter area. In both cases, however, a lack of rigorous treatment of the potential role of confounding risk

factors, such as co exposures (lead, copper, and cadmium), maternal age, lifestyle/socioeconomic status and smoking habits, have cast doubts over the validity of these findings . Other studies involving arsenic exposure via drinking water have produced conflicting results. Zierler et al. (63) found no evidence of an increased frequency of congenital heart disease in infants born to women consuming drinking water containing arsenic leveis between 0.8-22 ug/L. A 1.4-foid increase in spontaneous abortions and a 2.8-fold increase in still births were, however, observed in a group of "exposed" individuals (arsenic concentrations in water samples > 100 ug/L, N = 25,648) compared with a "low" exposure group (unspecified low arsenic concentration in water samples, N = 20,836) from the south eastern part of Hungary.

In sum, there does not appear to be consistent evidence linking any one particular reproductive outcome to arsenic exposure, and at the present time it is generally accepted that there is insufficient evidence to support the notion that arsenic causes reproductive effects in humans.

Arsenical Skin Lession

Arsenical Skin Lession

Arsenical Skin Lession

1.13 Diagnosis

Humans are exposed to arsenic (As) primarily from air, food and water. However, elevated inorganic As in drinking water is the major cause of As toxicity. Most of the reports of chronic As toxicity in man focus attention on skin manifestations because of its diagnostic specificity, but As often affects most systems of the body. The clinical manifestations of chronic As intoxication are dependent on host susceptibility, the dose and the time course of exposure. The symptoms are often insidious in onset and varied in nature. However in a few epidemiological studies no significant clinical features of toxicity were attributed to chronic intake of As contaminated water.

Although chronic As toxicity produces varied non malignant manifestations as well as cancer of skin and different internal organs, dermal manifestations such as hyper pigmentation and hyperkeratosis are diagnostic of chronic arsenicosis. The pigmentation of chronic As poisoning commonly appears in a finely freckled, "raindrop" pattern of pigmentation or depigmentation that is particularly pronounced on the trunk and extremities and has a bilateral symmetrical distribution- Mild pigmentation (a) Diffuse melanosis (with mild keratosis), (b) Mild spotty pigmentations, (c) Mild spotty depigmentations. (20) (a) Moderate pigmentation, (b) Severe pigmentation. Pigmentation may sometimes be blotchy and involve mucous membranes such as the undersurface of the tongue or buccal mucosa (4, 20, 40). The raindrop appearance results from the presence of numerous rounded hyper pigmented or hypo pigmented macules (typically 2-4 mm in diameter) widely dispersed against a tan-to-brown hyper pigmented background (20). Although less common, other patterns include diffuse hyper pigmentation (melanosis) and localized or patchy pigmentation, particularly affecting skin folds (20). So-called leukodermia or leukomelanosis, (20) hypo pigmented macules take a spotty, white appearance usually occur in the early stages of intoxication.

Arsenical hyperkeratosis appears predominantly on the palms and the plantar aspect of the feet, although involvement of the dorsum of the extremities and the trunk have also been described. In 3 the early stages, the involved skin might have an indurated, grit like character that can be best appreciated by palpation; however, the lesions usually advance to form raised, punctuated, 2-4 mm warlike keratosis that are readily visible . Occasional lesions might be larger (0.5 to 1 cm) and have a nodular or horny appearance occurring in the palm or dorsum of the feet. In severe cases, the hands and soles present with diffuse veracious lesions (a) Mild keratosis, (b) moderate keratosis (i) moderate diffuse thickening of the palm, (ii) a few nodules over thickened palm (associated lesions : Bowen's disease of the abdomen and squamous cell carcinoma on the finger). (19) and Severe keratosis (a) Veracious lesion of the palm with keratotic horn, (b) Big nodules over the dorsum of feet (associated lesion : Squamous cell carcinoma). (19) Cracks and fissures may be severe in the soles (38). Histological examination of the lesions typically reveals hyperkeratosis with or without parakeratosis, acanthosis, and enlargement of the rete ridges. In some cases, there might be evidence of cellular atypical, mitotic figures, in large vacuolated epidermal cells (11) classified arsenical keratosis into two types: a benign type A, further sub grouped into those with no cell atypical and those with mild cellular atypia; and a malignant type B, consisting of lesions of Bowen's disease (intraepithelial carcinoma, or carcinoma in situ), basal-cell carcinoma, or squamous-cell carcinoma. The later might arise in the hyperkeratosis areas or might appear on nonkeratotic areas of the trunk, extremities, or head (42).

Though spotty depigmented spots, similarly distributed are also diagnostic for this condition, sometimes blotchy depigmented spots are seen and these need to be differentiated from other depigmented skin lesions like tinea versicolor, seborrheic dermatitis. Diffuse hyperkeratitic lesions of the palms and soles are distinctive lesions of chronic arsenicosis. However, manual labourers, who work with bare hands, might have thickening of the palms. The thickening of palms in manual labourers are usually localised in the pressure points. Bare footed farmers who work in the fields might have diffuse thickening of the soles. However, when the lesions become nodular the diagnosis becomes obvious. The duration of the patient's As exposure with the date of onset of symptoms does not follow a particular time frame. Arsenical skin lesions have been reported to occur in West Bengal after drinking As contaminated water for one year or even less (50). In Taiwan, the youngest patient drinking As contaminated water who developed hyperpigmentation was 3 years old . Among the population exposed to As in drinking water in the Antofagasta region of Chile, cases of cutaneous arsenicosis, including both hyperpigmentation and hyperkeratosis, have been described in children as young as 2 years of age . The mean As dose in Antofagasta was estimated to be approximately 0.06 mg/kg per day for subgroups of children aged 3.13±3.33 years but was approximately 0.02 mg/kg per day for subgroups in their teens and twenties and 0.006 mg/kg per day for a subgroup in their sixties, indicating an inverse relationship between daily As dose rate/kg body weight and age .

1.13.1 Diagnostic criteria of chronic arsenicosis. (19)

1. At least 6 months exposure to arsenic levels of greater than 50 mg/L or exposure of high arsenic level from food and air. 2. Dermatological features characteristic of chronic arsenicosis.

3. Non carcinomatous manifestations: Weakness, chronic lung disease, non cirrhotic portal fibrosis of liver with/without portal hypertension, peripheral neuropathy, peripheral vascular disease, non pitting edema of feet/ hand.

4. Cancers : Bowens disease, Squamous cell carcinoma, Basal cell carcinoma at multiple sites, occurring in unexposed parts of the body.

5. Arsenic level in hair and nail above 1 mg/kg and 1.08 mg/kg respectively and/or arsenic level in urine, above 50 mg/L (without any history of taking seafood).

1.13.2 Dermatological criteria and grading of severity of chronic arsenic toxicity. (19)

Grade I : Mild

a) Diffuse melanosis.

b) Suspicious spotty depigmentation / pigmentation over trunk /limbs.

c) Mild diffuse thickening of soles and palms.

Grade II: Moderate

a) Definite spotty pigmentation / depigmentation on the trunk and limbs, bilaterally distributed.

b) Severe diffuse thickening (with/without wart like nodules of the palms and soles).

Grade III: Severe

a) Definite spotty pigmentation/depigmentation as above with few blotchy pigmented/depigmented macular patches over trunks or limbs.

b) Pigmentation involving the undersurface of tongue and/or buccal mucosa.

c) Larger nodules over thickened palms and soles occasionally over dorsal aspect of hands and feet. Diffuse veracious lesions of the soles with cracks and fissures and keratotic horns over palms/soles.

Again, Arsenic could be categorised in to 3 sequential stages:

1. Melanosis

2. Keratosis with or without anemia, Conjuntivities, bronchities, gastroenterities & Black foot diseases

3. Develoed keratosis & skin cancer

A few epidemiological studies have highlighted that none of the exposed population to environmental Arsenics show any clinical manifestation of chronic Arsenics toxicity. Further, there is a wide variation in the incidence of chronic arsenicosis in an affected population. Even not all members of an affected family show clinical effect. The reasons for such variation of disease expression are an enigma. However, as the As exposed people are at risk for developing As related cancer, they should be subjected to prolonged surveillance.

1.13.4 Biomarkers with special focus exclusively on diagnosis.

On the basis of As metabolism data, important biomarkers of internal exposure are: the urinary excretion of the element and its concentration in hair and nail (blood concentrations are generally too low and transient). Despite some encouraging reports, the use of As measurements in hair and nail as indices of absorbed dose appears limited. Efforts are needed to develop a standardized procedure to solve the problem of external contamination of samples. The relationship between As air concentration and urinary excretion of inorganic arsenic, and of mono and dimethyl arsenic acid, appears better. As urinary excretion (seafood As excluded) as a function of As oral intake via drinking water in steady state conditions, has been reported by several authors from different countries. Despite possible ethnic and environmental differences, reported results display a quite satisfactory consistency. Most strikingly, an increased excretion rate is observed when the water As concentration reaches 100 - 200 mg/L.

1.13.3.1 Urine

The concentration of total As in urine has often been used as an indicator of recent As exposure because urine is the main route of excretion of most As species (6, 52). The half-time of inorganic As in humans is about 4 days. Average background concentrations of As in urine are generally below 10 mg/L in Europe (2), somewhat higher in some parts of the US in people living near point source emissions, especially copper smelters, and around 50 mg/L in Japan (52) In certain areas in the US, an average concentration of As of 10 mg/L or less has been reported for children. Urinary As concentrations have also been shown to correlate with As intake in drinking-water. A survey was conducted by Harrington, et al. (1978) among a population in an area with elevated As concentrations in well water. Drinking well water with an As content exceeding 100 mg/L (mean 401 mg/L and an estimated total daily intake of 324 mg/L of As) gave an average urinary total As concentration of 178 mg/L (atomic absorption spectrophotometer). Drinkers of well water containing an average As concentration of 31 mg/L (estimated daily intake of 46 mg of As) had a mean urinary As concentration of 41 mg/L. Seafood in the diet may influence urinary As measurements. Certain seafoods (particularly cold water fin fish, crustaceans, and molluscs) may contain large amounts of organo arsenic compounds that have no known mammalian toxicity. In addition, certain edible marine foods, such as seaweed or kelp, may contain arsenosugars that are without recognized toxicity. These compounds are well absorbed from the gastrointestinal tract, and in the case of arsenobetaine, are largely excreted unchanged in the urine. When a clinical laboratory measures and reports the total As content in urine, the value may be markedly elevated (up to hundreds or thousands of µg/L) if 13 they have ingested seafood within the past 1-2 days. In an effort to avoid the contribution of complex organo arsenicals in seafood, some clinical laboratories use a speciation method that only measures inorganic As, or its metabolites, monomethylarsnoic acid (MMA) and dimethylarsonic acid (DMA). However, certain marine organisms, particularly bivalves such as clams, may contain over one hundred micrograms of dimethylarsonic acid in a typical serving, and may thus elevate urine As values even when the more restrictive speciation methods of analysis are used. Consequently, a urine As measurement may not be a valid reflection of As ingestion from drinking water if there has been any consumption of seafood (including seaweed products) within the past three days.

1.13.3.2 Hair and Nail.

Arsenic is normally found in higher concentrations in human hair and nails than in other parts of the body. This has been explained by the high content of keratin in these tissues (40). Hair As levels can provide useful information in chronic As poisoning but undue weight should not be given to the results. Several problems confront the toxicologist when using this test: there is only a very approximate relationship between hair As concentration and As toxicity. Thus, patients with chronic As poisoning may have hair concentrations varying, from 10 ppm (10 mg/kg hair) to 100 ppm whereas levels of around 45 ppm have been reported in Aa-related fatalities. Results derived from the analysis of a single hair or of one site along the shaft of a single hair are much less reliable than mean levels from larger hair samples because the inter and intra-hair variations in As content can be very large. Thus, samples should consist of at least one gram of hair cut close to the scalp and derived from several sites on the head and the whole sample should be analysed. External contamination of the hair by As must be excluded in order to use hair As concentrations to assess toxicity. Ingested As and As derived from external contamination are both avidly bound to the outer surface of the hair and these two sources cannot be differentiated by any known technique. External contamination can produce As concentrations of several thousand ppm and therefore can mislead investigators attempting to diagnose chronic As poisoning. Despite these pitfalls, the test can give useful information if carefully interpreted (21).

1.13.3.3 Blood

Most inorganic and organic As in blood is cleared fairly rapidly in man. Blood As will therefore reflect exposure for only a short period following absorption and will be very time dependent. Only if exposure is continuous and steady, as is sometimes the case with exposure through drinking-water, will As reach steady-state in the blood and thus make it possible to discern a relationship between blood As and exposure. Even so, there are no data that indicate a quantitative relationship in man between As exposure and blood As concentrations. The short half-life of As in the blood compared with the half-life in the body makes it difficult to discern a relationship between blood As concentration and total body As burden or As concentrations in different organs.

Partial speciation of As in blood has been reported in few cases (60). When using total As in blood as an indicator of exposure to inorganic As, the interference from organic As compounds originating from seafood has to be considered. Furthermore, because of the low concentrations, the analytical error might be significant, unless relatively sensitive methods are used. Data on concentrations of As in blood in people with no known exposure to As are in the range 0.3 – 2 mg/L . In people exposed to As in drinking water (200 mg/L) in northern Argentina, the mean blood As concentration was about 10 mg/L (145). In studies carried out in California and Nevada, an As concentration of 400 mg/L in water corresponded to about 13 mg/L in blood, and 100 mg/L in water corresponded to

3-4 mg/L in blood . Obviously, compared with urine, blood is a much less sensitive biomarker of exposure to As via drinking water.

Chapter-2

2.1. Rationale

Arsenic poisoning has emerged as a fresh blow to Bangladesh, a country that is known as a land of frequent natural calamities. After analyzing the data so far available, the experts opined that groundwater arsenic contamination and sufferings of people in Bangladesh might be the biggest arsenic calamity and the biggest mass poisoning in the world.(13, 33, 37) 3.035 million tube-wells were tested by the January 2005, and .886 million of them were found contaminated by unacceptable concentrations of arsenic and the rate of contamination is 29.19 %. According to the BAMWSP, total house hold surveyed are 9.44 million of total population is 50.45 million and out of them 29500 patients of arsenicosis have so far been identified in the country. Total number of Upazillas screened for Arsenicosis are 190. There are many reports of estimates of the number of people at risk of arsenic poisoning in Bangladesh ranging from 20 to 70 million out of the total 130 million (11,32). Arsenic in drinking water in Bangladesh is attracting much attention.

The important reasons for this include it being a unfamiliar problem (to the people, including concerned professionals); the number of people who may be exposed; and fear for dramatic future health effects as a result of water already consumed.(11) The health hazards due to arsenic contamination of drinking water has raised the serious concern for public health because of the disease arsenicosis that is borne by drinking arsenic contaminated water. In 1997, the World Health Organization (WHO) acknowledged that arsenic in drinking water was a "major public health issue" which should be dealt with on an "emergency basis".(56)

Chronic arsenic poisoning, the type that is found in Bangladesh, can manifest a wide range of disease conditions involving various human systems and organs, including the reproductive system. But, so far, reproductive effects of inorganic arsenic on humans have not been well studied. Most of the studies that were conducted in the area examined impacts of inhaled inorganic arsenic (from the copper smelter or the semiconductor industry) on reproductive health; studies on the reproductive health impacts of arsenic-contaminated water intake are very few. Arsenic affects peoples regardless of sex. It is a known carcinogen (24), and has mutagenic and teratogenic effects. Chronic exposure of Arsenic may affect all of the organ and system of human body.

Arsenic readily cross the placental barrier and thus affect foetal development. Reproductive and developmental effects of inorganic Arsenic on human and animal species have been reported (33,35) in some studies. Again, results of these studies indicate that further research in this field is needed. In contrast, there are few reports (1, 27) published about effects of arsenic in drinking water on human pregnancy outcome. In that report, higher Spontaneous abortion, Still birth and Neonatal death were observed in the high arsenic area, compared to control area. Moreover published studies are not providing sufficient information on pregnancy outcome in relation to arsenic exposure through drinking water in Bangladesh. So, there is important knowledge gap. In this context, the present study will be able to contribute to fill up this knowledge gap, and this study will be a pioneering one in the area of reproductive health impacts of arsenic contamination of groundwater. This study will contribute to the knowledge of the planners, policy makers and administrators to chalk out pragmatic policy for arsenic contamination mitigation programmes and for reduction of maternal and infant morbidity and mortality in Bangladesh.

2.2. Objective

General Objective:

- To study the Reproductive Health Impact of arsenic contamination in drinking water in selected area of Bangladesh.

Specific Objective:

- To study the socioeconomic characteristics of the women who are taking arsenic contaminated tube well water.
- To find out the diseases of the women who are taking arsenic contaminated tube well water.
- To study the reproductive health impacts of women in terms of the Spontaneous abortion, Still birth and Neonatal death who are taking arsenic contaminated tube well water.

2.3. Hypothesis

Long continued use of arsenic contaminated tube well water by women of reproductive age might have impact on Reproductive Health leading to Spontaneous abortion, Still birth and Neonatal death.

2.4. Operational definition

Reproductive health

Reproductive health has been defined as a state of complete physical mental and social well-being and not merely the absence of disease or infirmity, in all maters relating to the reproductive system and to its function and processes. Reproductive health therefore implies that people are to have satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how after to do so. Implicit in this last condition are the rights of man and women to be informed and having access to safe, effective affordable and acceptable method of family planning of their choice.

Reproductive health is a crucial part of general health, not only that it is a key element of health during adolescence and adulthood. It also sets the pace of health beyond their productive years for both women and men and has pronounced inter generational effects. (Beijing conference)

The area of reproductive health care has seven sub areas

- Safe motherhood
- Family planning
- Prevention and control of RTI / STD / AIDS
- Maternal nutrition
- Adolescent care
- Infertility
- Neo-natal care.

Here in this study, the safe motherhood issue has to discuss. Safe motherhood encompasses antenatal care, detection and management of pregnancy complications and screening of high risk pregnancies, delivery of trained personnel, obstetric first and referral services for complicated delivery and post natal care.

Here the study will highlight the some major pregnancy output like, Live birth, Spontaneous abortion, Still birth, Neonatal death, Antenatal care, complication during delivery and delivery related information.

Chronic arsenicosis: May be defined as a chronic condition due to prolong exposure of arsenic above safe level usually manifested by characteristics skin lesion with or without involvement of internal organ and malignancies.

Spontaneous abortion: Spontaneous abortions generally referred to as miscarriages, occur when an embryo or fetus is lost due to natural causes. It is spontaneous loss of the embryo or fetus before 20^{th} week of development. Spontaneous abortions after the 20^{th} week are generally considered preterm deliveries. Early embryonic development is an error prone process, and the body may spontaneously abort if a fetus is not viable or when the womb is unable to support the development of the fetus. Other causes can be infection, immune responses, or serious systemic diseases of the mother.

Melanosis : Hyperpigmentation (dark spot on the skin) and Hypopigmentation (white spot on the skin) are collectively known as Melanosis.

Keratosis : It is a condition, when the skin hardens and develops in to raised wart like nodules.

Blackfoot diseases: It is a peripheral vascular diseases results in gangrene in the extremities and usually occures in conjunction with skin lession

Stillbirth: When pregnancy ends without a live birth due to natural causes, including pregnancy loss, miscarriage or spontaneous abortion. It is the delivery of an infant, which is dead at birth, regardless of the stage of development. Infant delivered showing no sign of life after 24 weeks gestation.

Neonatal death: Neonatal death was defined as the death of newborn within 28 days after birth.

2.5. Major outcome variable

The following clinical and laboratory characteristics were used as major outcome variables to assess the treatment effect.

Clinical variables:

- Skin manifestation
- Thickening of the palm and soles
- Unwanted abortion / Spontaneous abortion / Miscarriage
- Still birth
- Neonatal death.
- Hypertension
- Diabetics Mellitus
- Anemia
- Measles
- Height
- Weight
- Weakness
- Headache
- Nausea
- Bad. Pain
- Diarrhea
- Cough
- Haemoptysis
- Parasthesia, Eclampsia

Chapter-3

3. LITERATURE REVIEW

3.1. Effects on laboratory mammals and vitro test system

Reproductive toxicity, embryo toxicity, and teratogenicity

3.1.1. In vivo embryo and fetal toxicity

Inorganic arsenic is toxic to mouse and hamster embryos and fetuses after oral, parenteral or inhalation administration to the dams, with arsenite 3–10-fold more potent than arsenate (3, 7 , 22, 57). The hamster embryo and fetus is more sensitive to this effect than the mouse. The toxicity is characterized by decreases in fetal weight, crown–rump length, embryo protein content, the number of somites, and growth retardation and lethality. Arsenite-induced lethality is dependent on dose and day of gestation in mice after a single oral dose (3) or in hamsters after an intravenous dose (57). Arsenite administered orally (20–25 mg/kg) is less effective than parenteral dosing (2.5–5 mg/kg) with respect to mortality (22) evaluated the developmental toxicity of arsenic acid administered by oral gavage to CD-1 mice and New Zealand white rabbits. Rabbits received doses of 0, 0.19, 0.75 or 3.0 mg/kg per day on gestation days 6–18 and mice received 0, 7.5, 24 or 48 mg/kg per day on gestation days 6–15. Developmental toxicity in the form of increased fetal resorptions and decreased fetal weight were observed only at exposure levels resulting in maternal toxicity (severely decreased weight gain, mortality). On the basis of the no observed adverse effect levels (NOAELs) identified in this study, rabbits (NOAEL = 0.75 mg/kg per day for maternal and developmental toxicity) were more sensitive to the effects of arsenic acid than mice (NOAEL = 7.5 mg/kg per day).

Ferm & Hanlon (18) implanted osmotic mini-pumps containing sodium arsenate (150–250 mg/ml) subcutaneously into pregnant hamsters on one of days 4–7 of gestation. The pumps release the solution at a rate of 1 µl/h. The dams were killed on day 13 of gestation and the fetuses examined. Fetal weight decreased and resorption rate increased in the offspring of treated dams, and these effects were dose-dependent and more marked the earlier the arsenate was implanted. There was also a trend of smaller crown–rump length with increased exposure time. The decrease in crown–rump length on day 4 was also dose-dependent.

The developmental effects of gaseous arsenic after repeated inhalation exposure were examined in rats.(29). Pregnant rats and virgin controls were exposed to 0, 10, 37 or 75 mg/m^3, 6 h/day, during gestation days 4–19. Although the rats exhibited signs of pulmonary toxicity, which included dyspnoea, and grey mottled lungs, there were no effects on maternal body weights. No embryotoxic effects were observed. Concentration-related growth retardation, as shown by decreased fetal body weight, was statistically significant at 37 mg/m^3. The NOAEL for developmental toxicity is 10 mg/m^3. The fetus had an arsenic concentration of 2.2 mg/g at 75 mg/m^3 on gestation day 20, but this level was considerably lower than that detected in maternal blood. Gallium concentration on gestation day 20 was greater in the fetus than in the dam (1.3 vs. 0.5 µg/g at 75 mg/m^3, respectively).

3.1.2. *In vitro embryo and fetal toxicity*

Several *in vitro* studies have examined the effect of inorganic arsenic at pre- and post-implantation stages of development. Mirkes et al. (29) examined the effect of sodium arsenite on two-cell mouse embryos at pre-implantation stages, which is approximately 30–32 h after conception. Arsenite-induced lethality occurs at a concentration of 100 µmol/litre, but other effects occur at much lower doses. Micronuclei form at 0.7 µmol/litre arsenite, and the ED_{50} for inhibition of blastocyte formation and blastocyte hatching respectively is 0.65 µmol/litre and 0.45 µmol/litre. Cell proliferation is decreased by arsenite in a dose-dependent manner.

After implantation, arsenite and arsenate are toxic (decreases in crown–rump length, number of somites, protein content, head length, yolk sac diameter) and lethal to embryos of mouse (8, 48). Tabacova et al. (48) observed that as gestational age increased when the mouse embryos are isolated and exposed to arsenic, resistance to toxicity or lethality increased. As observed in the *in vivo* studies, arsenite was more potent *in vitro* with respect to embryo and fetal toxicity than arsenate.

3.1.2.1. Teratogenicity

a) *In vivo*

There are many older studies of the teratogenic potential of arsenic in animals : many of these were carried out using the intravenous or intraperitoneal routes, which are not considered to be the most appropriate route of arsenic exposure for the fetus. In general the teratogenic effects are seen at levels that produce maternal toxicity.

Inorganic arsenic elicits teratogenic effects in the mouse (3, 19, 22, 31, 57) after oral, parenteral or inhalation administration. The malformations are dependent on the dose of arsenic administered as well as the gestational age. Sodium arsenite is more potent than sodium arsenate in inducing a teratogenic response, and parenteral administration of arsenic is more effective than oral administration. Administration of an acute oral dose of arsenite that is toxic to or near the lethal dose of pregnant mice (40–45 mg/kg) or hamsters (20–25 mg/kg) (22) induces a low incidence of teratogenic malformations.

The major teratogenic effect induced by inorganic arsenic in laboratory animals is cephalic axial dystrophic disorder, or neural tube defect. The defect is characterized by anencephaly and encephalocele, which are non-closure and partial closure of the cephalic neural folds, respectively (7). Anencephaly and encephalocele occur rarely in laboratory rodents. Other malformations which occur to a minor extent after exposure to arsenic include fused ribs, renal agenesis, macromedia, facial malformations, twisted hind limb, microphthalmia and exophthalmia.

Administration of inorganic arsenic to dams on days 7–9 of gestation results in neural tube defects in the developing organism. The most sensitive time in mouse embryos to arsenate is when the dams are administered chemical on day 8. Of the fetuses that survived a single dose of sodium arsenate (45 mg/kg) administered intraperitoneally to dams on day 8, 65% or more were epencephalic (31). After administration of a similar dose of arsenate on day 7 or 9, 3% or fewer of the surviving fetuses were epencephalic.

The neural tube defects seem to result from an apparent arsenic-induced arrest or delay in neural-fold apposition. Tanaka (50) examined the changes induced by an embryo-lethal dose of arsenic acid (30 mg/kg arsenic acid) administered to pregnant rats intraperitoneally on day 9 of gestation. At 4 h after exposure, there was some cellular necrosis in the neuroectoderm and mesoderm of the embryos. By 12 h, abnormal mitotic and interphase cells were observed in both tissues, and necrotic cells and debris from these cells were also present. By 24 h, inoculation no longer proceeded, as evidenced by the presence of the V-shaped neural fold that is normally closed by this time.

Willhite (57) examined the time course of effects on embryos isolated from pregnant hamsters administered sodium arsenate (20 mg/kg) intravenously on day 8 of gestation. There were no differences between embryos from control and arsenate-treated dams at 2 h. Changes became evident at 6 h and more so at 10 h after treatment, with a delay in elevation of the neural fold and closure of the neural tube. There were fewer cells in the cephalic mesoderm of treated embryos than in control embryos of an equivalent gestational age. The author suggested that the damage to the paraxial mesoderm may be associated with the skeletal effects induced by arsenic.

In studies by Morrissey & Mottet (31), pregnant mice were sacrificed 6–21 h after intraperitoneal administration of sodium arsenate (45 mg/kg) on day 8 of gestation. They observed that the neural folds were widely separated and not positioned for closure in the prospective hindbrain. Necrotic debris was also found primarily in the neuroepithelium of the prospective forebrain and sometimes in the mesenchyme, but it was not clear if this was the main lesion associated with anencephaly.

Results from Morrissey et al. (31) may explain, in part, the reason for inorganic arsenic-induced neural tube defects. They report that 24 h after intravenous administration of radiolabel led arsenic acid (0.4 µg As/kg) to pregnant mice on day 7 of gestation, the neuroepithelium has the highest concentration of radiolabel led arsenic of all embryonic tissue examined.

Fisher (19) examined the effect of sodium arsenate (45 mg/kg) on DNA, RNA and protein levels in developing rat embryos after intraperitoneal administration. The rats were killed on day 10, having received arsenate 4 h or 24 h before euthanasia. The embryos were removed and the macromolecule levels were determined then, or at 24 or 42 h after being placed in culture media. *In utero* exposure to arsenate for 4 h did not affect the macromolecule levels. A 24-h *in utero* exposure to arsenate resulted in a significant decrease in DNA, RNA and protein accumulation. The levels were still significantly lower than control at 24 h; by 42 h, the RNA and DNA were still significantly lower, but the protein levels had recovered. After 24 h in culture, and 48 h after exposure to arsenate, morphological changes in the arsenate-exposed embryos included a failure to rotate to a ventroflexed position, failure of closure of the anterior neuropore, no establishment of visceral yolk sac circulation, and no fusion of the allantoises sac in placental formation. The latter effect may reflect problems in formation of the urogenital system.

Nordstrom et al. (33) did not observe any teratogenic effects in mice or rabbits orally administered arsenic acid. In this study, mice were administered 0–48 mg/kg per day arsenic acid on gestation days 6–15. Rabbits were administered 0–3 mg/kg per day arsenic acid on gestation days 6–18.

