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Drinking Arsenic Water May Contribute to *Mycobacterium ulcerans* Infection

Alfred Allan Duker[1*], Samuel Ndur[2], Edward Matthew Osei Jnr[1], Isaac Awuku Acheampong[1], Gloria Afua Apedo[1]

[1]Department of Geomatic Engineering, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

[2]Department of Environmental & Safety Engineering, University of Mines and Technology, Tarkwa, Ghana

[*]**Corresponding author:** Alfred Allan Duker, Geomatic Engineering Department, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. Tel: +23324651024; Email: duker@alumni.itc.nl

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Abstract

Drinking water sources can be contaminated by toxic metals and metalloids such As arsenic (s), which occurs naturally in the earth's crust. Exposure to high levels of arsenic may cause adverse health effects because it provides a favourable environment for harmful microorganisms to grow. Buruli ulcer (Bu), a skin disease caused by *Mycobacterium ulcerans* MU infection is common in the Bomfa sub-district Ashanti region, Ghana.

This study investigated the possible link between Buruli ulcer incidence and drinking water arsenic in the Bomfa sub-district of Ghana. Drinking water sources in the study area were sampled and analyzed for arsenic. Surface map of arsenic concentration overlaid with locality map of BU incidents show localities with high incidents falling into regions of relatively high arsenic concentration. The exposure response relationship model showed a positive relationship between BU and drinking water arsenic. (i.e. R^2=0.54, p=0.1).

Statistical analysis of the data reveal that a high proportion of settlements with high BU prevalence utilize arsenic contaminated water sources. It was therefore concluded that arsenic likely contributes to MU infections in the study area.

Keywords: Arsenic; Buruli ulcer; Drinking Water, GIS; *Mycobacterium ulcerans*

Introduction

Arsenic contamination of drinking water sources is a major environmental concern and has been discussed extensively because it is present in many parts of the world. Arsenic is a potentially toxic, naturally occurring trace element, which is present at low concentrations in water, soil, rock and many foods. Its toxicity and increased appearance in the biosphere have generated a lot of public concern in recent years. Arsenic is introduced into the biosphere through wood preservatives, glass manufacturing, powder production (as contained in coal ash and petroleum residues), fertilization with poultry and hog manure containing arsenic from feed additives. Much of these reach natural waters. Mining-related activities have historically been linked with release of high levels of arsenic into soils and water bodies.

Human exposure to As can cause both short and long-term health effects. Consumption of drinking water containing As in excess of 10 micrograms per litre over long periods of time can lead to arsenicosis, a chronic illness that produces skin disorders, gangrene and organ cancers. Other diseases associated with arsenic exposure are hypertension, diabetes, infant mortality and birth defects. A recent report indicates that arsenic interferes with hormones making it a potent endocrine disrupter. In his study of the effects of arsenic exposure, Lantz established that As could predispose to defect the immune system [1]. Meanwhile subjects exposed to high levels of As concentrations were reported to have had impaired immune response [2]. Down-regulation of the immune system is known to be a risk factor for the development of BU [3]. Several studies including but not limited to e.g., Rosales-Castillo, et al. [4], have reported of impaired resistance to viral/bacterial infection via As ingestion.

Individuals vary in capacities in relation to how much As methylation remains in tissues. Studies [5] have shown that diet plays an important role in methylation efficiency. Thus, the amount of As retained in the body is related to diet and hence susceptibility to microbial infections. The poor socio-economic status of the village communities enhances and/or increases As burden and therefore As toxicity. Furthermore, the ability of arsenic to draw ferritin [6] could also enhance the adhesion of bacteria to human tissues [7,8] to establish infection.

