PREVALENCE OF SKIN CANCER IN CHRONIC ARSENICOSIS IN CHITTAGONG MEDICAL COLLEGE HOSPITAL

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Summary

A descriptive study was done in the Department of Dermatology and Venereology, Chittagong Medical College Hospital, Chittagong, during the period of July 2004 to June 2008, to find out the prevalence of skin cancer among various skin manifestations of chronic arsenicosis. All suspected patients of chronic arsenicosis coming from endemic zones of Bangladesh were the study population A total number of 234 patients of chronic arsenicosis were included in this study. The patients were diagnosed by physical examination and by estimation of arsenic level of scalp hair. The majority of the patients came from Noakhali, Chittagong, Feni, Laxmipur, Comilla & Chandpur districts. The mean age of the patients was 27.80 years ± 10.22 SD (Range: 12-70 years). About 70% patients were around 30 years of age. The male & female ratio was 1.9:1. Most of them came from average socio-economic status. About 28.6% patients were students, 25% patients daily labour. Majority of the patient (94%) used tube well as drinking water source, 12.8% had family history of chronic arsenicosis and about 19% took alternative medicines (homeopathic/kobirajee) for treatment of the same or other illness. The cent percent patients presented with hypo and hypermelanosis (rain drop pigmentation), while 90.6% were with hyperkeratosis in palms and soles. The measurement of arsenic in scalp hair was done. The mean arsenic level of scalp hair was found to be 2.63 ± 1.39 SD (range : 2.0 - 17.6 mg/kg). Skin biopsy for histopathology was done for suspected patients and skin lesions of 21.4% patients were detected as arsenical keratosis. Among the total patients, 6 (six) patients were found to develop skin cancers (2.6%). Among them, 3 patients developed Squamous Cell Carcinoma (SCC), 1 Basal Cell Carcinoma (BCC), while Bowen's disease and Melanoma was found in 1 patient each. Regarding treatment response, about 48% patients showed good response with topical keratolytics- 6% to 12% salicylic acid and potent corticosteroid- clobetasol propionate .05% & systemic antioxidants (Vit A, E & C). Arsenic is an emerging chemical carcinogen. In addition to the social problems, skin cancer along with other internal malignancies will be a serious health hazards in our country in near future. It is established that drinking tube-well water is the main source of chronic arsenic intoxication and different skin cancers are the due to arsenic. So safe arsenic free drinking water may prevent chronic arsenicosis and its complications.

Key words: chronic arsenicosis; prevalence; skin cancer

Introduction

Arsenic (As) along with Antimony (Sb) and Bismuth (Bi) belong to group V of the periodic table, was amongst the earliest elements to have been isolated and it was known before either Nitrogen [1772] or Phosphorous [1669] had been obtained as the free elements. The properties of arsenic sulfide and related compounds have been known to physicians and professional as poisons since the fifth century BC though their use is no longer recommended by either group of practitioners. Arsenic contaminates water when present in toxic amount. We ingest arsenic as small quantity in vegetable, fruits, fish, drinking water and in some medicine like Flower's solution and Asiatic Pill. Arsenic absorption, exertion and retention are influenced by the amount and the chemical forms in which it is ingested. Arsenic in the forms that ordinarily present in drinking tubewell water, food and the organic compounds of arsenitic acid, 3 nitro- 4 hydro phenyl arsenic acid and arsenobengene used as health and growth stimulants are well absorbed. After absorption arsenic is distributed rapidly and widely to all tissues of the human body such as liver, spleen, kidney, heart, lung, stomach, pancreas, muscles, thyroid, brain, spinal cord, skin, hair and nails. This study aim that to findout skin cancer in chronic arsenicosis.

Materials and methods

Type of study

The type of study undertaken was based upon randomized sampling and this was observational and

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descriptive type of study.

Study place and duration of study

The study was conducted in the Department of Dermatology and venereology, Chittagong Medical College Hospital during the period of July 2004 to June 2008.

Study population

A total number of 234 patients with suspected chronic arsenicosis were selected as study population.

Arsenicosis case definition

Arsenicosis was defined in this study as the 'Presence of characteristic arsenical skin lesions with a history of drinking arsenic contaminated water for at least 6 months'. This definition was also validated by other reports[1]. The diagnosis of arsenical skin lesions were reported in earlier publications[2].