Repeated inhalation exposure of GaAs to pregnant rats (see section 7.1.5.1) on gestation days 4–19 resulted in an increased incidence of skeletal variations. This effect became statistically significant at 37 mg/m^3 GaAs. Repeated inhalation exposure of GaAs to pregnant rats on gestation days 4–19 resulted in an increased incidence of skeletal variations.

b) *In vitro*

Inorganic arsenic is teratogenic to cultured mouse embryos (day 8), with sodium arsenite (1–4 µmol/litre) being approximately 10-fold more effective than sodium arsenate (10–40 µmol/litre) after a 48-h incubation (8). The most sensitive *in vitro* effect of arsenic is hypoplasia of the pros encephalon. Other effects include failure of neural tube closure and development of limb buds and sensory placode, somite abnormalities and, in the arsenate-exposed embryos, hydro pericardium.

Arsenite inhibits chondrogenesis in chick limb bud mesenchymal cells, with complete inhibition at 25 µmol/litre (8). Arsenate was ineffective at concentrations up to 200 µmol/litre, but when added with arsenite, gave an apparent dose-dependent additive effect.

Sodium arsenite (50 µmol/litre) induces dysmorphology in rat embryos (10 days old) after 2.5 h exposure and followed by a 21.5 h incubation without arsenic.

This effect is characterized by hypopiastic prosencepahon, miid sweliing of the rhomb encephaion, and abnormal somites and flexion of the tail (31).

Tabacova et al. (49) examined the teratogenicity of arsenite (1–30 μmoi/iitre) and arsenate (5–100 μmol/litre) in mouse embryos isolated from pregnant dams on day 9 of gestation. The embryos were incubated with various concentrations of arsenic, for different lengths of time, and at various stages of somite development. Arsenic induced effects such as non-closure of the neural tube, collapsed neural folds, pros encephalic hypoplasia, exophthalmia, pharyngeal arch defects and abnormal somites. The malformation rates were dependent on the dose and oxidation state of arsenic. Arsenite was generally 3–4 times more potent than arsenate in inducing these effects. As the age of the embryos advanced, a higher dose of arsenic was required to elicit the effect. The most sensitive developmental effect to inorganic arsenic was forebrain growth, neural tube closure, eye differentiation, axial rotation (dorso- to ventroflexion) and pharyngeal arch development, which were induced by a 1-h exposure to inorganic arsenic. The authors suggested that, because the *in vitro* malformation pattern is similar to that observed *in vivo* after maternal administration, inorganic arsenic is the toxicant.

3.1.2.2 Effect of methylated arsenicals MMA & DMA

The methylated arsenicals MMA and DMA have been examined for toxic effects in embryos and fetuses, because they are *in vivo* metabolites of inorganic arsenic, which is a reproductive toxicant in laboratory animals.

***In vivo* embryo and fetal toxicity**

A single intravenous administration of MMA (disodium salt) or DMA (sodium salt) on day 8 of gestation at dose levels of 20–100 mg/kg elicited a low resorption rate (10%) in pregnant hamsters (57). At higher doses of DMA (sodium salt, 900–1000 mg/kg) administered intraperitoneally to pregnant hamsters on one of days 8–12 of gestation higher resorption rates occur, ranging from 30–100% of the litters (22). The disodium salt of MMA (500 mg/kg) is less toxic after intraperitoneal administration than DMA, with 6–21% of the litters resorbed. Fetal growth was retarded after administration of MMA on days 9, 10 or 12.

DMA administered orally to pregnant mice (200–600 mg/kg per day) and rats (7.5–60 mg/kg per day) on days 7–16 of gestation resulted in significant fetal mortality in mice at 600 mg/kg per day and rats at 50–60 mg/kg per day . A significant decrease in fetal weight gain was observed in mice at 400–600 mg/kg and rats at 40–60 mg/kg.

3.1.2.3 Teratogenicity of MMA & DMA

MMA (disodium salt, 20–100 mg/kg) and DMA (sodium salt, 20–100 mg/kg) induced a low percentage of malformations (□ 6%) after intravenous administration on day 8 of gestation in pregnant hamsters (57). The effects were characterized by fused ribs, renal agenesis or encephalocele, with the latter anomaly observed only with DMA. Neither MMA nor DMA caused maternal toxicity after intravenous administration in these animals.

DMA (sodium salt, 900–100 mg/kg) induced more (3–100% of fetuses) gross (cleft palate and lip, micromelia, syndactyly, anencephaly, talipes) and skeletal (fused ribs) fetal malformations than MMA (disodium salt, 500 mg/kg) (< 4% of fetuses) after intraperitoneal administration on one of days 8–12 of gestation (22). Up to 50% and 37% respectively of the pregnant hamsters died after intraperitoneal administration of DMA and MMA (22).

Cleft palate in the mice was the major teratogenic response of DMA, and was observed at the two highest doses. There was also a significantly decreased incidence of supernumerary ribs. In the 400 mg/kg per day group, four mouse fetuses had irregular palatine rugae. In the rat, the average number of sternal and caudal ossifications was decreased at the two highest doses and the percentage of irregular palatine rugae increased significantly with dose. A dose-related decrease in maternal weight gain and increase in lethality occurred at the highest dose for the mice (59%) and the two highest doses for the rat (14–67%).

3.2. Effects on Human

Series of reproductive outcomes have been examined among female employees and women living close to the Rönnskär copper smelter in Sweden. Nordstrom et al. (33) compared birth weights of all offspring of women employed at the Rönnskär smelter during a 2-year period (1975–1976), categorized in three main groups according to their work location: factory, laboratory and administration. Information was also collected for infants of women who lived in four areas close to the smelter but at increasing distances. Births from the University Hospital in Umeå, a city distant from the smelter, were used as external controls. The average birth weight of infants of Rönnskär employees and of women living closer to the smelter were significantly lower than those from the two more distant areas and from Umeå. Among employees, those working in the laboratory had larger babies than those in the factory or in administration. In general, the effect was mainly observed in higher pregnancy orders (second born or later). Contrary to what is generally observed, there was a decrease in the average birth weight of offspring of higher parity among employees.

Nordstrom et al. (33) reviewed data from hospital files on over 4427 pregnancies of women born in or after 1930 who lived in four areas of increasing distances from the smelter. A control group of 4544 pregnancies was used from a hospital in Umeå, a non-exposed town. There was a clear dose–response relationship between the occurrence of spontaneous abortions and residential proximity to the smelter. In particular, women in the closest town (< 10 km from the smelter) had the highest rates (11% vs. 7.6%, $p < 0.005$). In the most exposed area, 4 of 20 women with abortions had had 2 abortions and no normal pregnancies. No women with such reproductive history were found in the other three areas.

In a further study (35), the previous analysis (34) was expanded to cover 662 births among women employed in or living near the smelter and in the unexposed town of Umeå in 1930–1959. Personal questionnaires were used to assess exposure and confounding factors. The average birth weight of babies born to employees was significantly lower than those born in Umeå ($p < 0.05$); in addition, birth weight was lower if the mother worked in the highest exposure categories (e.g. smelting and cleaning operations) rather than in lower exposure jobs. Most differences were found for the birth weight of third or later-born infants, which the authors proposed to be caused by the cumulative exposure with age. The differences were not found to be confounded by the gestational ages. Spontaneous abortions were highest when the mother was employed during pregnancy (14%) or before pregnancy and living near the smelter. Within employment categories, significantly higher rates of abortion were observed in high exposure jobs (28% vs. 14%, NS). The abortion rate was even higher if the father also worked at the smelter, not just the mother (19% vs. 14%; statistical significance not provided). Individual smoking data was not given, although no differences were found between the smoking rates of the different groups.

Nordstrom et al. (35), in an investigation of the occurrence of congenital malformations, found rates of 5.8% among infants born to female employees who worked at the smelter during pregnancy, compared to 2.2% among female employees who did not work ($p < 0.005$) and 3% among residents in the larger region. Multiple malformations were four times more common among employees working during pregnancy than among residents in the larger region.

Most of these studies by Nordstrom and co-workers had an ecological design with little or no information on other factors. Although arsenic exposures in and around the Rönnskär smelter were high, confounding from lead or copper could not be excluded. In addition, no adjustments were made for the effects of other potential confounding risk factors, such as maternal age, which is known to have a strong relationship to spontaneous abortion and congenital anomalies.

Zierler et al. (63) compared 270 cases of infants born with congenital heart disease and 665 controls from Massachusetts (USA). The POR, adjusted for all measured contaminants, source of water, and maternal education, for any congenital heart disease in relation to any arsenic exposure above the detection limit of 0.8 µg/litre, was not elevated. However, for a specific malformation, coarctation of the aorta, there was a significant POR of 3.4 (1.3–8.9). The exposure was quite low, the 90th percentile level being 1 µg/litre.

On the basis of information from a previous case–control study of spontaneous abortions in Boston, Aschengrau et al. (2) examined 286 women who experienced spontaneous abortions and 1391 controls in relation to the content of their water supplies. An adjusted odds ratio of 1.5 was found for the group with the highest arsenic concentrations. However, this exposure group had low levels of arsenic in water (1.4–1.9 µg/litre), close to or lower than laboratory analytical detection limits, and the possibility of chance or unaccounted confounders could not be discounted.

A study in an area of south-east Hungary (5) with exposure to arsenic from drinking-water examined the rates of spontaneous abortions and stillbirths for the period 1980–1987. Two populations were compared: one with levels of arsenic in drinking-water > 100 µg/litre (n = 25 648 people) and one control area with low arsenic levels (n = 20 836) (no information on analytical method, or timing or frequency of sampling was available). Both outcomes were significantly higher in the exposed groups, with a 1.4-fold increase in spontaneous abortions (p = 0.007) and a 2.8-fold increase in stillbirths (p = 0.028). Although both populations were reported to be similar in several characteristics, such as smoking, lifestyle, occupation and socio-economic status, no information was provided, and other important factors such as smoking and maternal age were not accounted for. Furthermore, no mention was made of other potential environmental exposures; in populations of roughly similar size, the number of live births during the study period, 1980–1987 was 5218 in the high- and 2112 in the low-exposure area; it was stated that no significant differences were observed in the cancer frequency; the frequency of spontaneous abortions was unusually low, 7 and 5%, respectively.

Another study in Bulgaria (49) included 34 maternal–infant pairs from the smelter area and 15 from a non-smelter area free from industrial exposures. Information regarding lifestyle characteristics, occupation, residence and medical history was ascertained by personal interviews. Samples of maternal and cord blood and placenta were obtained for analysis of arsenic, cadmium and lead concentrations. Infants born in the proximity of the smelter had lower birth weight (3012 vs. 3193 g). Although the study was small, these differences were also observed when divided into smoking and parity sub-groups. Placental concentrations of arsenic were three times higher ($p < 0.001$) in the smelter area, but cadmium levels were also elevated although the difference was not statistically significant. There was no difference in average lead levels in the two exposure areas.

A study conducted in the USA (16) investigated mortality from vascular diseases in the 30 counties with the highest average levels of arsenic in drinking-water for the period 1968–1984. The levels ranged from 5.4 µg/litre in Pierce County, Washington to 92 µg/litre in Churchill County, Nevada. When counties were grouped in three arsenic exposure categories, defined as 5–10, 10–20 and > 20 µg/litre, there appeared to be an increase in mortality from congenital anomalies of the heart only for females in the highest exposure group (SMR = 130, 90% CI (100–180), and for both sexes for congenital anomalies of the circulatory system (female SMR = 200, CI (110–340); male SMR = 130, CI (70–240). Slight increases in congenital anomalies of the heart and other anomalies of the circulatory system were found for two counties in the highest exposure group (29 and 46 μg As/litre in water, respectively), but none were found for Churchill County, which has the highest arsenic levels (92.5 μg/litre).

A hospital case–control study in the USA investigated the occurrence of stillbirths in relation to residential proximity to an arsenical pesticide production plant in Texas. Exposure was categorized in three groups according to arsenic air levels. An increasing, but not significant, trend in the risk of stillbirths was observed. The number of stillbirths was significantly elevated for the high-exposure group. When stratified by ethnicity, however, the findings remained significant for Hispanics only. Other exposures from the chemical plant were possible and were not measured in the study.

An ecological study examined infant mortality rates in three Chilean cities over a 46-year period (1950–1996) (23) . Antofagasta, in northern Chile, experienced very high arsenic levels in drinking-water for a period of 12 years. In 1958 a new water source which contained arsenic concentrations around 800 μg/litre was introduced as the main supplier of public water. In 1970, because of the overt signs of arsenicism observed in several studies, an arsenic removal plant was installed, and levels decreased initially to around 100 μg/litre, and then gradually over time to around 40 μg/litre. The changes in late fetal, neonatal and post-neonatal mortality rates over time in Antofagasta were compared to those in Valparaiso, another Chilean city with similar demographic characteristics but low in arsenic, and the capital, Santiago, with similarly low concentrations arsenic in the drinking-water. A close temporal relationship was observed between the high arsenic period and a rise in mortality rates in Antofagasta, whereas the other two cities had a steady decline in infant mortality. Fig. 5 shows the rates for neonatal mortality. Although data on other contaminants or factors related to infant mortality were not presented, the temporal relationship strongly suggests a role for arsenic exposure.

Two case-control studies addressed the association between arsenic in community drinking water and adverse reproductive outcomes. In a study of 270 cases of children with congenital heart disease compared to 665 control patients, Zierler *et al,* (62) examined the association between four cardiac defects and *in utero* exposure to nine metals. The authors found an increased frequency of coarctation of the aorta (Prevalence Odds Ratio = 3.4; 95% CI:1.3-8.9) among children born to mothers residing in areas with detectable levels of arsenic in the community water supply during the first trimester of pregnancy. No association was detected between arsenic levels in water and occurrence of the three other cardiac lesions investigated. Because of limitations in the study design, including assessment of multiple exposures and outcomes and lack of information regarding actual consumption of drinking water among the pregnant women, it is not possible to conclude from this study that the association with the observed heart defect is not explained by chance alone, or to eliminate the possibility that other malformations may be associated with exposure to inorganic arsenic.

In another study, Aschengrau *et al.,* (2) evaluated exposure to arsenic in 286 women with evidence of spontaneous abortion compared to 1391 control women. The crude odds ratio of exposure to inorganic arsenic in drinking water among cases compared to controls was 1.3 (95% CI: 1.0-1.6). Exposure to water containing higher arsenic levels was more strongly associated with spontaneous abortion than exposure to lower arsenic levels. After adjustment for multiple cofounders using a multiple logistic regression model, only exposure to higher levels of arsenic (1.4-1.9 μg/L) was found to be associated with spontaneous abortion and the magnitude of association was small and not statistically significant (Exposure Odds Ratio 1.5; 95% CI: 0.4-4.7).

There are three case reports of inorganic arsenic poisoning in pregnant women. In all cases, the mothers survived under clinical care. In one case, the mother ingested arsenic at 30 weeks gestation and delivered a premature infant 3 days later which died the same day. In the second case, 28 weeks pregnant, intrauterine death occurred 4 days after poisoning and toxic levels of arsenic were found in fetal tissues (Bollinger, *et al.,* 1992). In the third case, 20 weeks pregnant, chelation therapy was immediately initiated and a healthy infant was delivered at 36 weeks (12).

Hopenhayn-Rich C et al(23) also found positive association between arsenic drinking water exposure and adverse reproductive outcomes (spontaneous abortion, still birth, low birth weight). These studies provide supportive evidence for the findings for the findings of the study by ahmed et al.(1)

In the historical cohort study of Ahmed et al. (1), the incidences of three adverse pregnancy outcomes (spontaneous abortion, still birth, preterm birth) were determined by interviews using a questionnaire and check list. Respondents (n=96 per group) were randomly selected from the exposed population and controls were matched for age, education and socio-economic status. Statistical comparisons were made between a low exposure community (drinking water concentration < 0.02 mg As/L) and a high exposure community (drinking water concentration > 0.05 mg As/L in 85% of Wells). Subgroups within the high exposure community with briefer and longer exposures (5-15 years or > 15 years) were also compared. The risk of spontaneous abortion, still birth or preterm birth in the exposed group was more than double that of the unexposed group ($p < 0.05$, Fishers exact test , one sided). Comparisons of these adverse pregnancy outcomes between shorter and longer exposures were also statistically significant.

Milton. A.H et ai (27) in his study " Exposure to arsenic increase risk of adverse pregnancy outcomes" was conducted over married , non smoking females of reproductive age ranging from 15-49 years with the mean age of 31.22 years with a history of at least one pregnancy. They were studied to determine the association between chronic arsenic exposure through drinking water and spontaneous abortion, still birth and neonatal death.

Excess risks for spontaneous abortion, still birth and neonatal death were observed among the participants exposed to increasing concentration of arsenic in drinking water, after adjusting for participants' education, age at marriage, antenatal care and parity. The study findings further largely suggested that chronic arsenic exposure can increase the risk of adverse pregnancy outcome.

To investigate the relationship between community drinking water and spontaneous abortion, ***A Aschengrau*** *et al (2) in study "Quality of community drinking water and the occurrence of spontaneous abortion"* compared trace elements mainly arsenic levels in the drinking water of 286 women having a spontaneous abortion through 27 wk gestation with that of 1391 women having live births. Trace elements level were gathered from routine analysis of public tap water supplies from the communities where the women resided during pregnancy. After adjustment for potential confounders, an increase in the frequency of spontaneous abortion was associated with detectable level of high level of arsenic.

Chapter-4

4. Material and Methods

This study has been carried out as a case comparative cross sectional study among the arsenic affected married women (15-49) of Bera and Sujanagar Upazllas(exposed area) and arsenic free women of Santhia Upazilla (unexposed area) of Pabna.

Study population:

The study population was composed of marrled women of reproductive age (15-49 years) who prevlously had at least one pregnancy, of Sujanagor, Bera and Santhia upazillas of Pabna district. The exposed group (Bera & Sujanagar) consisted of women who had been drinking arsenic contaminated water (> 0.05 mg/l) for at least three years, where as the non exposed group (Santhia) consisted of respondents who had been drinking arsenic free safe water.

For the exposed group

Inclusion criteria

All married women of reproductive age (15-49 years) group with history of exposure to arsenic contaminated water and signs / symptoms of chronic arsenicosis may or may not present as determined by the following characteristics were included:

- Only marrled women were included.
- Using arsenic contaminated water
- Age- 15-49 years of age

- At least one pregnancy
- No history of smoking
- Had been living in the study area since their marriage and to have drunk water from the respective tube well before and during the pregnancy,
- Voluntary consent for participation.
- Skin manifestation may or may not be present: melanosis, keratosis and keratomelanosis.

Exclusion criteria

- Unmarried women
- Not taking arsenic contaminated water
- Age below 15 and over 49 years
- No more pregnancy
- Temporarily living in the study area and to not to have drunk water from the respective tube well before and during the pregnancy,
- History of smoking
- Patients refusing consent.
- Patient having concurrent illness due to other causes such as tuberculosis, known skin infections or other chronic illness.

For Non exposed group

Inclusion criteria

All married women of reproductive age (15-49 years) group with no history of exposure to arsenic contaminated water and no signs / symptoms of chronic arsenicosis as determined by the following characteristics were included.

- Only married women were included.
- Age- 15-49 years of age
- At least one pregnancy
- No history of smoking
- Had been living in the study area since their marriage and to have drunk water from the respective tube well before and during the pregnancy,
- Voluntary consent for participation.
- Drinking arsenic free water from the beginning
- Skin manifestation is absent: melanosis, keratosis and keratomelanosis.

Exclusion criteria

- Unmarried women
- Patients refusing consent.
- Drinking arsenic contaminated water for the long time (At least five year, from the time of detection)
- Patient having concurrent illness due to other causes such as tuberculosis, known skin infections or other chronic illness.

Baseline information

In this study, baseline information was taken from Department of public Health Engineering (DPHE) and Dhaka Community Hospital trust (DCHT). Dhaka

Community Hospital trust conducted several surveys in the Bera and Sujanagar Upazilla of Pabna District. The ground water survey already carried out by the Department of public Health Engineering (DPHE) and Dhaka Community Hospital trust in the above-mentioned areas. The base line information included the following :

- Age, sex, personal data
- Socioeconomic data.
- Area, location , household number
- Family size
- Water use data
- Arsenic detection of the tube well water
- Skin manifestation.

Sample size determination

To calculate the sample size the researcher consider the hypothesis of two population proportions. For a one-sided test the formulae used :

$$n = \{z_{1-\alpha}\sqrt{[2\overline{P}(1-\overline{P})]} + z_{1-\beta}\sqrt{[P_1(1-P_1)+P_2(1-P_2)]}\}^2 / (P_1 - P_2)^2$$

Where $\overline{P} = (P_1 - P_2)/2$

In this study P1=proportion of women who have spontaneous termination exposed to arsenic contamination water.

P2= Proportion of women who have spontaneous termination unexposed to arsenic contamination water

Different study says that spontaneous termination lies between 5 % to 10 % (ICDDRB, annual report 2004).

Assumption based on P1=5 % and due to the adverse effect of arsenic poisoning the rate increases up to double then with 95 % confidence interval and 90 % power the estimated sample for one sided test is 474 (S.K. Lwanga and S Lemeshow, p 36). Considering 5 % missed information we have collected 500 respondents for each of the two groups.

The women were asked starting from a corner of the Arsenic contaminated area and Arsenic free area & ended as soon as 500 women were interviewed.

The study was cross sectional case comparative study. The study was carried out among the married pregnant woman of three upazilias. The information about exposed and control were collected from both upazillas through questionnaire.

Study Place

The following three upazillas of pabna district were selected for the study

- Sujanagar
- Bera,
- Santhia

Sujanagor upazilla- 20 KM away from pabna town, Area: 334 sqkm, Population: 274213, Male: 144033, Female: 130180, Total union : 10, Total Village : 172

Total household: 45246, Total eligible couple: 45671, Total 15-49 years women: 53700

Bera upazilla- 50 KM away from pabna town. Area : 249 sq km, Total population : 264535, Male : 136938, Female : 127597, Total village : 166, Total union : 8

Total household: 46979, Total eligible couple: 45863, Total 15-49 years age women: 55870

Santhia upazilla- 40 KM away from pabna town. Area : 266 sq km,Total population : 359896, Male : 186518, Female : 173378,Total village :Total union : 11,

Total household: 66475, Total eligible couple: 68057

Total 15-49 years age women: 89073

Justification for selecting of the places of study

Pabna is one of the districts, where a huge number of community people were affected by arsenicosis.

Considerable numbers of arsenicosis patient were detected in DPHE (BAMWSP) & Dhaka Community Hospital trust (DCHT) authority according to WHO definition.

Communication with the selected study area was good.

Laboratory Method

The following equipment used :

Atomic Absorption Spectrophotometer with hydride Generation (AAS-HG) and flow injection system and a continuous flow of hydride generation atomic absorption spectroscopy system.

Research Instrument

After a preliminary observation and literature review a questionnaire was developed which included question on some selected parameters related to chronic arsenic poisoning of the pregnant women, outcome of pregnancy in relation to arsenic poisoning. The questionnaire included both open ended and close-ended type. The questionnaire was finalized after modification following pre-testing.

Data collevtion & Field surveillance

The selected trained field workers visited each household daily and interviewed the patients and all relevant data on the questionnaire according to the time schedule collected. The women were asked starting from a corner of the exposed and non exposed area and ended as soon as 500 women were interviewed.

Training of field staff

The field staffs were recruited and trained in field survey methods including home visit procedures, interview techniques, distribution of questionnaire, data collection and observations.

Research Manpower

There were one part time medical officer, two full time female supervisor (one for the exposed area and one for the control area) , two trained paramedic and ten field workers for the exposed and control area. These field staff was kept blind to the arsenic concentration of the tube well water to reduce bias, although complete blindness was not possible because most of the tube wells had previously been painted red or green to identify the presence or absence of arsenic concentration. The purpose of the interview was explained to the participants, and verbal consent was obtained before beginning each interview.

Training session were organized in the field office of Dhaka Community Hospital in Bera upazilla included clinical demonstration of arsenic affected patients, characterization of skin changes in palm and sole, recording of body weight, height, blood pressure, and other parameters. Field workers were also trained in collection of water samples from tube wells, ponds, river, and filters. Body weights were taken by calibrated wet machine. Body height was measured with vertical length board measuring nearest to 1 mm. Blood pressure was obtained in patients in lying position using standard sphygmomanometer. Random blood sugar was done by using the mobile glucometer

Quality assurance procedure

It has carefully followed all data quality assurance procedures during the progress of the study. Field workers visited every day under the supervision of field supervisor. The data were collected by asking question, observation and in-depth-interview with the client and recorded in the supplied questionnaire form In addition, medical officer monitored and supervised activities at all levels. Samples were collected following standard procedures, properly transported and preserved appropriately. Collected data at field were entered in to computer and kept under strict confidentiality until final analysis was complete. Samples of water were sent to the laboratory under special codes without reference to names and identity of patients to prevent observer's bias.

Ethical consideration:

Participation in the study was voluntary although collection of data were done among the listed arsenic affected women < 15-40 yrs > of exposed samples group. The study objective was informed to all participants and their parents in advance. The interviews were done at suitable time and convenient location to the participants was maintained.

Data analysis

All data were collected according to the prescribed interview schedule and directly entered in to computer without intermediate coding. Statistical analysis was carried out by using standard software package, such as SPSS, EpiInfo etc.

Limitation of the study:

Recall bias: Women were asked to recall their pregnancy history regarding early termination. There is possibility of misclassification of early termination with menstrutation especially for the first trimester of the pregnancy. Women can also hide their early termination history because of social problems. Recal bias of early termination to be an under estimation of the incidence rate of abortion for the selected arsenic contamination area. In the arsenic free area, this recall bias will be minimum since the risk early termination is half compare to the contamination area.

Selection bias: The women were asked starting from a corner of the contaminated area and ended as soon as 500 women were interviewed. There is a possibility have minor sample error if there is any difference between the arsenic level of women who were interviewed and the women who were not interviewed within the contaminated area.

Chapter-5

5. FINDINGS

Table-1: Household, eligible women, tube well tested by total number.

Result	Exposed	Non exposed	Total
Total household	425	416	841
Eligible women interviewed (15-49	500	500	100
Total tube well tested	174	181	355

Among, 500 respondents, 425 households in the exposed group, and 416 in the non exposed group. Among the households, 174 tube well were tested in the exposed (Red mark) group and 181 tube well in the non exposed group.The same represented below by figure.

Figure-1

Number of total household, total elligible women, total tube water tested

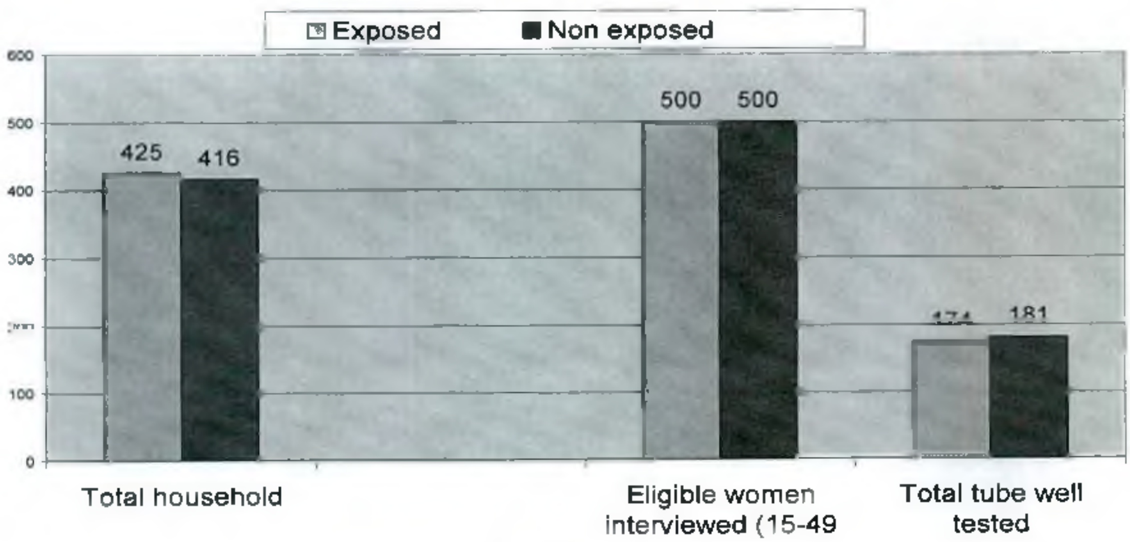


Table-2: House hold population of the female respondents and Percentage distribution by age group 15-49 years

Cross tabulation

Age	Exposed	Non exposed	Total
15-19	130 (26.1 %)	140 (28.2 %)	270 (27 %)
20-24	115 (23.2%)	105 (21.1 %)	220 (22 %)
25-29	90 (18.4 %)	82 (16.4 %)	172 (17 %)
30-34	63 (12.6 %)	73 (14.6 %)	136 (13.6 %)
35-39	53 (10.6 %)	46 (9.2 %)	99 (9.9 %)
40-44	25 (5.1 %)	31 (6.2 %)	56 (5.6 %)
45-49	24 (4.0 %)	23 (4.3 %)	44 (4.4 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

The above table shows the distribution of age of married women both in the exposed and non exposed groups. Average age of the female respondents was 15-19 years, and about 26 % in the exposed group and 28 % in the non exposed group. The second highest age group were 20-24 years and included 23 % in the exposed and 21 % in the non exposed group.

