



Research Article

NATURAL HISTORY OF CHRONIC ARSENIC TOXICITY FOLLOWING INTERVENTION TO REDUCE ARSENIC EXPOSURE, A STUDY FROM WEST BENGAL, INDIA

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ARTICLE INFO

Article History:

Received 06th May, 2020

Received in revised form 14th

June, 2020

Accepted 23rd July, 2020

Published online 28th August, 2020

Key words:

Arsenicosis in Nadia, Natural history, Pigmentation, Keratosis, Arsenic exposure

ABSTRACT

Background & Objective: Ground water arsenic contamination is an important cause of chronic arsenic toxicity in West Bengal, India. As natural history of arsenic related skin lesion following intake of safe water is scanty, a study was carried out to assess the outcome in regard to skin lesion following intervention to reduce arsenic exposure in West Bengal. **Methods:** Cohort Follow up study was carried out during 2017-2020 on a population of 7162 having arsenical skin lesion, studied previously during 2006-07, in the district of Nadia, West Bengal. Arsenic exposure data of all available past and present study subjects were used for exposure assessment. **Results:** Out of the population studied, 843 arsenicosis cases had skin lesion in the past, the lesions persisted in 249 (29.5%) cases while cleared in 594 (70.5%) subjects during current study. Further, 15 (0.21%) cases with new skin lesion were seen currently. Arsenic exposure data showed that 36.3% of individuals were drinking water with arsenic level ≥ 0.01 mg/L previously, but currently taking safe water (As < 0.01 mg/L). **Conclusion:** Clearance of arsenic skin lesion occurred in many cases following intake of safe water in arsenic exposed population in Nadia, West Bengal. However, safe water intake could not prevent occurrence of new skin lesion in a few cases.

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INTRODUCTION

People of states like West Bengal, Jharkhand, Bihar, Uttar Pradesh Assam and Manipur in eastern India and Chhattisgarh state in central India have been chronically exposed to ground water arsenic contamination above permissible limit.¹ Though various states of eastern India have been affected with the arsenic problem, West Bengal has been affected most and the calamity has been reported as early as 1984.²⁻⁵ It is well known that chronic arsenicosis is associated with skin manifestations like Pigmentation and Keratosis as a result of drinking of arsenic contaminated ground water for a prolonged period^{2-4,6-15}. Since the detection of the problem, supply of arsenic free safe water had been initiated by PHED, Govt. of West Bengal in a programmatic mode by installing safe deep-tube wells, surface water supply through spot sources and pipe line system in all the affected districts of the state.

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Information on natural history of arsenic related skin lesion following supply of safe water in arsenic exposed population in India is scanty. The current study was carried out to assess the natural history of arsenic related skin lesion following intervention to reduce arsenic exposure after a gap of ten years of initial study on a cohort of large arsenic exposed population with evidence of arsenicosis studied previously in the district of Nadia, West Bengal during 2006-07. Current study ascertained any change in frequency and severity of past skin lesions and appearance of any new lesion in those who had no such lesion in the past. Current arsenic exposure of the participants were also assessed following supply of safe water by the PHED in the study population

MATERIALS AND METHODS

This Cohort Follow up study was carried out during 2017-2020 on a population of 10469 people from 17 arsenic affected blocks of Nadia district, West Bengal. Earlier in 2006-07, during the first wave of data collection, 1,616 patients who had clinical evidence of arsenical skin lesion and were exposed to arsenic through drinking water were identified from 2297

households in those blocks¹⁶. In the current study, information could be captured from 2233 households, accounting for 8206 persons studied earlier. The remaining population either migrated or were absent during the current study. Further, a total of 1044 persons were found dead out of the total surveyed population of 8206. Out of the total of 7162 participants who could be clinically examined for skin lesion during the current study arsenic exposure data through water was not available for the past and present study from 32 participants. Hence, correlation of arsenic exposure data was done for 7130 participants for the past and present study. (Fig-1) Present study envisaged to estimate the burden of arsenic related skin lesion in the cohort who were recruited out of the people studied earlier along with determination of current arsenic exposure in their drinking water.

Field Study

The field study was designed to minimize subjectivity in examination of skin lesions diagnostic of arsenicosis. A pre designed, pre tested and semi structured case record form was used to capture the information. 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. Characteristics of skin lesions of keratosis and pigmentation were as follows: Keratosis was characterized by diffuse bilateral thickening of palms and/or soles with or without nodules of various shapes and sizes. Pigmentation was identified if there were areas of mottled dark brown pigmentation bilaterally distributed on the trunk. Sometimes spots of depigmentation also occurred, but these characteristics were not regarded as essential for the diagnosis¹⁷. A scoring system has been adopted to classify the degrees of severity of skin manifestations¹⁸. Institutional review board of DNGM Research Foundation, Kolkata, has approved the protocol of the study. Informed consent was obtained prior to participation for the interview.

