Clinics in Oncology

Research Article
Published: 08 Jun, 2020

Prevalence and Mortality of Skin Cancer in an Arsenic Exposed Population in District of Nadia, West Bengal, India

Guha Mazumder DN[1], Kunal Kanti Majumdar[2,4], Pramit Ghosh[3,4] and Aloke Kumar Ghosh[4]*

[1]Department of Medicine and Gastroenterology, Institute of Post Graduate Medical Education & Research, India

[2]Department of Community Medicine, KPC Medical College and Hospital, India

[3]Department of Community Medicine, Deben Mahatma Government Medical College, DNGM Research Foundation, India

[4]DNGM Research Foundation, India

Abstract

Background: Ground water arsenic contamination is an important cause of chronic arsenic toxicity in West Bengal, India. Though many studies on skin and systemic manifestations were done earlier, but no study had been done assessing prevalence of skin cancer and its mortality in arsenic exposed population in India.

Methods: A cross sectional study was done on a population of 8,206 residing in 2,233 household in Nadia district, West Bengal. A total of 7,162 participants were clinically examined for determination of prevalence of skin lesion including skin cancer during the study. Death due skin cancer was determined by verbal autopsy from total death due to cancer out of 1,044 persons who were found dead during the study. Arsenic exposure data was obtained from testing of arsenic in drinking water sources from 7,130 participants.

Results: Prevalence of skin lesion was found to be 3.68% out of the population of 7,162 studied. Skin cancer was found to be present in 44 cases, the prevalence being 0.61%. Significantly more male and aged people (Mean 63 years) had skin cancer. Difference between proportion affected with skin cancer exposed to arsenic above or below 50 µg/L was found to be statistically significant (p-value = 0.03). Death due to skin cancer was found to occur in 6 (4.96%) subjects out of total cancer deaths of 121 recorded out of 8,206 populations surveyed.

Conclusion: Our community-based study has provided, for the first time, data on arsenic exposure, prevalence and mortality of skin cancer from a large arsenic exposed population in India.

Keywords: Pigmentation & Keratosis; Skin cancer prevalence; Skin cancer mortality; Arsenic exposure; Skin cancer

OPEN ACCESS

Correspondence:
Guha Mazumder DN, Department of Medicine and Gastroenterology, Institute of Post Graduate Medical Education & Research, DNGM Research Foundation, New Alipore, Kolkata 700053, India, E-mail: guhamazumder@yahoomail.com

Received Date: *19 May 2020*
Accepted Date: *04 Jun 2020*
Published Date: *08 Jun 2020*

Citation:
Guha Mazumder DN, Majumdar KK, Ghosh P, Ghosh AK. Prevalence and Mortality of Skin Cancer in an Arsenic Exposed Population in District of Nadia, West Bengal, India. Clin Oncol. 2020; 5: 1709.

Introduction

Arsenic pollution in groundwater, used for drinking purposes, has been envisaged as a problem of global concern. Arsenic contamination in drinking water has been reported from many countries like Taiwan, China, Argentina, Chile, Mexico, Cambodia, Thailand, Myanmar, Nepal, USA [1], but the severity of this contamination in India and Bangladesh is unprecedented.

In India, occurrence of arsenic in groundwater has been reported from West Bengal, Bihar, Jharkhand, Chhattisgarh, Uttar Pradesh and Assam [1]. Though many states have been identified with significant arsenic contamination in groundwater in India, the major affection was detected as early as 1983 in West Bengal [2]. Today, in West Bengal, the arsenic contamination in ground water has been detected in 8 districts of the state [1]. Of these, the major affected districts are Malda, Murshidabad, Nadia, and North and South 24 Parganas. It is suspected that 6 million people are exposed to arsenic contaminated ground water in West Bengal [1].

Predominant manifestation of chronic arsenic toxicity is skin lesions characterized by pigmentation and keratosis [3]. Skin cancer is a commonly observed malignancy related to drinking of arsenic contaminated water [1]. The working group of International Agency for Research on

Figure 1: Arsenical skin cancer over the chest.

Figure 2: A case of Bowen's disease.

Cancer [1] evaluated ecological studies from Taiwan, Mexico, Chile and the USA, cohort studies from Taiwan and a case-control study from the USA. Numerous cases of skin cancer have been documented from communities with arsenic contaminated drinking water.

Several epidemiological studies on skin lesion and systemic manifestations have been carried out in the past in many arsenic affected districts, of West Bengal, India [4-9]. But no epidemiological study related to prevalence of skin cancer and its mortality has so far been done in arsenic exposed population in India.

