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Different cutaneous and mucous membrane manifestations of chronic arsenicosis, a study of Chittagong, Bangladesh

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ABSTRACT

Background: Chronic arsenicosis is a serious health problem in Bangladesh now due to the intake of arsenic contaminated groundwater above the safe level of 0.05 mg/L by shallow tube well, throughout the country. About 25 million people of Bangladesh are at risk of chronic arsenic toxicity. Arsenic toxicity is also an alarming situation in many countries of the world. Hence, the study on health hazard of arsenic contamination, its prevalence, presentation, complication, and management is an important one.

Aim: The purpose of this study is to evaluate different cutaneous and mucous membrane manifestations of chronic arsenicosis.

Method: The study descriptive was conducted in the Department of Dermatology and Venereology in Chittagong Medical College Hospital. A total 105 patients of clinically diagnosed chronic arsenicosis were selected for the study. Clinical manifestations of chronic arsenicosis patients were analyzed for different mucocutaneous findings.

Result: Evaluation and analysis of findings showed chronic arsenicosis patients had characteristic features of melanosis or leukomelanosis (raindrop pigmentation) in 100% patients. Another characteristic finding of palmoplantar punctate hyperkeratosis was found in 69.5% of patients of chronic arsenicosis. Other mucocutaneous findings of chronic arsenicosis were cutaneous malignancy such as basal cell carcinoma, squamous cell carcinoma, and Bowen's disease. Others cutaneous and systemic diseases were also observed in patients of chronic arsenicosis.

Conclusion: Characteristic mucocutaneous findings of chronic arsenicosis were melanosis, leukomelanosis (raindrop pigmentation), palmoplantar punctate hyperkeratosis, and cutaneous malignancy. As chronic arsenicosis is a serious health problem in our country, it demands more research on chronic arsenicosis.

Key words: Chronic arsenicosis, leukomelanosis, melanosis, pigmentation

INTRODUCTION

Arsenicosis is a chronic health condition arising from prolonged ingestion of arsenic above the safe dose for at least 6 months, usually manifested by characteristic skin lesions of melanosis and keratosis, occurring alone or in combination, with or without the involvement of internal organs.[1] Arsenic exposure occurs in variety of occupations, during work in industries and during use of weed killer or insecticides and different chemical compounds. However, arsenic-containing groundwater intake is the main cause of arsenic toxicity now. About 25 million people of Bangladesh and a similar number of people of surrounding countries are at threat of arsenic-contaminated drinking water.[2] Hence, described as the Bangladesh arsenic condition, "largest mass poisoning in the world."

Arsenic exposure causes different types of toxic effect to human. Acute arsenic poisoning with an ingested dose of only 70–180 mg of arsenic trioxide is fatal to human. Acute arsenic poisoning presents with severe abdominal pain, burning of the lips and mouth, projectile vomiting and severe blood stained diarrhea, restlessness, thirst, severe muscle cramp, oliguria and proteinuria leading to collapse, shock, and death. Acute arsenic poisoning usually occurs as suicidal, homicidal, and accidental poisoning.[3]

Chronic arsenic exposure causes chronic arsenicosis. The World Health Organization (WHO)[1] describes algorithm using following two diagnostic criteria of arsenicosis:

a. The presence of pigmentary and keratotic skin lesions and
b. Evidence of exposure to elevated levels of arsenic established by the history of intake of arsenic contaminated water, or by arsenic concentration in hair or nails.

The first diagnostic criteria are clinical criteria, which require the presence on physical examination of any of the pigmentary or keratotic skin signs. The second criteria are laboratory criteria,

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in which a reliable history of consuming drinking water with an elevated concentration of arsenic for at least 6 months is sufficient to establish exposure.[4] In the absence of adequate information regarding a subject's exposure history, the finding of elevated levels of arsenic in a subject's hair or nails could offer presumptive evidence of elevated arsenic exposure.[5] Arsenic testing should be conducted using standardized sample collection methods and acceptable laboratory techniques. Normal limit of arsenic in nail and hair is up to 1 mg/kg.