Field workers were provided with information regarding the village and the families from the record of the earlier study with previous exposure data and case records. Each member of the household was interviewed and clinically examined. Each participant was questioned about his or her current sources of drinking and cooking water along with duration of water use from those sources. After taking history from the participant, general medical examination was carried out, including a careful inspection for arsenical skin lesions.

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 analysed for measurement of arsenic level by Atomic absorption spectrophotometer with flow-injection hydride generation system at Reference laboratory of PHED, Govt. of West Bengal. Water samples were collected from all available current private and public tube wells used for drinking and cooking purposes by recruited household members in the past study. Peak arsenic level recorded from drinking water from all collected sources for each household member was recorded for assessment of peak past arsenic exposure. Data available

from last wave were used to analyse the change in arsenic exposure of an individual over last decade.

RESULTS

A total of 8206 participants was surveyed during the three years of study out of past population of 10469 studied during 2006-07 in all the 17 blocks of Nadia district. The remaining population either migrated or absent during the current study. A total of 1044 deaths occurred out of the total surveyed population of 8206. Thus a total of 7162 participants could be clinically examined for skin lesion during the current study. However, arsenic exposure data through water was not available for the past and present study from 32 participants. Hence, arsenic exposure data was analysed from 7130 participants for the past and present study. (Fig-1) A total of 843 arsenicosis cases having skin lesion in the past could be reviewed during current examination. The lesions were found to persist in 249 (29.5%) cases while cleared in 594 (70.5%) subjects. A total of 15 (0.21%) new cases of arsenical skin lesion were detected currently among the study population who had no such lesion during last phase.

Demographic characteristics and arsenic exposure data of 7162 participants studied in the past (843 with and 6319 without skin lesion) are given in Table 1. Past exposure of arsenic was significantly ($p < 0.0001$) higher in arsenicosis cases with skin lesion than those without skin lesion. Further males and aged persons (> 60 years) were significantly more in subjects with skin lesion than without. It needs to be mentioned that arsenical pigmentation was found to be present in most of cases who had skin lesion while only 28% of cases had keratosis. It could be seen that arsenical pigmentation was found to be present in 823 (11.49%) cases out of the total cases studied in the past. Further, keratosis was found to be present in 236 (3.3%) cases of the past subjects studied. Both pigmentation and keratosis were found to be mild in nature for majority of cases.

Arsenical skin lesion was found to be present in 264 cases during the current phase among population of 7162 subjects studied previously. Thus prevalence of skin lesion during current study was 3.68%. Analysis of clinical data of patients who has been found to have skin lesion during the present study has been given in Table 2. It could be seen that 76.2% of these patients with skin lesion are male, 52.6% being in the age group of 60 years and above. A total of 231 cases with pigmentation was found to be present in those who had skin lesion during the current study. Out of these 220 cases of pigmentation were found to be present during past study while 11 new cases of pigmentation were found during current study. Thus, pigmentation was found to be present during past and present study in 220 (3%) cases out of 7162 participants surveyed. It is shown in Table 1 that pigmentation was present in 823 (11.49%) cases during the past study. Thus clearance of skin lesion of pigmentation was found to occur in (823-220) 603 (73%) patients out of the population studied.

Further, a total of 61 cases of keratosis was found to be present during the current study in the surveyed population. Out of these, 57 cases of keratosis was found to be present during past study while 4 new cases of keratosis were found during current

study. (Table 2) Thus, 57(0.8%) cases of keratosis were found to be present during past and present study out of 7162 participants surveyed. It is shown in Table 1 that keratosis was present in 236 (3.3%) cases during past study. Thus clearance of skin lesion of keratosis was found to occur in (236-57) 179 (75.8%) patients out of the population studied following a gap of 10 years. Correlation of arsenic exposure through drinking water in arsenicosis cases during the past and current study Data on arsenic exposure through water was available for 7130 subjects which included 837 past patients and 264 current patients. Frequencies of different level of arsenic exposure in the studied population in the past and present are given in Table -3. It could be seen that frequency of arsenic exposure of <0.01mg/L was found to be 28.3% in the past and 57.2% in the present examination. Further, arsenic exposure of the study population was ≥ 0.05 mg/L in 42.2 % in the past while in 17.8% in the present examination.