Methodology

A cross sectional study was done during 2017-2020 in which information was collected from residents' of 2,233 households selected from 17 arsenic affected blocks of Nadia district, West Bengal. Selection of households was based on the methodology adopted during a study on assessment of health impact on arsenic affected population in the same district during 2006-07 [9]. It was noted that a total of 8,206 persons were studied earlier in those 2,233 households. A total of 1,044 persons were found dead during the current study out of the total surveyed population of 8,206. So, a total of 7,162 participants could be clinically examined for skin lesion including skin cancer during the current study.

Cause of death due to skin cancer was ascertained through verbal autopsy done on 1,044 persons who were found dead during current field survey carried out in 2,233 households.

Field study

The field study was designed to minimize subjectivity in examination of skin lesions diagnostic of arsenicosis. Demographic characteristics and socio-economic condition of the participant were recorded in a proforma. All participants were examined in the field by the physician who had experience in diagnosing arsenic-caused skin lesions in the past.

Each member of the household was interviewed and clinically examined. Careful inspection of skin was carried out for arsenical skin lesions during general medical examination. Skin lesion of arsenical pigmentation and keratosis were ascertained as follows: Pigmentation was identified if there were areas of mottled dark brown pigmentation bilaterally distributed on the trunk. Keratosis was characterized by diffuse bilateral thickening of palms and/or soles with or without nodules of various shapes and sizes [3]. Skin cancer was clinically diagnosed on the basis of lesion being rough, nodular, ulcerated (non-healing) lesion present over the skin along with keratotic lesion of palm or sole or on non- keratotic areas of the trunk and extremities (Figure 1). Further lesions of Bowen's disease were also included in this diagnosis of skin cancer (Figure 2). The lesion appears as sharply demarcated round plaque or has an irregular polycyclic lenticular configuration. The lesions are erythematous, pigmented, crustated, fissured, keratotic and nodular. The diameter of the lesions may vary from 0.8 cm to 3.5 cm. The lesions are multiple and occur on the sun-protected areas of the skin [10-12]. Each participant was questioned about his or her current sources of drinking and cooking water along with duration of water use from those sources.

Water samples were collected by the field team from current private and public tube wells used for drinking and cooking purposes by each studied household. All the water samples were analyzed for measurement of arsenic level by atomic absorption spectrophotometer with flow-injection hydride generation system at reference laboratory of PHED, Govt. of West Bengal. Arsenic exposure data through water was not available for the study from 32 out of 7,162 participants; hence, analysis of arsenic exposure data was done for 7,130 participants for the study.

Verbal Autopsy

In this study cause of death was ascertained by verbal autopsy method adopting the VA-formats used by RGI [13]. The semi-structured format used by the enumerator included a description of events preceding the event of death. List of cardinal symptoms like cancer, hypertension, diabetes, tuberculosis etc. were used for probing. Both narrative and close-ended questions were used to assign the underlying cause of death. Initial contact with household was done to obtain consent to participate in the study and was followed by interview to access medical records including death certificate if the death had occurred in a hospital and was followed by carrying on interview for verbal autopsy. Interview of relatives, or those acquainted and associated with the deceased was done to extract relevant information preceding death. Information on sequence of events, circumstances leading to death, signs & symptoms of any illness etc. were collected. One of the enumerators, who collected the information, was arsenic expert physician. Two independent experts (clinicians) reviewed all the information, positive & negative symptoms and opined about the probable cause of death based on available information. Following review of completed questionnaires assignment of causes of death was done. In case of any discrepancy third expert was consulted. About 10% of cases were re-evaluated by a separate team for quality check and till date performance of teams were found to be satisfactory.

Institutional Ethical Committee of DNGM Research Foundation,

Table 1: Demographic characteristics and clinical features of 7,162 participants studied.

Characteristics	Arsenicosis cases (pigmentation and/or keratosis present)		Non cases (No pigmentation or keratosis)	
	N=264		N=6898	
Age	N	%	N	%
<12	0	0	0	0
12- <18	0	0	20	0.29
18- <30	3	1.14	666	9.65
30- <60	122	46.21	4885	70.82
>60	139	52.65	1327	19.24
Sex				
Male	202	76.52	2409	34.92
Female	62	23.48	4489	65.08
Pigmentation	231	3.2	0	
Keratosis	61	0.8	0	
Skin Cancer	44	0.61	0	

Table 2: Age distribution of studied population with and without skin cancer.