It is estimated that approximately 57 million people are drinking groundwater with As concentrations above the World Health Organization's standard of 10μg/L [9]. In Bangladesh 100,000 cases of skin lesions caused by As have occurred Arsenic down-regulates the immune system and thus enhances bacterial / viral infection [10]. This raises potential risk of Buruli ulcer (Bu) development in areas where people are exposed to arsenic. Buruli ulcer is a skin disease caused by *Mycobacterium ulcerans* [11]. Healing is protracted and often results in deformity and disability, particularly in children [12]. The impact of the disease on the few health facilities in the affected areas is enormous. The long hospital stay, often more than 3 months (and sometimes one year) per patient, represents a huge loss in productivity for adult patients and family caregivers, and loss of educational opportunities for children. In developing countries, socio-cultural beliefs and practices strongly influence the health-seeking behaviours of people affected by Bu [13,14]. Duker, et al. [15], established that BU prevalence in settlements along As-enriched drainages and farmlands is greater than elsewhere. The study also indicated that BU prevalence along As-enriched drainages were greater than As-enriched farmlands.

This study hypothesizes that arsenic in drinking water may be a contributory factor to MU infections. The study therefore looks into a possible link between BU and As in drinking water sources in the Bomfa sub-district.

In this paper we aimed at:

a) Ascertaining the presence and concentrations of As in drinking water in the Bomfa sub-district of the Ashanti region;

b) Establishing the relationship, if any, between As and MU infections in the area in a GIS environment.

GIS technology provides opportunities for epidemiologists to study associations between environmental exposures and spatial distribution of disease [16].

Geographic Information System (GIS) and Health

Disease maps demonstrate the distribution of diseases in space and inevitably stimulate the formation of causal hypothesis. Geographic Information System (GIS) is more than mere visualization of spatially referenced disease data - disease mapping. GIS is a system for the collection, storage, integration, analysis and display of spatially referenced data [17]. Due to its ability to combine data from many sources for identification and mapping of environmental factors associated with disease vectors, GIS is particularly suited for environmental and geographical epidemiology. It provides a tool for probing links between diseases and the physical environment while controlling for lifestyle factors and permits studies of disease clustering and association with spatial phenomenon such as point and line sources of pollution. Moreover, GIS permits exploration of disease risk around a point source of pollution or along a river [17]. GIS can facilitate modelling exposure- action and activity spaces- to permit an understanding of the contemporary patterns of a disease such as BU. GIS analysis can illumine causation and/or contributory factors and give clues for primary prevention.

Materials and Methods

Study Area

The Ashanti Region of Ghana is one of the worst affected regions, accounting for 60% of all reported cases [18]. The Ejisu-Juaben district lies between latitudes 6^{o}25'N and 6^{o}50'N and longitudes 1^{o}15'W and 1^{o}35'W. It covers an area of 678 km^2. The district capital is Ejisu. The district is located in the central part of the Ashanti Region. It shares boundaries with Sekyere East and Asante Akim North districts to the east, Kumasi Metro and Kwabre districts to the west and the Bosomtwe Atwima Kwanwoma and the Asante Akim South districts to the south. The major river that runs through the area is the Banko River (Figure 1).

The population of the district is 124,176, which forms 3.4% of the total population of the region. The average growth rate for the district is 2.6%. Males form 47.98% and females form 52.02%.

Bomfa is a sub-district in the Ejisu-Juaben district. It is made up of 22 localities; prominent among them are Bomfa, Adumasa, Nobewam, New Koforidua, Duampompo, Buamadumase, Kubease, Hwereso, Onaa and Bukuruwa. The area is covered by topographic sheet 0602B3, published by the Survey of Ghana. BU reported cases per settlement in the area range from 3 to 23.

About 54% of the population engages in farming, hunting and forestry. Inhabitants of the settlements depend on both groundwater and/or surface water for drinking and other domestic purposes. Seventy percent of the population use groundwater while 11% use surface water. The vegetation type in the area is the moist semi-deciduous forest, which contains different species of tropical wood of high economic value.