Arsenic contamination in drinking water is a serious health problem in Bangladesh, in South East Asian region and different countries of the world. First arsenic contamination in groundwater was detected in 1993, in our country in Chapai Nawabganj district. Now tube well water of 61 districts out of 64 districts is affected with arsenic contamination. 5 million people are suffering from arsenic-related skin and systemic diseases in Bangladesh. Safe level of arsenic in drinking water, according to the WHO standard, is 0.01 mg/L (10 ppb) and Bangladesh standard is 0.05 mg/L (50 ppb). Arsenic compounds undergo various reactions and release arsenic to underground water.

Metabolism of arsenic in the human body is very complex. After intake and absorption of arsenic, it is metabolized in the liver. It is detoxified by conversion in monomethyl arsenic acid (MMA) and dimethyl arsenic acid (DMA) and excreted mostly (90%-95%) as MMA, DMA and inorganic form through urine. A portion of absorbed arsenic is deposited in the skin, hair, nail, and other organs.[6]

Arsenic affects all organs and systems of the body. Skin lesions of melanosis, leukomelanosis, and palmoplantar punctate hyperkeratosis are most common characteristic findings and diagnostic. Clinical manifestations of chronic arsenicosis develop after a latent period of 6 months to 2 years or more depending on the amount of arsenic intake. Arsenic-induced cutaneous malignancies are squamous cell carcinoma (SCC), basal cell carcinoma (BCC), melanoma, and Bowen's disease. Average latency periods for carcinoma are 18 years with a range from 3 to 40 years.[7] Arsenic-associated others cutaneous manifestations include diffuse alopecia of the scalp, hypo, and hyperhidrosis, peripheral neuropathy, black foot disease (pigmentation, ulceration, and gangrene in lower extremities), and nail dystrophy.

Chronic arsenic toxicity produces various systemic manifestations; among important are chronic lung diseases such as chronic obstructive pulmonary disease, and bronchiectasis, liver disease such as non-cirrhotic portal fibrosis, polyneuropathy, peripheral vascular disease, ischemic heart disease, diabetes mellitus, and asthenia.[8] Cancer of lung, liver, and urinary bladder is important cancers associated with chronic arsenic toxicity.[9]

Treatment of chronic arsenicosis is not satisfactory. To avoid drinking of arsenic contaminated tube well water is necessary. Safe arsenic free water can be taken from surface water (boiled, organism free), deep tube well water, pipe supply water, rainwater harvesting, and treatment of arsenic contaminated water by filter. Antioxidant with a combination of Vitamin- A, Vitamin - E, and Vitamin - C is used by some physicians. Spirulina, blue-green microalgae, found beneficial to chronic arsenicosis.[10] Symptomatic treatment is given for other presentation.

As arsenic contamination in drinking water is a serious health problem in Bangladesh and many other countries, it is important to find out different clinical presentation including mucocutaneous manifestations, diagnosis, and management of chronic arsenicosis. Chart 1: Total 73 palmo-planter hyperkeratosis patient were found out of 105 patients. Among them, mild, moderate and severe were found 20, 46 and 7 respectively. Chart 2 illustrates that scalp hair arsenic level found high in 21 patients.