Patients' selection

Patients who attended the arsenic clinic, Department of Dermatology & Venereology, Chittagong Medical College Hospital (CMCH) with typical clinical manifestations of chronic arsenicosis as per standard instruction and recommendation. Considering the endemicity of disease in the region, only clinical criteria were used for diagnosis.

Inclusion criteria

1. Patients who had given verbal consent and were willing to comply with this study process.

2. Chronic Arsenicosis patients of both sex groups of more than 5 years.

3. Patients having history of consumption of arsenic contaminated tube-well water more than 6 months with or without family history of chronic arsenicosis.

4. Patients coming from endemic zones presented with acquired palmo-plant punctuate hyperkeratosis.

5. Patients who had hyper pigmentation or leucomelanosis on the trunk and extremities and other typical signs and symptoms of chronic arsenicosis.

Exclusion criteria

1. Patients who refused to be included in the study.

2. Patients with age below 5 years.

3. Mottled pigmentations since birth.

4. Drug induced hypo or hyper pigmentation.

5. Occupational or hereditary or other skin diseases associated with palmo-planter hyperkeratosis.

Data collection procedure

A close ended pre-tested questionnaire was used to collect information on sociodemographics, water use and occupation. Skin lesions of chronic arsenicosis i.e. melanosis, lencomelanosis and keratosis was examined by dermatologists under daylight (Appendix-I). A total of 234 patients were enrolled. Different skin manifestations of chronic arsenicosis were analyzed. Skin biopsy from the lesion of hyperkeratosis for histopathology done to find out different types of skin cancers. A total of 234 scalp hair samples were collected and all these preserved hair samples were sent to Atomic Energy Centre, Dhaka where these were analyzed by flow-injection hydride generation atomic absorption spectrophotometer (FIHG-AAS). The minimum detection level for this method is 3 mg / kg.

Statistical analysis

All analyses were performed using SPSS software (Version 12). Baseline chrematistics of the study populations were calculated and comparison between different baseline variables was done using student t-test, chi-square test and Pearson's correlation test.

Observations and results

A total of 234 cases, 154 (65.8 %) males, 80 (34.2%) females, fulfilling the inclusion criteria were enrolled during the study period (Table I). The mean age of the patients was 27.80 years ± 10.22 SD (Range: 12 - 70) (Fig 1). About 70 % patients were under 30 years of age. The Male: Female ratio was 1.9: 1. Most of the patients were students (28.6%) and daily labours (24.8%) (Fig 2). About 74% came from average socio-economic status (Table II). Noakhali was found most endemic area in southern part of Bangladesh (Fig 3, 4). Maximum patients are tube-well water user (94%) (Table III). About 13% patients had family history of Arsenicosis (Fig 5), and about 19% had history of using homeopathic medications.

Various types of skin manifestations were found. Among them, the most common was Rain Drop Pigmentation (100%). 90.6% patients showed Palmo-planter Punctate Keratosis was present in 90.6% of patients.

Arsenic level of Scalp hair was estimated (Table IV, V, VI). The mean Arsenic level was detected to be as 2.63 mg/Kg ± 1.39 SD (Range : 2.0-17.6).

Arsenicosis (73mg/kg) was deccted among 27.87% of the total patients (Fig 6). Skin Biopsy for histopathology was done for suspected patients, and skin lesions of 21.4 % patients were detected as Arsenical Keratosis (Table VII). Among the total patients, 6 (Six) patients were found to develop Skin Cancer (2.6 %). Among them, 4 patients developed Squamous Cell Carcinoma, while Bowen's Disease and Melanoma was found in 1 patient each. Clinical improvement after treatment of patients were observed. Hyperkeratosis was improved clinically and good response was observed in about 48 % patients. About 33 % patients were found to be as non responders (Table VIII).

Table I : Sex distribution of study population

Sex	N	%
Male	154	65.8
Female	80	34.2
Total	234	100.0

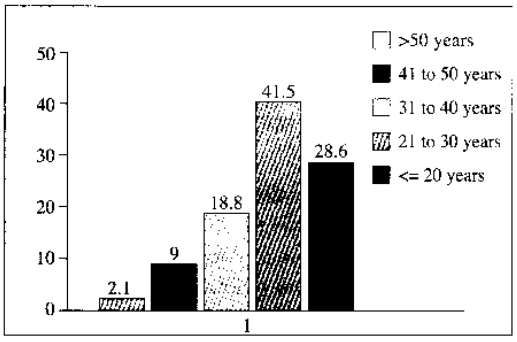

Fig 1 : Age group of study population (n=234)