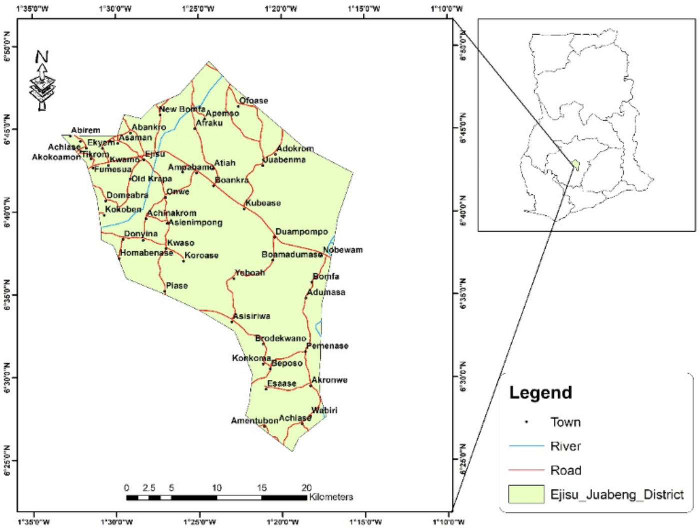

Figure 1: Ejisu-Juabeng District.

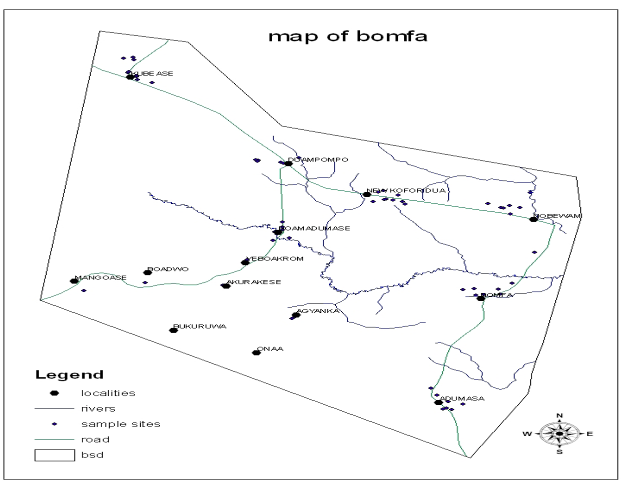

Figure 2: General map of Bomfa.

Materials

The following are the sources of spatial data input to the GIS.

1. Reported incidents of BU from 2002 - 2006 were obtained from Bomfa Health Centre (Bomfa), Huttel Health Centre (Boamadumase) and Global Evangelical Hospital at Apromase; all in the Ejisu-Juaben district of Ashanti.

2. Settlement population estimate for 2000 was obtained from the Ghana Statistical Service (GSS), Kumasi and projected to obtain population estimates for 2006.

3. Handheld GPS was used to capture positional data for sample sites and some settlements within the study area.

Method

Water Sampling and Analysis

Water samples were collected at 61 sites during the dry season, from surface and ground water sources where inhabitants abstract water. Water samples were collected in 500 ml plastic containers. The containers were soaked in nitric acid (HNO_3) solution overnight, thoroughly rinsed with distilled water and dried before use. This was to ensure there was no contamination of the samples.

Duplicate samples were collected at each abstraction point. To keep the as in solution, each of the two samples from was acidified with nitric acid to PH<2. The acidified samples were filtered through a 0.45µm filter, to remove particulates, into test tubes and refrigerated. The samples were then analyzed for as using the Spectra AA 220 Atomic Absorption Spectrophotometer (AAS) at the Environmental Laboratory of AngloGold Ashanti (Obuasi) mine.

Handheld GPS was used to determine the geographic coordinates of the sample sites and settlement sites, which were not located on the study area map. 'FUGRO', coordinate transformation software was used to transform the geographic coordinates into the local coordinate system.

Spatial Data Capture

All the analogue maps obtained were scanned and geo-referenced. Spatial data were then captured by on-screen digitizing using the ArcGIS program. Spatial data of rivers/streams, roads (digitized as line segments) settlement locations captured as points were overlain to create a map view of the study area (Figure 2).

