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Bladder Carcinoma in Arsenic Affected Districts of West Bengal

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Abstract:

Objectives: *To evaluate distribution of bladder carcinoma patients in various districts of West Bengal classified accordingly ground water arsenic level.*

Methods: *It was a retrospective observational survey. All operated patients with histo-pathologically proven transitional cell carcinoma of urinary bladder, who presented in our outpatient department (OPD)from August 2013 to August 2015, were included in study. As our institute is the main tertiary referral center in eastern India, we calculated bladder cancer incidence-person-year according to our records, using West Bengal census-2011 data for population at risk in various districts.*

Results: *From August 2013 to August 2015, 279 patients were diagnosed as transitional cell carcinoma of urinary bladder. Out of 279 patients, 242 were from severely affected districts, 28 were from mildly affected districts, and rest of 9 patients from arsenic safe districts. Three categories were similar in terms of duration of symptoms, smoking habit. Bladder carcinoma incidence-persons-year in severely affected districts was more than the other two categories. (Severely affected - 0.211, mildly affected - 0.106, and in arsenic safe - 0.021). Bladder carcinoma incidence in male was more than female in all the three categories of the districts. Mean age of Bladder carcinoma patients in severely affected districts was less than the other two categories (Severely affected 55.18 yrs, mildly affected 59.28 yrs, and in arsenic safe 60.55 yrs). Patients from severely affected category was presented with higher stage and grade than the other two categories.*

Conclusions: *Arsenic might be a major risk factor causing bladder carcinoma in this region. Bladder cancer in the severely affected districts comparatively does occur at an earlier age, and with higher stage and grade.*

Keywords: *arsenic, bladder, carcinoma, West Bengal*

1. INTRODUCTION

Urinary Bladder cancer has a strong association with environmental exposures. This association is particularly strong for arsenic as evident from arsenic induced malignant transformation of human bladder urothelial cells, and correlates to the same endemic areas where populations were identified with arsenic-induced skin cancer[1,2]. Excess inorganic arsenic in drinking water from artesian wells is a major health hazard in certain parts of the world and is associated with an increased risk of urothelialtumors in addition to other diseases[3,4,5]. Peoples residing in Bengal Delta Plain in India, no comprehensive study has yet been done in this respect considering arsenic as the major risk factor. According to a reported work done by the School of Environmental Studies (SOES), Jadavpur university on ground-water contamination of West Bengal in nine districts (Malda, Murshidabad, Nadia, North-24 Parganas, South-24 Parganas, Barddhaman, Haora, Hugli and Kolkata), are categorized as severely affected (arsenic concentrations > 50 µg/L) , five districts (Koch Bihar , Jalpaiguri , Darjiling , North Dinajpur and South Dinajpur) as mildly affected (arsenic concentrations 11-50 µg/L) and the rest five districts (Bankura, Birbhum, Purulia, Medinipur East And Medinipur West), as unaffected or arsenic safe (arsenic concentration < 10 µg/L)[6].

We tried to find out if there was any association exists between geographical distribution of bladder carcinoma cases with the reported ground water contamination of Arsenic level in respective districts

in West Bengal. Therefore, this study included analysis of arsenic as a risk factor so that avoidance of such factor could decrease the incidence of the disease significantly as well as to designing effective treatment plan for the bladder carcinoma patients.

2. METHODS

It was a retrospective observational survey. In this study we included all the histopathologically proven bladder carcinoma patients. These patients were either operated in our institute or operated elsewhere and then presented to our outpatient department (OPD). Case Report form (CRF) was made for every patient including demographical data, smoking habits, clinical, radiographical and histopathological data. Person residing for a minimum period of 5 year in particular district was considered as resident of that district. We used West Bengal census 2011 data [Table-1] for considering population at risk to calculating incidence-person-year for 2 years from August 2013 to August 2015. We calculated incidence-person-years for every district. We categorised districts according to reported work done by the School of Enviromental Studies, Jadavpur university (SOES) on ground-water contamination of West Bengal[6] in three categories – (1) Severely affected, (2) Mildly effected, (3) Safe / Unaffected.