Table-3: Level of education: Women

Total number of Respondents and their Percentage distribution by level of education

Level of education	Exposed	Non exposed	Total
No education	200 (40 %)	160 (32 %)	360 (36 %)
Primary incomplete	145 (29 %)	155 (31 %)	300 (30 %)
Primary completed	40 (8 %)	40 (8 %)	80 (8 %)
Secondary incomplete	95 (19 %)	115 (23 %)	210 (21 %)
Secondary completed & above	20 (4 %)	30 (6%)	50 (5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

According to Table 3, majority of respondents (40 % in the exposed group and 32 % in the non exposed group) had no education. Only 6 % in the exposed group, 4 % in the non exposed group attended or completed secondary education.

Table-4: Level of education of the Male (Respondents husband)

Total number of the male and their Percentage distribution by level of education.

Level of education	Exposed	Non exposed	Total
No education	150 (30 %)	160 (31 %)	310 (31 %)
Primary incomplete	170 (34 %)	320 (32 %)	320 (32 %)
Primary complete	40 (8 %)	90 (9 %)	90 (9 %)
Secondary incomplete	90 (18 %)	170 (17 %)	170 (17 %)
Secondary complete & higher	50 (10 %)	110 (11 %)	110 (11 %)
Total	**500(100 %)**	**500(100 %)**	**1000(100 %)**

The above table shows that 34 % of the respondents in the exposed group & 32 % in the non exposed group did not complete primary level education. Only 10 % in the exposed group 11 % in the non exposed group completed the secondary education.

Table-5: Employment status: Women

Total respondents and their Percentage distribution by employment status

Employment status	Exposed	Non exposed	Total
Not employed	405 (81 %)	390 (78 %)	795 (79.5 %)
Work all year	60 (12 %)	50 (10 %)	110 (11 %)
Work seasonally	20 (4 %)	35 (7 %)	55 (5.5 %)
Work Occasionally	15 (3 %)	25 (5%)	40 (4 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100%)**

According to table-5, out of the respondents 81 % in the exposed group and 78 % in the non exposed group were not currently employed. Only 12 % in the exposed group and 10 % in the non exposed group are currently employed during the year

Table-6: Employment status: Male (Respondents Husbands)

Total number of male and their percentage by employment status

Employment status	Exposed	Non exposed	Total
Not employed	75 (15 %)	90 (18 %)	165 (16.5 %)
Work all year	360 (72 %)	340 (68 %)	700 (70 %)
Work seasonally	50 (10 %)	30 (6 %)	80 (8 %)
Work Occasionally	15 (3 %)	40 (8 %)	55 (5.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

The above table shows 15 % in the exposed group & 18 % in the non exposed groups donot have any employment, whereas 72 % in the exposed & 68 % in the non exposed group had employment.

Table-7: Household characteristics

Distribution of Respondents by household charecterstics

Total Households= 425 (In the exposed area), 416 (in the non exposed area)

Charecterstics	Exposed	Non exposed	Remarks
Electricity			
Present	32 %	35 %	
Absent	68 %	65 %	
Total	**100.0 %**	**100.0 %**	
Sanitation facility			
Modern toilet/ septic tank	4.1 %	3.8 %	
Water sealed latrine	11.6 %	12.5 %	
Pit latrine	37.1 %	38.8 %	
Open latrine	28.2 %	30.1 %	
Hanging latrine	2.3 %	1.1 %	
No other facility	16.7 %	13.7 %	
Total	**100.0 %**	**100.0 %**	
Food consumption			
Deficit in whole year	15.1 %	13.0 %	
Sometime deficit	40.2 %	37.2 %	
Neither deficit nor surplus	38.7 %	41.1 %	
Surplus	6 %	8.7 %	
Total	**100.0 %**	**100.0 %**	
Cooking fuel			
Wood	33.7 %	35.1 %	
Crop residue	52.1 %	54.4 %	
Dung cakes	13.2 %	9.6 %	
Liquid gas	0	0	
Other	1 %	.9 %	
Total	**100.0 %**	**100.0 %**	
Main roof material			
Mud / Jute / Bamboo	49.0 %	46.6 %	
Wood	1.1 %	1.5 %	
Brick / Cement	5.1 %	6.8 %	
Tin	44.8 %	45.1 %	
Total	**100.0 %**	**100.0 %**	
Floor material			
Earth (Kacha)	95.0 %	93.0 %	
Wood	0	0	
Cement	5.0 %	7.0 %	
Total	**100.0 %**	**100.0 %**	

The above table represents that 32% had electricity in exposed group , while 35% in non exposed group. Water sealed latrine 11.6% and 12.5 % had in exposed and non exposed groups respectively.Food consumption were found deficit in the whole year 15.1 % and 13% in the exposed and non exposed groups. In regard to find for cooking majority 52% and 54% used in exposed and non exposed group respectively. Majority respondents <49% exposed and 46% used mud, jute, bamboo as roof materials and almost similar percentage used tin. Allmost all < 95% exposed group and 93% non exposed group> had kacha floor and only 5% and 7% had cement floor for exposed and non exposed group respectively.

Table-8: House hold land ownership

Respondent's household possession and percentage distribution by land ownership

Ownership pattern	Exposed	Non exposed	Remarks
Owns a homestead	460 (92 %)	470 (94 %)	930
Own other land	260 (52 %)	230 (46 %)	490
None of the above	40 (8 %)	30 (6 %)	70

According to the table, 92 % in the exposed group and 94 % in the non exposed group owned a house for living. Whereas 52 % in the exposed group and 46 % in the non exposed group own land other than homestead.

Table-9: House hold composition

Distribution of Percentage of household by size

Family member	Exposed	Non exposed	Total
1 (One)	10 (2 %)	15 (3 %)	25 (2.5%)
2 (Two)	25 95 %)	30 (6 %)	55 (5.5 %)
3 (Three)	65 (13%)	55 (11 %)	120 (12%)
4 (Four)	120 (24 %)	130 (26 %)	150 (15%)
5 (Five)	80 (16 %)	70 (14 %)	180 (18%)
6 (Six)	85 (17 %)	95 (19 %)	150 (15%)
7 (Seven)	45 (9 %)	55 (11 %)	100 (10%)
8 (Eight)	30 (6 %)	20 (4 %)	50 (5%)
9 (Nine)+	40 (8 %)	30 (6 %)	70 (7%)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100%)**

Table 7 shows that 24 % in the exposed and 26 % in the non exposed group of house hold composed of 4 members. Both the exposed and non exposed group 57 % of the household composed of 3-5 members.

Table-10: Sources of drinking water

Distribution of percentage of sources of drinking water

Sources of water	Exposed	Non exposed	Total
Tube well	450 (90 %)	440 (89 %)	890 (89 %)
Deep tube well	15 (3 %)	20 (4 %)	35 (3.5 %)
Surface water	20 (4 %)	15 (3 %)	35 (3.5 %)
Pond	10 (2 %)	20 (4 %)	30 (3 %)
River	4 (.8 %)	5 (1 %)	9 (.9 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

This table shows that most of the respondents (90 % in the exposed & 89 % in the non exposed group) used tube well water for drinking purposes.

Table-11: Sources of cooking water

Distribution of percentage of cooking water

Sources of water	Exposed	Non exposed	Total
Tube well	420 (84 %)	430 (86 %)	850 (85%)
Deep tube well	20 (4 %)	25 95 %)	45 (4.5%)
Surface water	20 (4 %)	15 (3 %)	35 (3.5%)
Pond	30 (6 %)	25 (5 %)	55 (5.5%)
River	10 (2 %)	5 (1 %)	15 (1.5%)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

According to this table, most of the respondents (84 % in the exposed & 86 % in the non exposed group) used tube well water for cooking purposes.

Table-12: Water for washing purpose by sources

Sources of water	Exposed	Non exposed	Total
Tube well	275 (55 %)	300 (60 %)	575 (57.5 %)
Deep tube well	20 (4 %)	30 (6 %)	50 (5 %)
Surface water	50 (10 %)	35 (7 %)	85 (8.5 %)
Pond	150 (30 %)	125 (25 %)	275 (27.5 %)
River	5 (1 %)	10 (2 %)	15 (1.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

The above table shows that most of the respondents (55 % of the respondents in the exposed & 60 % of the respondents in the non exposed group of the household) used tube well water for washing purposes.

Table-13: Use of bathing water by sources

Percentage distribution of household source of bathlng water

Sources of water	Exposed	Non exposed	Total
Tube well	310 (62%)	275 (55%)	585 (58.5%)
Deep tube well	40 (8%)	50 (10%)	90 (9%)
Surface water	25 (5%)	50 (10%)	75 (7.5%)
Pond	100 (20%)	125 (25%)	225 (22.5%)
River	25 (5%)	15 (3%)	40 (4%)
Total	**500 (100%)**	**500 (100%)**	**1000 (100%)**

This table shows that most of the respondents (62 % of the respondents in the exposed & 55 % of the respondents in the non exposed group of the household) used tube well water for bathing purposes.

Table-14: Abstain from drinking tube well water

Percentage distribution of abstain from drinking tube well water

Abstain from drinking tube well water	Exposed	Non exposed	Total
Yes	180 (36 %)	65 (13 %)	245 (24.5 %)
No	320 (65 %)	435 (88 %)	755 (75.5 %)
Total	**500 (100 %)**	**500 (100%)**	**1000 (100 %)**

Most of the respondents 65% in the exposed group and 88% in the non exposed group , told that shallow tube-well were the only source of water for drinking water and they are not abstain to drink the tube well water.

Table-15: Cause of abstaining

Percentage distribution of abstaining of drinking water by causes.

Cause of abstaining	Exposed	Non exposed	Total
Fowl smell	10 (.5 %)	3 (0.6 %)	13 (1.3 %)
Body spot	144 (28.8 %)	Nil	144 (14.4 %)
Spot to other	16 (3.2 %)	7 (1.4 %)	23 (2.3 %)
Due to advice of GO / NGO	8 (1.6 %)	10 (2 %)	18 (1.8 %)
Others	2 (0.4 %)	45 (9 %)	47 (4.7 %)
NA	320 (64 %)	435 (88 %)	755 (75.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

Most of the respondents (29 % in the exposed group) were not taking tube well water due to black spot of others body.

Table-16: Continuing to drink tube well water by causes

Reasons of continuing to drink tube well water	Exposed	Non exposed	Total
All are drinking the same water	64 (12.8 %)	348 (69.6 %)	412 (41.2 %)
Difficult to collect alternate water	134 (26.8 %)	-	134 (13.4 %)
Contaminated dug well	96 (19.2 %)	-	96 (9.6 %)
No other arsenic free water	13 (2.6 %)	-	13 (1.3 %)
Other	13 (2.6 %)	87 (17.4 %)	100 (10.0 %)
NA	180 (36 %)	65 (13 %)	245 (24.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

In this table, 13% of the respondents in the exposed group told that they were drinking the water because most of the peoples were taking and drinking water from the shallow tube well, 27 % told that it was very difficult for them to bring the water, in the exposed group. In the exposed group 19% respondent told the cause of contaminated dug well. On the other hand most of the respondents (69 %) of the non exposed group were continuing to drink the tube well water because they had no such type of information about arsenic

Table-17: Tube well water checked by Govt. / NGO

Percentage distribution of tube well water checked by GO / NGO

Tube well water checked by GO / NGO	Exposed	Non exposed	Total
Yes	480 (96 %)	490 (98 %)	970 (97 %)
No	20 (4 %)	10 (2 %)	30 (3 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

Table 15 shows that most of the respondent in the exposed and non exposed group (96 %, 98% respectively) opined that the representatives from Govt. / NGO had checked their tube well water for arsenic contamination and also put the red mark by using the field kit and collect water for laboratory test.

Table-18: Median age at first marriage

Percentage showing the median age of first marriage among the respondents

Age in Year	Exposed	Non exposed	
15-49	Omitted, because 50 % of the women married for the first time		
20-24	16.1	16.4	
25-29	15	15.3	
30-34	14.8	15.1	
35-39	14.1	14.8	
40-44	13.9	14.2	
45-49	13.6	13.9	
20-49	14.5	14.9	

According to tabie –16, the median age at first marriage rises from 13.6 years for exposed and 13.9 years for non exposed group (for woman age 45-49) to 16.1 years for exposed and 16.4 years for non exposed group (for those age 20-24.). It has been increasing overtime.

Table-19: Suffering from arsenicosis

Percentage distribution among those were sufferings from arsenicosis

Arsenicosis	Exposed	Non exposed	Total
Yes	146 (29 %)	0	146 (14.6 %)
No	354 (71 %)	500 (100 %)	854 (85.4 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

In the exposed group, 29 % thought that they were suffering from arsenicosis and in the non exposed group, 100 % thought that they were not suffering from that case.

Table-20: Presence of black spot in the body

Percentage distribution of black spot in the body

Black spot/ white spot	Exposed	Non exposed	Total
Yes	146 (28 %)	0	146 (12 %)
No	354 (78%)	500 (100 %)	854 (86%)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

Tabie -18 reavealed that only 28 % of the respondents in the exposed group narrated the black spot / white spot in their body, where as in the non exposed group <100 %> no spot in their body.

Figure-3

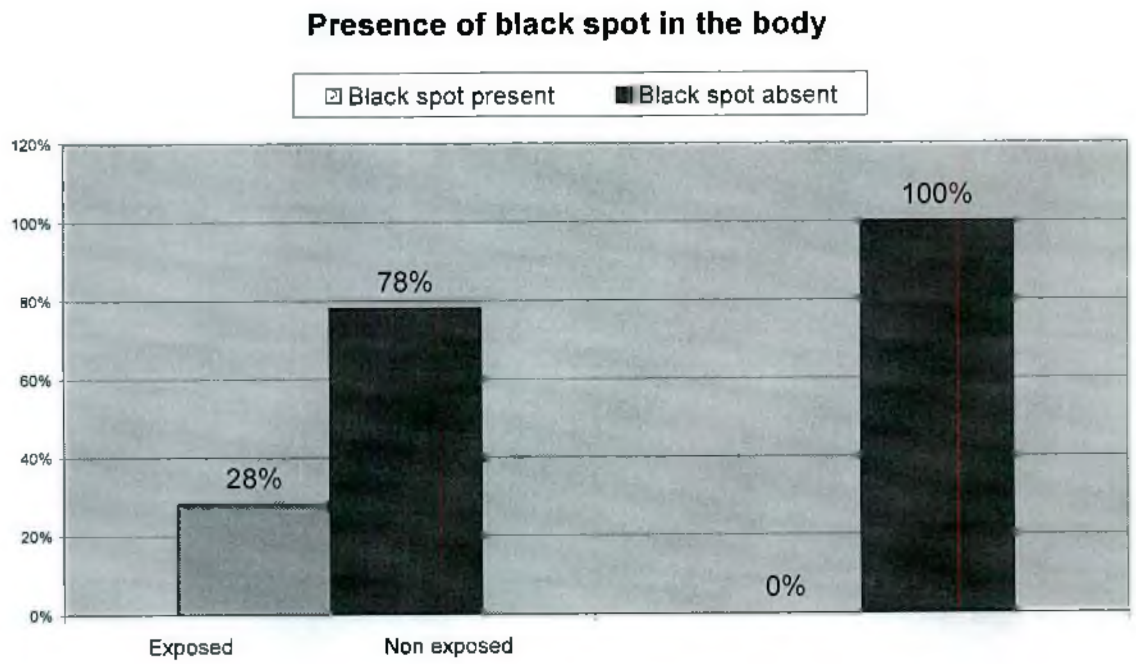


Table-21: Thickening of sole and palm

Percentage distribution among those were developed thickening of sole and palm <Keratosis>

Thickening of palm and sole	Exposed	Non exposed	Total
Yes	67 (13.4 %)	15 (3 %)	82(8.2%)
No	433 (86.6 %)	485 (97%)	918(91.8%)
Total	**500(100 %)**	**500(100 %)**	**1000(100 %)**

Table-20, shows that, only 13.4 % of the respondents in the exposed group skin thickened where 86.6% answered negative.

Figure-4

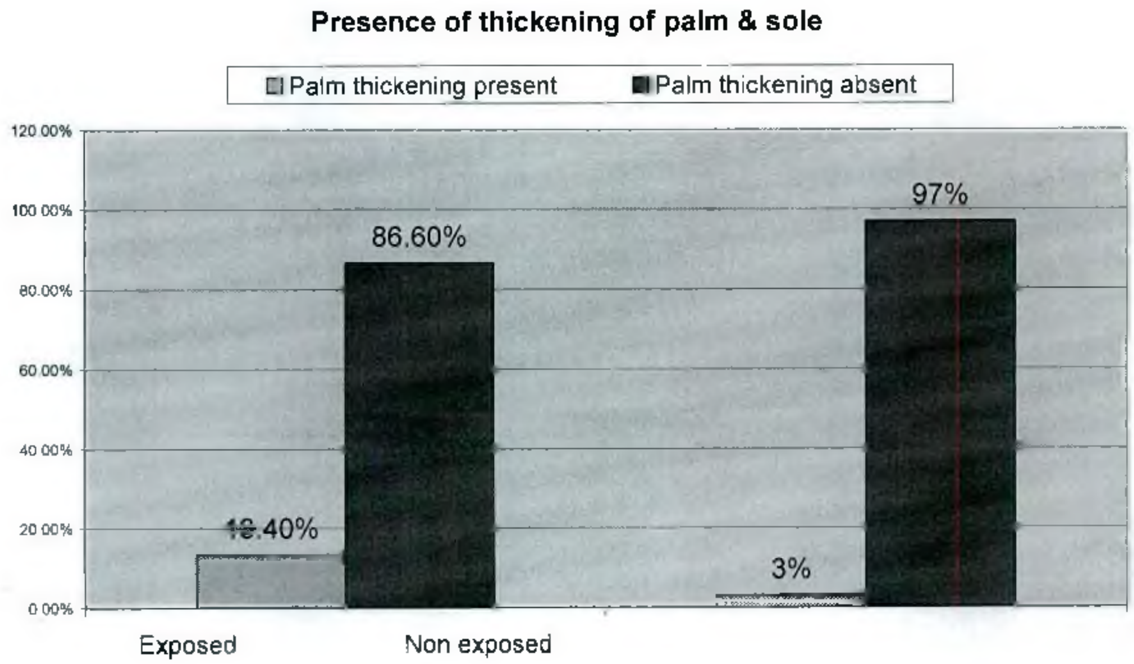


Table-22: Baseline characteristics of the respondents by Clinical findings.

Characteristics	Exposed	Non exposed
Body weight, kg mean ± Sd	43.4 ± 12.5	43.3± 12.8
Body height, inches, mean ± sd	60.7 ± 3.9	61.2 ± 3.1
Body mass index (BMI) %		
Malnourished (BMI <20)	74.1	73.7
Normal (BMI 20-24.9)	25.8	26.7
BMI, Mean ± SD	17 ±2.1	18.8 ± 2.4

The mean body weight of the exposed group is 43.4 ± 12.5 and the non exposed i 43.3± 12.8.

The mean body height of the exposed group is 60.7 ± 3.9 and the non exposed group is 61.2 ± 3.1.

Table-23: Symptom of the diseases

Distribution of percentage of the symptom presented by respondent.

Symptom	Exposed	Non exposed
Weakness	335 (67%)	266 (53%)
Cough	250 (50 %)	185 (37%)
Headache	166 (33%)	140 (28 %)
Nausea	75 (15 %)	60 (12 %)
Burning of the eye	200 (40 %)	210 (42%)
Pain abdomen	240 (48 %)	225 (45 %)
Haemoptysis	46 (9%)	25 (5 %)
Dspnea	135 (27 %)	125 (25 %)
Parasthesia	260 (52%)	115 (23 %)

In the above table, most of the respondents complained more than one symptoms .67 % complained of weakness, 50 % complained of cough, 9% of haemoptysis and 52 % compained of parasthesia in the exposed group. On the other hand, 53 % complained of weakness, 37 % of cough, and 23 % of parasthesia in the non exposed group.

Figure-5

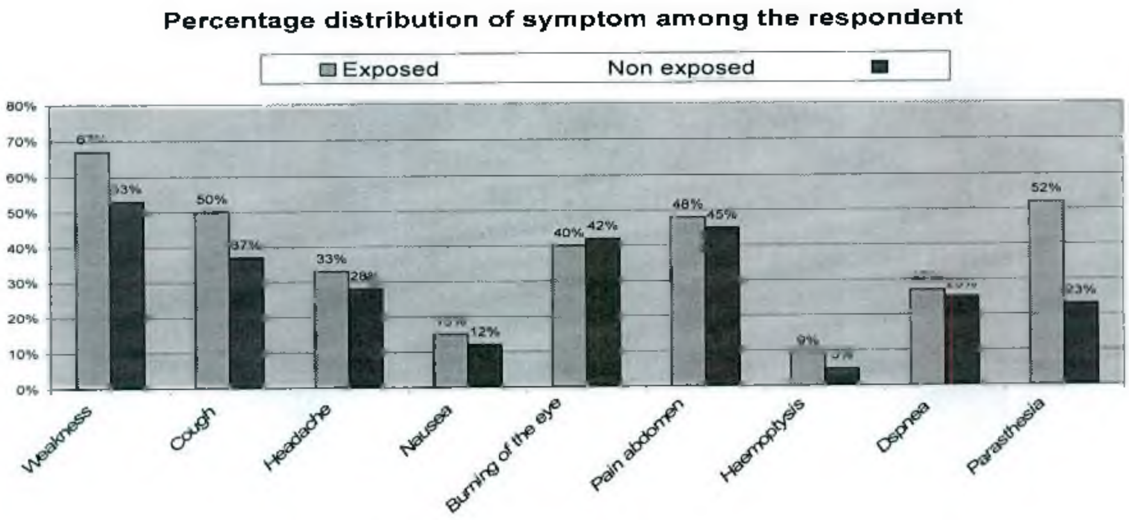


Table-24: Sign, Presented by the respondents

Distribution of percentage by signs of the diseases

n=500

Sign	Exposed	Non exposed
Anemia	270 (54%)	260 (52%)
Hepatomegaly	84 (16.8%)	23 (4.6%))
Spenomegaly	71(14%)	17 (3.4%)
Ascitites	10 (2 %)	2 (.5 %)
Odema	45 (9 %)	10 (5 %)
Sign of polyneuropathy	90 (18%)	25 (5 %)
Sign of lung diseases	165 (33 %)	40 (8 %)
Hypertension	81 (16%)	68 (13. 50%)
Diabetis mellitus	77(15%)	59 (12%)

In this table, most of the respondents (54% & 52 %), for both the exposed and non exposed group respectively, found anemia, 16.8% of the exposed group and 4.6 % in the non exposed group showed hepatomegaly, 14 % in the exposed and 3.4 % in the non exposed, showed spleenomegaly. 16 % in the exposed group and 13.5% in the non exposed group showed hypertension. In the exposed group 15 % showed DM.

Figure-6

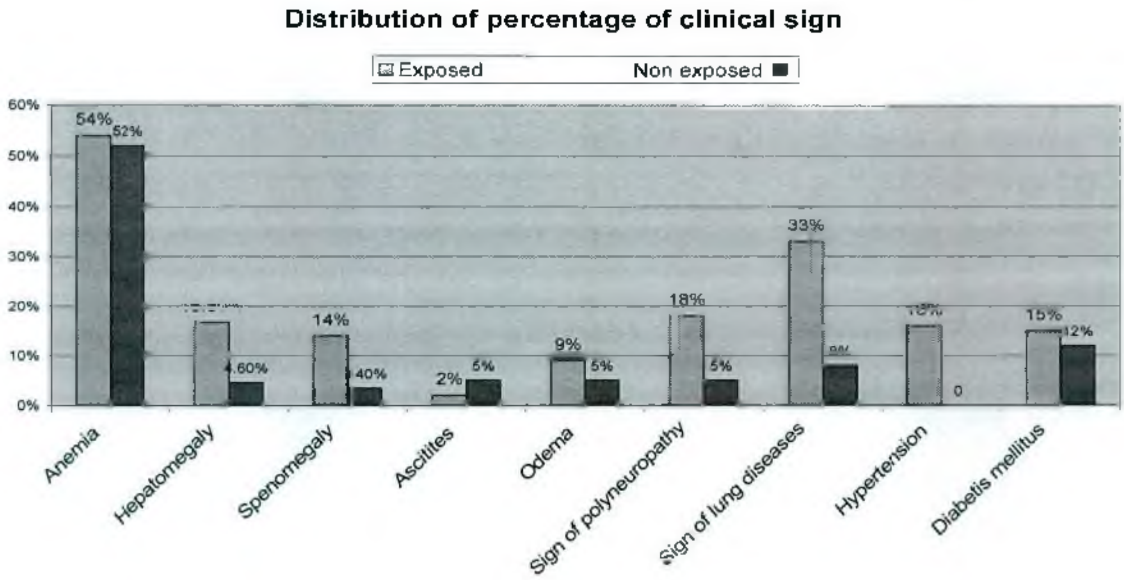


Table-25: Perception about the disease

Percentage distribution among the respondents perception about the diseases

Ideas	Exposed	Non exposed	Total
Arsenic skin diseases	104 (20.8 %)	8 (1.6 %)	112 (11.2 %)
Other than arsenic skin diseases	42 (8.4 %)	20 (4 %)	62 (6.2 %)
Other	454 (90.8 %)	472 (94.4 %)	926 (92.6 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100%)**

In the exposed group 20.8 % of the respondents seems that the arsenic caused it. 8.4% seems that it was not due to arsenic and probably other than arsenic.

Table-26: Visited by Government organization (Govt.) and Private organization

Percentage distribution of GO / NGO visit

GO / NGO visited the village	Exposed	Non exposed	Total
Yes	446 (89.1 %)	450 (90 %)	896 (89.6 %)
No	54 (10.9 %)	50 (10 %)	104 (10.4)
Total	**500 (100 %)**	**500 (100 %)**	**1000(100 %)**

Most of the respondents of both the group (89 % in the exposed and 90 % in the non exposed group) told that the representatives from Govt. / NGO had visited their villages, tested their tube well water, examined their condition and discussed their duties about to prevent the arsenicosis.

Table-27: Comment of the representatives of Gogernment organization (GO) / Non government organization (NGO)

Percentage distribution of the opinion of representative of GO / NGO

Comment	Exposed	Non exposed	Total
Suffering from arsenicosis	140 (28 %)	0	140 (14 %)
Skin diseases	45 (9 %)	56 (11.2 %)	101 (10.1 %)
NA	315 (63 %)	444 (88.8 %)	759 (75.9 %)
Total	**500 (100%)**	**500 (100%)**	**1000 (100%)**

Table-27,shows that the representatives of different GO / NGO opined that 28 % in the exposed group are suffering from chronic arsenicosis whereas in the un exposed group no one is suffering from arsenicosis. There were also some other skin diseases (9 % in the exposed & 11.2 % in the non exposed group) of the both survey group.

Table-28: Suggestion given by the representatives of Govt. / NGO to prevent arsenicosis

Percentage distribution of given suggestion of the representative of Govt. / NGO

Suggestion	Exposed	Non exposed	Total
Yes	485 (97 %)	470 (94 %)	955 (95.5 %)
No	15 (3 %)	30 (6 %)	45 (4.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000(100 %)**

Table –28, Shows that most of the respondents in both groups (97 % in the exposed & 94 % in the unexposed) told that the representatives of Govt. / NGO made some suggestion about arsenic contamination.

Table-29: Suggestion provided to the respondent about use of water

Suggestion details	Exposed	Non exposed	Total
1.To avoid arsenic contamination water	500 (100 %)	0	500
2. To collect water from alternate water source	490 (98 %)	34 (6.8 %)	524
3. To take vitamin and other supplement	165 (33 %)	55 (11 %)	220

In this table all of the respondents (100 %) in the exposed group were suggested to avoid the arsenic contaminated water. 98 % of the respondents were also advised at the same time to collect the arsenic free water from alternate water source. And at the same time 33 % of the respondents were also advised to take vitamin and other food supplement.

On the other hand no one is suggested to take arsenic free water in the non exposed group. 34 % of the respondents were suggested to take alternate water and at the same time both the group (11 %) were suggested to take vitamin and other supplement.

Table-30: Diagnosis of Arsenicosis by physician

Percentage distribution of the diagnosis

Diagnosis	Exposed	Non exposed	Total
Suffering from arsenicosis	146 (29.1 %)	0	140 (14 %)
Skin diseases	22 (4.5 %)	56 (11.2 %)	101 (10.1 %)
NA	332 (66.4 %)	444 (88.8 %)	759 (75.9 %)
Total	**500 (100%)**	**500(100%)**	**1000 (100%)**

In this table, 29 % of the respondents in the exposed group, were diagnosed by the physician that they were suffering from arsenicosis. A small amount of percentage (4.5 % in the exposed 11.2 % in the non exposed I group) were suffering from skin diseases.