Comparing age	Mean	N	Std. Deviation	Median	Minimum
None	46.49958	7118	14.68207	45	12
Skin cancer	*63.90909	44	13.06659	66.5	36
Total	46.60653	7162	14.73482	45	12

*Age was significantly higher for those with skin cancer (p value <0.0001)

Kolkata, has approved the protocol of the study following ICMR guidelines. Informed consent was obtained prior to participation for the interview.

Data collected were digitized and stored. Analysis was done using MS excel and Epi-info version 7.2. Descriptive statistical methods like proportion, measures of central tendency and dispersion were calculated. Statistical significance of various socio demographic variables, arsenic exposure etc. was calculated for dependent factors like mortality/and morbidity using chi-square test or t-test depending on the data character.

Results

Clinical and demographic features of study population are given in Table 1. Arsenical skin lesion was found to be present in 264 cases out of the study population. Thus, prevalence of skin lesion was found to be 3.68% out of the population of 7,162 studied. Skin pigmentation and keratosis were present in 231 (3.2%) and 61 (0.85%) cases respectively. Majority (52.65%) of subjects with arsenical skin lesion were found to be elderly, i.e. >60 yrs. Further, more male (76.52%) subjects had arsenical skin lesion.

Skin cancer was found to be present in 44 cases out of 7,162 persons examined the prevalence being 0.61%. Mean age of skin cancer was found to be 63.9 years, significantly higher than the rest (mean 46.5 years) of the study population (Table 2). It was found that 0.22% of females and 1.3% of males were affected with skin cancer. The difference of prevalence of the disease among males & females were statistically significant; OR is 5.99 for disease occurrence among males (Table 3).

Arsenic exposure data was available from 7,130 participants and it showed that 4,079 (57.2%) participants were taking water with arsenic level <10 µg/L. It was further observed that 155 (58.7%) cases out of 264 patients with skin lesion had current arsenic exposure of

Table 3: Sex distribution of studied population with and without skin cancer.

	Female	Male	Total	p value
Skin cancer	10	34	44	<0.0001
None	4541	2577	7118	
	4551	2611	7162	

Table 4: Different level of arsenic exposure of participants with and without skin cancer.

As Level	Skin cancer	None	Total	%
<10 mg/L	9	2012	2021	0.45%
10-50 mg/L	9	2101	2110	0.43%
50-90 mg/L	13	1215	1228	1.06%
90-170 mg/L	7	1038	1045	0.67%
170-330 mg/L	2	419	421	0.48%
330-640 mg/L	3	239	242	1.24%
>640 mg/L	1	62	63	1.59%
	44	7086	7130	0.62%

Difference between proportion affected with skin cancer exposed to arsenic level above or below 50 µgm/L is statistically significant (p-value = 0.03).

<10 µg/L. Different levels of arsenic exposure of patients with skin cancer are given in Table 4. It could be seen that nine cases of skin cancer were exposed to drinking water with arsenic level <10 µg/L. The problem affected more persons from those exposed to higher as level, especially those who were exposed to As level >50 µg/L. Difference between proportion affected with skin cancer exposed to arsenic level above (0.88%) or below (0.44%) 50 µg/L is statistically significant (p-value = 0.03).

Cause of death was ascertained by Verbal autopsy on 1,044 subjects who were found dead during the survey of a population of 8,206. Death due to cancer was found to occur in 121 (11.6%) subjects

Table 5: Skin cancer death out of total cancer deaths among studied population (n=121).

Sites	Frequency	Proportion
Skin cancer death	6	4.96%
Total Cancer death	121	100.00%

out of which death due to skin cancer was found to occur in 6 (4.96%) subjects.

Discussion

This is the first study in which prevalence of skin cancer has been ascertained on a large arsenic exposed population in India. In the current study a total of 44 cases (Prevalence 0.61%) of skin cancer was identified out of the population of 7,162 studied. Prevalence study conducted on the largest population of 40,421 in arsenic endemic area of Taiwan showed presence of skin cancer in 1% cases [14]. Further, an ecological study based on prevalence of skin cancer in Mexico showed prevalence of skin cancer of 1.4% in the people in arsenic exposed (average, 410 µg/L) town (1,488 inhabitants) compared to nil (average, 5 µg/L) in people in unexposed town (998 inhabitants) [15]. However data of the present study showed slightly lower prevalence of skin cancer in study population of West Bengal, India. In a population-based case-control study of incident of skin cancers, 284 and 524 age- and sex-matched controls from New Hampshire, USA, there was evidence of an increased risk of skin cancer (OR=2.07, 95% CI=0.92, 4.66) among those with the highest levels of toenail arsenic concentration compared to those with the lowest levels of toenail arsenic concentration [16]. In the present study the mean age of cases with skin malignancy was 63.9 years, more males being affected than females, and the OR is 5.99 for disease occurrence among males. The male-to-female ratio was 2.9:1 for skin cancer, the prevalence increased steadily with age in Taiwan study [14].