Correlation of different level of arsenic exposure in the studied population in the past and present is shown in Table 4. It could be seen that 1492 subjects had arsenic exposure of <0.01mg/L while 637 subjects were exposed to arsenic > 0.05 mg/L in the past. Overall 38.4% of participants were exposed to same arsenic level throughout the decade of which 21% individuals were having safe water with Arsenic level <0.01mg/L all through. Further 36.3% individuals were exposed to ≥ 0.01 mg/L arsenic previously, but currently were having safe water with Arsenic level <0.01mg/L (Table-4).

Frequency of different level of arsenic exposure in the past and natural history of skin lesion is given in Table-5. It is to be noted that 199 cases of arsenicosis with skin lesion had peak arsenic exposure of <0.01mg/L in the past. Further 4 cases who had development of new skin lesion had peak arsenic exposure of <0.01mg/L in the past.

Observation of so many cases with arsenical skin lesion with peak arsenic exposure <0.01mg/L in the past appears to be due the fact that these patients had exposure of arsenic before collection of water samples from their households earlier. As lifetime water history was not obtained from the studied population in the past this observation appears to be due to missing of arsenic exposure data from all sources in the studied population in the past. However it is apparent that higher the arsenic exposure higher the incidence of skin lesion in the past.

It could be seen in table 6 that skin lesion cleared in 69.4% of cases who had such lesion in the past following drinking of water with As level <0.01mg/L. However new skin lesion occurred in 11 (0.3%) out of 4079 subjects currently drinking safe (As level <0.01mg/L) water.

Table 1 Characteristics of 7162 participants studied in the past (2006-07) in regard to their clinical features and Arsenic exposure through drinking water

Characteristics	Cases (With pigmentation and/or keratosis) N=843 (11.77%)	Controls (without pigmentation or keratosis) N=6319	P value
As concentration in drinking water (mg/L)			
Minimum	BDL	BDL	
Maximum	0.89	1.362	

Mean	0.109	0.071	<0.0001		
Median	0.046	0.035			
SD	0.160	0.111			
Age	N	%	N	%	
<12	NIL	NIL	NIL	NIL	
12-<18	0	0	20	0.3%	
18-<30	5	0.6%	664	10.5%	
30-<60	389	46.1%	4618	73.1%	
>60	449	53.3%	1017	16.1%	<0.0001
Sex					
Male	449	53.3%	2162	34.2%	<0.0001
Female	394	46.7%	4157	65.8%	
Clinical Features			N		
Pigmentation	823(11.49%)				
Mild	707	83.9%	NIL	NIL	
Moderate	107	12.7%	NIL	NIL	
Severe	9	1.1%	NIL	NIL	
Keratosis 236 (3.3%)					
Mild	196	23.3%	NIL	NIL	
Moderate	39	4.6%	NIL	NIL	
Severe	1	0.1%	NIL	NIL	

Table 2 Characteristics of 7162 participants studied in regard to their current clinical features

Characteristics	Arsenicosis cases (pigmentation and/or keratosis present) N=264		Non cases (No pigmentation or keratosis) N=6898	
	N	%	N	%
Age				
<12	0	0.00	0	0.81
12-<18	0	0.00	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 (220-Past, 11 new)				
Mild	193 (184, Past, 9 new)	73.11	0	0.00
Moderate	32 (30, Past, 2 new)	12.12	0	0.00
Severe	6	2.27	0	0.00
Keratosis 61 (57-Past, 4 new)				
Mild	43 (39, Past, 4 new)	16.29	0	0.00
Moderate	16	6.06	0	0.00
Severe	2	0.76	0	0.00

Table 3 Frequency of different level of arsenic exposure in 7130 studied population in the past and present. [Arsenic exposure data through water was not available for the past and present study from 32 participants]

Peak As level	Frequency (past)	Frequency (Current)
<0.01mg/L	2020 (28.3%)	4079 (57.2%)
0.01-0.05 mg/L	2109 (29.6%)	1780 (25.0%)
0.05-0.3mg/L	2649 (37.2%)	1244 (17.4%)
0.3-0.6mg/L	262 (3.7%)	23 (0.3%)
≥ 0.6 mg/L	90 (1.3%)	4 (0.1%)
Grand Total	7130	7130

Table 4 Correlation between frequency of different level of arsenic exposure in the studied population in the past and present