Table-31: Suggestion given by the physician for prevention

Percentage distribution of the physician's suggestion

Suggestion given by the physician	Exposed	Non exposed	Total
Yes	474 (94.9 %)	490 (98 %)	964 (96.4 %)
No	26 (5.1 %)	10 (2 %)	36 (3.6 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

Table- 31, shows that most of the respondents (95 % in the exposed, 98 % in the non exposedl) told that doctors gave some suggestion about to prevent the arsenicosis.

Table-32: Complianced and Non complianced physicians' suggestion

Percentage distribution to follow the physician's suggestion about arsenicosis

Follow the physicians suggestion	Exposed	Non exposed	Total
Yes	180 (36 %)	435 (87 %)	615 (61.5 %)
No	320 (64 %)	65 (13 %)	385 (38.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

In this table most of the respondents (64 %) told that they did not followed the suggestion given by the doctors, in the exposed group.

On the other hand 87 % of the respondents in the non exposed group, followed the suggestion of the physician

Table-33: Reasons not followed the advice of the doctor

Percentage distribution among the respondent those did not followed the advice

Reasons not followed the doctors suggestion	Exposed	Non exposed	Total
Access to arsenic free water was not easy	140 (28 %)	0	140 14 %
Lack of motivation	35 (7 %)	30 (6 %)	65 (6.5 %)
Other peoples drink the water	60 (12 %)	25 (5 %)	85 (8.5 %)
Others	85 (17 %)	10 (2 %)	95 (9.5 %)
NA	180 (36 %)	435 (87 %)	615 (61.5 %)
Total	**500 (100%)**	**500 (100%)**	**1000 (100%)**

The main advice of the doctors was, not to drink the arsenic contaminated water and take alternate arsenic free water. Here 28 % of the respondents in the exposed group told that the main difficulties of access the safe water were the distance, time and carriers. 7 % in the exposed & 6 % in the non exposed told that actually they were not followed the advice due to lack of interest, because they were not motivated for doing this. 12 % in the exposed group & 5 % in the non exposed group told that they were following the others about drinking tube well water.

Table-34: Distribution of concentration of Arsenic in Tube well water

Percentage distribution of concentration of Arsenic in Tube well water

Arsenic concentration (ug/l)	**Exposed** (No of tube well)	**Non exposed** (No of tube well)	Total
< 50	0	181 (100 %)	187
50-200	61 (35.05%)	Nil	61
> 200	113(64.95%)	Nil	113
Total	**174**	**181**	**355**

Most of the tube wells (65%) were higher concentrations of arsenic than the maximum allowable limit for Bangladesh (50 ug / l).

Table-35: Duration of using of tube well water

Percentage distribution of duration of using tube well water

Year using tube well water	exposed	Non exposed	Total
< 8 Year	310 (62%)	290 (58%)	600 (60%)
> 8 Year	190 (38%)	210 (62%)	400 (40%)
Total	500 (100%)	500 (100%)	1000 (100%)

62 % of the respondents were using tube well water around 8 years or less than 8 years, in the exposed group.

Figure-7

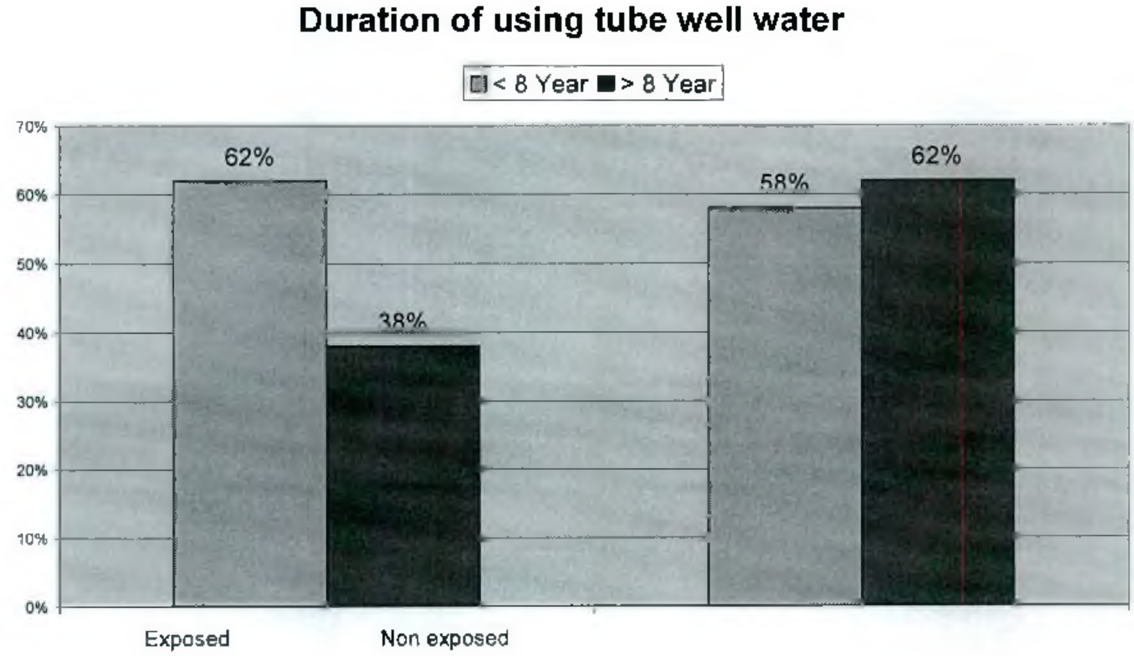


Table-36: Red painted tube well

Percentage distribution for red painted tube well

Painted red mark tube well	Exposed	Non exposed	Total
Yes	171(98.28 %)	0	171
No	03 (1.72 %)	181	184
Total	**174**	**181**	**355**

Table- 36, shows that most of the respondents (98 %) tube well were painted as red mark in the exposed group. On the other hand 100 % of the tube well in the non exposed group were free of red mark.

Table-37: Pregnancy outcome

Distribution of the percentage of respondent by pregnancy outcome

Pregnancy outcome	Exposed	Non exposed	Total
Live birth	775 (81.6 %)	823 (89.5 %)	1598 (85.5 %)
Spontaneous abortion	69 (7.3 %)	38 (4.1 %)	107 (5.7 %)
Still birth	44 (4.6 %)	26 (2.8 %)	70 (3.7 %)
Neonatal death	62 (6.5 %)	33 (3.6 %)	95 (5.1 %)
Total	950 (100 %)	920 (100 %)	1870 (100 %)

Table-37, shows that the live births were 81.6 % in the exposed group and 89.5 % in the non exposed group. About Spontaneous abortion. 7.3 % occurred in the exposed group and 4.1 % in the non exposed group , about Stillbirth, 4.6 % in the exposed group and 2.8 % in the non exposed group. For Neonatal death, 6.5 % in the exposed group and 3.6 % in the non exposed group.

Figure-8

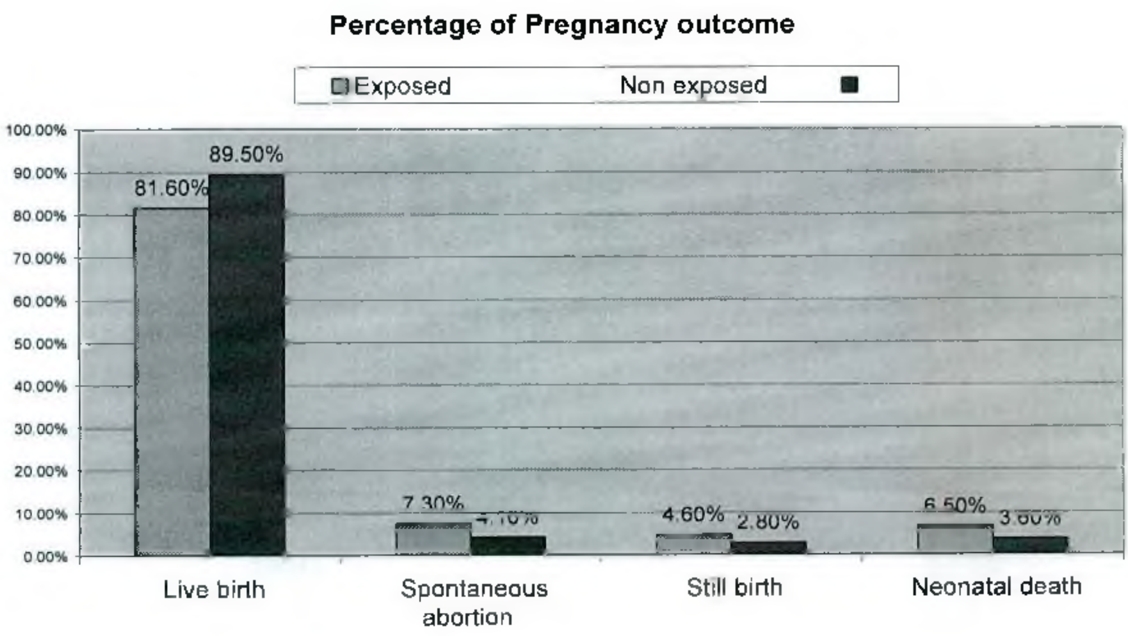


Table-38: Present status of the pregnancy outcome

Distribution of respondents by status of the pregnancy outcome during study period.

Present status of child	Exposed	Non exposed	Total
Alive child	775 (81.5 %)	823 (89.46 %)	1598
Dead child	175 (18.7 %)	97 (11.2 %)	272
Total	950 (100 %)	920 (100 %)	**1870**

According to the above table, 81.3 % of the child were alive in the exposed group, 88.9 % of the in the unexposed group.

On the other hand 18.7 % of the children were dead in the exposed group and 11.2 of the child in the unexposed group.

Table-39: Antenatal care

Distribution of Percentage of the respondents by categories antenatal care

Received antenatal care (ANC)	Exposed	Non exposed	Total
Qualified doctor	225 (23.68 %)	240 (26.09 %)	465 (24.87 %)
Nurse / Midwife / Paramedic	140 (14.74 %)	127 (13.80 %)	267 (14.28 %)
Medical assistant (MA) / SACMO	4 (.42 %)	7 (.76 %)	11(.59 %)
HA / FWA	30 (3.16 %)	23 (2.50 %)	53 (2.83 %)
Trained birth attendant	5 (.53 %)	9 (.98 %)	14 (.75 %)
Untrained birth attendant	6 (.63 %)	4 (.43 %)	10 (.53 %)
Unqualified provider	22 (2.32 %)	17 (1.85 %)	39 (2.09 %)
Other	12 (1.26 %)	14 (1.52 %)	26 (1.39 %)
No Antenatal care	506 (53.26 %)	479 (52.07 %)	985 (52.67 %)
Total	950 (100 %)	920 (100 %)	1870 (100 %)

Table-39, shows that 23.68 % of the respondent in the exposed group and 26 % in the non exposed group received the antenatal care from the qualified doctor . Whereas 53.26 % of the respondents in the exposed group and 52.07 % of the respondent in the non exposed group received no antenatal care.

The other care providers were Nurse/ Midwife / Paramedic, Medical assistant/ SACMO, TBA, untrained birth attendant and others.

Table-40: Complication during antenatal care

Distribution of respondents by complication during antenatal period.

Complication	Exposed	Non exposed	Total
No complication	180 (36 %)	205 (41 %)	355 (35.5 %)
Pre-eclampsia	95 (19 %)	75 (15 %)	180 (18 %)
Convulsion	15 (3 %)	10 (2 %)	25 (2,5 %)
P/V bleeding	45 (9 %)	30 (6 %)	75 (7.5 %)
Fever	50 (10 %)	60 (12 %)	110 (11.0 %)
Leaking membrane	60 (12 %)	50 (10 %)	130 (13 %)
Oedema	40 (8 %)	50 (10 %)	90 (9.0 %)
DM	15 (3 %)	20 (4 %)	35 (3.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100%)**

According to the above table,

- 19 % in the exposed and 15 % in the non exposed group complained of Pre-eclamptic toxemia.
- 8 % in the exposed group, 10 % in the non exposed group complained of oedema
- 9 % in the exposed and 6 % in the non exposed group complained of PV bleeding,
- Whereas 36 % in the exposed and 41 % in the non exposed group did not have any complication.

Figure-10

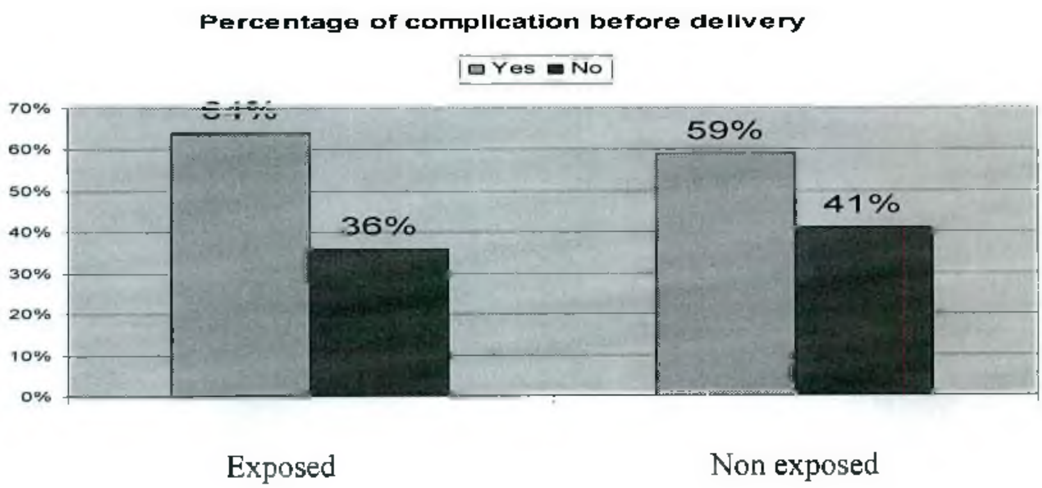


Table-41: Complication during delivery

Percentage distribution of complication during delivery

Complication	Exposed	Non exposed	Total
No complication	280 (56 %)	300 (60 %)	580 (58 %)
Prolonged labour	120 (24 %)	110 (22 %)	230 (23 %)
Excessive bleeding	65 (13 %)	50 (10 %)	115 (11.5 %)
Convulsion	10 (2 %)	5 (1 %)	15 (3 %)
Baby's hand and feet came first	5 (1 %)	25 (.5 %)	30 (3.0 %)
Discharging fowl smell	5 (1 %)	5 (1 %)	10 (1.0 %)
Retained placenta	15 (3 %)	27 (5.5 %)	42 (4.2 %)
Total	**500 (100%)**	**500 (100%)**	**1000(100%)**

The above table shows that , 24 % of the respondent in the exposed and 22 % in the non exposed group complained of prolonged labour, 13 % of the respondents in the exposed and 10 % of the respondent in the non exposed group complained of excessive bleeding during delivery.

Other complications namely retained placenta, convulsion, hand or feet came first,both the group were also found.

Figure-11

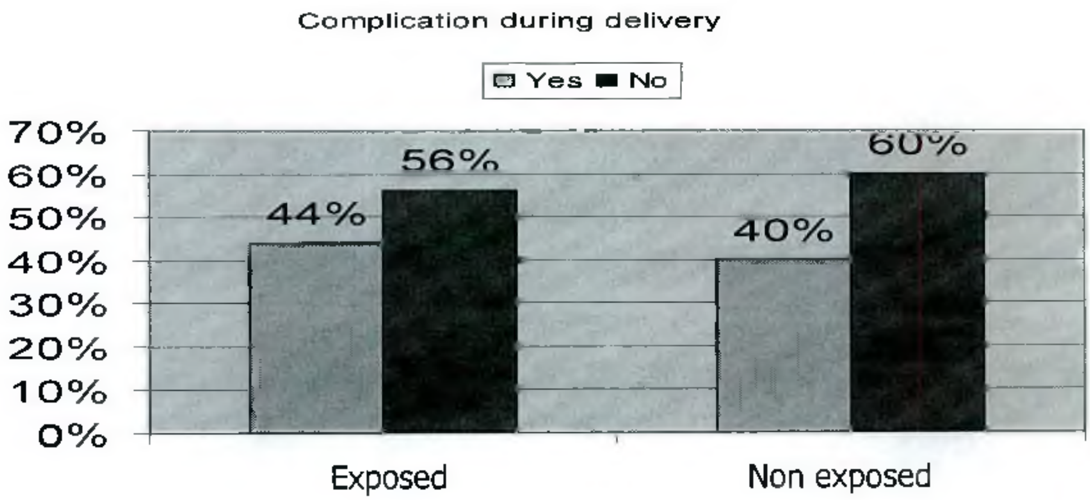


Table-42: Post partem complications

Distribution of Respondents by Post partem complication

Complication	Exposed	Non exposed	Total
No complication	360 (72 %)	380 (76 %)	740 (74 %)
Fever	55 (11 %)	65 (13 %)	120 (12 %)
Severe bleeding	60 (12 %)	40 (8 %)	100 (10 %)
Fowl discharge	15 (3 %)	10 (2 %)	25 (2.5 %)
Convulsion	10 (2 %)	5 (1 %)	15 (1.5 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000(100 %)**

The table reavealed that, most of the women complained of PV bleeding <12%, in the exposed group and 8 % in the non exposed group>. Most of the complications were higher in the exposed group than in the non exposed group.

Figure-12

Complication during post partem

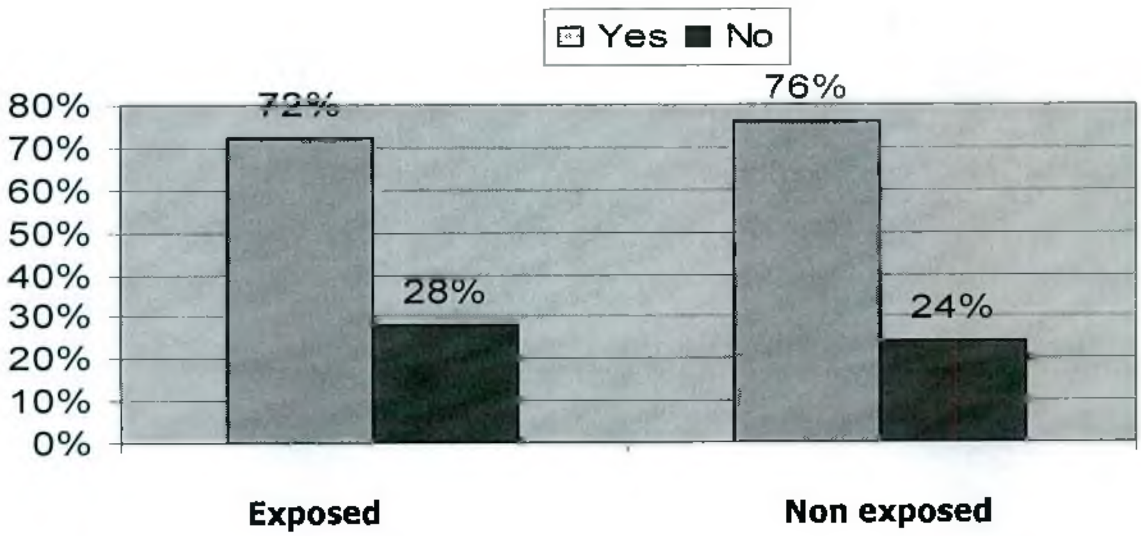


Table-43: Complication before delivery

Complication	Exposed	Non exposed
Yes	320 (64 %)	295 (59 %)
No	180 (36 %)	205 (41 %)
Total	**500 (100 %)**	**500 (100%)**

The table shows that 36 % of the respondents in the exposed and 41 % of the respondents in the non exposed group complained of no complication. Whereas, 64 % of the respondents in the exposed group and 59 % of the respondents in the non exposed group complained of some complication before delivery.

Table-44: Complication during delivery

Complication	Exposed	Non exposed	Total
Yes	220 (44%)	200 (40%)	420 (42%)
No	280 (56%)	300 (60%)	580 (58%)
Total	**500 (100%)**	**500 (100%)**	**1000 (100%)**

P = .20, Odd ratio = 1.18

According to this table, 44 % respondents in the exposed and 40 % respondents in the non exposed group complained for some complication during delivery.

The association is not statistically significant.

Table-45: Complication in post partem

Complication	Exposed	Non exposed	Total
No complication	360 (72 %)	380 (76 %)	740 (74 %)
Complication	140 (28 %)	120 (24 %)	260 (26 %)
Total	**500 (100 %)**	**500 (100 %)**	**1000 (100 %)**

P =.14, Odd ratio =1.23

The above table shows that 28 % of the respondents in the exposed group developed some complication whereas in non exposed group 24 % developed no complication, after delivery. Association is not satistically significant.

Table-46: Place of delivery

Distribution of Respondents by place of delivery

Place of delivery	Exposed	Non exposed	Total
Public health facility	38 (4 %)	46 (5 %)	84 (4.49 %)
Private health facility	14 (1.47 %)	20 (2.17 %)	34 (1.82 %)
Home	893 (94 %)	846 (92 %)	1739 (92.99 %)
Others	5 (.53 %)	8 (.87 %)	13 (.70 %)
Total	**950 (100%)**	**920 (100%)**	**1870 (100%)**

Table-46 presents only 4 % in the exposed group and 5 % in the non exposed group, births occurred at a public health facility, while almost (94 % in the Exposed and 92 % in the non exposed) all other delivered in the home.

Figure-13

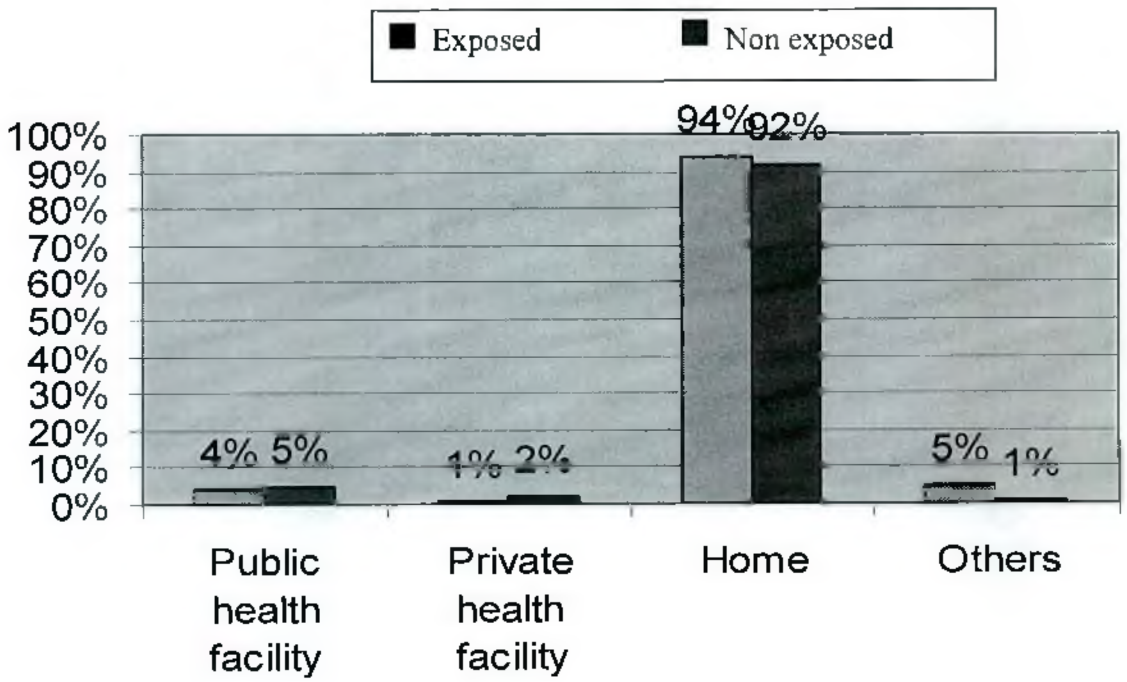


Table-47: Association of Black spot and Spontaneous abortion by relationship.

Spontaneous abortion	Presence of black spot		Total
	Yes	No	
Absent	103 (70.5 %)	328 (92.66%)	431 (87.6 %)
Present	43 (29.5%)	26 (7.44 %)	69 (12.4 %)
Total	146 (100%)	354 (100%)	500 (100%)

P<.05

Table 47, shows that 29.5 % patient had black spot and at the same time developed spontaneous abortion. The association is statistically significant.

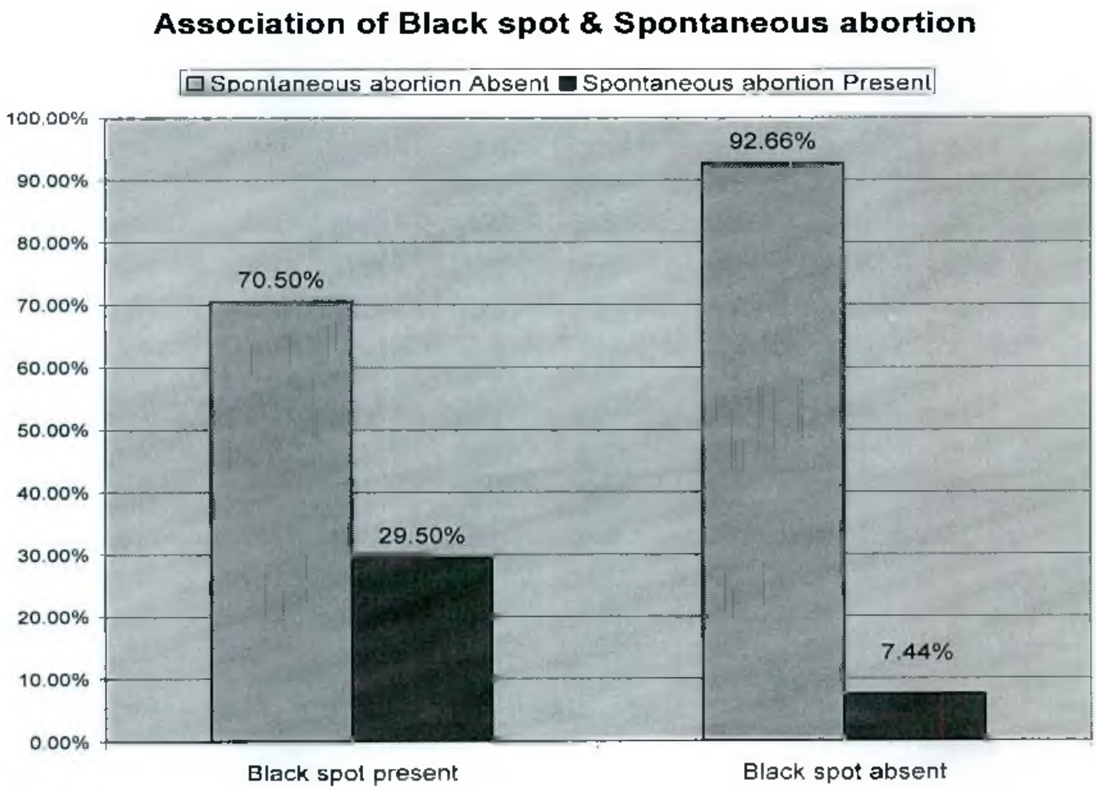


Table-48: Association of Black spot and Still birth

Still birth	Presence of black spot		Total
	Yes	No	
Absent	118 (82%)	337 (96%)	456 (91.0%)
Present	28 (18%)	17 (4%)	44 (9.0%)
Total	146 (100%)	354 (100%)	500 (100%)

$P<.05$

Table shows that 18 % patient had black spot and at the same time developed still birth . The association is also statistically significant.

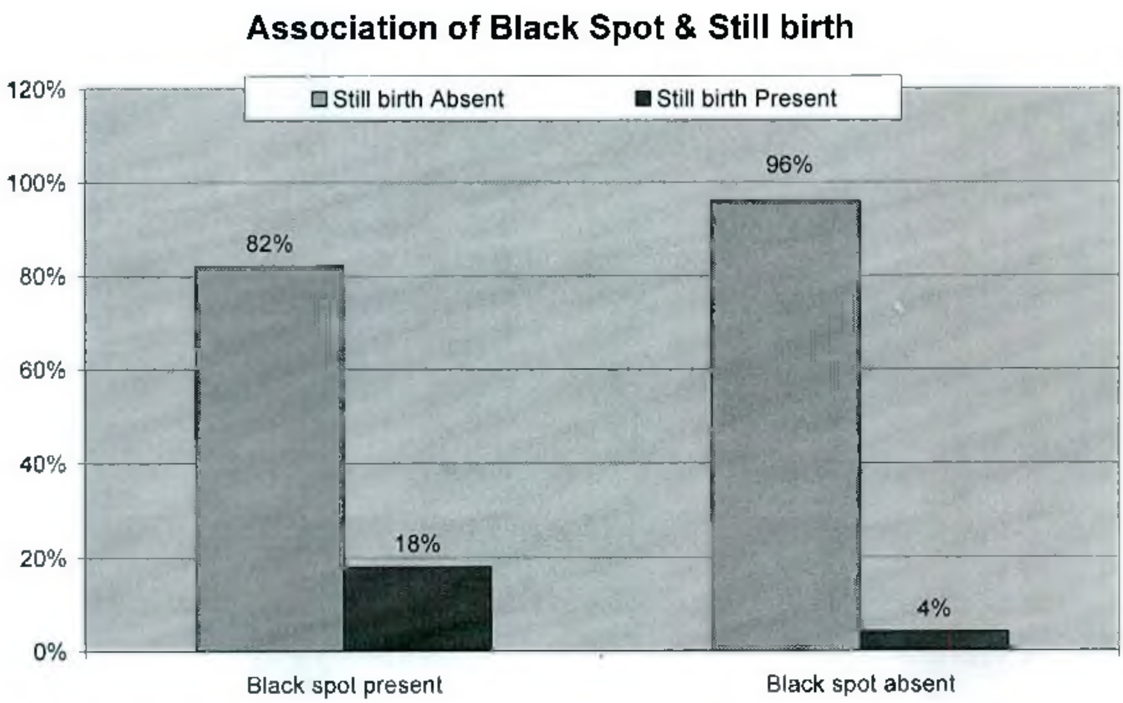


Table-49: Association of black spot and Neonatal death

Neonatal death	Presence of black spot		Total
	Yes	No	
Absent	122(84%)	317 (90%)	440 (88%)
Present	24 (16%)	37(10%)	62 (12%)
Total	146 (100%)	354 (100%)	500 (100%)

P<.06

Table shows that 15.8 % patient had black spot and at the same time developed Neonatal death.