In the present study difference between proportion affected with skin malignancy exposed to arsenic level above (0.88%) or below 50 µg/L (0.44%) was found to be statistically significant (p-value = 0.03). In Taiwan study also prevalence rate for skin cancer showed an ascending gradient according to the arsenic content of the well water, *i.e.*, the higher the arsenic content, the more patients had skin cancer [14].

In the present study 155 (58%) cases with skin lesion of pigmentation and keratosis and 9 (22.4%) cases with skin cancer were found to be taking water with arsenic level <10 µg/L currently. As the study was conducted more than 30 years after the problem of ground water arsenic contamination detected in West Bengal and as life time water data was not collected for the study participants in the current study the occurrence of skin pigmentation and keratosis and skin malignancy in good number of cases with current arsenic exposure <10 µg/L could be explained by possible high arsenic exposure in these subjects earlier.

The reported incidence of skin cancer in India is less than 1% of all the cancers [17]. Skin cancers constituted 2.4% (77/3154) of patients with cancer treated in the surgical oncology department of a Regional Cancer Centre in India [18]. In a retrospective study the incidence of skin cancers was found to be 3.18% of all the cancer patients registered over a period of one year at one medical centre in Punjab, India [19]. The mortality of skin cancer in arsenic exposed population in our study was found to be 4.96% of all cancer deaths, higher than that reported from hospital-based population in India. As compared with the general population in Taiwan, both the Standardized Mortality Ratio (SMR) and cumulative mortality rate were significantly high in black foot disease-arsenic endemic areas for cancer of skin, the SMRs being, 534, for males, and 652 for females [20]. Mortality rates from skin cancer was studied between arsenic exposed region of Antofagasta and the unexposed control Region VIII of Chile in 1976-92 during an Ecological study, the SMR for skin cancer was 3.2 (95% CI, 2.1 to 4.8) [21]. Smith et al. [22] compared sex- and site-specific mortality for the years 1989-93 in arsenic exposed Region II of Chile with national mortality rates. The SMR for skin cancer was 7.7 (95% CI, 4.7 to 11.9) among men and 3.2 (95% CI, 1.3 to 6.6) among women.

Limitation of the study was that lifetime record of water sources used for drinking purpose could not be collected as the study was done many years after the ground water arsenic contamination occurred in the study population. Further, as cross-sectional study was carried out on a large population, no histological confirmation of diagnosis of skin cancer could be done because of technical reason. However, the clinical characteristics were quite diagnostic of skin cancer.

Conclusion

Though many studies on skin and systemic manifestations were done earlier, but no study had so far been done assessing prevalence of skin cancer and its mortality in arsenic exposed population in India. Skin cancer was found to be present in 44 cases, the prevalence being 0.61% studied on a population of 7,162. Death due to skin cancer was found to occur in 6 (4.96%) subjects out of total cancer deaths of 121 recorded out of 8,206 populations surveyed. Present study provided, for the first time, data on arsenic exposure and prevalence of skin cancer and its mortality from a large arsenic exposed population in India.

Acknowledgement

The paper was prepared on the basis of study carried out on a research project implemented with funding from ICMR Ad-hoc Research Project Grant, vide sanction letter no. Re: No: 5/8/4-15(ENV)/2015-NCD-1 dated 19.03.2017. Water samples collected from households of study participants were tested by chemist of PHED Department from the Nadia District laboratory for which we offer gratitude to Director, WSSO, PHED for giving permission. The contents of the paper are solely the responsibility of the authors and not necessarily represent the official view of ICMR. The authors express great appreciation to all the team members of the study, Shyamasree Mukherjee, Pramit Kumar Majumder, Ranjit Sardar, Ayan Karar, Kaushiki Pada Chakraborty for the tireless service given by them during field work and data management at the office, without which the study would not have been possible.