BU incidents and projected population estimates for 2006 were recorded as spatial attributes of the settlements. Arsenic concentrations in samples were recorded as spatial attribute of the sample sites. For each of the settlements with incidents of BU, the percentage prevalence of BU was calculated. Prevalence expresses cases of a disease in terms of the proportion of the population afflicted at a specified time [19]. It is expressed here as the number of BU cases divided by the population estimate, multiplied by 100 to yield a percentage.

$$\text{Thus, \%prevalence} = \frac{\text{No. of BU Cases}}{\text{Population}} * 100$$

Spatial Data Analysis

The spatial data analysis was carried out using the ArcGIS geostatistical analyst. The Inverse Distance Weighting (IDW) method of interpolation was used to estimate the arsenic concentration of each settlement from the sample concentrations within the study area. Subsequently, surface map of arsenic concentration and locality map of BU incidents represented in proportional circles were created and overlaid so as to visually determine the spatial distribution of arsenic and BU prevalence, and the correlation between them in the area as shown in Figure 3. Quantitatively, exposure-response model was used to determine the spatial relationship between As in drinking water and BU prevalence.

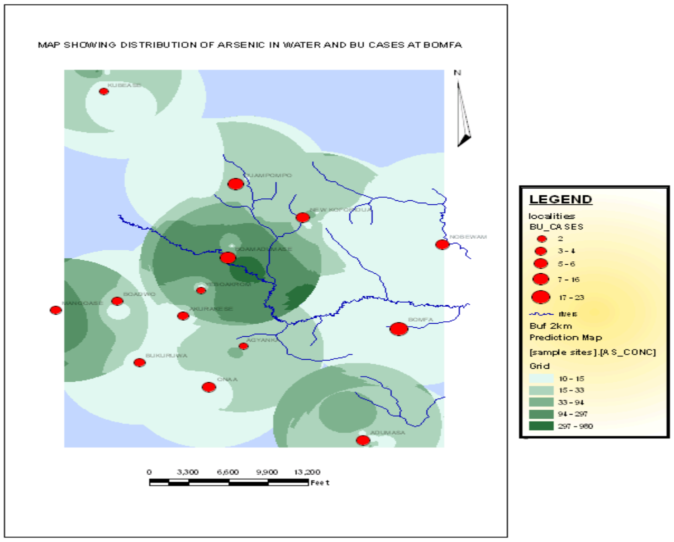

Figure 3: Surface map of As concentration overlaid with locality map of BU incidents in the study area.

Results and Analysis

Spatial Distribution of Arsenic and BU Incidents in the Study Area

Visual inspection of Figure 3 indicates that generally localities with high incidents of BU falls within areas with high arsenic concentration. This shows a positive relationship between arsenic in water and BU incidents in the study area. However, Bomfa does not show such significant positive relationship with regards to arsenic in water and BU incidents.

Analysis of Arsenic Levels in Water

The range of as concentrations in water in the study area is 10-980 µg/l. Of the 61 abstraction points sampled, 34% had As levels exceeding the 10 µg/l limit of the WHO guidelines maxima for As [20]. Seventy-nine percent (79%) of the water samples recorded exactly 10µg/l As. Table 1 shows the statistical analysis of as concentrations in drinking water in the study area. It is, however, not easy to tell who is drinking what type of water; but consumption of such As-enriched water over a long period of time will accumulate As in the body. Such accumulation is deleterious to human health, even at the WHO 10 µg/l maximum [21].

	Min	Median	Mean	St dev.	Max
As (µg/l)	10	10	37.5	126.0	980

Table 1: Statistical analysis of water as concentrations in Bomfa Sub-district.