Figure-16

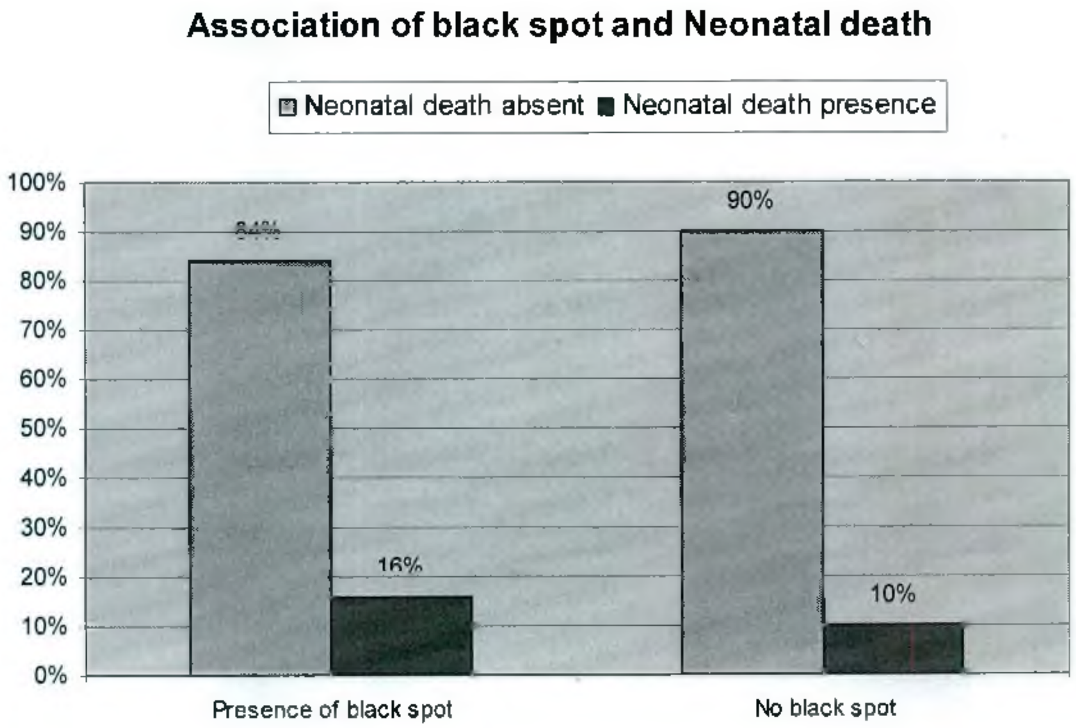


Table-50: Association of Keratosis and Spontaneous abortion

Spontaneous abortion	Presence of keratosis		Total
	Yes	No	
Absent	47 (76%)	384 (90%)	431 (87.6%)
Present	20 (24%)	49 (10%)	69 (12.4%)
Total	67 (100%)	433 (100%)	500 (100%)

P< .05

Table shows that 24 % patient had keratosis and at the same time developed spontaneous abortion. The association is statistically significant

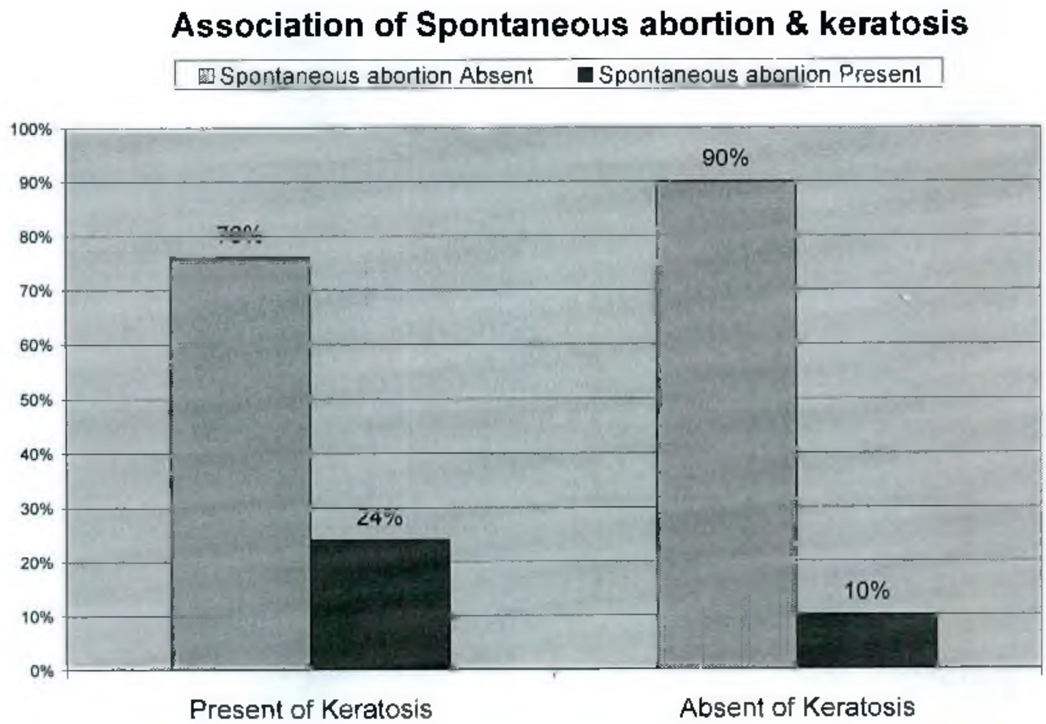


Table-51: Association of keratosis and Still birth

Still birth	Presence of Keratosis		Total
	Yes	No	
Absent	54(84%)	401(93%)	455(91.8%)
Present	12(16%)	32(7%)	44(8.2%)
Total	66 (100%)	433(100%)	500(100%)

P<.05

Table shows that 16 % patient had keratosis and at the same time developed Still birth. The association is statistically significant.

Figure-18

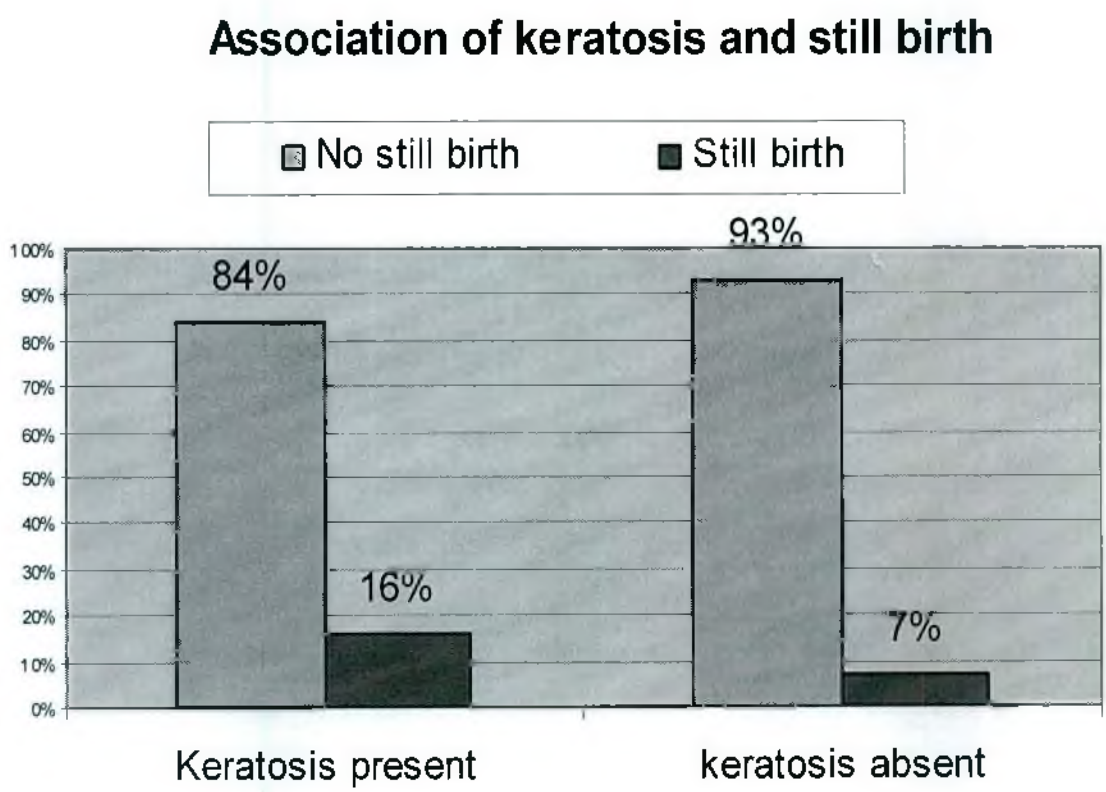


Table-52: Association of keratosis and Neonatal death

Neonatal death	Presence Keratosis		Total
	Yes	No	
Absent	53(81%)	385(89%)	438(88%)
Present	14(19%)	48(11%)	62(12%)
Total	67 (100%)	433(100%)	500(100%)

P < .10

Table shows that 19 % patient had keratosis and at the same time developed Neonatal death. The association is significant (P < .10)

Figure-19

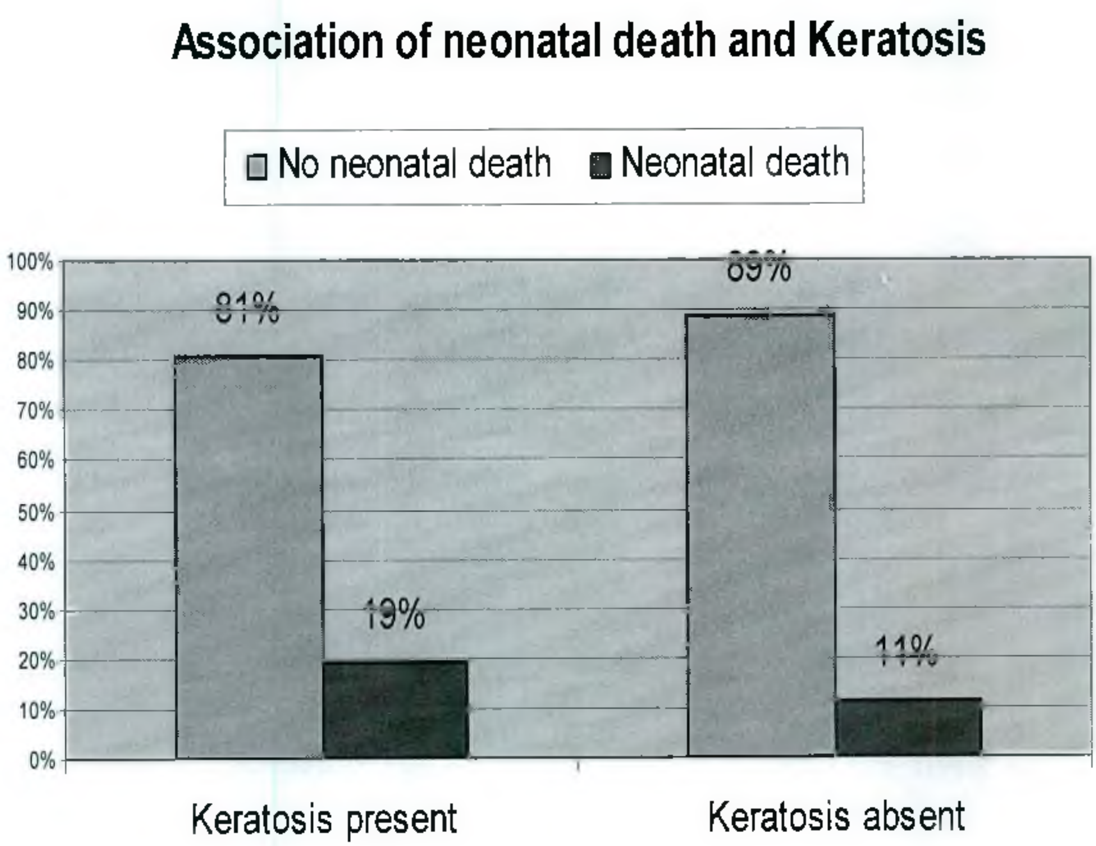


Table-53: Association of Black spot and level of arsenic

Black spot	Level of Arsenic		Total
	<200 ug/l	>200 ug/l	
Yes	52 (15.7%)	94 (56%)	146 (29.2%)
No	280 (84.3%)	74 (44%)	354 (70.8%)
Total	332 (100%)	168 (100%)	500 (100%)

P<.001 OR=6.84, CI=4.38, 10.07

According to this table, 56 % of the respondents had black spot and at the same time the level of arsenic in the tube well water was more than 200 ug/l , where as 15% have black spot at the level of less than 200 ug/l arsenic in tube well water.

Figure-20

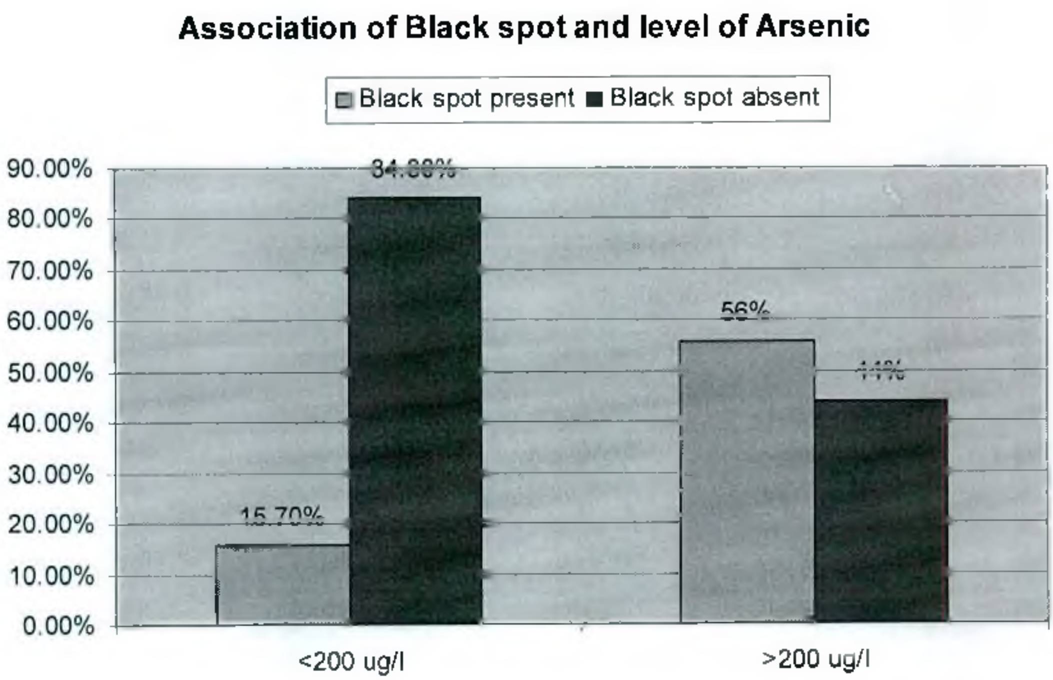


Table-54: Association of keratosis and level of arsenic

Keratosis	Level of arsenic		Total
	<200 ug/l	>200 ug/l	
Yes	29 (8.7%)	38 (22.6%)	67(13.4%)
No	303(91.3%)	130(77.4%)	433(86.6%)
Total	332(100%)	168(100%)	500 (100%)

P<.001, OR=3.05, CI=1.75, 5.34

This table shows that, 22.7 % of the respondents had keratosis and at the same time they had >200 ug /l arsenic in the drinking water. On the other hand, 8.7% had keratosis at the level of <200 ug/l.arsenic in the drinking water.

Figure-21

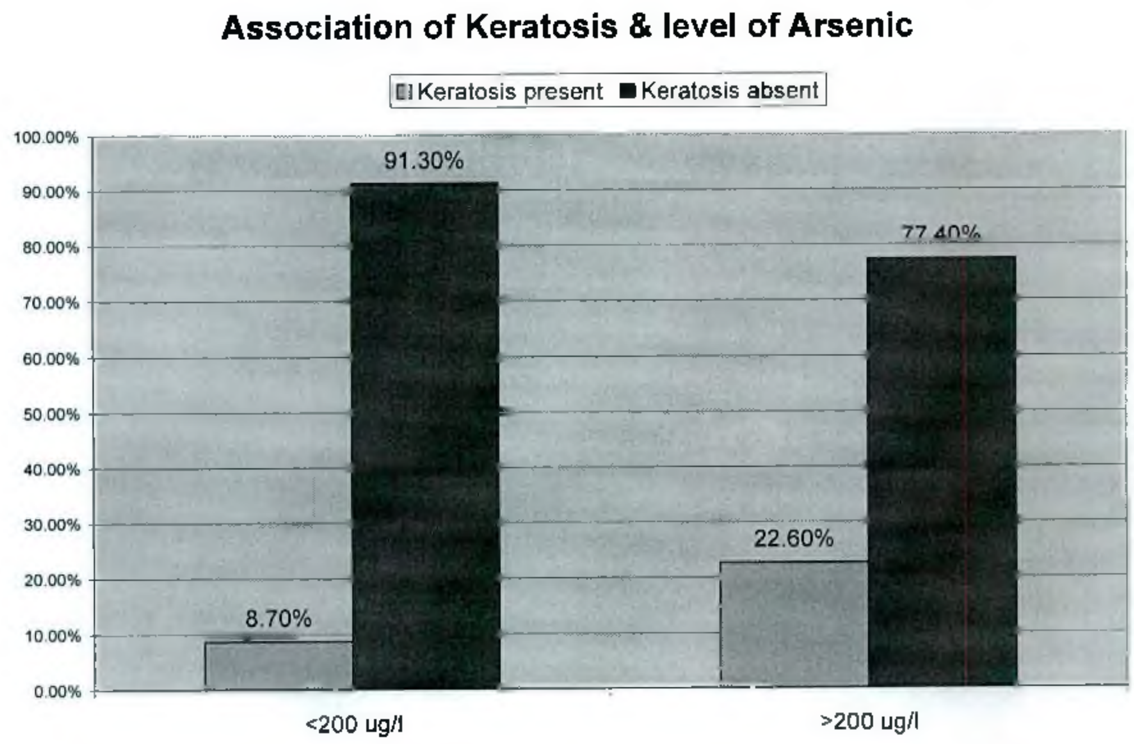


Table-55: Difference of pregnancy outcome in two areas

Outcome	Exposed	Non exposed	Odd ratio	Confidance Interval	P value
Live birth	775	823	1.94	1.48, 2.55	<.001
Spontaneous abortion	69	38	2	1.31, 3.07	<.001
Still birth	44	26	1.77	1.07, 2.95	<.05
Neonatal death	62	33	2.07	1.32, 3.27	<.001

The total live birth in the exposed area 775 and non exposed area is 823. The association of the two areas outcome is statistlcaly significant ($p < .001$).

In the exposed area, the number of spontaneous abortion is 69, and 38 in the non exposed area. The odd ratio is 2 and confidance Interval is 1.31, 3.07. The association is statistlcaly significant (P value <.001).

Still birth, in the exposed area is 44 and 26 in the non exposed area. The odd ratio is 1.77 and the CI is 1.07, 2.95. Here, the association is also statlsticaly significant (< .05).

The total number of Neonatal death is 62 in the exposed area and 33 in the non exposed area. The odd ratio is 2.07, confidence Interval is 1.48, 2.55. Here the association is also statisticaly significant (p value < .001)

Table-56: Relationship of pregnancy complication of the Exposed and non exposed area

Area	Complication present	Complication absent	Total
Exposed	220	744	964
Non exposed	186	782	968
Total	406	1526	1932

Odd Ratio =1.24 (0.99 <OR < 1.56)

Complications were higher in the exposed than in the non exposed area with odd ratio 1.25, P<.06

Table-57: Association of Arsenic concentration with Spontaneous abortion, Still birth, Neonatal death.

Outcome	Arsenic level		Odd ratio	Confidance Interval	P value
	< 200 ug/l	>200 ug/l			
Live birth	544	231			
Spontaneous abortion	27	42	3.62	2.12, 6.19	<.01
Still birth	22	24	2.66	1.39, 5.07	<.01
Neonatal death	36	26	1.68	.96, 2.03	=.051

In this table, the level of arsenic is divided in to <200 ug/l and >200 ug/l. The association of the level of arsenic in the tube well water with spontaneous abortion and still birth are statisticaly significant (p value is <.01). The association with neonatal death is very close to significant (p value = .051)

Chapter-6

6. Discussion

The study was conducted among married women of age group 15 to 49 years with the prime objective to compare the reproductive health impacts of women (exposed group) in Arsenic contamination and non-Arsenic areas (non exposed) through a structured pretested interview schedule.

The married female (15-49) respondents who gave a history of exposure of arsenic through drinking of contaminated tube wells water and presented with or without dermal manifestation, (keratosis, melanosis, pigmentation) were initially identified by the field workers during their home visit in the exposed area. Only married reproductive age group women (15-49) were included in the study. It was considered that both the married women (Dermal manifestation present or not) in each household initially for the both exposed and non exposed group. The exposed feature (dermal manifestation) present with the married women was examined by medical doctors and a diagnosis of arsenic poisoning was confirmed by clinical examination and determining arsenic contents in tube well water. Each of the respondents was asked to sign an informed, voluntary consent form for their participation in the study.

The Negative outcome (Spontaneous abortion, Still birth, Neonatal death) of the women again checked by history taking to exclude all other confounding factor related to Spontaneous abortion, Stillbirth & Neonatal death.

Sujanagar & Bera Upazilla of Pabna district has been identified as arsenic affected area, and Santhia upazilla (most of the tube well) is free from arsenic affected tube well, according to DPHE report. There were about 174 tube wells in the exposed area, were found arsenic contaminated. On the otherhand, 181 tube wells in the unexposed area, all of them were free from arsenic contamination . Under the government programme, the contaminated tube wells had been identified by field tests kit and these were painted red. The villagers were cautioned not to drink and cook with water from these tube wells. However the villagers continued to drink from the contaminated tube wells, because they did not have access to alternative source of arsenic free water. Moreover when the red paint disappears after few months, the villagers thought it safe and started using it again. Also the level of contamination of a particular tube well did not remain constant over a certain length of time. A number of factors influenced the level of arsenic content of a particular tube well, these include, location, time of sampling, season, rate of use, depth of pipes, salinity, and mineral content of soil.

It was also difficult to determine how long the population has been exposed to toxic levels of arsenic through contaminated drinking water because the dates of installation of the tube well were not recorded. Some were installed by the government and others by private initiatives. According to users recall, these people have been drinking arsenic contaminated water for 7-10 years.

There are much arsenic contamination of ground water and its potential risks to human health created an alarming situation for both the population at risk and the health authorities. Within the last ten years or so, massive arsenic contamination of ground water has been detected in Bangladesh. The magnitude of arsenic contamination of ground water in Bangladesh is colossal. There are more than 80 million already exposed, majority of them are below the age of 15.

Different aspects of the study findings have been discussed as follows:

Section-1: Sociodemograhic characteristics

In this study socio demographic information includes social, economic and demographic characteristics of the household of those women of reproductive age 15-49, (exposed and non exposed group,) who were taking arsenic contaminated tube well water or not taking arsenic contaminated water.

In this study, the reproductive age (15-49 years) of the married women's are included both for exposed and non exposed group. The total female respondents were 500 in the exposed and 500 in the non exposed group.

According to the table-1, the percentage of highest age group was 15-19 in the both exposed and non exposed group. The percentage of the both group were very close.It indicates that the both groups represents the same socioeconomic class which is very important for this study. The percentage of age group is decreasing gradually when the age of the respondents increasing. Bangladesh Demographic and Health survey of BDHS, 2004 (3) shows that the highest age group is 15-19 year in the rural and urban area also, which is similar to this study. Overall, the proportion of persons of younger age groups is substantially larger than the proportions in the older age groups for each sex and in both urban and rural areas.

Ability to read or write is an important determinant of social and economic well-being of the population. Education is the key determinants of the lifestyles and status of an individual enjoys a society. It affects many aspects of life, including demographic and health behavior. Many studies have shown that education attainment has strong effects on reproductive behavior, contraceptive use, fertility, mortality, morbidity, and attitude awareness related to family health and hygiene. Most of the respondents (female) in this study got no education both in the exposed and non exposed group and the percentage is 40 and 32 for the exposed and non exposed group respectively (Table-3). Four percent only completed the secondary education in the exposed and six percent in the non exposed group.

Bangladesh Health and demographic survey of BDHS, 2004 (3), also shows that majority of the females (36%) have no education, while 3.7 % completed the secondary education, which is similar to the study. BDHS also shows that educational attainment is higher in urban areas. The percentage of respondents who completed the secondary education increased during last few years, according to BDHS.

Female education has been found to be an important determinant of fertility decline in many under developed countries and an important differentiator of fertilities within countries. Several explanations have been offered toward this relationship. Improvement of female education is likely to delay marriage and suggest a vocational career as an alternative to minimise childbearing. Higher education level may also be associated with increased economic security, which in turn, is related to smaller families. In addition, education also affects attitude and values of person in such a way that they begin to question the traditional practice of their parents or other authority figures. Education enhances the status of women, thereby increasing their exposure to new information and ideas reduce social and cultural prejudices and thus induce behavioral changes. Furthermore, literate person tend to be more open to innovations and have a greater opportunity to come in to contact with agent of change, such as health planners or family planning counselors and are more exposed to mass media.

Education is an important determinant of social and economic status of individuals in a society. To understand the wellbeing of women in a country, it is important to examine the education status of women compared to their male counterpart. Literacy is one of the very basic indicators of educational status. Other possible indicators of education are related to school and college enrollment, number of women teacher in schools, colleges and universities etc.

Again, the same information collected from the respondent's husbands and patterns of the percentage of education profile more or less same. In the exposed group 30 % and in the non exposed group 31 % has got no education (Table-4). The percentage of completion of secondary education of husbands is higher than women. BDHS survey also shows the same scenario about the male education.

Current employment status of women, most of the women in the exposed and non exposed group were unemployed where around twelve percent in both the group were working round the year (Table-5). But the employment status of the respondents' husband was reverse. Most of the men were working round the year for both the group (Tabie-6). This result reflects the study of BDHS survey, also it is proved that both the exposed and non exposed group were taken from the same socio-economic status. Like other traditional societies, many women in Bangladesh, do not work outside their home or its immediate vicinity. However, women perform many directly productive and income earning activities with the home plot. For example, post harvest operations of agriculture products are carried out by women within the house. In Bangladesh, participation in productive, income generating activities by women is considered employment to define the labour force. In 1996, total labour force of Bangladesh was about 56 million and women constitute a third of this total (3). In urban areas, about 27 % of total labour forces are women while the proportion is about 40 % for rural areas. In 1996, total labour force of Bangladesh was about 56 million and women constitute a third of this total. In terms of employment conditions, more than a third of all women in labour force are actually unpaid family workers. Most of these women are involved in family-run production activities, including processing of agricultural outputs. In recent years women work force has become very important in the production sector, especially in the garment industries of the country.

Household income or employment might also be related to technique used for water purification in the village. The example of water storage practice in the Laxipur area of Bangladesh can be given. In this area water is stored in small vessels to allow the iron oxide to settle on the bottom of the vessel and this enhances the concentration of adsorbed arsenic in the sludge. Higher income / employed household might have greater storage facilities for their tube well year for both the group (Table-6). This result reflects the study of BDHS survey, also it is proved that both the exposed and non exposed group were taken from the same socio-economic status. Like other traditional societies, many women in Bangladesh, do not work outside their home or its immediate vicinity. However, women perform many directly productive and income earning activities with the home plot. For example, post harvest operations of agriculture products are carried out by women within the house. In Bangladesh, participation in productive, income generating activities by women is considered employment to define the labour force. In 1996, total labour force of Bangladesh was about 56 million and women constitute a third of this total (3). In urban areas, about 27 % of total labour forces are women while the proportion is about 40 % for rural areas. In 1996, total labour force of Bangladesh was about 56 million and women constitute a third of this total. In terms of employment conditions, more than a third of all women in labour force are actually unpaid family workers. Most of these women are involved in family-run production activities, including processing of agricultural outputs. In recent years women work force has become very important in the production sector, especially in the garment industries of the country.

