Arsenic in drinking water and childhood mortality: A 13-year follow-up findings

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ABSTRACT: Around 51 million children globally are exposed to elevated levels of arsenic in drinking water. However, the extent to which exposure is related to deaths from cancer at a young age is unknown. We assembled a cohort of 58,406 children aged 5–18 years from Health and Demographic Surveillance System of icddr in Bangladesh and followed during 2003–2015. The follow-up period was 543,415 person-years. We observed a significant association between childhood cancer mortality and arsenic exposure in the highest exposure tertile (HR = 2.70, 95% CI = 1.25–5.83). Arsenic exposure was associated with substantial increased risk of deaths at young age from cancers where child (5–11 years) had a higher risk of death compared to adolescent (12–18 years).

1 INTRODUCTION

Our previous study (Rahman *et al.*, 2007, 2009) followed up childhood residents of Matlab for 7 years and found a significant dose-response relationship between cumulative arsenic exposure and all cancers and cardiovascular combined deaths. Therefore, this study continued with same population of 58,406 Matlab residents who had been followed up for an average of 13 years in an effort to elucidate the dose-response relationship between ingested arsenic exposure and mortality risks. The large number of study participants, longer period of follow-up with more incident cases, and wide range of arsenic exposure levels provided us with a unique opportunity to further investigate the association. However, further aim included analyzing the modifying effects of surviving children and attained education that have been exposed to arsenic through the consumption of tubewell water.

2 METHODS/EXPERIMENTAL

We assembled a population-based cohort study on childhood mortality with excess drinking arsenic water registered in Matlab Health Demographic Surveillance System (HDSS) from January 01, 2003 to December 31, 2015. All childhood deaths (age 5–18 years at baseline) were ascertained. Cardiovascular causes of death were defined as ischemic heart diseases, I20–I25 (International Classification of Disease, 10th Revision (ICD-10)), and cerebrovascular

diseases (stroke), I60–I69 (ICD-10) and cancer C1–C99. Causes of deaths were identified from routine VA conducted by specially trained field staff of HDSS who were unaware of the arsenic exposure of the household members.

Follow-up time in person-years was calculated as the number of days between the baseline interview and date of death, out migration, or report of being alive on December 31, 2015 whichever came first. Participants with an accident-related cause of death such as road traffic accident, drowning or other accidental deaths or being alive were censored. The association in baseline and average exposures were calculated for each individual. The association between maternal age at birth, sex, education, asset score, and individual level arsenic exposures were analyzed in order to assess possible associations ($P \leq 0.10$), using chi square or Spearman's correlation coefficients was considered appropriate for the data. The mortality risks of arsenic exposures were estimated by Cox proportional hazards models, adjusting for potential confounders. Factors crudely associated with mortality at 5% level of significance, were included in the model.

3 RESULTS AND DISCUSSION

Of the 58,406 children, 313 died during follow-up. Baseline arsenic exposure was associated with increased all cancer cause of childhood mortality (Table 1). Children were exposed in current arsenic well water ($>138.71 \mu\text{g L}^{-1}$) had 2.32 times higher

Table 1. Association between baseline and average exposures and childhood mortalities, hazard ratios (HRs) and 95% confidence interval (95% CI).

Exposure variables	aHRs 95% CI, baseline exposure	aHR and 95% CI, average exposure
≤1.10	1.00	1.00
1.11–138.71	1.89 (0.83–4.28)	0.97 (0.40–2.40)
>138.71	2.70 (1.25–5.83)	2.32 (1.09–4.93)

chance of deaths than those who were exposed to $\leq 1.10 \mu\text{g L}^{-1}$ level of arsenic contamination after adjusting age, sex, education attainment and SES.

We noted a higher mortality rate among both cancer and non-cancer children deaths (8.92% and 7.03%, respectively) that had no educational attainment. An earlier study reported that ensuring arsenic free drinking water would increase educational attainment among the Bangladeshi males (Murray & Sharmin, 2015). And also education is a known factor that correlates with the populations' perception about arsenic poisoning. We also demonstrated that the highest mortality rate (9.09 per 100,000 person-years) in 2015 was prevalent among the cancer suffered children in those who exposed $>138.71 \mu\text{g L}^{-1}$.