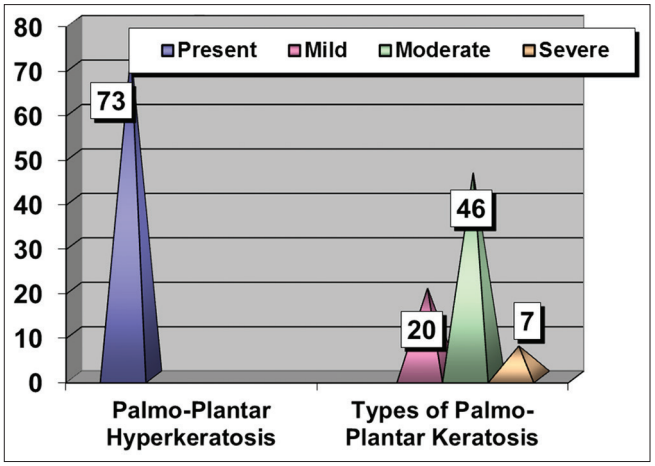

Chart 1: Distribution of palmoplantar hyperkeratosis

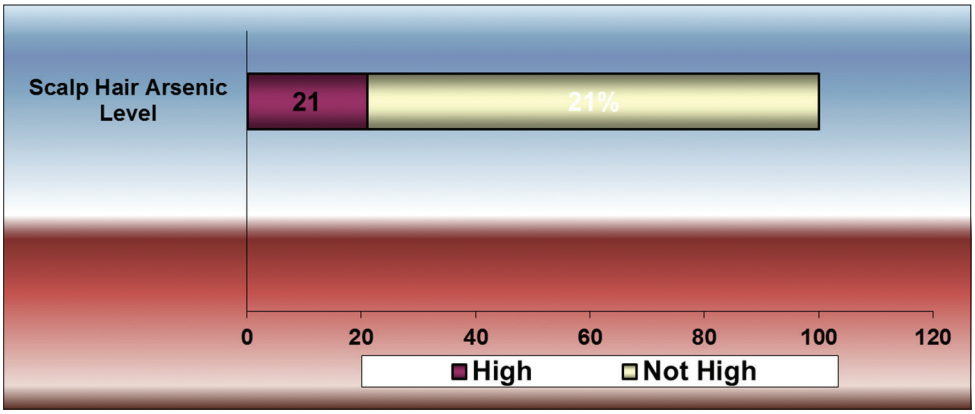

Chart 2: Distribution of scalp hair arsenic measurement levels

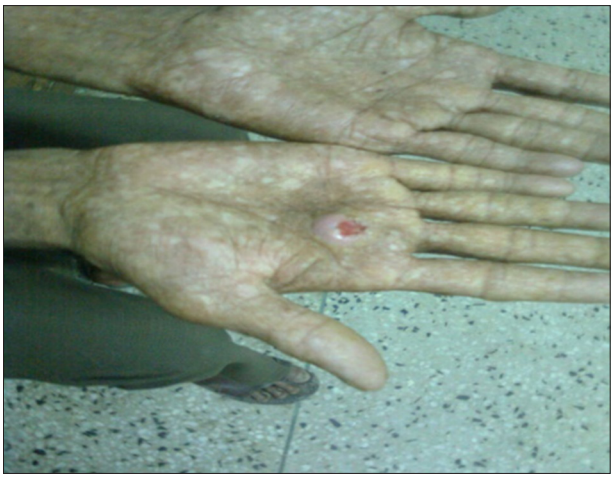

Figure 1: Patient of chronic arsenicosis with squamous cell carcinoma

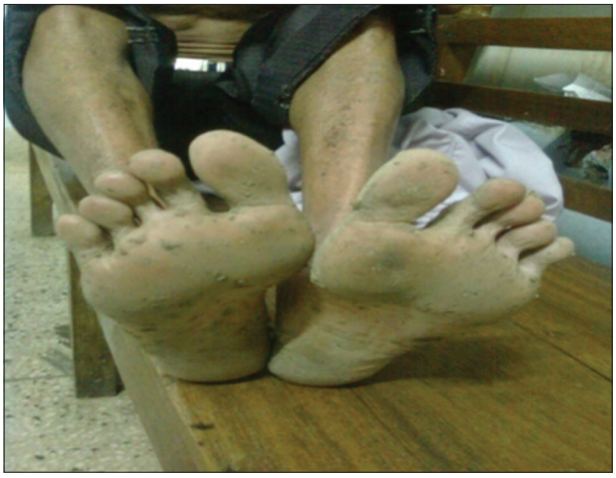

Figure 4: Patient of chronic arsenicosis with planter hyper keratosis

Figure 2: Patient of chronic arsenicosis with basal cell carcinoma

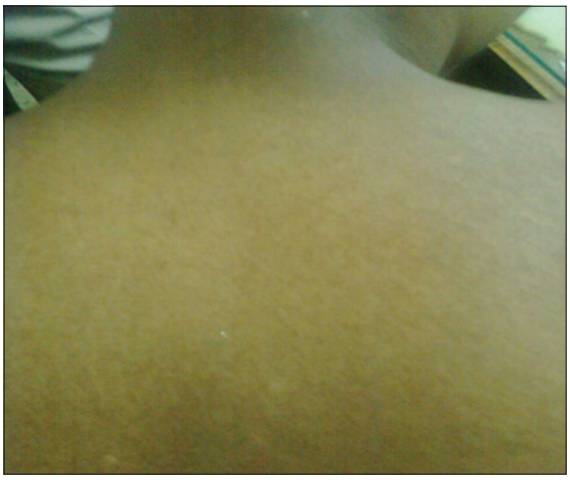

Figure 5: Patient of chronic arseniccosis with raindrop pigmentation

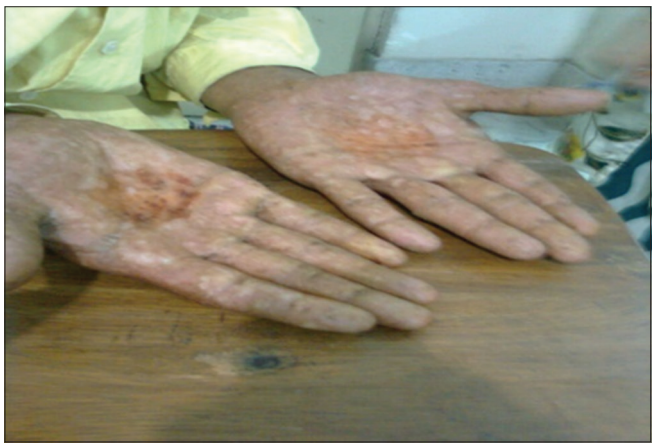

Figure 3: Patient of chronic arsenicosis with palmer hyper keratosis

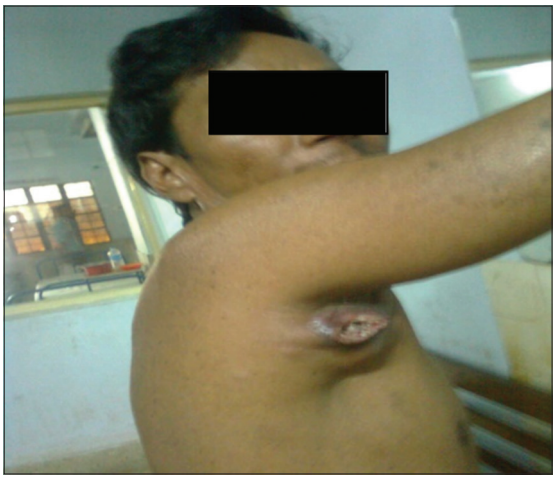

Figure 6: Patient of chronic arseniccosis with squamous cell carcinoma with metastasis to axillary lymph node

METHODS AND MATERIALS

This descriptive study was conducted in the Department of Dermatology and Venereology in Chittagong Medical College Hospital (CMCH) during the period from October 2008 to September 2009. A total of 105 patients of chronic arsenicosis had been included in the study. Inclusion criteria were patients of both sexes, age group from 6 to 60 years and voluntarily give consent to participate in the study. Exclusion criteria were hypomelanosis/ melanosis since birth, appearance related to any drug intake

or occupation, present in the face only. The study protocol was approved by the technical committee, Ethical Committee, and peer review committee of Chittagong Medical College. All the patients were informed of the nature of study in detail. Then, written consent was taken from each patient or the patient's guardian before enrollment into the study.

The history, physical examination including investigation findings had been recorded after taking informed consent of the patient or the patient's guardian. All data had been collected in individual "case record form," and the necessary investigation results have been collected and recorded in an attached sheet. Data were processed and analyzed using computer software Statistical Packages for the social Sciences-Version 15 [Figures 1-6].