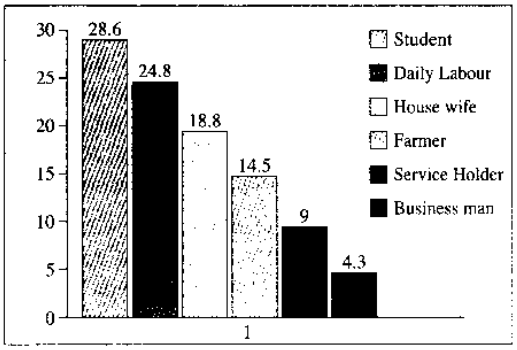

Fig 2 : Occupations of study population (n=234)

Table II : Socio-economic status of study population (n=234)

SES	N	%
Low	60	25.6
Average	174	74.4
Total	234	100.0

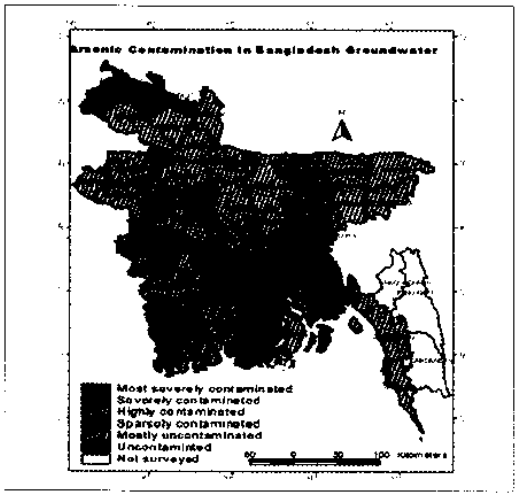

Fig 3 : Arsenic contamination in Bangladesh groundwater

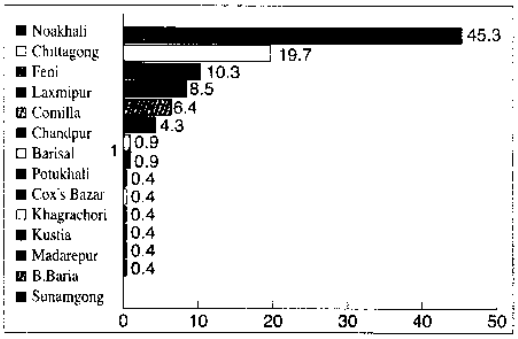

Fig 4 : Distribution of inhabitance of study population (n=234)

Table III : Source of drinking water of study population (n=234)

Sources	N	%
Tube Well	220	94.0
Surface Water	8	3.4
WASA	6	2.6
Total	234	100.0

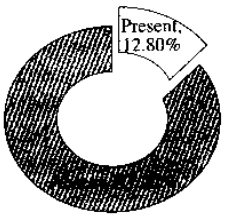

Fig 5 : Family history of arsenicosis (n=234)

Table IV : Arsenic Status in scalp hair of study population (n=234)

	N	%
Normal	169	72.2
Arsenicosis	65	27.8
Total	234	100.0

Table V : Skin biopsy for histopathology (n=234)

	N	%
Not Done	184	78.6
Arsenical Keratosis	50	21.4
Total	234	100.0

Table VI : Mean differences among arsenic status with t-test results

Continuous Variables	Arsenic Status in Scalp Hair	N	MEAN	SD	T	P
Age (Years)	Normal	169	24.64	8.58	8.791	0.000 (<0.001)
	Arsenicosis	65	36.02	9.57		
Arsenic Level in Scalp Hair(mg/Kg)	Normal	169	2.00	0.00	10.095	0.000 (<0.001)
	Arsenicosis	65	4.27	1.81		
Duration of Illness (Years)	Normal	163	2.21	0.99	5.655	0.000 (<0.001)
	Arsenicosis	64	3.15	1.18		

Table VII : Skin cancer detected by histopathology (n=234)