Table1. *Urinary Bladder Carcinoma Incidence in Various Districts Using West Bengal Census -2011 Datas*

District	Population	Male	Female	Total cases	Male cases	Female cases	Incidence	Incidence (male)	Incidence (female)
Malda	3997970	2061593	1936377	18	14	4	0.225	0.339	0.103
Murshidabad	7102430	3629595	3472835	31	25	6	0.218	0.344	0.086
Nadia	5168488	2655056	2513432	21	17	4	0.203	0.32	0.079
North 24 parganas	10082852	5172138	4910714	44	36	8	0.218	0.348	0.081
South 24 parganas	8153176	4182758	3970418	34	27	7	0.208	0.322	0.088
Barddhaman	7723663	3975356	3748307	31	26	5	0.2	0.327	0.067
Haora	4841638	2502453	2339185	21	17	4	0.216	0.339	0.085
Hugli	5520389	2819100	2701289	23	18	5	0.208	0.319	0.092
Kolkata	4486679	2362662	2124017	19	16	3	0.211	0.338	0.071
Koch bihar	2822780	1453590	1369190	5	4	1	0.088	0.137	0.036
Jalpaiguri	3869675	1980068	1889607	9	7	2	0.116	0.177	0.053
Darjiling	1842034	934796	907238	4	3	1	0.108	0.16	0.055
South dinajpur	1670931	855104	815827	3	3	NIL	0.089	0.175	NIL
North dinajpur	3000849	1550219	1450630	7	6	1	0.116	0.193	0.034
Bankura	3596292	1840504	1755788	2	2	NIL	0.027	0.054	NIL
Birbhum	3502387	1791017	1711370	2	2	NIL	0.028	0.055	NIL
Puruliya	2927965	1497656	1430309	1	1	NIL	0.017	0.033	NIL
East medinipur	5094238	2631094	2463144	2	1	1	0.019	0.019	0.02
West medinipur	5943300	3032630	2910670	2	1	1	0.016	0.016	0.017

We calculated incidence-person-year in each category. We compared demographical data, smoking habits, staging and grading of tumors between each category. For statistical analysis data were tabulated into a Microsoft excel spreadsheet and then analysed by SPSS 20.0.1 and Graph Pad Prism version 5. Data have been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. The median and the inter quartile range have been stated for numerical variables that are not normally distributed. Student's independent sample's t-test was applied to compare normally distributed numerical variables between

groups; unpaired proportions were compared by Chi-square test or Fisher's exact test, as appropriate. Confidence interval was 95%.

3. RESULTS

From August 2013 to August 2015, 279 patients were diagnosed as transitional cell carcinoma of urinary bladder. Out of 279 patients, 242 were from severely affected districts, 28 were from mildly affected districts, and rest of 9 patients from arsenic safe districts.

There was no statistically significant difference (P-value-0.958) between three categories for the gender distribution of cases. We did smoking quantification by pack-year and found that difference between three categories for smoking habits was not statistically significant (P-value-0.965)[Table-2]

There was statistically significant difference between mean age (P-value 0.0009), showed younger age of bladder carcinoma patients in severely affected districts. Mean (±SD) age of the patients was 55.1860 (±6.7081) years [Range: (36.0-73.0)] for severely affected category, 59.28 (±6.6380) years [Range: 43.0-71] for mildly affected districts, and 60.55 (±3.7454) years [Range: (55.0-67.0)]. [Table-2]

Bladder carcinoma incidence in male was more than female in all the three categories of the districts (severely affected category male-0.667, female-0.165), (mild affected category male-0.339, female-0.077), (safe category male-0.064, female-0.019). [Table-1]

Incidence-persons-year was more in severely affected districts (0.211) than the mildly affected (0.106) and safe districts (0.021) categories. Incidence-persons-year was least in arsenic safe category districts. [Table-3]

There was statistically significant difference between diagnosed stage and grade at presentation between three categories (P-value for staging 0.043, and for grade P-value <0.0001). Patients from the severely affected districts category were diagnosed with higher stage and grade of tumour than the other two categories. [Table-2]

Table2. *Age, Gender, Smoking Habit, and Histopathological Parameters of Different Categories of Districts*