Past Arsenic level (peak)	Current water data (peak Arsenic level)					Grand Total
	<0.01mg /L	0.01-0.05 mg/L	0.05-0.3mg/L	0.3-0.6mg/L	>0.6mg/L	
<0.01mg/L	1492	346	182			2020
0.01-0.05 mg/L	1232	610	265		2	2109
0.05-0.3mg/L	1278	737	624	10		2649
0.3-0.6mg/L	64	52	132	12	2	262
≥ 0.6 mg/L	13	35	41	1		90
Grand Total	4079	1780	1244	23	4	7130

Table 5 Frequency of different level of arsenic exposure in the past and natural history of skin lesion

Past peak As level	Total	Total skin lesion in the past	Skin lesion both past & present	Skin lesion cleared	New skin lesion only	Never any skin lesion	incidence of skin lesion over 10 years
<0.01mg/L	2020	199 (9.9%)	54	145 (72.9%)	4	1817 (89.9%)	0.22%
0.01 to <0.05mg/L	2109	235(11.1%)	56	179 (76.5%)	6	1868 (88.5%)	0.37%
0.05 to <0.3mg/L	2649	317 (11.9%)	104	213 (67.6%)	3	2329 (87.9%)	0.21%
0.3 to <0.6 mg/L	262	60 (22.9%)	21	39(65.0%)	1	201 (76.7%)	0.50%
>0.6mg/L	90	26 (28.9%)	14	12 (46.2%)	1	63(70%)	1.56%
Grand Total	7130	837 (11.7%)	249	588 (70.5%)	15	6278 (88.1%)	0.29%

Table 6 Frequency of different levels of arsenic exposure in the present and natural history of skin lesion

Current peak As level	Total exposed	Total skin lesion in the past	Skin lesion both past & present	Skin lesion cleared	New skin lesion	Never any skin lesion	incidence of skin lesion over 10 years
<0.01mg/L	4079	470 (11.5%)	144	326 (69.4%)	11	3598 (88.2%)	0.31%
0.01 to <0.05mg/L	1780	249 (13.9%)	64	184 (74.2%)	2	1529 (85.9%)	0.19%
0.05 to <0.3mg/L	1244	112 (9%)	36	74 (67.3%)	2	1130 (90.8%)	0.35%
0.3 to <0.6 mg/L	23	5 (21.7%)	1	4 (80%)	0	18 (78.3%)	0.000%
>0.6mg/L	4	1 (25%)	1	0	0	3(75%)	0.000%
Grand Total	7130	837	249	588 (70.5%)	15	6278 (88.1%)	0.29%

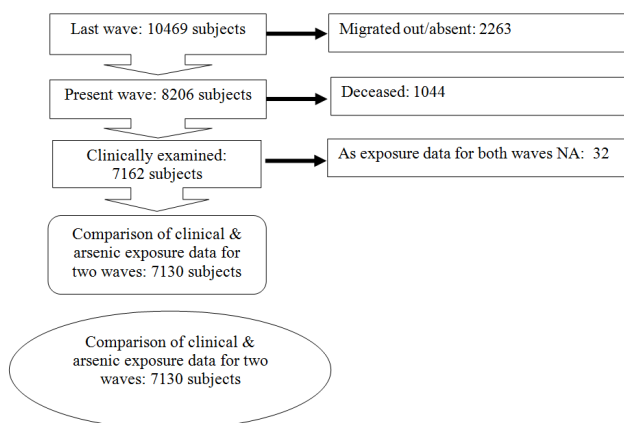


Figure 1 Subject recruitment during cohort follow-up after a decade

DISCUSSION

Not many reports are available on the natural history of arsenic related skin lesion following intake of safe water in arsenic exposed population. Arsenic safe drinking water was supplied to the past study population by PHED, Govt. of West Bengal after the initial study done during 2006-07. Out of the total surveyed population of 8206 studied earlier a total of 7162 participants could be clinically examined for skin lesion during the current study. A total of 843 arsenicosis cases having skin lesion in the past could be reviewed during current examination. The lesions were found to persist in 249 (29.5%) cases while cleared in 594(70.5%) subjects. A total of 15 (0.21%) new cases of arsenical skin lesion were detected currently among the study population who had no such lesion during last phase. Further clearance of pigmentation and keratosis was observed in 73% and 75.8 % cases respectively. Analysis of arsenic exposure data of the population studied in the past and present showed that 21% individuals were having safe water with arsenic level <0.01mg/L all through. Further 36.3% individuals were exposed to ≥0.01mg/L arsenic previously, but were currently having safe water with arsenic

level <0.01mg/L.(Table 4) Thus drinking of safe water has played important role in clearance of arsenic skin lesion in many cases.