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In the household interview, respondents were asked about the characteristics of their own hold, including electricity, sanitation food cooking fuel, main housing materials.

Here table-7, summarizes this information 32 % of the household in the exposed group and 35 % in the non exposed group have access the electricity.

The important determinants of health are access to adequate sanitation facilities for the community. 83 % of the household in the exposed and 86 % in the non exposed group have some type of facility, including 53 % in the exposed and 54 % in the non exposed group that have hygienic toilet (septic tank, modern toilet, water sealed latrines, and pit latrines) The sanitation facilities vary between rural and urban areas.

To get a measure of household economic vulnerability, the respondents were asked whether they thought their household was a surplus or deficit household in terms of food consumption. !5 % of the household in the exposed group and 13 % in the non exposed group seems to experience food deficit throughout the year, while 40 % of the household face food deficit some time in the year. Only 6 % of the household reported their food as a surplus.

A question about fuel for cooking was also asked in the interview. Two types fuel are predominantly used for cooking in Bangladesh: wood and crop residue. 52 %

of the respondent in the exposed and 54 % of the household in the non exposed use crop residue or straw for cooking. None of the household using the liquid gas.

Here Tin is the main roof material of the survey area, accounting 45 % of the exposed group and 44 % in the non exposed group are used tin . However , urban and rural households vary widely in the cement or concrete roofs.

About floor material, 95 % of the household in the exposed and 93 % in the non exposed used earth as a floor material. Only 5 % in the exposed and 7 % in the non exposed group are using cement as a floor material.

In regard to Respondents household ownership, more than ninety percent of the respondents in the exposed and non exposed group household own a homestead and slightly more than half own land other than a homestead (Table-8). BDHS survey also shows the percentage 95 percent and at the same time it is shown that homestead or land is less common in urban than in rural areas.

Fifty one percent of household in the rural area composed of three to five members (Table-9). Average household size composed of five members. Also BDHS survey shows the same study results. Urban household size is marginally smaller than rural household size.

About the sources of drinking water, most of the respondents had been drinking tube well water before they were enrolled in the study. Information of household water source is very important, because potentially fatal diseases, including typhoid, cholera, and dysentery are prevalent in the unprotected water. Tube well is the predominant sources throughout the Bangladesh. Most of the respondents of the group exposed and non exposed accustomed to drink tube well water and at the same time, arsenic contamination also been identified in tube well water.

For the most of the respondent's, tube well water was the only sources of cooking, washing and bathing purposes(Table-11,12,13). Water from other sources was used in little amount for both the exposed and non exposed group. Bangladesh health and demographic survey revealed that more than nine in ten thousands in rural areas and seven in ten thousands in urban areas obtain drinking water from tube well, not only for drinking purpose, but also for other domestic purposes. Pipe water is accessible only in urban areas. Around one third of urban household using the piped water as safe water. Access to safe water supply is one of the most important determinants of health and socioeconomic development.

Water intended for human consumption should be both safe and wholesome. The health benefits from reducing water related diseases could in some circumstances be transmuted in to a greater work capacity, which may contribute to increase production and overall economic development. Safe water for household is dependent on the time and labour used in the collection of water, the time and resources used in boiling / sterilizing the water and in managing water within the household.

Arsenic poisoning in communities has numerous effects and family are likely to use a range of coping mechanisms. An important issue arises when families first become aware of the hazards of the use of the arsenic contaminated water. While an individual or household may not even be exposed to arsenic, or if exposed, onset of arsenicosis may not have started, how will families decide to protect themselves and ensure access to safe water? The absence of minimum information for making house hold decision in regard to the risk and to safety of the customary water source of drinking, laundry and other purposes might cause inefficiencies and stress. By using water of nearby tubewells in the past, women and children saved travel time for distant water sources.

It is important to point out that the potential physical access to safe water is no gurantee that families can use this source. For example, access to safe water may be difficult for social reasons. Families may have to negotiate the use of water with others who own a hand pump, a yard connection, a storage tank or a rain water harvesting system with storage. However class cast relationship, such as rich poor or landlord tenant farmer, may impede sharing of water between families of different socioeconomic backgrounds

When the question arises about abstaining from the contaminated tube well water in the exposed and non exposed group, then most of the respondents (Table-14) had been drinking tube well water which is arsenic contaminated (in the exposed group) before they were enrolled in the study. Although it was very difficult to determine how long the tube well had been contaminated, the average duration of exposure has been estimated 4- 10 years. This estimate was based on the time of the installation of the tube well as recalled or reported by the owner of the tube well. No written record was available to ascertain the time of installation of the tube well. Although, most of the respondents were cautioned to drink contaminated water from the tube wells marked as red (in the exposed area) , most of the villagers continued to drink contaminated water from these tube well because of lack of an access to an alternative sources of arsenic free water. Moreover, when the red paint disappears after a few months, the villagers thought it safe and started uses it again. On the other hand respondents usually drink the tube well water (they had no such type of arsenic contamination problem) in the non exposed group.

Among those who were abstaining from drinking water, most of the causes were to see the black spot on the others body(Table-15). Because, they informed that the black spot is the sign of the chronic arsenicosis.

In the area selected for exposed and non exposed, most of the tubewells water was checked by the government or non government organization (NGO). In the exposed area the representatives from Govt. / NGO put the red mark on the tube well, for not to drink the water in the exposed area. Most of the organizations used the field kit to test the tube wells water. A few tubewells were the only source of drinking water in the area. Under the government programme, the contaminated tube wells had been identified by field test and these were painted red, the villagers were cautioned not to drink and cook with water from these tube wells. The level of contamination of a particular tube well did not remain constant over a certain period of time. A number of factors influence the level of arsenic content of a particular tubewell; these include location, time of sampling, season, rate of use, depth of pipes, salinity and mineral content of soil.

Marriage in most Asian societies indicated the onset of the socially acceptable time for childbearing. Women, who marry early, will have, on average, a longer period of exposure to pregnancy, often leading to a higher number of children ever born. In this study, it showed that median age at first marriage has been increasing over time for both the group, exposed & non exposed groups (Table-18). According to the BDHS survey (3) since 1993, revealed that although the median age at first marriage for women 20-49 has increased over time, there was a decrease from a median of 15 years at the time of the 1999-2000 BDHS to 14.8 years in 2004. In Bangladesh the legal age of marriage is 18 years for women; however a large proportion of marriage still takes place before the legal age. BDHS data 2004 showed that 68 percent of women age of age group 20-24 were married before the age of 18. Data indicate that over the last two decades, the proportion of marrying before the legal age had been gradually declining; but in recent years, it has increased again. According to BDHS survey (2004), the median age of marriage increases with level of education and with household income status. For example, among women age 15-49, the median age of first marriage is 14.9 years for those with no education and 19.6 years for those who have at least completed secondary education. Like wise, for the same age group, the median age at marriage 14.7 years for women in the lowest wealth quintile and 15.2 years for those in the highest wealth quintile. BDHS survey shows that urban women tend to marry almost one year later.

A publication of BBS shows (April 1999) that the average age at first marriage for women was only 19 years while it was 26 years for male. The most of the women in Bangladesh get married when they are at the age range 15 to 19 years. Such a low age at marriage adversely affect their health status, social situation and economic independence. It is interesting to note that for all educational status categories from no formal education to secondary schooling, the age at first marriage increases only slightly from 17.4 years to 18.2 years. Therefore, encouraging girls to attend the secondary schools will not improve the age at marriage significantly. Completion of school certificate examination or other higher degrees affect age at marriage by couple of years. The average age of first marriage for women is also more or less constant by the occupation of the household. For agricultural households, the average age at marriage was found to be 18.1 years, according to BBS. While for non agricultural households the average age was 18.3 years. In contast, average age at marriage increases very significantly with non agricultural occupation of men, from 24 years to about 33 years.

In this section, the findings of the variables used in both the exposed and non exposed are very close, which indicates that the samples were taken from the same socio demograhic area? The study findings are very much similar with Bangladesh Health and Demographic Survey (BDHS) 2004 findings. Moreover there was no statistically significant difference ($p > 0.05$) for socio-demographic status, age at marriage, educational status etc. among the respondents of exposed and non exposed group.

Section: 2: Morbidity pattern of the women

The most common clinical presentation of the patients was skin pigmentation, predominantly in the form of cutaneous melanosis over the trunk and back. The next common feature was palmer and planter keratosis. The prevalence of liver and spleen enlargement were low and no case of cancer or death was observed. In contrast, several clinical involement of patient due to chronic arsenicosis have been reported from west Bengal, by India by Guha Mojumder et al (20). The authors examined 156 patients in 6 districts in West Bengal and observed 77 % cases of hepatomegaly, 31 % splenimegaly, 53 % severe lung diseases and 2 cases of liver cirrhosis, I case of skin cancer, and 5 deaths. The Indian patients seem to have the worst form of illness than that observed among 40421 in Taiwan where 18 % showed skin pigmentation and 7 % of keratosis. Arsenic pollution of ground water has been detected for more than 20 years earlier in West Bengal than in Bangladesh indicating that west Bengal population might have been exposed for substantially longer period than those in Bangladesh. The other possibilities could be the difference in arsenic concentrations in drinking water, water use pattern, level of malnutrition, genetic predisposition between these two population groups.

The morbidity from skin lesion (Black spot and thickening of palm and sole) due to chronic arsenic toxicity, in this study showed a high prevalence rate of hyper pigmentation and thickening of skin, 28 % and 13.4 % respective in the case group (Table- 20, 21). No more case was found in the non exposed group. Guha mozumdar (20) in his study shows that though pigmentation was seen in all cases, keratosis was found in 61.5% of the cases. After detection of the case of melanosis (biack spot / hyper pigmentation) and keratosis (thickening of the skin) by the interviewer, a physician (trained in Arsenicosis) had confirmed those case by physical examination.

Black spot and thichening of palm and sole means dermal manifestations such as hyperpigmentation and hyperkeratosis are diagnostic of chronic arsenicosis. The pigmentation of chronic Arsenic poisoning commonly appears in a finely freckled, "raindrop" pattern of pigmentation or depigmentation that is particularly pronounced on the trunk and extremities and has a bilateral symmetrical distribution- Mild pigmentation (a) Diffuse melanosis (with mild keratosis), (b) Mild spotty pigmentations, (c) Mild spotty depigmentation. (47) (a) Moderate pigmentation, (b) Severe pigmentation. Pigmentation may sometimes be blotchy and involve mucous membranes such as the undersurface of the tongue or buccal mucosa (4, 20). The raindrop appearance results from the presence of numerous rounded hyperpigmented or hypopigmented macules (typically 2-4 mm in diameter) widely dispersed against a tan-to-brown hyperpigmented background. Although less common, other patterns include diffuse hyperpigmentation (melanosis) and localized or patchy pigmentation, particularly affecting skin folds (20). So-called leukodermia or leukomelanosis, hypopigmented macules take a spotty, white appearance usually occur in the early stages of intoxication.

Arsenical hyperkeratosis appears predominantly on the palms and the plantar aspect of the feet, although involvement of the dorsum of the extremities and the trunk has also been described. In the early stages, the involved skin might have an indurated, gritlike character that can be best appreciated by palpation; however, the lesions usually advance to form raised, punctated, 2-4 mm wartlike keratosis that are readily visible (20). Occasional lesions might be larger (0.5 to 1 cm) and have a nodular or horny appearance occurring in the palm or dorsum of the feet. In severe cases, the hands and soles present with diffuse verrucous lesions (a) Mild keratosis, (b) moderate keratosis (i) moderate diffuse thickening of the palm, (ii) a few nodules over thickened palm (associated lesions: Bowen's disease of the abdomen and squamous cell carcinoma on the finger) (50) and severe keratosis (a) Verrucous lesion of the palm with keratotic horn, (b) Big nodules over the dorsum of feet (associated lesion: Squamous cell carcinoma).

Though spotty depigmented spots, similarly distributed are also diagnostic for this condition, sometimes blotchy depigmented spots are seen and these need to be differentiated from other depigmented skin lesions like tinea versicolor, seborrheic dermatitis. Diffuse hyperkeratitic lesions of the palms and soles are distinctive lesions of chronic arsenicosis. However, manual labourers, who work with bare hands, might have thickening of the palms. The thickening of palms in manual labourers are usually localised in the pressure points. Bare footed farmers who work in the fields might have diffuse thickening of the soles. However, when the lesions become nodular the diagnosis becomes obvious. The duration of the patient's Arsenic exposure with the date of onset of symptoms does not follow a particular time frame.

Here in this study, most <62%> of the respondents received arsenic contaminated water more than 8 years but when they were not aware about the first exposure of arsenical skin lesion. They were confused about the time of first exposure.

The duration of the patient's Arsenic exposure with the date of onset of symptoms does not follow a particular time frame. Arsenical skin lesions have been reported to occur in West Bengal after drinking Arsenic contaminated water for one year or even less (50). In Taiwan, the youngest patient drinking Arsenic contaminated water who developed hyperpigmentation was 3 years old . Among the population exposed to Arsenic in drinking water in the Antofagasta region of Chile, cases of cutaneous arsenicosis, including both hyperpigmentation and hyperkeratosis, have been described in children as young as 2 years of age. The mean Arsenic dose in Antofagasta was estimated to be approximately 0.06 mg/kg per day for subgroups of children aged 3.13±3.33 years but was approximately 0.02 mg/kg per day for subgroups in their teens and twenties and 0.006 mg/kg per day for a subgroup in their sixties, indicating an inverse relationship between daily Arsenic dose rate/kg body weight and age.

It is found from this study, that those women who were taking highly arsenic contaminated water (> 200ug/l) having more black spot (56%) and thickening of the skin (22.6%) than those who were taking less concentrated arsenic water (< 200ug/L) (Table-54, 55). The association of black skin (Hyperpigmentation) and high level of arsenic in tube well water is statistically significant (P<.001) where odd ratio is 6.84, CI= 4.38, 10.07. And also the association of thickening of the skin (Keratosis) and high level of arsenic in tube well water is also statistically significant (P<.001) odd ratio 3.05, CI= 1.75, 5.34. This finding suggest the definite association of the level of Arsenic in the tube well water and Arsenicosis i.e black skin (Hyperpigmentation) and thickening of skin (Keratosis)

The percentage of black skin (Hyperpigmentation) is more than thickening or keratosis. (Odd ratio: 3.05, confidence interval 1.75, 5.34 and P <.001) which supported Guha Mozumder's study

The presence of a stable population in rural villages with different degrees of arsenic exposure enabled me to study the dose response pattern of skin lesions in the case group. There are some limitations, however, such as the lack of information on deaths caused by high exposure to arsenic, and the lack of information on the amount of water consumed by the individual. On the other hand, each individual had only one main source of drinking water with a known arsenic concentration (in the exposed group) even if the concentrations might have varied in the same well over time. In the exposed group, there is no information in this respect, however, arsenic analyses,in some places had not previously been performed in the villages under study.

Saha (40) have studied the incidence of arsenical dermatosis in 14 villages of West Bengal, India . According to his study the lowest arsenic concentration in water producing dermatosis was 100 ug / L. He also showed that more arsenical skin lesions in those patients who were taking high concentration of arsenic in the drinking water, which is similar to this study.

After detection of the case of Melanosis / hyperpigmentation & keratosis by the interviewer, a physician (Trained for arsenicosis) has confirmed the diagnosis by history & physical examination.

Morbidity other than melanosis / hyperpigmentation and keratosis, generalized sign, symptom and other clinical findings was observed by a graduate physician, specially trained in arsenicosis.

The symptoms like generalized weakness, headache, nausea, burning of the eye, abdominal pain, were close to the non exposed group. But the percentage of cough haemoptysis and parathesia are significantly high.(Table-23), which may be due to Chronic Arsenic poisioning. Guha mazumder in his study also found the similar findings (20) where the generalized weakness, hemoptysis, cough and parasthesia were more complined by the arsenic affected patients.

About the clinical findings, the percentage of hepatomegaly, splenomegaly, haemoptysis, Ascities and poluneuropathy were higher in the exposed group than in the non exposed group. The findings are statistically significant (P <.005). The percentage of Diabetes and hypertension were also higher in the exposed group than in the non exposed group. Guha Mozunder et al (20) also found the high incidence of hepatomegaly, splenomegaly, haemoptysis, Ascities, poluneuropathy, Diabetes and hypertension, which is similar to this study. So the above-mentioned clinical signs are responsible may be due to arsenic in the exposed group.

With history of chronic arsenic exposure and arsenical skin lesions, (indicators of chronic arsenicosis are weakness, anemia, burning eye, feel too hot, cough, peripheral neuropathy, hepatomegaly and peripheral vascular diseases) (59). Most of them complained of generalized weakness with some other feature. These features are manifested variably in different exposed populations and may also be caused by arsenic unrelated condition. Infrequent manifestations, which have been reported to occur by some investigators in people giving a history of chronic arsenic exposure and which may be as arsenic related condition. Guha mozumdar in his study shows that though pigmentation was seen in all cases, keratosis was found in 61.5%, and skin cancer was detected in 13% cases. Weakness was a predominant symptom (70%) while anemia was present in 47% of cases. Nausea, anorexia, abdominal pain and diarrhoea were present in 58.3%) Symptoms of respiratory disease were found in 57.1%) cases. (20).

From above discussion, it is clear that the patients were suffering from the above mentioned signs and symptoms, may be due to excess arsenic poisoning in the tube well water.

The majority of the respondents from both the groups, exposed and non exposed, mentioned that their tubewells were screened for arsenic by different organization (Table-26). Representatives from Govt. / NGO visited their villages, tested their tube well water, examined their condition and made some suggestion to prevent arsenicosis. As per latest information of BAMWSP that the screening of the tube well of 190 upazillas completed. The total 3035 million tube well were screened,(House hold number= 9.44 million) . Among them 0.886 million were contaminated and DPHE, UN organization, Dhaka community hospital trust (DCHT), BRAC, WHO, UNICEF etc took part actively in the survey for arsenic screening.

Among the respondents in the exposed group, only 28 % were recognized as arsenicosis (Table-27) by the health worker of different organization. And the percentage of Arsenicosis in the non exposed group was absent. Nobody was detected as arsenicosis in the non exposed group. Majority of the respondents from the both groups were being suggested by the organizations about their duties to prevent arsenicosis (Table-28). In the exposed group 100 percent were advised to avoid the arsenic contaminated water and they were advised to collect water from the alternate source like deep tube well, ring well, rain water harvesting, treatment of surface water, treatment of arsenic contaminated water(Table-29).

The respondents in the exposed group were also diagnosed as arsenicosis by the physician also (Table-30).Most of the respondent were advised by the physician not to drink the arsenic contaminated water(Table-31) and advised to take water from the alternate option. Majority of the respondents did not follow the suggestion. The reasons of not to follow were, (a) access of arsenic free water was not easy,(b) lack of motivation,(c) followed the other peoples who did not gave importance to doctors suggestion. The follow up visit (Table-33) was not done by those organizations and it is the main reason to continue to drink the water. The other important causes were, dug well contamination, lack of arsenic free filtered water, lack of vitamin or other drugs.

Most of the respondents (62%) in the exposed group, had been using the tube well less than 8 Years (Table-38). Although it was very difficult to determine how long the tube well had been contaminated. This estimate was based on the time of installation of the tube well as recalled or reported by the owner of the tube well.

Out of 174 tube wells 171 tube well were red painted by the organization, in the exposed group and none of the tube well in the non exposed group (n=181).

In this section, it could be assumed that womens were suffering from diseases more in the exposed group due to arsenic contamination in the tube well water

Section: 3
"Impact of Arsenic contamination on Reproductive Health"

This study revealed, that reproductive health impact of chronic arsenic contamination in drinking water (adverse pregnancy outcome, eg. Spontaneous abortion, still birth, neonatal death) is assessed in the women (15-49 yrs) of the exposed and non exposed area. The study also reavealed the sociodemographic pattern and morbidity of those respondents, of the selected area.

Reproductive health is defined by WHO as a state of physical, mental, and social well-being in all matters relating to the reproductive system at all stages of life. Reproductive health implies that people are able to have a satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when, and how often to do so. Implicit in this are the right of men and women to be informed and to have access to safe, effective, affordable, and acceptable methods of family planning of their choice, and the right to appropriate health-care services that enable women have safe pregnancy and childbirth.

In this study, the impact of reproductive health like pregnancy outcome considered as four main categories, live birth, unwanted abortion/ spontaneous abortion / miscarriage, still birth and neonatal death.

There was no good documentation of pregnancy outcome available in the study area, so we had to rely on the respondents when obtaining information.

A pregnancy that terminates normally and timely and fetus survive to become a live infant, called live birth. A pregnancy that losses prior to 20 weeks gestation are considered as spontaneous abortion. Miscarriage is the common term for the natural or accidental termination of a pregnancy at a stage where the embryo or fetus is incapable of surviving. Miscarriage is the most common complication of pregnancy. Women experiencing a miscarriage might have bleeding for 2 weeks or more. Bleeding for more than 10 days, or the presence of abdominal pain, may indicate incomplete miscarriage and warrant review by a doctor. Although a literatures suggest that a miscarriage should not be much heavier than a period, a miscarriage from 8 weeks or so can involve extremely heavy bleeding, to the extent that it may be difficult to go out. Severe bleeding may require medical attention. Spontaneous abortion / Miscarriage occurs more often than people think. About 25 % of women will experience one in their lives. Up to 78 % of all conception may fail in most cases before the women even know she is pregnant. A fifth of confirmed pregnancies have some bleeding occurring in the first 20 weeks and in all 15 % proceeds to spontaneous abortion. After the age of 35, the risk of miscarriage increases considerably: 1 in 5 or 6. After 40, the risk increases to 1 to 3, and after 45 it is 1 in 2.

Most such terminations occur very early in pregnancy, during the first trimester, and many people restrict the term miscarriage to early losses. Pregnancy losses in the second trimester are much less common. Spontaneous abortion frequently occurs so early that the women are not even aware that she is pregnant; these are preclinical pregnancy losses. Some women are prone to miscarry; the term "habitual abortion" is more and more replaced by pregnancies have terminated before 20 weeks gestation. Miscarriage or spontaneous abortion can occur for many reasons, not all of which can be identified. They are most frequent during the first trimester. About 30 % of fertilized eggs are actually lost before the women know she is pregnant and may only be noticeable by slightly more important blood loss. First trimester losses are in many cases due to aneuploidy. A chromosomal abnormality occurs where the genetic material from the sperm and egg don't fuse together appropriately. The resulting baby does develop properly. Other possible but much less common causes include physical trauma, exposure to certain chemicals, infection, and immune factors. A number of studies have examined lifestyle factors. Thus obesity, high caffeine intake (>300 gm / day), alcohol consumption, and use of NSAIDs have all been linked to higher miscarriage rates in general. All women undergoing fertility therapy tend to have higher miscarriage rates.Pregnancy losses in the second trimester may be due to fetal abnormalities, uterine malformation, cervical problem, infection, trauma, immune factors, and medical diseases.

In this study, no more women was found, age over 35 years had conceived & both the group and no such type of history of obesity, high caffeine and NSAID intake that might play role for developing spontaneous abortion.

The exposure in this study, both arsenite and arsenate exposures are relavent, because arsenate is converted to arsenite by glutathione during biomethylation in the human body. Arsenite has been observed to be more potent than arsenate. Recent studies reported that arsenic croses the human placenta(23), although more than 90 % of the arsenic in plasma and urine was in the form of dimerhylarsine acid, indicating an increase in the methylation of arsenic during pregnancy. Maternal toxicity has also been found to be associated with the adverse developmrntal effects of arsenic exposure(27). Maternal toxicity may in some instances be the causative factor in abnormal development of the embryos. This is probably the result of induction of metallothionein in the maternal liver that leads to a systemic redistribution of zinc and a transitory but developmentally adverse, zinc deficiency. These effects were produced in pregnant rats by arsenate (22).. Exposure to arsenic also exerted direct adverse effects on explanted rodent embryos exposed to arsenic outside the maternal system. However there was a poor correlation between maternal and developmental toxicity in an extensive literature analysis. Therefore, arsenic is likely to have direct toxic effects on embryos in vivo, but its effects might be excerabated by external toxicity (23).

Arsenic was listed under proposition 65 as known to the state to cause reproductive toxicity (developmental toxicity), effective May1, 1997 (24). For purposes of preposition 65 , arsenic (As) oxide include arsenate and arsenite salts, arsenic tri-oxide, arsenic pentoxide, arsenic acid, arsenous acid and other arsenic compounds that dissociate to the oxyanion species. The proposition 65 listing of arsenic (inorganic oxides) was based on a finding by the Developmental and Reproductive Toxicant (DART) Identification Committee, (54) the proposition 65 states qualified experts for reproductive toxicity, that the chemicals had been clearly shown by scientifically valid testing according to generally accepted principles to cause developmental toxicity. As part of its deliberation the committee was provided with the document "Evidence on Developmental and Reproductive Toxicity of Arsenic" developed. Exposure at a time 1000 times greater than the MADL (Maximum allowable dose level) is expected to have no observable effect. MADLs are derived from No Observable Effect Levels (NOELs), the highest exposure level at which no effect was observed or Lowest Observable Effect Level (LOELs), the lowest exposure levels at which an observe effect was observed under the specific conditions.(55)

The NOEl for MADL development is required to be based on the most sensitive study deemed to be sufficient quality. A recent study from the human literature of the effects of elevated drinking water arsenic on pregnancy outcome in Bangladesh (1) was considered to be of sufficient quality and to provide adequate exposure information. Studies from animal literature indicated that higher doses of arsenic were required to produce developmental toxicity in animals. The lowest doses producing developmental toxicity in rodent studies were 8-13 mg As / kg/ d as compared to 0.017 mg As / kg/d/ (0.0986 mg/ d in a 58 kg woman) in the study of Ahmed et.al. (1) This is consistent with reviews concluding the humans are more sensitive to arsenic toxicity than laboratory animal species, probably due to well documented species differences in arsenic absorption, distribution, metabolism, and excretion (52). The incidence of three adverse pregnancy outcomes (Still birth, preterm birth and spontaneous abortion) and the statistical comparisons were made between a low exposure community (drinking water concentration < 0.02 mg As / L) and a high exposure community (drinking water concentration > 0.05 mg As/L in 85% of wells). Subgroups within the high exposure community with briefer and longer exposure

(5-15 years or > 15 years) were also compared. Aktar et al showed, that the risk of negative outcome in the exposed group was more than double that of the unexposed group and comparison of these adverse pregnancy outcomes between shorter and longer exposures were also statistically significant.

In this study 7.3 % of the respondents complain of spontaneous abortion or miscarriage in the exposed group and 4.1 % in the non exposed group.(Table-37). The rate of spontaneous abortions were higher in the exposed group than the non exposed group and the association is statistically significant (P <.001), where odd ratio: 2, Confidence interval is 1.31, 3.07. (Table-56). The rate of spontaneous abortions were also high in that group those who had black spot and keratosis in comparison to that group had no black spot and keratosis.(Table-48,51) and the association is statistically significant (p<.05). In this study it is proved that women with Arsenicosis had more spontaneous abortion than the group of women took arsenic contaminated water but no arsenicosis or sign developed. Again it was reaveled that the group had more spontaneous abortion, were taking high concentration of Arsenic contaminated tube well water (> 200 ug/l) , which is also statistically significant.(p <.01 , odd ratio 3.62, confidence interval; 2.12, 6.19) So, in this study, it is clear that the spontaneous abortion were more in those women were taking high concentration (> 200 ug/l) of Arsenic contaminated tube well water.

Nordstrom et al. (33) conducted a study of 662 of women employed in or living near the arsenic smelter area. In that study it is showed that spontaneous abortion was highest when the mother was employed during pregnancy (14 %) or before pregnancy and living near the arsenic smelter. Within employment categories, significantly higher rate of abortions were observed in high exposure job where 28 % in the exposure group and 14 % in the non exposure group. Here it was also interesting that the abortion rate were higher among the father worked at the smelter. Again, Nordstrom reviewed data from hospital files on over 4427 pregnancies of women born in or after 1930 who lived in four areas of increasing distances from the smelter. A control group of 4544 pregnancies was used from a hospital in Umeå, a non-exposed town. There was a clear dose–response relationship between the occurrence of spontaneous abortions and residential proximity to the smelter. In particular, women in the closest town (< 10 km from the smelter) had the highest rates (11% vs. 7.6%, $p < 0.005$). In the most exposed area, 4 of 20 women with abortions had 2 abortions and no normal pregnancies. So this study result supports the relationship of Spontaneous abortion and arsenic.