		Safe	**Mild**	**Severe**	**TOTAL**	**p-value**
	Number (%)	**9(3.2)**	**28(10.0)**	**242(86.7)**	**279(100.0)**	
Sex	**Female**	2 3.8	5 9.4	46 86.8	53 100.0	0.958
	Male	7 3.1	23 10.2	196 86.7	226 100.0	
Smokers	**No**	3 3.4	9 10.3	75 86.2	87 100.0	0.982
	Yes	6 3.1	19 9.9	167 87.0	192 100.0	
Smoking pack years	**Mean (range)**	7.6 (5.0-12.0)	7.7(5.0-12.0)	7.7(5.0-12.0)		0.965
	SD	2.7019	1.7589	1.358		
	Median	7.0	8.0	8.0		
Age (Years)	**Mean (range)**	60.55(55.0-67.0)	59.28(43.0-71)	55.1860(36.0-73.0)		0.0009
	SD	3.7454	6.6380	6.7081		
	Median	60.0	59.0	55.0		
Stage	**pTa**	6 6.5	15 16.3	71 77.2	92 100.0	0.043
	pT1	3 3.1	10 10.4	83 86.5	96 100.0	
	pT2	0 0.0	2 3.8	50 96.2	52 100.0	
	pT3	0 0.0	1 3.4	28 96.6	29 100.0	
	pT4	0 0.0	0 0.0	10 100.0	10 100.0	
Grade	**High**	2 1.1	9 4.9	172 94.0	183 100.0	<0.0001
	Low	7 7.3	19 19.8	70 72.9	96 100.0	

Table3. *Overall Incidence of Bladder Carcinoma in Different Categories of Districts According to Ground Water Arsenic Contamination*

Districts category	Incidence-person- year
Severe	0.211
Mild	0.106
Safe	0.021

4. DISCUSSION

Although causal relationships are mostly explained from case-control and cohort studies for known human carcinogens, with little, if any, evidence from ecological studies. But for arsenic in drinking-water, ecological studies provide important information on causal inference, because of large exposure contrasts and limited population migration. Because of widespread exposure to local or regional water sources, ecological measures provide a strong indication of individual exposure and the ecological estimates of relative risk are often so high that potential confounding with known causal factors cannot explain the results[7].

Contamination of groundwater by arsenic was first detected in the West Bengal in one village in the 24-Parganas district; in 1983 (Garai *et al*., 1984)[8].Since then extensive research in West Bengal has revealed that this region has one of the most serious problems with groundwater contamination by arsenic in wells used for drinking-water[9, 10]. Arsenic association with bladder carcinoma was showed in many studies done outside india[11-15], but no study yet been done in this region.

Chiang *et al*. (1993) showed that the age-adjusted incidence of bladder cancer in the Blackfoot disease-endemic area of Taiwan was higher than that in a neighbouring area of Taiwan and in the country as a whole[16]. Similarly an ecologic study done by Guo et al (1997) using the proportions of wells with various specified arsenic levels in each township as indicators of exposure and evaluated the effects of urbanization and smoking by an urbanization index and the number of cigarettes sold per capita. In both genders, they observed associations of high arsenic levels in drinking water with transitional cell carcinomas of the bladder, kidney, and ureter and all urethral cancers combined. After adjusting for urbanization and age, the proportion of wells with arsenic levels above 0.64 ppm had positive associations with the incidence of transitional cell carcinomas of the bladder, kidney, and ureter and all urethral cancers combined in both genders[17]

Likewise in our study, there was wide variation in bladder carcinoma incidence with level of arsenic contamination. We found more incidence of bladder carcinoma in severely affected districts category than other two districts categories.

According to study done by Steinmaus et al. (2003) of arsenic ingestion and bladder cancer using individual data on water sources, water consumption patterns, smoking, and other factors they found that smokers who drink water containing arsenic at concentrations near 200μg/day may be at increased risk of bladder cancer compared with smokers at lower arsenic exposures[18].

Likewise in our study we found no statistically significant difference for smoking habits between three categories but there was high incidence of bladder carcinoma in severely affected districts category than the other two categories. It showed that in these districts arsenic might be the major risk factor for causing bladder carcinoma. As majority of the population in this region is smoker, there might be some additive effect of arsenic with other risk factors like smoking, which may be the cause of such a high incidence of bladder carcinoma in this region.

In this study we found that bladder carcinoma incidence was highest in severely affected districts than the other two categories, also in these districts bladder carcinoma presented in comparatively in younger age group and with higher stage and grade. So according to our study we found that bladder carcinoma in severely affected districts were more aggressive than the other two categories.

Further studies needed to evaluate the role of arsenic as a risk factor for urinary bladder carcinoma, role of individual metabolic system to handling arsenic because although all the person exposed to arsenic in a particular district, but not everyone developed urinary bladder carcinoma. Further studies also needed to evaluate cellular and molecular changes that are responsible for inducing carcinoma because of arsenic.