Appearance of 15 (0.21%) new cases of arsenical skin lesion in the participants who did not have skin lesion in the past are important finding. It may be due to delayed appearance of skin lesion from past arsenic exposure in these subjects. Recorded arsenic data of those who had new skin lesion showed that arsenic exposure in 4 cases in the past and in 11cases in the present was safe (<0.01mg/L) (Table 5 and 6).Further, 199 cases of arsenicosis with skin lesion had peak arsenic exposure of <0.01mg/L in the past. As lifetime water data was not collected during past study, it was likely that these subjects might have higher arsenic exposure earlier than water data collected during past study. Current safe water intake could not prevent occurrence of such new lesion.

Another follow up study was done during 2010-11 on a population of 2620 out of the past surveyed population of 5562 of previous epidemiological study done from a cohort of arsenic exposed population of 7683 surveyed during 1995 in South 24 Parganas, West Bengal assessing impact on arsenical skin lesion following consumption of arsenic safe water¹⁹.Skin pigmentation was found to clear in 128 (56.64%) out of 226 cases and skin keratosis in 60 (65.9%) out of 91 cases diagnosed in earlier study.Further11 (0.44%) cases of new skin lesion was found to appear out of the studied population having no lesion in the past. The improvement of skin lesion of pigmentation and keratosis was found to be lower compared to the improvement of those lesions in current study carried out in Nadia district .Further, lower number (0.21%) of new lesion appeared in study population of Nadia district compared to new lesion appeared (0.44%)in study population of South 24 Parganas. Less improvement of skin lesion and higher incidence of new lesion in the study of South 24 Parganas might be due to higher past arsenic exposure (BDL to 3.4 mg/L) of the study population of South 24 Parganas²⁰than the past peak arsenic exposure (BDL-1.362mg/L) (Table-1)observed in the study population of Nadia district

Oshikawa *et al.*²¹ investigated the changes in severity of skin lesions over a period of 10 years among an affected cohort in an area having arsenic-contaminated shallow wells due to tin mining activities in southern Thailand where interventions to reduce arsenic-contaminated water had been implemented. Over the 10-year period, both regression and progression of lesions occurred, although the majority of the subjects followed up remained the same. Drinking predominantly arsenic-free water increased the probability of regression in subjects with mild-stage lesions, but not in those with more advanced-stage lesions. In a study carried out in Inner Mongolia, China, Sun *et al.*²² reported that skin lesions improved in affected individuals to some extent after they had been drinking water containing low levels of arsenic for 1 year. However, a 5-year follow-up study showed no further significant improvement in skin lesions.

However, last cited studies were carried out on small number of participants. Further individual arsenic exposure data in the past was not considered for assessing the outcome results of

follow up study. Thus, a major strength of this paper is that it is based on the largest population-based study with individual arsenic exposure data, followed up after a prolonged period of drinking arsenic safe water, providing critical information in regard to exposure-response relationship on effect of drinking arsenic safe water. However, limitation of the paper is that lifetime water history was not taken during the initial study of the arsenic exposed population in Nadia district during 2005-06. Hence, significant number (199) of cases of skin lesion was seen with past arsenic exposure of <0.01mg/L during the past study.

CONCLUSION

Information on natural history of arsenic related skin lesion following supply of safe water in arsenic exposed population in India is scanty. Report of current study carried out during 2017-2020, after a gap of ten years of initial study, contributed outcome of supplying safe water to a large (7162) arsenic affected population of Nadia district of West Bengal. Out of the population studied, arsenical skin lesions cleared in significant (70.5%) number of cases while persisted in some (29.5%) who had lesion in the past. Further, new appearance of skin lesion occurred in a few (0.21%) who had no lesion in the past. Drinking of arsenic safe water has played important role in clearance of arsenic skin lesion in many cases.

Acknowledgement

The project was 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, RanjitSardar, AyanKarar, KaushikiPada 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.

Conflict of Interest: The authors declare no conflict of interest.

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How to cite this article:

DN Guha Mazumder *et al* (2020) 'Natural History of Chronic Arsenic Toxicity Following Intervention to Reduce Arsenic Exposure, A study from West Bengal, India', *International Journal of Current Advanced Research*, 09(08), pp. 22980-22985. DOI: <http://dx.doi.org/10.24327/ijcar.2020.22985.4543>