A case–control study of spontaneous abortions in Boston, Aschengrau et al. (2) examined 286 women who experienced spontaneous abortions and 1391 controls in relation to the content of their water supplies. An adjusted odds ratio of 1.5 was found for the group with the highest arsenic concentrations. However, this exposure group had low levels of arsenic in water (1.4–1.9 µg/litre), close to or lower than laboratory analytical detection limits, and the possibility of chance or unaccounted confounders could not be discounted. In another study of Aschengrau evaluated of exposure to arsenic of two groups. The crude odds ratio of exposure to inorganic arsenic in drinking water among cases compared to controls was 1.3 (95% CI: 1.0-1.6). Exposure to water containing higher arsenic levels was more strongly associated with spontaneous abortion than exposure to lower arsenic levels. After adjustment for multiple cofounders using a multiple logistic regression model, only exposure to higher levels of arsenic (1.4-1.9 μg/L) was found to be associated with spontaneous abortion and the magnitude of association was small and not statistically significant (Exposure Odds Ratio 1.5; 95% CI: 0.4-4.7).

A study in an area of south-east Hungary (6) with exposure to arsenic from drinking-water examined the rates of spontaneous abortions for the period 1980–1987. Two populations were compared: one with levels of arsenic in drinking-water > 100 μg/litre (n = 25 648 people) and one control area with low arsenic levels (n = 20 836) (no information on analytical method, or timing or frequency of sampling was available). Both outcomes were significantly higher in the exposed groups, with a 1.4-fold increase in spontaneous abortions (p = 0.007) . Although both populations were reported to be similar in several characteristics, such as smoking, lifestyle, occupation and socio-economic status, no information was provided, and other important factors such as smoking and maternal age were not accounted for. Three additional studies (23) also found positive association between arsenic drinking water exposure and spontaneous abortion.

In the historical cohort study of Ahmed et ai. (1), the incidences of three adverse pregnancy outcomes (spontaneous abortion, still birth, preterm birth) were determined by interviews using a questionnaire and check list. Respondents (n=96 per group) were randomly selected from the exposed population and non exposeds were matched for age, education and socio-economic status. Statistical comparisons were made between a low exposure community (drinking water concentration < 0.02 mg As/L) and a high exposure community (drinking water concentration > 0.05 mg As/L in 85% of Wells). Subgroups within the high exposure community with shorter and ionger exposures (5-15 years or > 15 years) were also compared. The risk of spontaneous abortion, in the exposed group was more than double that of the unexposed group ($p < 0.05$, Fishers exact test , one sided). Comparisons of these adverse pregnancy outcomes between shorter and longer exposures were also statistically significant.

Milton. A.H et al (27) in his study "Exposure to arsenic increase risk of adverse pregnancy outcomes" was conducted over married, non smoking females of reproductive age ranging from 15-49 years with the mean age of 31.22 years with a history of at least one pregnancy. They were studied to determine the association between chronic arsenic exposure through drinking water and spontaneous abortion.

To investigate the relationship between community drinking water and spontaneous abortion, *A Aschengrau et al <2> in study "Quality of community drinking water and the occurrence of spontaneous abortion"* compared trace elements mainly arsenic levels in the drinking water of 286 women having a spontaneous abortion through 27 wk gestation with that of 1391 women having live births. Trace elements level was gathered from routine analysis of public tap water supplies from the communities where the women resided during pregnancy. After adjustment for potential confounders, an increase in the frequency of spontaneous abortion was associated with detectable level of high level of arsenic.

The rate of possible confounding factors like Hypertension, Diabetes Meiiitus (DM), were also very close to the both group. The percentage of other factors like advanced maternal age, height, weight, drug history, history of trauma, which often causes spontaneous abortion, were nearly same in the both group.(Table-22). The difference was not statistically significant.

Here in this study. excess risks for spontaneous abortion is observed among the respondents exposed to increasing concentration of arsenic in drinking water, after adjusting for participants' education, age at marriage, antenatal care and parity and other confounding factor. The study findings largely suggested that chronic arsenic exposure can increase the risk of spontaneous abortion.

Here in the study, Still birth is 4.6 % in the exposed group and 2.8 % in the non exposed group. (P < .001). It was observed that rate of still births were higher in the exposed group than the unexposed group (Table-37). The association is statistically significant (P < .001). The possible confounding factors were adjusted here in the study.

The association was also statisticaly significant (P < .001,) for the comparison of still birth with black spot / melanosis/ hyperpigmentaion and thickening of skin/ keratosis. Here it was observed that those women had black spot and keratosis, also had more stillbirth, than those no black spot and keratosis, in the exposed group (Table- 49, 52). Here in this study, this association proved that women with arsenicosis had more still birth than women with no arsenicosis. Still birth were also higher for those women of taking high level (> 200 ug /l) of arsenic contaminated tube well water in comparison to less concentrated< 200 ug/l

Arsenic contaminated tube well water (Table-58), which is also statistically significant ($p <.01$, odd ratio, 2.66, confidance interval, 1.39, 5.07).

It is already established in the previous discussion that exposure to water containing higher arsenic levels was more strongly associated with still birth than exposure to lower arsenic level

Two populations were compared in an area of south east Hungary with exposure to arsenic from drinking water examined the rates of still births for the period 1980-1987. Among two population, one with levels of arsenic in drinking water > 100 µg/liter (n = 25 648 people) and one control area with low arsenic levels (n = 20 836) (no information on analytical method, or timing or frequency of sampling was available). The outcome was significantly higher in the exposed groups, and a 2.8-fold increase in stillbirths (p = 0.028). Although both populations were reported to be similar in several characteristics, such as smoking, lifestyle, occupation and socio-economic status, no information was provided, and other important factors such as smoking and maternal age were not accounted for. Furthermore, no mention was made of other potential environmental exposures; in populations of roughly similar size, the number of live births during the study period, 1980–1987 was 5218 in the high- and 2112 in the low-exposure area. This study also supports the present study findings here.

Inorganic arsenic is also toxic for reproductive system in mammals like mouse and hamster was found in some study."Developmental toxicity assessment of arsenic acid in mice and rabbits" a study conducted (25) and evaluated potential effects of exposure to inorganic arsenic throughout major organogenesis, CD-1 mice and white rabbits were gavaged with arsenic acid dosages of 0,7.5, 24 or 48 mg / kg/ d on gestation days 6 through 15 (mice) or 0,0,19, 0.75 or 3.0 mg / kg/ d/ on Gestational days 6 through (18) rabbits and examined at sacrifice (GD 18 mice : GD 29, rabbits) for evidence of toxicity. Two high dose mice died, and survivors at the high and intermediate doses had deceased weight gains. At the high dose in rabbits, seven died or became moribund, decrease fetal weight and prenatal mortality / still birth was increased.

A hospital case–control study (21) in the USA investigated the occurrence of stillbirths in relation to residential proximity to an arsenical pesticide production plant in Texas . Exposure was categorized in three groups according to arsenic air levels. An increasing, but not significant, trend in the risk of stillbirths was observed. The number of stillbirths was significantly elevated for the high-exposure group. When stratified by ethnicity, however, the findings remained significant for Hispanics only. Other exposures from the chemical plant were possible and were not measured in the study.

A study was performed in Taiwan (58) to compare the risk of adverse pregnancy outcomes (Preterm delivery. low birth weight) between an area with historic high well water arsenic level, arsenic exposed area (AE) and a comparison area with no historic evidence of arsenic water contamination , non –arsenic- exposed area (NAE). Arsenic exposed area (AE) had a higher rate of preterm delivery than NAEs (3.74 % vs 3.43 %). The result of this study suggests that, after adjustment for potential confounders arsenic exposure from drinking well water was associated, with an odd ratio of 1.1 (0.91-1.33). The result of mean birth weight in the AEs and NAEs were 3132.6 and 3162.6 g. respectively. It was also found that babies born in AEs were on average 30 g lighter than those born in NAEs.

"Exposure to arsenic increase risk of adverse pregnancy outcomes" study was conducted by Milton, A.H. et al (27), in females of reproductive age ranging from 15-49 years with the mean age of 31.22 years with a history of at least one pregnancy. In this cross sectional study, 533 women were interviewed. The respondents reported use of a total of 223 tube wells, for 208 wells. Excessive risk of still birth were observed among the participants chronically exposed to higher concentration of arsenic in drinking water after adjusting for participants height, history of hypertension and diabetes and age at first pregnancy. Here the odd ration were 2.5 (95 % confidence interval = 1.3 -4.9). This study also supports the present study findings which also related to the excessive risk with high level of Arsenic contaminated water.

The similar result was found on the study (1) "Arsenic in drinking water and pregnancy outcomes". This cross sectional study was carried out in two villages in Bangladesh with a comparison to exposed group and non exposed group. The study subjects were married women of reproductive age who previously had at least one pregnancy. There were 96 exposed and unexposed women included in the study. Of the exposed group 98 % had been drinking water that contained more than 0.10 mg/ l arsenic and 43.8 % of these had been drinking this water for 5-10 years. Statistical comparisons were made between a low exposure community (drinking water concentration < 0.02 mg As/L) and a high exposure community (drinking water concentration > 0.05 mg As/L in 85% of Wells). Subgroups within the high exposure community with briefer and longer exposures (5-15 years or > 15 years) were also compared. The risk of still birth or preterm birth in the exposed group was more than double that of the unexposed group ($p < 0.05$, Fishers exact test , one sided). Comparisons of these adverse pregnancy outcomes between shorter and longer exposures were also statistically significant. Three studies (23) also found positive associations between arsenic drinking water exposure and adverse pregnancy outcome (Still birth).

In this study, BMI, Mean $\pm$ SD in the exposed group 17 $\pm$ 2.1 and the non exposed group ii was 18.8 + 2.4 (Table-22). The difference was not statistically significant in this study. Because maternal obesity is the important factor for Still birth & Neonatal death. A cohort study (58) was conducted in Aarthus university hospital in Denmark_ and it was found that the maternal obesity had double risk of Still birth(Odds ratio 2.8 , CI 1.5- 5.3)_and Neonatal death (odd ratio -2.6, CI- 1.2- 5.8) compared of women with normal weight. But no statistically significant increased risk of stillbirth or neonatal death was found among underweight women. It was Adjustment for maternal cigarette smoking, alchohol intake, maternal age, parity, hypertensive disorder and Diabetis Mellitus (DM) etc in that study.

Socioeconomic status is a less important determinant of Neonatal mortality risk, there is no estimated impact of wealth (nor of paternal education). Similarly location (division of residence, rural / urban) does not exert an important effect on neonatal survival chances, once non exposedling for others factor. Services such as clean water and sanitation, electrification, and antenatal and delivery care are key determinants of neonatal survival. Newborn have significantly better survival chance when they live in household with both piped water in to the dwelling and sanitary toilet facilities. In addition, newborn living in electrified dwellings have significantly better survival chance than others.

Maternal characteristics are important determinants of Neonatal mortality. New born have better survival chances if their mother are more mobile

In this study (Table- 37), 6.5 % of the Neonatal death occured in the exposed group and 3.6 % in the non exposed group. (p < .001, odd ratio 2.07, confidence interval 1.32, 3.27) The rate of Neonatal death is higher in the exposed than the non exposed group.

Here it was observed that those women had black spot and keratosis, had more Neonatal death, than the exposed group but no black spot and keratosis .Here in this study, this association proved that women with arsenicosis had more Neonatal death than those were taking arsenic contaminated water but no keratosis and the non exposed group. Stillbirth was higher for those women of taking high level >200 ug /l of arsenic contaminated tube well water. (p = .051, odd ratio 1.68, confidence interval .96, 2.03)

An ecological study examined infant mortality rates in three Chilean cities over a 46-year period (1950–1996) (24). Antofagasta, in northern Chile, experienced very high arsenic levels in drinking water for a period of 12 years. In 1958 a new water source which contained arsenic concentrations around 800 µg/litre was introduced as the main supplier of public water. In 1970, because of the overt signs of arsenicism observed in several studies, an arsenic removal plant was installed, and levels decreased initially to around 100 µg/litre, and then gradually over time to around 40 µg/litre. *The changes in late fetal, neonatal and post-neonatal mortality rates over time* in Antofagasta were compared to those in Valparaiso, another Chilean city with similar demographic characteristics but low in arsenic, and the capital, Santiago, with similarly low concentrations arsenic in the drinking-water. A close temporal relationship was observed between the high arsenic period and a rise in mortality rates in Antofagasta, whereas the other two cities had a steady decline in infant mortality.

A cross sectional study on "Chronic arsenic exposure and adverse pregnancy outcomes in Bangladesh" was conducted by Milton, A.H, (27) 533 were interviewed. Excessive risks for Neonatal death was observed among the participants chronically exposed to higher concentration of arsenic in drinking water after adjusting for participant's height, history of DM and hypertension, age at first pregnancy. Comparing exposure to arsenic concentration of greater than 50 ug / l with 50 ug /l or less, the odd ration was 1.8 (95 % confidence interval = 0.9-3.6) for neonatal death. These study findings suggest that chronic arsenic exposure may increase the risk of neonatal death which support the present study findings.

There are some biological factors associated with higher Neonatal mortality are gender (male) , multiple birth, short proceeding birth interval, death of previous sibling, and very low or very high birth order (the estimated turning point is between birth order 6 and 7). Mother age has a convex effect on mortality risk, the coefficient suggesting that that the mother's optimal age for child birth is during her late 20s

The above findings suggest an association between chronic arsenic exposure through drinking water and neonatai death which is statistically significant.

Impact of antenatal care

A pregnancy brings with it great hope for the future, and can give women a special and highly appreciated social status. It also brings great expectations of health care that is often willingly sought at this time. This explains, at least in part, the extraordinary success of antenatal care consultation. Women want confirmation that they are pregnant. At the same time they know that pregnancy can be dangerous particular in the developing world. In many countries pregnant women are likely to know of maternal death, stillbirth and newborn death among their own standard family or in their community.

In high income and middle-income countries today, use of antenatal care by pregnant women is almost universal-except among marginalized groups such as migrants, ethnic minorities, very poor and those live in isolated rural communities.

Antenatal care is not just a way to identify women at risk of troublesome deliveries. While less prominent than the dangers that can occur during child birth, those surrounding pregnancies are so far from being negligible. Women expect that antenatal care will help them deal with the health problem that can occur during pregnancy itself. The cares are, first, the complication of pregnancy itself, second, diseases that happen to affect a pregnant women and which may or may not be aggravated by pregnancy, and third, the negative effects of unhealthy lifestyles on the outcome of pregnancy. All have to be tackled by antenatal care.

BDHS<3> shows that there are sharp differences in antenatal care coverage subgroups in Bangladesh. Antenatal care from a medically trained provider is received more often by young mothers than older mothers and for lower order births than for higher order births. Antenatal coverage also increases with level of mother's education and household economic status. It is also showed that nine out of ten mothers who completed secondary education received antenatal care from a medically trained provider, compared with only three in ten mothers with no education. The antenatal coverage is quite large in urban than rural areas.

In this study, it shows that the percentage from the both exposed and non exposed groups are receiving antenatal care from different categories of providers were, in close, indicates the same socio-economic group. 46.5 % of the respondents in the exposed and 48 % in the non exposed group are receiving antenatal care some how (Qualified and unqualified) from the care provider (Table-40). The BDHS survey, 2004 shows that 49 % are received care from the above mentioned care provider. In this study, 23.68 % of the respondents in exposed and 26.09 % in the non exposed are receiving antenatai care from the qualified doctors, whereas the BDHS percentage are 25 % , receiving the antenatal from the said provider. The percentage of the type of Ante-natal care received in the both group. had no special impact on pregnancy outcome.

Maternal morbidity is divided in to obstetic complications, preexisting medical conditions. and cesarean delivery. An obstetic complication is a condition caused by the pregnancy itself or by its management. A pre-existing medical complication is an underlying condition that may be aggrevated by the pregnancy. Classic complication of pregnancy include pre-eclampsia and eclampsia which affect 2.8 % of pregnancies in developing countries and 0.4 % in developed countries (12), leading to many life threatening cases and over 63000 maternal death world wide every year. Haemorraghe following placental abruption or placenta previa affects about 4 % or pregnant women (13). Less common, but very serios complications include ectopic pregnancy and molar pregnancy.

Morbidity during antenatal period

Two thirds of the women (64 % & 59 %) of the exposed and the non exposed group respectively, reported that they had experienced at least one complication during the period of antenatal care or before delivery. The rest (36 %, 41 %) for both the group did not report any such complications of condition. Here the patterns of complication are showing the same socio-economic condition for the group.

The study results are similar to the result of ICDDR,B study result (39) done in Motlab. That study showed that 66 % of the respondents were facing somehow complication.

But, nearly one fifth (19 %) of the respondents reported having the condition, pre-eclampsia (PET), in the exposed group and 15 % in the non exposed group (Table-41). This may be due Arsenic contamination in the tube well water in the exposed group. . In exposed group the percentage of PV bleeding, Leaking membrane, convulsion were still high that the non exposed group. The ICDDR,B study results also showed the same result as like the non exposed group. Here , Arsenic may be responsible to develop the above complication during antenatal period, (p=.20)

Morbidity during delivery

Forty four percent respondents in the exposed group and forty percent in the non exposed group (Table-42) complain of at least one morbid complication during their period of delivery. The percentage of prolonged labour, excessive bleeding and convulsion were still higher than the non exposed group, which may be due to Arsenic contamination in the tube well water, in the exposed group. The other condition like, retained placenta, fowl smell, baby's hand and feet came first were the close percentage.

Complication after delivery / post partem morbidity

Twenty eight percent of the women in the exposed group and twenty four percent of the women in the non exposed group at least one type of morbid condition within 42 days of delivery. Fever was reported 11 percent & 13 percent in the exposed and non exposed group respectively. The percentage of severe bleeding (12 %) was higher than the non exposed group (8%). The other conditions were like, convulsion and fowl discharge, more or less close. The higher rate in the exposed group may be due to the presence of arsenic contamination and the association is not significant. (p=.14).

Confounding factors

Hypertensive disorder of pregnancy: It is one of the risk factor for pregnancy. Hypertensive disorder of pregnancy is a group of health problem that all refer to high blood pressure during pregnancy. There are two types of hypertensive disorder. a. Pregnancy induced hypertension. b. Pre-existing hypertension or essential hypertension. The pregnancy-induced hypertension is believed to be a result of maternal mal adaptation to placental tissue and reduced maternal placental perfusion. Women with the high risk of this disorder include young women, older women, nulliparous women and obese women

Here in this study, 16 % respondents in the exposed group and 13.5 % in the non exposed group were observed as hypertension. The increased rate of hypertension in the exposed group might be due to chronic arsenic exposure. Because there are some studies proved that there is a relationship among hypertension and Chronic arsenic exposure. The association of hypertension with the spontaneous abortion, stillbirth, and neonatal death was not identified. The association was not also statistically significant.(Table-24)

Diabetes Mellitus

Diabetes in pregnancy can be the result of diabetes mellitus present before pregnancy, or of gestational diabetes. Gestational diabetes Mellitus (GDM) may be induced by pregnancy or it may be maternity onset diabetes first recognized during pregnancy.

Here in this study, 15 % respondents in the exposed group and 12 % in the non exposed group were observed as Diabetes Mellitus (DM). The increased rate of diabetes in the exposed group might be due to chronic arsenic exposure. Because there are some studies proved that there is a relationship among diabetes and Chronic arsenic exposure The association of DM with the spontaneous abortion, stillbirth, and neonatal death was not identified. The association was not also statistically significant.(Table-24)

Smoking and alcohol consumption:

Harmful lifestyles behavior of the mother, such as smoking and alcohol abuse, also have adverse effect on the health status of the fetus and new born. In exposed of cigarette smoking, not only smoking during pregnancy but also lifetime smoking history and environmental cigarette smoking seems to have adverse effect. Tobacco chewing, which occurs more frequently in developing countries, also appears to have some adverse effects. The relationship between smoking or alcohol consumption and adverse pregnancy and birth outcome is complex and likely to be confounded at least to some extend by factor such as other negative life style behavior, malnutrition, and psychological stress, socio economic factor.

Smoking during pregnancy contributes to several adverse outcome including reduced weight and length, LBV, intrauterine growth retardation, abruption placenta, placenta previa, preterm birth, spontaneous abortion, still birth, prenatal mortality

In this study, all of the respondents for both the group exposed and non exposed were totally non-smoker and non alcoholic.

Anemia ;

Anemia is a quite common disorder in pregnancy. Maternal anemia has been said to lead to increased risks of IUGR, LBW, preterm birth, prenatal mortality and maternal morbidity. The adverse effect of anemia are limited unless the anemia is share or complicated by other condition, pre-eclampsia, abruption placenta. Further a high level of more than 13 g / dl has been associated with adverse outcome, such as preterm birth, LBW, perinatal mortality and pre eclampsia.

The percentage of anemia identified for both the group (54 % in the exposed and 52% in the non exposed group) which is not statistically significant.

Advanced maternal age

Frequently, an age 35 years or over is applied to denote women at increased risk of experiencing complication especially in refuse to women who are pregnant at the first time. Advance maternal age has been associated with many adverse outcomes for maternal and fetal health status.Advance maternal age has been associated with many adverse outcomes for maternal or fetal health status. Adverse outcome that are frequently mentioned in relation to advanced maternal age are: chromosomal anomalies, spontaneous abortion, still birth, gestational diabetes, placenta previa, abruptio placentae, preterm birth and perinatal mortality.

Moreover various factor may confound the observed association between maternal age and advance pregnancy and pregnancy outcome. Post natal confounder include, parity, education, race, history of reproductive difficulties and complication, smoking and drinking behavior, pre-existing health problem. In USA, 35.5 % of the women bears child within the age 35 years. 13 % of women over the age 35 but below the age 40 years. 2.2 % over the age 40 years. The highest maternal age was 54 years (6 live birth).

In regard to this study, relationship between advanced age with still birth and spontaneous abortion appeared, not significant. The majority of the respondents delivered their child before the age of 35.

So, all of the above possible confounding factors for the negative pregnancy outcome were not responsible for the higher rate of Spontaneous abortion, Still birth and Neonatal death, in this study.

The above findings suggest an association between chronic arsenic exposure through drinking water and spontaneous abortion, stillbirth and Neonatal death which is statistically significant.

Chapter-7

Conclusion & Recommendation

Conclusion

When most of the people have developed the habit of drinking tube-well supplied groundwater in Bangladesh, arsenic has been found in unacceptable concentrations in tube-well water in many parts of the country, and in consequence many people are suffering from chronic arsenic poisoning. Arsenic, a naturally occurring metalloid, is one of the most common and important trace elements with toxic properties. Arsenic causes adverse health effects if taken in high amounts, when the intake of arsenic exceeds the limit of tolerance.

Arsenic poisoning episodes have been reported all over the world. Exposure to arsenic may come from natural sources, from industrial sources, or from food and beverages. In the South-East Asia Region, arsenic contamination of groundwater has been reported in Bangladesh, India, and Thailand and to a limited extent in Nepal and Myanmar. In India and Bangladesh, and possibly Nepal and Thailand, arsenic is of geological nature originating from the natural aquifers.

Arsenic contamination at higher level than the WHO recommended value was found in the tube-wells of 52 districts out of the 60 surveyed. Of these, the level of arsenic presence exceeds the maximum permissible limit in the tube-wells water of 41 districts. In 11 districts, the level of arsenic concentration was found more than the WHO recommended value, but less than the maximum permissible limit. The survey in 41 districts revealed a more dangerous fact.

According to WHO more than 1.0 mg/l arsenic in water may create a disastrous situation. This concentration is 100 times higher than the WHO recommended value and 20 times higher than the maximum permissible limit.

Chronic arsenic poisoning can manifest a wide range of disease conditions involving various human systems and organs, including the reproductive system.

The main objective of the study is to study the reproductive health impact of arsenic contamination of drinking water on married women including their pregnancy outcomes.

Chronic arsenic poisoning, the type that is found in Bangladesh, can manifest a wide range of disease conditions involving various human systems and organs, including the reproductive system. But, so far, reproductive effects of inorganic arsenic on humans have not been well studied. There is an important knowledge gap in the areas of reproductive health impacts of arsenic-contaminated water intake.

Most of the studies that were conducted in the area examined impacts of inhaled inorganic arsenic (from the copper smelter or the semiconductor industry) on reproductive health; studies on the reproductive health impacts of arsenic-contaminated water intake are very few. Again, results of these studies indicate that further research in this field is needed.

In this study, it was revealed that those women were suffering more with black spot & keratosis also receiving high concentration of arsenic in the tube well water (drinking water). And at the same time, in this group, the rate of adverse pregnancy outcomes were high in comparison to those women were taking low arsenic concentrated water.

The rate of Spontaneous abortions, Still birth and Neonatal death were higher in the exposed group than the non exposed group and the association was statistically significant. The rate of Spontaneous abortions, Still birth and Neonatal death were also high in that group those who had black spot and keratosis in comparison to that group had no black spot and keratosis and the association was statistically significant . In this study it is proved that women with arsenicosis developed more adverse pregnancy outcome than the group of women took arsenic contaminated water but no arsenlcosis or sign developed. Again it was reaveled that the group had more adverse pregnancy, were taking high concentration of arsenic contaminated tube well water (> 200 ug/l), which was also statistically significant. So, in this study, it is clear that the adverse pregnancy outcome were more in those women taking high concentration (> 200 ug/l) of Arsenic contaminated tube well water.

Finally, it was observed that negative reproductive health impacts (Spontaneous abortion, Still birth & Neonatal death) were more common among women who were taking high arsenic contaminated drinking water.

So, the results of this study are in consistence with the hypothesis of the study

Attention has been drawn to the fact that ingestion of arsenic contaminated water leads to series of skin diseases & increase number of Spontaneous abortion, Still birth & Neonatal death. It is important to prevent the increase of arsenicosis for both health & economic reason. It is clear that mitigation methods need to be implemented urgently, not least for reasons of poverty alleviation. It is important to assess the future health & socioeconomic impacts of alternative mitigation methods

In this context, the present study will be able to contribute to fill up this knowledge gap, and this study will be a pioneering one in the area of reproductive health impacts of arsenic contamination of groundwater. I hope that this study can be an input in the further discussion and will contribute to the knowledge of the planners, policy makers and administrators to chalk out pragmatic policy for arsenic contamination mitigation programmes and for reduction of maternal and infant morbidity and mortality in Bangladesh.

RECOMMENDATION

a. Build awareness through mass communication not to take arsenic contaminated water.

b. Provide safe drinking water.

c. Provide symptomatic treatment and identify patients / population at risk.

d. Strengthen diagnostic facilities at local level.

Chapter-8

Annex-1

Bibliography

1. Ahmad SA, Sayed MHSU, Barua Sampa, Jalil MA, Ahmed R. Arsenic in Drinking Water and Pregnancy Outcomes.J.Envirionmental Health Perspective 2001 June 15; 109(6):629-631.

2. Aschengrau A, Zierler S, Cohen A. Quality of community drinking water and the occurrence of spontaneous abortion. Arch Environ Health 1989 June 4; 44(3):283-290.

3. "Bangladesh Health & Demographic Survey 2005"

4. Black M.D. Prolong ingestion of Arsenic. Pharm 1967 J (Dec 9) 593-597

5. Borgono JM, Vincent P, Venturino H. Arsenic in the drinking water of the city of Antofagasta: Epidemiological and clinical study before and after installation of a treatment plant. Environ Health Perspect 1977 May 19: 103-105.

6. Borzsonyi M, Bereczky A, Rudnai P, Csanady M, & Horvath A . Epidemiological studies on human subjects exposed to arsenic in drinking water in Southeast Hungary. Arch Toxicol 1992 Jun 4 ; 66 : 77-78.

7. Carpenter SJ. Developmental analysis of cephalic axial dysraphic disorders in arsenic-treated hamster embryos. Anat Embryol 1987 ;176:345-365.

8. Chaineau E, Binet S, Pol D, Chatellier G, Meiningen V . Embryotoxic effects of sodium arsenite and sodium arsenate on mouse embryos in culture. Teratology 1990 ; 41:105- 112.

9. Chatterjee A, Das D, Mandal BK, Chowdhury TR, Samanta G & Chakraborti D. Arsenic in ground water in six districts of West Bengal, India: the biggest arsenic

calamity in the world. Part 1. Arsenic species in drinking water and urine of the affected people 1995 ; 120: 643-650.

10. Chatterjee A, Das D, & Chakraborti D. A study of ground water contamination by arsenic in the residential area of Behala, Calcutta due to industrial pollution. Environ. Pollut1993; 80: 57-65

11. Das D, Chatterjee A, Mandal BK, Samanta G and Chakraborti D. Arsenic in ground water in six districts of West Bengal, India: the biggest arsenic calamity in the world. Part 2. Arsenic concentrations in drinking water, hair, nails, urine, skin-scale and liver tissue (biopsy) of the affected people. Analyst, 1995 ; 120: 917-924.