RESULTS AND OBSERVATIONS

Table 1: Distribution of sex among the study subject

Sex	Frequency (%)
Male	73 (69.5)
Female	32 (30.5)
Total	105 (100.0)

Table 2: Distribution of background information among the study subjects

Intake of tube well water	Frequency (%)
Yes	105 (100.0)
No	00 (0.0)
Intake of homeo/herbal medicine	
Yes	32 (30.5)
No	73 (69.5)
Source of arsenic toxicity	
Water	105 (100.0)
Total	105 (100.0)

Table 3: Distribution of mucocutaneous manifestations among the study subjects

Melanosis/leukomelanosis	Frequency (%)
Present	105 (100.0)
Absent	00 (0.0)
Palmoplantar hyperkeratosis	
Present	73 (69.5)
Absent	32 (30.5)
Total	105 (100.0)
Types of palmoplantar keratosis	
Mild (Grade 1)	20 (27.4)
Moderate (Grade 2)	46 (63.0)
Severe (Grade 3)	07 (9.6)
Total	73 (100.0)

Table 4: Distribution of cutaneous malignancies among the study subjects

Cutaneous malignancy	Frequency (%)
Present	08 (7.6)
Absent	97 (92.4)
Total	105 (100.0)
Types of cutaneous malignancy	
SCC	05 (62.5)
BCC	02 (25.0)
Bowen's Disease	01 (12.5)
Total	08 (100.0)
Skin biopsy for histopathology	
Done	10 (9.5)
Not Done	95 (90.5)
Total	105 (100.0)

BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma

Table 5: Distribution of other manifestations among the study subjects

Leg edema	Frequency (%)
Present	03 (2.9)
Absent	102 (97.1)
H/o repeated conjunctivitis	
Present	23 (21.9)
Absent	82 (78.1)
Cancer of internal organ	
Present	03 (2.9)
Absent	102 (97.1)
Total	105 (100.0)

Table 6: Distribution of scalp hair arsenic measurement levels among the study subjects

Scalp hair arsenic level	Frequency Percentage (%)
High (>3 mg/Kg)	22 (21.0)
Not high	83 (79.0)
Total	105 (100.0)

Table 7: Distribution of systemic diseases present among the study subjects (*n*=20)

Systemic diseases	Frequency (%)
Asthenia	05 (25.0)
Hypertension	05 (25.0)
Diabetes mellitus	02 (10.0)
Hepatic diseases	02 (10.0)
Renal diseases	02 (10.0)
Respiratory diseases	02 (10.0)
Nervous system diseases	02 (10.0)
Total	20 (100.0)

DISCUSSION

This study was done to evaluate mucocutaneous manifestations of chronic arsenicosis in CMCH. Chronic arsenicosis is a condition due to prolonged exposure of arsenic above safe level, for more than 6 months. Drinking contaminated tube well water with arsenic is the main cause of this. As 25 million people of Bangladesh are at risk of arsenic contamination and 5 million people are already suffering from diseases associated with arsenic toxicity, it is important to find out patients due to arsenic toxicity.

Statistical analysis reveals that among the patient's males were 73 (69.5%) and females were 32 (30.5%) [Table 1]. In Nepal in a community-based study, among 93 patients of chronic arsenicosis

64 (69%) were male and 29 (31%) were female.[11] In our study increased male number is due to more male attendance in CMCH.

In our country and also worldwide, arsenic-contaminated drinking water is the main cause of arsenic toxicity.[2] It has been reflected in this study. 100% study population had taken tube well water for drinking [Table 2] Arsenic contaminated tube well water was the only source for drinking found in patients of chronic arsenicosis in a community-based study in Nepal.[11] In this study, a total of 105 patients (100%) are suggestive of arsenic toxicity due to tube well water intake.

Most important skin and mucous membrane manifestations that have came out in this study are the pigmentary changes of melanosis or leukomelanosis (100%) and palmoplantar punctate hyperkeratosis (69.5%) [Table 3], which were found, respectively, in 105 and 73 patients of chronic arsenicosis patients of this study. In a study in West Bengal, India, in 156 patients of chronic arsenicosis,[4] found pigmentation disorder in 156 (100%) and keratosis in 96 (61.5%) patients. In our study, 3 types of palmoplantar punctate hyperkeratosis were found. Among these mild form in 20 (27.4%), moderate in 46 (63.0%), and severe in 7 (9.6%) patients were found [Table 3]. In the WHO description, it has been included as diagnostic findings.[2]