Analysis of Exposure-response of Arsenic in Water and BU Prevalence

The 'MINITAB' software was used to model an exposure-response relationship for the study area. It can be seen that BU incidence depends on population and to a lesser extent on drinking water arsenic concentrations. The results of the regression analysis are shown in Table 2.

As (µg/l)	Sub Population	BU Incidents	%Prevalence
≤10	19088	90	0.47
10 - 49	7534	25	0.33
50 - 99	12589	36	0.29
100 - 150	3893	22	0.57
>150	1560	16	1.03

Table 2: Exposure - response relationship between BU prevalence and Arsenic in water.

The relationship between BU prevalence and arsenic in water shows a relatively significant positive relation (i.e. $R^2 = 0.54$, $p = 0.1$). The graphical representation is shown in Figure 4 below.

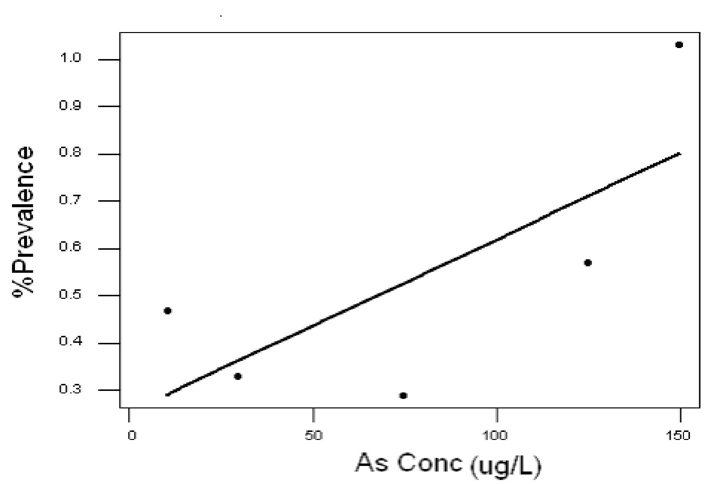

Figure 4: Regression plot of As concentration against % prevalence of BU infection. There is a positive correlation between Water Arsenic and % prevalence.

Discussion

The surface map of As concentrations of abstraction points overlaid with locality map of BU incidents (Figure 3), shows localities of high incidents falling in regions of high As concentration. This is an indication of a positive relationship between As in water and BU incidents. The sole exception is one settlement (Bomfa), which has low As concentration but high BU incidence. This also is understandable since ingestion of As over a long period could equally be harmful [21].

The range of As concentrations in water in the study area can in no uncertain terms be underestimated. Although WHO recommended 10µg/l As maximum level [20], further studies show that even this is still hazardous [21]. However, 79% of the samples recorded exactly 10µg/l As. Besides, 21% of the samples have As concentrations exceeding the 10µg/l and 13% had values that exceeded the guideline for Maximum Contaminant Level (MCL) of As of 50µg/l for developing countries like Ghana [22]. Arsenic is bio-cumulative and its accumulation in the body is inevitable if waters with high concentrations of As are consumed. This could contribute to MU infections since As down-regulates the immune system [1,21], and subsequently enhance vulnerability to bacterial infection [4], hence increase incidents of BU in such areas. Even though Bomfa, has a high rate of BU incidents, the region falls in a relatively low As concentrated region (10-15µg/l) (Figure 3). This level of exposure is still associated with decreased DNA repair capacity, with a potential mechanism for co-carcinogenic activity (i.e. increase in skin infection susceptibility) [21,23]. This could have been one reason for EPA to change MCL of As to 10µg/l. Other reasons for Bomfa's case could be due to: (i) borehole in disrepair and (ii) farming on As-enriched farmlands.

Increased number of Boreholes

About ten years ago (1997), the inhabitants of Bomfa had few boreholes, which for lack of maintenance later broke down. The community depended on surface water for consumption and domestic purposes. Surface waters, however, have high arsenic concentrations compared to ground waters. This probably explains the upward trend in BU occurrences observed in 2002 and which peaked in 2003. Borehole water was re-introduced at Bomfa, which provided a better source of drinking water for the inhabitants. Subsequent increase in the number of such borehole water was characterized by the simultaneous decline of BU incidents at Bomfa since 2003. The trend is graphically represented in Figure 5.