	N	%
Detected	6	2.6
Not Detected	228	97.4
Total	234	100

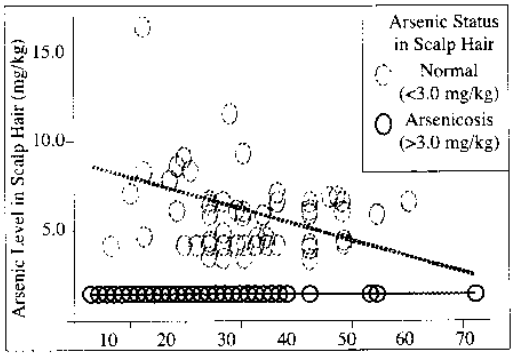

Fig 6 : Pearson's correlation between age and arsenic level : (r=0.290, P< 0.001)

Table VIII : Treatment response of chronic arsenicosis (n=234)

	N	%
Good response	112	47.90
Non responder	78	33.30
Discontinued treatment	44	18.80
Total	234	100.00

Discussion

The discovery of arsenic contamination of ground water in many nations, including Argentina, Chile, China, India, Mexico, Taiwan, Thailand, the United States and now, Bangladesh shows that this is a global problem. Bangladesh is facing with the largest mass poisoning of a population in history because ground water used for drinking has been contaminated with naturally occurring inorganic arsenic. It is estimated that about 77 million inhabitants of Bangladesh are at risk of drinking arsenic contaminated water [3]. The scale of this environmental disaster is greater than any seen before.

In Bangladesh, arsenic contamination of water in tube-wells was confirmed at first in 1993 in the Nawabganj district [4]. Further testing was done in the following years by different agencies and institutions like the Bangladesh Atomic Energy Commission, the Dept. of Public Health Engineering Laboratories, the National Institute of Preventive and Social Medicine in Dhaka. For Bangladesh Arsenic Concentration in drinking water recommended by WHO is ≤50 μg/L[5].

Chronic Arsenicosis appearing in rural population in an epidemic proportion at the 20th century in our

country is an alarming health hazard at present. Arsenic is widely distributed in body tissues like blood, skin, hair, nails. It can be detected long times after it has disappeared from the urine & feces. Rare acute Arsenic poisoning may occur in short time but chronic arsenicosis may take longer period. Mottled pigmentations or raindrop pigmentation occurs most commonly in the trunk and extremities. Palmo-planter punctuate Hyperkeratosis occurs after a long period of chronic Arsenic poisoning. Initially there may be dermatitis, hyperkeratosis, conjunctivitis, diarrhea & later on anemia, peripheral neuropathy & multi organ failure. In the last stage, patient may develop gangrene of limbs & skin cancers including SCC, BCC, melanoma, Bowen's Disease & other internal malignancies like carcinoma of stomach, lung & liver. Studies showed concentration of arsenic in tubewell water in endemic areas of Bangladesh was >50 μg/L[6,7].

Based on population density measured in 1998 this group estimated that the number of people exposed to arsenic consecrations above 50 μg /L. was about 21 million. This number would be approximately doubled or more if WHO's standard of 10 μg /L. were adopted. Further studies conducted by the School of Environment Studies and the Dhaka Community Hospital found that 59% of the 7800 ground water samples had arsenic concentrations greater than 50 μg /L[8].

In two other studies it was found that 30% of 7364 adults and 430 of 1481 adults developed skin concer due to arsenice [9,10,11].

The latency for arsenic-caused skin lesions (I.e., the time from first exposure to manifestation of disease), in particular Keratosis, is typically about 10 years[12]. In the 1997 consultancy, it was found that the youngest individuals with skin lesions caused by arsenic were about 10 years old[2] which was comparable with my study i.e. the youngest case of chronic Arsenicosis was 12 years old in my study. Other studies have shown that skin lesions also occur in children younger than 10 years. However, latency that is shorter or longer than 10 years may occur, and the rapidity of the appearance of skin lesions appears to be dose dependent. The typical latency of skin cancer is more than 20 years after the beginning of exposure to arsenic. A study of large population in Taiwan found a clear dose-response relationship between arsenic concentrations in drinking water and the prevalence of skin cancer[13]. In their study, the average concentration of arsenic in water was about 500 μg /L. and by age 60 more than 1 in 10 had developed skin can cancer [14]. In my study the arsenic level of scalp hair 2.63 mg/kg ± 1.39 SD (Range 2.0-17.6 mg/kg) (P<0.001) Though large number of skin cancers have been reported in Taiwan, the future burden of arsenic caused skin cancer in Bangladesh is uncertain. Differences in susceptibility between the populations of Taiwan and Bangladesh may exist that only time and further study will identify. However, as yet there is no evidence to indicate that the long-term risks of skin cancer would be any lower in Bangladesh than in Taiwan.