12. Daya MR, Irwin R, Parshley MC, Harding J, Burton BT. Arsenic ingestion in pregnancy. Vet Hum Toxicol 1989 ; 31: 347.

13. Dhaka Community Hospital Trust (DCHT). *Arsenicosis in Bangladesh* . Dhaka DCHT, 1998 ; 2: 2-5

14. Dhar RK, Biswas BK, Samanta G, Mandal BK, Chakraborti D, Roy S, Fafar A et al. Groundwater arsenic calamity in Bangladesh. Current Science, 1997, 73(1): 48-59.

15. Diaz-Barriga F, Santos MA, Mejia JD, Batres L, Yanez L, Carrizales L. Arsenic and cadmium exposure in children living near asmelter complex in San Luis Pososi, Mexico. Environmental Research 1993 ; 62:242-250.

16. Ellenhorn, MJ , Arsenic In: Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning Baltimore 1997 ; 2 : 1538-1542.

17. Farago M, Abernathy RL, Calderon WR, Chappell Eds. Exposure and Health Effects, Academic Publishers, London 1997; 5: 1–16.

18. Ferm VH, Hanlon DP (1985). Constant rate exposure of pregnant hamsters to arsenate during early gestation. Environ Res 1985 ; 37: 425-432.

19. Fisher DL. Cultured rat embryo accumulation of DNA, RNA, and protein following maternal administration of sodium arsenate. Environ Res 1982 ; 28:1-9.

20. Guha Mazumder DN, Das Gupta, Santra J, Pal A, Ghosh A, Sarkar Chattopathday S, Non Cancer effects of chronic arsenicosis with special reference to liver damage 1998 ; 5 : 112-123

21. Hindmarsh, JT, Hair arsenic as the index of toxicity, Proceding of the 3rd International confernence on arsenic exposure and health effects, San diegi, CA 1998; p-7

22. Hood RD, Harrison WP. Effects of prenatal arsenite exposure in the hamster.Bull Environ Contam Toxicol 1982; 29: 671-678.

23. Hopenhayn-Rich C, Smith AH, Goeden HM. Human studies do not support the methylation threshold hypothesis for the toxicity of inorganic arsenic. Environ Res 1993 ; 60 :161-177.

24. Hopenhayn-Rich C, Biggs ML, Fuchs A, Bergoglio R, Tello EE, Nicolli H, & Smith A. Bladder cancer mortality associated with arsenic in drinking water in Argentina. Epidemiol 1996 ; 7: 117-124.

25. Lewis DR, Calderon R, Southwick JW, Ouellet-Helstrom R, & Rench J. Drinking water arsenic in the U.S.: the Millard County, Utah mortality study. Submitted to Environmental Health Perspectives 1998 octobar 4.

26. Lin T-H, Huang Y-L, & Wang M-Y (1998) Arsenic species in drinking water, hair, fingernails, and urine of patients with blackfoot disease. J Toxicol Environ Health, Part A 1998; 53 : 85-93.

27. Milton AH, Smith W, Rahman B, Hasan Z, Kulsum U, Dear K.Rakibuddin M. Chronic Arsenic exposure and adverse pregnancy outcome, Bangladesh, Epidemology 2005; 16(1):82 – 86 .

28. Mandal BK, Chowdhury TR, Samanta G, Basu GK, Chowdhury PP, Chanda CR. Arsenic in groundwater in seven districts of West Bengal, India – The biggest arsenic calamity in the world. Current Science 1996; 70(11): 976-986.

29. Mirkes PE, Cornel L. A comparison of sodium arsenite- and hyperthermiainduced stress responses and abnormal development in cultured postimplantation rat embryos. Teratology 1992; 46:251-259.

30. Moderegger H, Schachl K, Kalcher K, *et al.* A new simple device for the determination of arsenic in drinking water at low levels. In: *Abstracts of the International Conference on Arsenic Pollution of Ground Water in Bangladesh: Causes, Effects and Remedies 1998 Feb 8-12 ;* 72 - 73.

31. Morrissey RE, Mottet NK. Arsenic-induced exencephaly in the mouse and associated lesions occurring during neurulation. Teratology 1993; 28:399-411.

32. Ng JC. Arsenic contamination: Scourge of millions. In: *Programme-Primer of the Rotary Conference for Arsenic-free Water: A Peace Programme of The Rotary Foundation 1999 Nov. 26-28; Calcutta.* : 26-29.

33. Nordstrom S, Beckman L, Nordenson I . Occupational and environmental risks in and around a smelter in northern Sweden III,Frequencies of spontaneous abortion. Hereditas 1987b ; 88 : 51-54.

34. Nordstrom S, Beckman L, Nordenson I. Occupational and environmental risks in and around a smelter in northern Sweden. V. Spontaneous abortion among female employees and decreased birth weight in their offspring. Hereditas 1979a; 90: 291-296.

35. Nordstrom S, Beckman L, Nordenson I. Occupational and environmental risks in and around a smelter in northern Sweden. VI. Congenital malformations. Hereditas 1979b ; 90 : 297-302.

36. Quadiruzzaman AM. Arsenic contamination in Bangladesh. *Daily Star*, suppl. 20 Dec. 1999: 17.

37. Rabbani GH, Anwar KS, Hossain A, *et al*. Arsenic poisoning in Bangladesh: Review of current situation : *Programme and Papers of the Inauguration Ceremony of the Bangladesh Arsenic Control Society (BACS) 1999 May 8; Dhaka*. Dhaka: BACS, 1999: 26-33.

38. RAHMAN M, TONDEL M, AHMAD S.A, & AXELSON O. Diabetes mellitus associated with arsenic exposure in Bangladesh. *Am. J. Epidemiol*. 1998 ; **148:** 198-203.

39. Rahman M, Ahmed MK, Van Ginnekenj J. Induced abortion in Motlab, Bangladesh, Trends and determinants(ICDDRB), Int.fam Plann perpective, 1998 ; 24: 128-32

40. Saha KC, Melanokeratosis from arsenic contaminated tubewell water. Ind.J. Dermat. 29(4): 37-46.

41. Shapiro H.A, Arsenic content of human hair and Nails. Its Interoretation, J. Forensic Medicine 14 : 65-71

42. Smith A H, Lingas EO, Rahman M. Contamination of drinking water by Arsenic in Bangladesh, a public health health emergency, Bulletin WHO 78: 1093-103

43. Scudlark JR & Church TM. The atmospheric deposition of arsenic and association with acid precipitation. Atmos Environ 1988; 22(5): 937-943.

44. Smith RA, Alexander RB & Wolman MG. Water-quality trends in the nation's rivers. Science 1987; 235: 1607-1615.

45. Sommers SC & Mc Manus RG, Multiplr Arsenical cancer of skin and internal organ, Cancer 6 ; 6: 347-359.

46. Symonds et al. Pathophysiology of pregnancy, Environ Health Perspect, 19:151-157.

47. Sullivan RJ. National Air Pollution Control Administration Publication No. APTD 69- 26 1969 ; 5 : 60.

48. Tabacova S, Hunter ES III, Gladen BC. Developmental toxicity of inorganic arsenic in whole embryo culture: Oxidation state, dose, time and gestational age dependence. Toxicol Appl Pharmacol 1996 ;138:298-307.

49. Tabacova S, Baird DD, Balabaeva I, Lolova D, Petrov I . Placental arsenic and cadmium in relation to lipid peroxides and glutathione levels in maternal-infant pairs from a copper smelter area. Placenta 1994 ; 15:873-881.

50. Tanaka T. Arsenic in the natural environment. Part II: Arsenic concentrations in thermal waters from Japan. Appl Organomet Chem 1990 4: 197-203.

51. Tseng WP, Chu Hp, How SW, Fong JM, et al. J. Natl. Cancer Inst 1968 453 ; 414.

52. Vahter M, Friberg L, Rahnster B, Nygren A, & Nolinder P. Airborne arsenic and urinary excretion of metabolites of inorganic arsenic among smelter workers. Int Arch Occup Environ Health 1986 ; 57:79-91.

53. Valentine JL, Kang HK, & Spivey G. Arsenic levels in human blood, urine, and hair in response to exposure via drinking water. Environ Res 1979 20:24-32.

54. Environmental Health Criteria 18, Geneva. World Health Organization 1981 ; 174-176

55. Arsenic and arsenic compounds. Environmental Health Criteria 22 (Second edition). Geneva, World Health Organization.2001.

56. World Health Organization (WHO). *World Health Organization Fact Sheet*. Fact Sheet No. 210. Geneva: WHO, 1999.

57. Willhite CC. Arsenic-induced axial skeletal (dysraphic) disorders. Exp Mol Pathol 1981 ; 34:145-158.

58. W Kirsten et ai " Maternal Obesity and pregnancy outcome"Am J Obstet Gynecol 1999 ;82 : 192-207.

59. Zaldivar R. Arsenic contamination of drinking water and foodstuffs causing endemic chronic poisoning. Beitr Path Bd 1994; 151: 384-400.

60. Zhang X, Cornelis R, De Kimpe J, Mees L, Vanderbiesen V, De Cubber A, & Vanholder R.Speciation of arsenic in serum, urine and dialysate of patients on continuous ambulatory peritoneal dialysis. Clin Chem 1996 43(2):406-408.

61. Zhuang GS, Wang YS, Tan MG, Zhi M, Pan WQ, & Cheng YD. Preliminary study of the distribution of the toxic elements As, Cd, and Hg in human hair and tissues by RNAA. Biol Trace Elem Res 1990; 12:729-736.

62. Zierler S, Theodore M, Cohen A & Rothman K. Chemical quality of maternal drinking water and congenital heart disease. Int J Epidemiol 1988 ; 17: 589-594.

63. Zierler S, Theodore M, Cohen A, Rothman KJ. Chemical quality of maternal drinking water and congenital heart disease. Int J Epidemiol 1988; 17: 589-594.

64. Zhang J, Klebanoff MA, Roberts JM. Prediction of adverse outcomes by common definitions of hypertension in pregnancy. Obstet Gynecol. 2001; 97: 261–267

65. Vinogradhov, A.P. Geochemistry of rare and dispersed chemical elements in soils. 2nd edition, Newyork.

66. Wedepohl KH, Onishi H. Hand book of Geochemistry, Springer-Verlag, Newyork1969: 2 : 33-39

67. Survey report of BAMWSP , 2005

68. Othmer K. Encyclopedia of Chemical Technology. 1970 : 88 : 243

Annex-2

টিউবওয়েল পানিতে আর্সেনিক দুষণ ও প্রজনন স্বাস্থ্যে প্রভাব ও ফলাফল বিষয়ক গবেষণার প্রশ্নমালা

ক) আর্থ সামাজিক অবস্থাঃ

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং

১। উত্তর দাতার নামঃ- ....

২। স্বামীর নাম ঃ- ....

৩। ঠিকানা ঃ- গ্রামঃ- ... ... ডাকঘরঃ- ... ...

উপজেলাঃ- ... ... জেলাঃ- ... ...

৪। আপনার বয়স কত (পূর্ন বছরে)ঃ- ... ... বছর

৫। আপনি কতদুর পড়াশোনা করেছেন ?

০ = করি নাই	১ = প্রাথমিক	২ = মাধ্যমিক	৩ = উচ্চ মাধ্যমিক
৪ = স্নাতক	৫ = স্নাতকোত্তর	৬ = ভোকেশনাল	৭ = অপ্রতিষ্ঠানিক
৮ = অন্যান্য			

৬। আপনার স্বামী কতদুর পড়াশোনা করেছেন ?

০ = করে নাই	১ = প্রাথমিক	২ = মাধ্যমিক	৩ = উচ্চ মাধ্যমিক
৪ = স্নাতক	৫ = স্নাতকোত্তর	৬ = ভোকেশনাল	৭ = অপ্রতিষ্ঠানিক
৮ = অন্যান্য			

৭। সংসারে আয় বৃদ্ধি করে এমন কোন পেশায় নিয়োজিত আছেন কিনা ?

১ = কোন কাজ করে না ২ = সারা বৎসর কাজ করে ৩ = বৎসরে নির্দিষ্ট সময় কাজ করে

৪ = মাঝে মধ্যে কাজ করে।

৮। আপনার স্বামীর পেশা ঃ ১ = কোন কাজ করে না ২ = সারা বৎসর কাজ করে
৩ = বৎসরে নির্দিষ্ট সময় কাজ করে ৪ = মাঝে মধ্যে কাজ করে।

৯। বসত বাড়ীর বৈশিষ্টঃ

ক) বিদ্যুৎ - ১ = আছে ২ = নাই

খ) স্যানিটেশন সুবিধা ১ = আধুনিক টয়লেট ২ = ওয়াটার সিল টয়লেট ৩ = পিট ল্যাট্রিন

৪ = খোলা ল্যাট্রিন ৫ = অন্যান্য

বসত বাড়ীর বৈশিষ্টঃ

গ) খাদ্য বিষয়ক- ১ = সারা বৎসর ঘাটটি থাকে ২ = মাঝে মধ্যে ঘাটতি থাকে
৩ = ঘাটতি / অতিরিক্ত থাকে না ৪ = অতিরিক্ত থাকে

ঘ) রান্নার জ্বালানী- ১ = কাঠ ২ = শুকনা বাঁশ ৩ = গোবর ৪ = গ্যাস ৫ = অন্যান্য

ঙ) বাসার ছাদ- ১ = টিন ২ = বাঁশ ৩ = ইট/সিমেন্ট / কাদা

চ) বাসার মেঝে- ১ = কাদা ২ = কাঠ ৩ = সিমেন্ট

১০। বসত বাড়ির মালিকানা - ১ = নিজের বাড়ি ২ = অন্যের বাড়ি/ভাড়া বাড়ি ৩ = কোনটাই না

১১। আপনার পরিবারের জনসংখ্যা কত ? ... ... জন।

খ) দৈনন্দিন পানির ব্যবহারঃ

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং

১২। খাবার পানি

১ = নলকুপ/টিউবওয়েল	২ = গভীর নলকুপ	৩ = পুকুর / ডোবা	৪ = কুয়া
৫ = নদীর পানি	৬ = বৃষ্টির পানি	৭ = অন্যান্য	... ...

১৩। রান্নার পানি

১ = নলকুপ/টিউবওয়েল	২ = গভীর নলকুপ	৩ = পুকুর / ডোবা	৪ = কুয়া
৫ = নদীর পানি	৬ = বৃষ্টির পানি	৭ = অন্যান্য	... ...

১৪। থালা বাসন ধোয়ার পানি

১ = নলকুপ/টিউবওয়েল	২ = গভীর নলকুপ	৩ = পুকুর / ডোবা	৪ = কুয়া
৫ = নদীর পানি	৬ = বৃষ্টির পানি	৭ = অন্যান্য	... ...

১৫। গোসলের পানি

১ = নলকুপ/টিউবওয়েল	২ = গভীর নলকুপ	৩ = পুকুর / ডোবা	৪ = কুয়া
৫ = নদীর পানি	৬ = বৃষ্টির পানি	৭ = অন্যান্য	... ...

১৬। বর্তমানে আপনার পরিবারের সদস্যরা টিউবওয়েল/তারা পাম্প/অগভীর নলকুপের পানি পান থেকে বিরত আছেন কি ? ১ = হ্যাঁ ২ = না ৩ = মাঝে মধ্যে

১৭। উত্তর "হ্যাঁ" হলে কেন এই পানি পান থেকে বিরত আছেন ?

১ = পানিতে দুর্গন্ধ ২ = আপনার গায়ে দাগ দেখা দেওয়ার ভয়ে

৩ = আপনার মত যারা পানি পান করতেন তাদের গায়ে দাগ দেখা দেওয়ার কারণে

৪ = অন্যান্য (নির্দিষ্ট করুন) ....

১৮। উত্তর "না" হলে কেন আপনি বর্তমানে ঐ টিউবওয়েলটির পানি পান করছেন ?

১ = নবাই ঐ টিউবওয়েল/তারা পাম্প/অগভীর নলকুপের পানি পান

২ = টিউবওয়েলটি অতি সম্প্রতি বসানো হয়েছে

৩ = অন্যান্য (নির্দিষ্ট করুন)

....

১৯। বর্তমানে যে টিউবওয়েল / তারা পাম্প / অগভীর নলকুপের পানি পান করছেন তা কি কোন সরকারী / বেসরকারী / অন্য কোন সংস্থা কর্তৃক পরীক্ষা করে নিরাপদ এই মর্মে কোন পরামর্শ দেয়া হয়েছে কিনা?

১ = হ্যাঁ ২ = না

গ) আর্সেনিক রোগ / লক্ষণসমূহঃ

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং
২০।	বর্তমানে আপনি কোন রোগে আক্রান্ত কিনা ? ১ = হ্যাঁ ২ = না	
২১।	আপনার শরীরে কোন ছোট ছোট কালো / বাদামী দাগ আছে কিনা ? ১ = হ্যাঁ ২ = না	
২২।	উভয় হাত ও পায়ের তালু শক্ত ও পুরু হয়েছে কিনা ? ১ = হ্যাঁ ২ = না	
২৩।	অংশগ্রহণকারীর শারিরীক অবস্থার বর্ণনা - ক) ওজন ... ... কে জি খ) উচ্চতা ... ... মিটার	
২৪।	বর্তমানে আপনার কি কি রোগের উপসর্গ (Symptom) আছে ?	
২৫।	বর্তমানে আপনার কি কি রোগের লক্ষণ (Sign) আছে ?	
২৬।	শারীরিক এই পরিবর্তন দেখে প্রথমে কি রোগ বলে ভেবেছিলেন ? ১ = চুলকানী বা পাঁচড়া ২ = অন্য কোন চর্মরোগ ৩ = অন্যান্য (নির্দিষ্ট করুন)	
২৭।	আপনার শরীরে এ ধরণের লক্ষণসমূহ প্রকাশ পাবার পর কোন সরকারী/বেসরকারী/স্বায়ত্বশাসিত/স্বেচ্ছাসেবী সংগঠনের কোন কর্মকর্তা/কর্মী আপনার গ্রামে এসে দেখে গেছেন কি ?	

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং
	১ = হ্যাঁ ২ = না	
২৮।	উত্তর হ্যাঁ হলে ঐ সংস্থার কর্তা/কর্মী কি রোগ হয়েছে জানিয়ে গেছেন ? ১ = চর্মরোগ ২ = আর্সেনিক রোগ ৩ = কুষ্ঠরোগ ৪ = অন্যান্য	
২৯।	ঐ সমস্ত সংস্থার কর্ত/কর্মী রোগ নিরাময়ের জন্য আপনাকে কোন পরামর্শ দিয়ে গেছেন কি ? ১ = হ্যাঁ ২ = না	
৩০।	উত্তর "হ্যাঁ" হলে কি ধরনের পরামর্শ দিয়েছেন ? উত্তরঃ	
৩১।	চিকিৎসক আপনার রোগ পরীক্ষা করে কি মন্তব্য করেছিলেন (অর্থাৎ আপনার কি ধরণের অসুখ হয়েছে বলে জানিয়েছেন) ? উত্তরঃ	
৩২।	উত্তর হ্যাঁ হলে চিকিৎসক আপনাকে কোন পরীক্ষার পরামর্শ/কোন উপদেশ দিয়েছিলেন কি ? ১ = হ্যাঁ ২ = না	
৩৩।	চিকিৎসকের পরামর্শ অনুযায়ী নিয়মিত চিকিৎসা/উপদেশ মেনে চলছেন কি ? ১ = হ্যাঁ ২ = না	
৩৪।	উত্তর "না" হলে কারণ উল্লেখ করুন কারণঃ-	

৩৫। টিউবওয়েলের পানিতে আর্সেনিকের পরিমান ও ব্যবহারের সময়ঃ

সময়	টিউটওয়েলের মালিকের নাম	বাড়ির নম্বর (ঠিকানা)	আর্সেনিকের পরিমান Mg/L	টিউবওয়েলে লাল রং দেওয়া হইয়াছে কি	ব্যবহারের সময় (বছর)
বর্তমান					

ঘ) প্রজনন স্বাস্থ্য সম্পর্কিত প্রশ্নমালাঃ

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং

৩৬। কত বছর বয়সে আপনার বিবাহ হয়েছিল ? .... বছর বয়সে

৩৭। সন্তান সন্ততির ইতিহাস (নীচের কোড অনুযায়ী পুরণ করুন)

গর্ভক্রম ↓ / কোড →	গর্ভের বয়স (মাস)	গর্ভের ফলাফল	জীবিত সন্তান ছেলে / মেয়ে	সন্তানের বর্তমান বয়স	গর্ভকালীন সেবা (ANC)	প্রসব পূর্ব জটিলতা	গর্ভকালীন জটিলতা	প্রসব পরবর্তী জটিলতা (৪০ দিনের মধ্যে)	প্রসবের স্থান
	(১)	(২)	(৩)	(৪)	(৫)	(৬)	(৭)	(৮)	(৯)
১।									
২।									
৩।									
৪।									
৫।									
৬।									

(২) = গর্ভের ফলাফল	১ = জীবিত সন্তান ২ = মৃত সন্তান ৩ = অনিচ্ছাকৃত গর্ভপাত ৪ = ইচ্ছাকৃত গর্ভপাত ৫ = এম. আর.
(৩) = জীবিত সন্তান	১ = ছেলে ২ = মেয়ে
(৪) = সন্তানের বর্তমান অবস্থা	১ = বর্তমানে জীবিত ২ = মারা গেছে
(৫) = গর্ভকালীন সেবা (ANC)	১ = সেবা নেই নাই ২ = MBBS ডাক্তার ৩ = সরকারী স্বাস্থ্য প্রতিষ্ঠান ৪ = বেসরকারী স্বাস্থ্য প্রতিষ্ঠান ৫ = পল্লী চিকিৎসক ৬ = অন্যান্য ....
(৬) = গর্ভকালীন জটিলতা	১ = কোন জটিলতা নাই ২ = গায়ে পানি ৩ = রক্ত ক্ষরণ ৪ = এক্লামশিয়া ৫ = ডায়াবেটিস ৬ = গর্ভপাত
(৭) = প্রসব কালীন সমস্যা	০ = কোন জটিলতা নাই অবস্থায় ১ = রক্তক্ষরণ ২ = গর্ভে বাচ্চা উল্টানো ৩ = প্রসবের প্রতিবন্ধকতা
(৮) = প্রসব পরবর্তী সমস্যা	০ = কোন জটিলতা নাই ১ = বাচ্চা আঘাত পাওয়া ২ = জন্ডিস ৩ = শ্বাস কষ্ট জনিত সমস্যা ৪ = অপূর্ণাবস্থায় ভূমিষ্ট বাচ্চা ৫= অঙ্গপ্রতঙ্গের অসম্পূর্নতা
(৯) = প্রসবের স্থান	১ = বাড়িতে ২ = সরকারী হাসপাতাল/ক্লিনিক ৩ = বেসরকারী হাসপাতাল/ক্লিনিক ৪ = মাতৃসদন ৫ = থানা হাসপাতাল ৬ = অন্যান্য ....

ক্রমিক নং	প্রশ্ন ও উত্তর	কোড নং

৩৬। কত বছর বয়সে আপনার বিবাহ হয়েছিল ? .... বছর বয়সে

৩৭। সন্তান সন্ততির ইতিহাস (নীচের কোড অনুযায়ী পুরণ করুন)

গর্ভক্রম ↓ / কোড	গর্ভের বয়স (মাস)	গর্ভের ফলাফল	জীবিত সন্তান ছেলে / মেয়ে	সন্তানের বর্তমান বয়স	গর্ভকালীন সেবা (ANC)	প্রসব পূর্ব জটিলতা	গর্ভকালীন জটিলতা	প্রসব পরবর্তী জটিলতা (৪০ দিনের মধ্যে)	প্রসবের স্থান
	(১)	(২)	(৩)	(৪)	(৫)	(৬)	(৭)	(৮)	(৯)
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২।									
৩।									
৪।									
৫।									
৬।									

(২) = গর্ভের ফলাফল	১ = জীবিত সন্তান ২ = মৃত সন্তান ৩ = অনিচ্ছাকৃত গর্ভপাত ৪ = ইচ্ছাকৃত গর্ভপাত ৫ = এম. আর.
(৩) = জীবিত সন্তান	১ = ছেলে ২ = মেয়ে
(৪) = সন্তানের বর্তমান অবস্থা	১ = বর্তমানে জীবিত ২ = মারা গেছে
(৫) = গর্ভকালীন সেবা (ANC)	১ = সেবা নেই নাই ২ = MBBS ডাক্তার ৩ = সরকারী স্বাস্থ্য প্রতিষ্ঠান ৪ = বেসরকারী স্বাস্থ্য প্রতিষ্ঠান ৫ = পল্লী চিকিৎসক ৬ = অন্যান্য ....
(৬) = গর্ভকালীন জটিলতা	১ = কোন জটিলতা নাই ২ = গায়ে পানি ৩ = রক্ত ক্ষরণ ৪ = এক্লামশিয়া ৫ = ডায়াবেটিস ৬ = গর্ভপাত
(৭) = প্রসব কালীন সমস্যা	০ = কোন জটিলতা নাই ১ = রক্তক্ষরণ ২ = গর্ভে বাচ্চা উল্টানো অবস্থায় ৩ = প্রসবের প্রতিবন্ধকতা
(৮) = প্রসব পরবর্তী সমস্যা	০ = কোন জটিলতা নাই ১ = বাচ্চা আঘাত পাওয়া ২ = জন্ডিস ৩ = শ্বাস কষ্ট জনিত সমস্যা ৪ = অপূর্ণাবস্থায় ভূমিষ্ট বাচ্চা ৫= অঙ্গপ্রতঙ্গের অসম্পূর্নতা
(৯) = প্রসবের স্থান	১ = বাড়িতে ২ = সরকারী হাসপাতাল/ক্লিনিক ৩ = বেসরকারী হাসপাতাল/ক্লিনিক ৪ = মাতৃসদন ৫ = থানা হাসপাতাল ৬ = অন্যান্য ....

Annex-3

সম্মতি পত্র

রোগীর আইডি নং-

গবেষণার নাম- বাংলাদেশের নির্দিষ্ট জেলায় দীর্ঘ মেয়াদী আর্সেনিক বিষক্রিয়ায় মহিলাদের প্রজনন স্বাস্থ্যের বিরূপ প্রভাব

আমি বুঝতে পেরেছি যে আর্সেনিকযুক্ত পানি পান করার ফলে আমি দীর্ঘ মেয়াদী আর্সেনিকোসিস রোগে আক্রান্ত একজন রোগী যার সুনির্দ্রিষ্ট কোন চিকিৎসা নাই। দীর্ঘ দিন আর্সেনিকযুক্ত পানি পান করার ফলে মহিলাদের (বয়স ১৫-৪৯এর ভিতরে) গর্ভ ধারনের বিরূপ ফলাফল লক্ষ্য করা যায়, যাহা বিভিন্ন দেশে গবেষনার মাধ্যমে প্রমানিত হইয়াছে।

বাংলাদেশের নির্দিষ্ট (পাবনা জেলায় বেড়া, সুজা নগর, সাথিয়া উপজেলা) স্থানে আর্সেনিকযুক্ত পানি পান করার ফলে দীর্ঘ মেয়াদী আর্সেনিকোসিস রোগে আক্রান্ত মহিলাদের গর্ভধারণের ফলাফল নিরূপনের জন্য একটি গবেষণা কার্য পরিচালিত হইবে।

যদি আপনি এ গবেষণা কার্যক্রমে অংশ গ্রহণ করিতে চান, তাহা হইলে নিম্নলিখিত শর্তাবলী আপনাকে মানিয়া চলিতে হইবে।

১. আপনাকে গবেষণায় অন্তর্ভুক্ত করা হইবে এবং অন্তর্ভুক্তির দিন হইতে বেশ কিছু দিন যাবৎ মাঠ কর্মী এবং চিকিৎসক গণ আপনাকে পরিদর্শন করিবে। আপনার দেওয়া সকল তথ্যাদি গোপন রাখা হইবে। কেবল মাত্র গবেষকগণ সেই সকল তথ্যাদি ব্যবহার করিতে পারিবেন।
২. মাঠ কর্মী এবং চিকিৎসকগণ আপনার অসুস্থতা, গর্ভধারণ এবং সন্তান সন্তানাদির বিষয়ে আপনাকে প্রশ্ন করবে এবং আপনার দেহের ওজন, উচ্চতা, রক্তচাপ, পুষ্টি সংক্রান্ত ও অন্যান্য শারীরিক পরীক্ষা নিরীক্ষা করিবেন।
৩. টিউবওয়েলের পানিতে আর্সেনিকের মাত্রা নিরূপনের জন্য মাঠ কর্মীগণ টিউবওয়েলের পানি সংগ্রহ করিবেন।
৪. এই গবেষণায় অংশ গ্রহণ করা অথবা না করার সিদ্ধান্ত সম্পূর্ণ আপনার। গবেষণায় অংশ গ্রহণের পরও যে কোন সময় আপনি আপনার নাম প্রত্যাহার করিতে পারিবেন।

আপনার সহযোগিতার জন্য ধন্যবাদ।

মনোনিত ব্যক্তির স্বাক্ষর অথবা বাম হাতের বৃদ্ধাঙ্গুলের ছাপ — তারিখ ঃ

গবেষকের স্বাক্ষরঃ — তারিখ ঃ