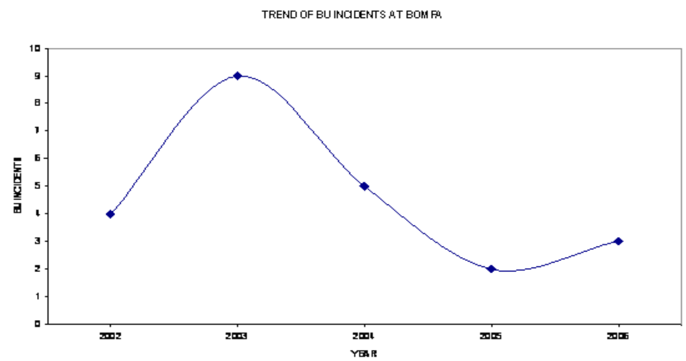

Figure 5: Yearly trend of BU incidents at Bomfa since 2002. There was decrease in occurrences after 2003.

The simultaneous decrease of the BU incidents with the introduction of boreholes may indicate a relationship between less As consumption from streams and rivers and the reduced BU incidents. This could contribute to low As consumption at Bomfa, and hence reduced number of BU (although the settlement has high number of BU incidents).

On the other hand, if MU existed in the river/stream environment, then there could be more infections during the period when the inhabitants began using the surface water. In this case As could inactivate enzymes [24] and induce immune suppression of persons ingesting As contaminated water; and immune-compromised persons are at risk with regards to MU infections [3].

However, the increased number of borehole in the area meant less visits to the surface water abstraction sites, and therefore, less infection. This could also explain the downward trend of the disease since the re-introduction of the borehole pipes.

Possibility of farming on As-enriched farmlands.

The effect of As on the inhabitants may not only occur in the riverine environments but also on the farms. Therefore, if water contains dissolved As, it may have more As in its sediments. These sediments during flood times are deposited on floodplains and/or agricultural soils where several farmers wished to farm or grow food crops. High concentrations of As in soils may be absorbed by the food crops grown there [25-27]. For example, As concentrations in the Banko River ranged from 10µg/l to 110µg/l.

The major occupation of the people in district is agriculture, with most of the people engaged in cultivating food crops in the low lands (flood plains). Some of the crops cultivated in the area are cocoyam, plantain, cassava, sugarcane, that have high As absorbing rate from the soil [25]. These suggest a possible exposure to arsenic through food crops.

A plot of As levels against BU prevalence showed a relatively significant positive relationship between As levels and BU prevalence (i.e. $R^2 = 0.54$, $p = 0.1$). This is an indication that As in water may play a role in MU infection. From the linear regression analysis of the exposure response model, there is no limit of As concentration that may be safe, especially when considered in the light of other social and environmental factors.

Conclusion

Inhabitants in most settlements in the Bomfa sub-district are prone to chronic ingestion of high levels of As because they consume arsenic-enriched water.

The results show that the concentration levels of As found in drinking water sources in the study area poses a major health threat especially with regards to bacterial infections including MU. Arsenic concentrations in water were found to be moderately significant, and positively associated with BU but not very conclusive.

It is therefore appropriate in this study area that drinking water must necessarily be all potable or water from boreholes that have not been contaminated with As. Also, soils especially from the floodplains must be remediated to avoid As occurring in the food crops.

Considering the limitation of exploratory data analysis and the size of the data sets there is some indication that elevated As levels in the community has some association with BU incidence.

Further investigation with a larger dataset is needed to confirm this study. For example, it will be determined whether or not it is the MU in the riverine environment alone which is the cause of the infections or the drinking water arsenic exposure or both. Other confounding and risk factors must also be considered.

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