Cutaneous malignancy was an important finding in this study, as mucocutaneous manifestation. Cutaneous malignancies were found in 8 (7.6%) patients of this study. Among this squamous cell carcinoma in 5 patients, basal cell carcinoma in 2 patients, and Bowen's disease in 1 patient were found. Diagnosis of cutaneous malignancy was done by histopathological examination [Table 4]. Prevalence of 10.6 skin cancers per 1000 patients of chronic arsenicosis had been described in Taiwan.[12] Arsenic-related cutaneous malignancies have been described in different studies and WHO[1] and United Nations Children's Fund [13] description.

One important finding of chronic arsenicosis was "Black foot" disease. This is an important finding recorded in patients of Taiwan.[14] However, in India and Bangladesh, it is not a common finding. In our study, one young boy was found with leg edema but no other systemic disease. Another two patients of leg edema were associated with systemic disease. Peripheral neuropathy was found in 6 (5%) patients of this study. Pedal edema was found in 11.5% and peripheral neuropathy in 13.4% patients of chronic arsenicosis in a study.[4] Scalp hair arsenic level was advised for every patient, among these 22 (21.0%) patients were with high level >3 mg/kg [Table 6]. The test was done at Atomic Energy Centre in Dhaka. It does not reflect arsenic toxicity properly, as a normal level of arsenic in scalp hair is 1mg/kg. Hair and nail arsenic level reflect evidence of arsenic exposure.[5]

Systemic diseases in chronic arsenicosis patients were found in this study as hypertension in 5(4.7%) patients, diabetes mellitus in 2 (1.9%), liver disease in 2 (1.9%), chronic respiratory disease in 2 (1.9%), kidney disease in 2 (1.9%), and nervous system disease in 2 (1.9%) patients [Table 7]. Increased prevalence of hypertension in 6.2%, hepatic disorder in 10.2% patients of chronic arsenicosis was reported. Increased incidence of 6-fold raised the ratio of diabetes mellitus, and cerebrovascular disease was observed in patients of chronic arsenicosis in Taiwan.[4] Out of 107 patients of chronic arsenicosis, 33 were found with pulmonary involvement among these 4 patients were with complicated lung diseases in a study Tables 5-7.[15]

Summary

Chronic arsenicosis is a serious health problem in our country now. Patients were selected as "clinically confirmed" cases of chronic arsenicosis according to the WHO guideline. The study population was evaluated for mucocutaneous manifestations due to chronic arsenic toxicity. In this study, it was observed that melanosis or leukomelanosis (raindrop pigmentation) is the main cutaneous findings in chronic arsenicosis, which was found in 100% patients of this study population. Another important cutaneous manifestation was the palmoplantar punctate hyperkeratosis, which was observed in 69.5% study population. Cutaneous malignancy of SCC, BCC, and Bowen's disease was observed in 8 (7.6%) patients of chronic arsenicosis. Other mucocutaneous findings that were found in patients of chronic arsenicosis were leg edema, diffuse alopecia, conjunctivitis, hyperhidrosis, peripheral neuropathy, and nail dystrophy.

CONCLUSIONS

Chronic arsenicosis is a serious health problem in Bangladesh and also in many countries of the world. Melanosis, leukomelanosis (raindrop pigmentation), palmoplantar punctate hyperkeratosis, and different cutaneous malignancies are the most important mucocutaneous manifestations of chronic arsenicosis. By these manifestations, the patients of chronic arsenicosis can be identified in the community and health service program. Hence, awareness about chronic arsenic poisoning is essential among mass people in Bangladesh. Mucocutaneous manifestations of chronic arsenicosis and associated cutaneous malignancy should be evaluated with due attention and observation in a large-scale study.

Recommendation

It is recommended that further multicenter study of mucocutaneous manifestations of chronic arsenicosis are necessary for early diagnosis and management and thus to minimize psycho-social stigma of chronic arsenicosis.

Limitations of the Study

The study was carried out on a small scale. Thus, the patients of chronic arsenicosis who were included in this study may not reflect the total scenario of Bangladesh.

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