Limitations of this study were that it was an ecological study, so definitive causal relationship could not be measured. Although our institute drained most of the patients in this region but further studies will be needed at larger scale.

5. CONCLUSIONS

Arsenic contamination seems major risk factor for causing high incidence of bladder carcinoma in this region. From our study we conclude that arsenic induced bladder carcinoma are comparatively more aggressive as presenting in early age with higher grade and stage. Further studies needed to established causal relationship of arsenic contamination with bladder carcinoma, cellular and molecular changes in arsenic induced bladder carcinoma.

REFERENCES

[1] Biagini, R.E. [Chronic hydroarsenicism and mortality from malignant cancers.] Semana med., (1972), 141, 812–816 (in Spanish).

[2] Chen CJ, Chuang YC, Lin TM, Wu HY. Malignant neoplasms among residents of a blackfoot disease-endemic area in Taiwan: high-arsenic artesian well water and cancers. Cancer Res. 1985 Nov;45(11 Pt 2):5895–9.

[3] 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 Apr 1;147(7):660–9.

[4] Chen Y, Ahsan H. Cancer burden from arsenic in drinking water in Bangladesh. Am J Public Health. 2004 May;94(5):741–4.

[5] Chang C-H, Liu C-S, Liu H-J, Huang C-P, Huang C-Y, Hsu H-T, et al. Association between levels of urinary heavy metals and increased risk of urothelial carcinoma. Int J Urol. 2016 Mar;23(3):233-9.

[6] Chakraborti D, Das B, Rahman MM et al, Status of groundwater arsenic contamination in the state of West Bengal, India, http://www.soesju.org/arsenic/wb.htm

[7] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Some drinking-water disinfectants and contaminants, including arsenic. IARC MonogrEvalCarcinog Risks Hum World Health Organ Int Agency Res Cancer. 2004; 84:1–477.

[8] Garai R, Chakraborty AK, Dey SB &Saha KC. Chronic arsenic poisoning from tubewell water. *J. Indian med. Assoc*. (1984), 82, 34–35.

[9] Steering Committee Arsenic Investigation Project. National Drinking Water Mission Submission Project on Arsenic Pollution in Groundwater in West Bengal (Final Report), Kalkota,Public Health and Environment Department, Government of West Bengal. (1991).

[10] Chowdhury UK, Biswas BK, Chowdhury TR, Samanta G, Mandal BK, Basu GC, et al. Groundwater arsenic contamination in Bangladesh and West Bengal, India. Environ Health Perspect. 2000 May; 108(5):393–7.

[11] Sommers SC, Mcmanus RG. Multiple arsenical cancers of skin and internal organs.Cancer. 1953 Mar; 6(2):347–59.

[12] Bergoglio RM. [cancer mortality in zones of arsenical waters of the province of cordoba, argentine republic. contribution to the regional pathology of cancer]. Prensa Médica Argent. 1964 Oct 23; 51:994–8.

[13] Chen CJ, Chuang YC, Lin TM, Wu HY. Malignant neoplasms among residents of a blackfoot disease-endemic area in Taiwan: high-arsenic artesian well water and cancers. Cancer Res. 1985 Nov; 45(11 Pt 2):5895–9.

[14] Chen Y, Ahsan H. Cancer burden from arsenic in drinking water in Bangladesh. Am J Public Health. 2004 May; 94(5):741–4.

[15] Huang Y-K, Huang Y-L, Hsueh Y-M, Yang M-H, Wu M-M, Chen S-Y, et al. Arsenic exposure, urinary arsenic speciation, and the incidence of urothelial carcinoma: a twelve-year follow-up study. Cancer Causes Control CCC. 2008 Oct; 19(8):829–39.

[16] Chiang HS, Guo HR, Hong CL, Lin SM, Lee EF. The incidence of bladder cancer in the black foot disease endemic area in Taiwan. Br J Urol. 1993 Mar; 71(3):274–8.

[17] Guo HR, Chiang HS, Hu H, Lipsitz SR, Monson RR. Arsenic in drinking water and incidence of urinary cancers. EpidemiolCamb Mass. 1997 Sep; 8(5):545–50.

[18] Steinmaus C, Yuan Y, Bates MN, Smith AH. Case-control study of bladder cancer and drinking water arsenic in the western United States.Am J Epidemiol. 2003 Dec 15; 158(12):1193–201.