Multiple studies conducted in the arsenic contaminated countries around the world found positive link with various types of cancers including urinary bladder, lung, kidney, hematolymphatic malignancy, skin cancers followed by mortality who are drinking arsenic contaminated water (Axelson *et al.*, 1978; Hopenhayn-Rich *et al.*, 1998; Karagas, 2010; Lewis *et al.*, 1999; Smith *et al.*, 1998; Wu *et al.*, 1989). We found only five childhoods cancer studies relevant to our study, however, these all were ecological and made no inference of all-cause mortality risks (Infante-Rivard *et al.*, 2001; Liaw *et al.*, 2008; Moore *et al.*, 2002; Rubin *et al.*, 2007). All of these studies reported a non-significant relative risk to various cancers including lymphoblastic leukemia from Canada cohort, all types of cancers combined from Chile and Nevada in United States (Infante-Rivard *et al.*, 2001; Liaw *et al.*, 2008; Moore *et al.*, 2002).

4 CONCLUSIONS

Despite some limitation, this study could have been done because of uniqueness of Matlab population having individual level As exposure data and the independent prospective demographic surveillance system covering 0.5 million population for about five decades. Further studies are needed with a longer follow up period to investigate if the risk is further enhanced and causal link becomes clearer though it might be hard enough to find similar population-elsewhere with exposure data for investigating the risk of death due to As exposure at young age.

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REFERENCES

- Axelson, O., Dahlgren, E., Jansson, C.D. & Rehnlund, S.O. 1978. Arsenic exposure and mortality: a case-referent study from a Swedish copper smelter. *Br. J. Ind. Med.* 35: 8–15.
- Hopenhayn-Rich, C., Biggs, M.L. & Smith, A.H. 1998. Lung and kidney cancer mortality associated with arsenic in drinking water in Cordoba, Argentina. *Int. J. Epidemiol.* 27: 561–569.
- Infante-Rivard, C., Olson, E., Jacques, L. & Ayotte, P. 2001. Drinking water contaminants and childhood leukemia. *Epidemiology* 12: 13–19.
- Karagas, M.R. 2010. Arsenic-related mortality in Bangladesh. *Lancet* 376: 213–214.
- Lewis, D.R., Southwick, J.W., Ouellet-Hellstrom, R., Rench, J. & Calderon, R.L. 1999. Drinking water arsenic in Utah: a cohort mortality study. *Environ. Health Perspect.* 107: 359–365.
- Liaw, J., Marshall, G., Yuan, Y., Ferreccio, C., Steinmaus, C. & Smith, A.H. 2008. Increased childhood liver cancer mortality and arsenic in drinking water in northern Chile. *Cancer Epidemiol. Prev. Biom.* 17: 1982–1987.
- Moore, L.E., Lu, M. & Smith, A.H. 2002. Childhood cancer incidence and arsenic exposure in drinking water in Nevada. *Arch. Environ. Health* 57(3): 201–206.
- Murray, M.P. & Sharmin, R. 2015. Groundwater arsenic and education attainment in Bangladesh. *J. Health Popul. Nutr.* 33: 20.
- Rahman, A., Vahter, M., Ekstrom, E.C., Rahman, M., Golam Mustafa, A.H., Wahed, M.A., Yunus, M. & Persson, L.Å. 2007. Association of arsenic exposure during pregnancy with fetal loss and infant death: a cohort study in Bangladesh. *Am. J. Epidemiol.* 165(12): 1389–1396.
- Rahman, A., Vahter, M., Smith, A.H., Nermell, B., Yunus, M., El Arifeen, S., Persson, L.Å. & Ekström, E.C. 2009. Arsenic exposure during pregnancy and size at birth: a prospective cohort study in Bangladesh. *Am. J. Epidemiol.* 169(3): 304–312.
- Rubin, C.S., Holmes, A.K., Belson, M.G., Jones, R.L., Flanners, W.D., Kieszak, S.M., Osterloh, J., Lubet, G.E., Blount, B.C., Barr, D.B., Steinberg, K.K., Satten, G.A., McGeehin, M.A. & Todd, R.L. 2007. Investigating childhood leukemia in Churchill County, Nevada. *Environ. Health Perspect.* 115(1): 151–157.
- Smith, A.H., Goycolea, M., Haque, R. & Biggs, M.L. 1998. Marked increase in bladder and lung cancer mortality in a region of Northern Chile due to arsenic in drinking water. *Am. J. Epidemiol.* 147: 660–669.
- Wu, M.-M., Kuo, T.-L., Hwang, Y.-H. & Chen, C.-J. 1989. Dose-response relation between arsenic concentration in well water and mortality from cancers and vascular diseases. *Am. J. Epidemiol.* 130: 1123–1132.