References

1. IARC, Some drinking-water Disinfectants and contaminants, including Arsenic. Monographs on the Evaluation of Carcinogenic risks to Humans Lyon, France, WHO. 2004;84:61-96.
2. Gorai R, Chakraborty AK, Dey SB, Saha KC. Chronic arsenic poisoning from tube well water. J Indian Med Association. 1984;82:34-5.
3. WHO Technical Publication. In: Caussy D, editor. A field guide for detection, management and surveillance of arenicosis cases. New Delhi: WHO Regional Office for South East Asia; 2005;30:19-22.
4. Guha Mazumder DN, Chakraborty AK, Ghosh A, Das Gupta J, Chakraborty DP, Dey SB, et al. Chronic arsenic toxicity from drinking tube-well water

in rural West Bengal. Bull World Health Organ 1988;66:499-506.

5. Guha Mazumder DN, Haque R, Ghosh N, De BK, Santra A, Chakraborty D, et al. Arsenic levels in drinking water and the prevalence of skin lesions in West Bengal, India. Int J Epidemiol. 1998;27(5):871-7.
6. Rahaman MM, Mondal BK, Roy Chowdhury T, Sengupta MK, Chowdhury UK, Lodh D, et al. Arsenic groundwater contamination and sufferings of people in north 24-parganas, one of the nine arsenic affected districts of West Bengal, India. J Environ Sci Health, Part A - Toxic Hazardous Substances Environ Engineering. 2003;38(1):25-59.
7. Rahaman MM, Sengupta MK, Mukherjee SC, Pati S, Ahamed S, Lodh D, et al. Murshidabad - one of the nine groundwater arsenic-affected districts of West Bengal, India. Part I: Magnitude of Contamination and Population at Risk. Clinical Toxicology. 2005;43:823-34.
8. Mukherjee SC, Saha KC, Pati S, Dutta RN, Rahman MM, Sengupta MK, et al. Murshidabad--one of the nine groundwater arsenic-affected districts of West Bengal, India. Part II: Dermatological, Neurological, and Obstetric Findings. Clin Toxicol(phila). 2005;43(7):835-48.
9. Guha Mazumder DN, Ghosh A, Majumdar KK, Ghosh N, Saha C, Guha Mazumder RN. Arsenic contamination of ground water and its health impact on population of district of Nadia, West Bengal, India. Indian J of Community Med. 2010;35:331-8.
10. Sommers SC, McManus RG. Multiple arsenical cancers of skin and internal organs. Cancer. 1953;6(2):347-59.
11. Yeh S. Skin cancer in chronic arsenicism. Hum Pathol. 1973;4:469-85.
12. Guha Mazumder DN. Chronic arsenic toxicity and human health. Indian J Med Res. 2008;128(4):436-47.
13. Prospective Study of One Million Deaths in India: Rationale, design and validation results RGI-CGHR Prospective Study Collaborators Final Version, 2005.
14. Tseng WP, Chu Hm, How SW, Fong JM, Lin CS, Yeh S. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J Natl Cancer Inst. 1968;40(3):453-63.
15. Cebrián ME, Albores Aguilar M, Blakely E. Chronic arsenic poisoning in the north of Mexico. Hum Toxicol. 1983;2(1):121-33.
16. Karagas MR, Stukel TA, Morris JS, Tosteson TD, Weiss JE, Spencer SK, et al. Skin cancer risk in relation to toenail arsenic concentrations in a US population-based case-control study. Am J Epidemiol. 2001;153(6):559-65.
17. Mahajan MK, Lal P, Biswal BM, Mohanti BK. Cancer of skin. In: Rath GK, Mohanti BK, editors. Text book of radiation oncology: Principles and practice. New York: B. I. Churchill Livingstone; 2000. p. 223-37.
18. Deo SV, Hazarika S, Shukla NK, Kumar S, Kar M, Samaiya A. Surgical management of skin cancer: Experience from a regional cancer Centre in India. Indian J Cancer. 2005;42(3):145-50.
19. Lal ST, Singh RPB, Bhatti DJ, Yadav HP. Changing trends of skin cancer: A tertiary care hospital study in Malwa region of Punjab. J Clin Diagn Res. 2016;10(6):12-5.
20. Chien-Jen C, Ya-Chien C, long-Ming L, Hsin-Yin W. Malignant neoplasms among residents of a Blackfoot disease-endemic area in Taiwan: High-arsenic artesian well water and cancers. Cancer Res. 1985;45:5895-9.
21. Rivara MI, Cebrián M, Corey G, Hernández M, Romieu I. Cancer risk in an arsenic-contaminated area of Chile. Toxicol Ind Health. 1997;13(2-3):321-38.
22. Smith AH, Goycolea M, Haque R, Biggs ML. Marked increase in bladder and lung cancer mortality in a region of northern Chile due to arsenic in drinking water. Am J Epidemiol. 1998;147:660-9.