In Argentina, a mortality study in the arsenic - exposed region of Cordoba found increased risks of bladder and lung cancer among men and women from 1986 to 1991, although arsenic concentrations were lower (average 178 μg /L.) than in Taiwan[15]. Using the current US Environmental Protection Agency standard of 50 μg /L it has been estimated that the life time risk of dying from cancer of liver, lung, kidney, bladder and skin while drinking 1 liter a day of water containing arsenic at this concentration could be as high as 13 per 1000 persons exposed[16].

The latest document on arsenic in drinking water, the US National Research Council concluded that exposure to 50 μg /L. could easily result in a combined (Skin & internal) cancer risk of 1 in 100[17].

In case of Bangladesh it can be inferred that since there are many people who currently have skin lesions caused by ingesting arsenic, many more cancers will occur if exposure to arsenic continues. It is established that mortality from cancers due to arsenic ingestions by any means will increase in future if sufficient latency for cancer formation has been allowed.

In our study, most of the patients came from endemic zone of greater Noakhali. M.A.I. Chowdhury et al, 2006 showed that Chandpur, Comilla, Noakhali, Munshiganj, Faridpur, Madaripur, Gopalgonj, Shariatpur and Satkhira are the most arsenic contaminated part of the country. It was found that about one-third of the total patients of our study had high level of arsenic in scalp hair, maximum patients were of middle age. About 13 % patients has got positive family history of Chronic Arsenicosis. Almost all patients used tube-well water for drinking purpose and some patients took

homeopathic & Kabirajee medicine for different illness for variable times before the development of chronic Arsenicosis.

6 (six) patients out of 234 cases developed skin cancers, like SCC, Bowen's Disease & Melanoma. The association between skin cancer and arsenic status of different body tissues was found to be Statistically Significant (P<0.001). Rong chun Yu et al., 2000 showed that chronic ingestion of arsenic from drinking water is associated with the occurrence of skin cancer [22]. They showed that skin lesion cases had had higher percents of inorganic arsenic, methylarsonic acid (MMA) and lower percent of dimethyl arsenic acid (DMA). It is established that individual with higher percentage of MMA (> 15.5%) had an odds ration of developing skin cancer 5.5 times (95% confidence interval) higher than those having a lower percentage of MMA. It is concluded that arsenic biotransformation including methylation capacity may have a role in the development of arsenic induced skin disorders.

None of the patients had manifestations or evidence of Diabetes Mellitus or other major endocrinopathy. Though some study reports show that arsenic is a probable contributor to causation of Diabetes mellitus and hypertension[23]. Advanced Keratoses on palms and soles are extremely vulnerable for superimposed infections such as fungal infections and cancer formation wish may cause serious problems. Providing topical Keratolytics and antifungls and systemic antioxidants may be beneficial and should be part of routine care in advanced cases. Urinary glucose should tasted in all patients with chronic arsenicosis and patient's blood pressure should be monitored routinely because arsenic exposure may induce hypertension[24].

The limitations of our study was that we were not able to do, arsenic estimation of tube well water during the time of examinations of patients of chronic arsenicosis. Serum Arsenic level or urinary arsenic level was not estimated due to lack of facilities in our country. The possibility of continuing exposure to arsenic via drinking water or food or by other means should be tasted by screening of arsenic in blood or urine samples. At present there is no kit for blood or urine sample testing. So a reference laboratory should be equipped to measure Arsenic in biological samples.

Conclusion

The present paper provides a scenario of muco-cutaneous manifestations of Chronic Arsenicosis in our people. In addition to the social problems, skin cancer along with other internal malignancies will be a serious health hazards in our country in near future.

Arsenic may be an emerging chemical carcinogen in near future. So further study is required to evaluate the status of chronic Arsenicosis including Malignancies among the peoples of endemic areas of Arsenic poisoning in Bangladesh. It is a great challenge for the Government to provide safe arsenic free drinking water for the population of Bangladesh.

Early case detection and early management with follow up treatment may prevent cancer formation and premature death. So a broad based study is necessary to find out the multiple sources of arsenic and different consequences of Chronic Arsenic poisoning, including cancers of different organs of the body.

It is necessary to take short and long term emergency intervention programme by Government and NGO's for prevention of further endemicity of chronic arsenicosis in the country.

Disclosure

All the authors declared no competing interestes.

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