

Chronic low-level arsenic exposure reduces lung function in male population without skin lesions

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Abstract

Objectives The respiratory effects of chronic low-level arsenic exposure from groundwater have been investigated in West Bengal, India.

Methods The participants (834 non-smoking adult males) were subdivided in two groups: an arsenic-exposed group ($n = 446$, mean age 35.3 years) drinking arsenic-contaminated groundwater (11–50 $\mu\text{g/L}$) and a control group of 388 age-matched men drinking water containing $<10 \mu\text{g/L}$ of arsenic. Arsenic in water samples was measured by atomic absorption spectroscopy. The prevalence of respiratory symptoms was documented by structured, validated questionnaire. Pulmonary function test (PFT) was assessed by portable spirometer.

Results Compared with control, the arsenic-exposed subjects had higher prevalence of upper and lower respiratory symptoms, dyspnea, asthma, eye irritation and headache. Besides, 20.6 % of arsenic-exposed subjects had lung function deficits (predominantly restrictive and combined types) compared with 13.6 % of control ($p < 0.05$). A positive association was observed between arsenic concentration in drinking water and the prevalence of

respiratory symptoms, while a negative association existed between arsenic level and spirometric parameters.

Conclusions The findings suggest that even low-level arsenic exposure has deleterious respiratory effects.

Keywords Arsenic · Groundwater · Respiratory symptoms · Lung function

Introduction

Groundwater arsenic (As) contamination is a serious public health concern in West Bengal, India. The threshold limit of inorganic As in drinking water, as recommended by the World Health Organization (WHO) and the US Environmental Protection Agency, is 10 $\mu\text{g/L}$ (USEPA 2001; WHO 1993). In line with this, the Bureau of Indian Standards (BIS) has revised the desired level of As concentration in drinking water from an earlier 50–10 $\mu\text{g/L}$ (Smith et al. 2002). However, 50 $\mu\text{g/L}$ is still the legally enforceable standard of As in India if alternative sources are unavailable (BIS 2009). A large number of aquifers in the entire Ganga–Brahmaputra basin of the Indian sub-continent have As contamination above the WHO recommended limit and the BIS desired level (Chakraborti et al. 2011).

Arsenic is a Class I human carcinogen (IARC 1987) and associated with increased risk of cancers of the skin, lung, liver, kidney and the urinary bladder (NRC 1999). Although the effects of As on elevated lung cancer risk is now well recognized, there has been relatively little research on its role in non-malignant respiratory illnesses (Chiou et al. 1995; Smith et al. 1998). This is important because As exposure is associated with several non-malignant clinical conditions like skin lesions (Caussy

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2005), peripheral neuropathy, cardiovascular problems, conjunctivitis, diabetes, weakness, anemia, diarrhea, hepatomegaly, fetal loss and infant mortality (Bhattacharjee et al. 2013).

The airways can also be affected by chronic As exposure. Studies from India (Mazumder et al. 2000), Bangladesh (Parvez et al. 2008), and Chile (Smith et al. 2002) have reported a high prevalence of respiratory symptoms like chronic cough, chronic bronchitis and shortness of breath among As-exposed individuals. Pronounced decrement of pulmonary function is common among people with arsenical lesions (Mazumder et al. 2000; De et al. 2004; von Ehrenstein et al. 2005; Mazumder et al. 2005). Restrictive type of lung function deficiency was observed in more than half of the subjects, and both obstructive and restrictive lung diseases in 41 % of As-exposed subjects examined in India (De et al. 2004). Remarkable increase in the risk of chronic obstructive pulmonary disease has been observed among people with arsenical skin lesions in India (Mazumder et al. 2005) and Chile (Smith et al. 2006).

These studies showing detrimental effects of arsenic on lung function and respiratory symptom prevalence were largely limited to people exposed to high As concentrations (>500 µg/L) who had visible As-related skin lesions like hyperkeratosis (De et al. 2004; von Ehrenstein et al. 2005). In contrast, the effect of chronic low-level As exposure (up to 50 µg/L for 5 years or more) on the respiratory system is largely unknown despite the fact that several million people of eastern India and elsewhere are drinking water contaminated with arsenic in that dose range. Against this background, the present study was undertaken to examine the effect of chronic low-level As exposure through drinking water on the respiratory system. We compared the respiratory symptom prevalence and pulmonary function data of two groups of adult males from eastern India—an ‘exposed’ group of 446 non-smoking men, without As-related skin lesions who were drinking water with As content 11–50 µg/L and a ‘control’ group of 388 non-smoking men who were matched for age and socio-economic conditions but drinking water with As content <10 µg/L.

Methods

Study areas and participants

The participants were enrolled from the As-endemic Narayanpur village in Haringhata block of Nadia district and arsenic-free Saguna and Majher Char villages in Kalyani block of the Nadia district of West Bengal, India. They were all apparently healthy individuals without any

As-related skin problems like raindrop pigmentation, palmar and plantar hyperkeratosis and hypo- or hyperpigmentation. A total number of 446 adult men, drinking As-contaminated water of Narayanpur village (11 and 50 µg/L), for at least 10 years were recruited between April 2011 and March 2012. The control group comprised 388 people from Saguna and Majher Char villages of Kalyani (within the same geographical area) where As content in groundwater was below 10 µg/L. The participants resided in houses with brick walls and concrete/tin/terracotta roof. Motor vehicles were rare in these villages; bicycles, cycle rickshaws and bullock carts were the principal modes of transport. Electricity was present in all the villages.

Inclusion and exclusion criteria

The inclusion criteria were (i) apparently healthy, never smoker adult male subjects; (ii) residing in that area for the past 5 years or more; (iii) tube well as the only source of drinking water. The exclusion criteria were persons with skin lesions, under medication, had a previous history of malignancy.

Demographic and socio-economic data and water samples were collected at the time of field visits. Arsenic-induced skin lesion status was evaluated by a dermatologist. The study protocol was approved by the Institutional Ethics Committee of Chittaranjan National Cancer Institute, Kolkata. Informed consent was obtained from all the participants before enrollment for this study.

Collection of water samples and measurement of arsenic

The water samples were collected from hand pumps in sterile polyethylene bottles with 0.1 % HCl. The tube wells were common tube wells which were used by all the families in the vicinity of the well. The As analysis in collected water samples was done by the Atomic Absorption Spectrophotometer Duo (Agilent Technologies) equipped with vapor generation assembly (Agilent VGA 77) according to the procedure of Behari and Prakash (2006). A stock solution of 1.0 mg/mL (1,000 ppm) As was prepared from As standard for AAS (Sigma-Aldrich) in milli Q water with 0.1 % HCl and diluted to form four standards 5, 10, 20 and 40 ppb for calibration. The instrument was calibrated using 5 M HCl in the acid channel and 0.6 % NaBH₄ and 0.5 % NaOH in the reduction channel in the working range of 10–50 ppb As standard. For pre-reduction experiment, the sample was prepared in 5 M HCl and 20 % potassium iodide (KI) was added and allowed to react up to 45 min at room temperature. For direct analysis, the unknown samples were

diluted in varying concentrations and pre-reduced in the same way as the standards. A standard curve was drawn with the prepared range of standards and the concentrations of arsenic in the unknown samples were ascertained from the standard curve with the help of the software Spectra AA. The samples were analyzed in duplicate and three readings were taken for each sample.

For quality control, inter-laboratory tests of the same samples were done along with School of Environmental Studies (SOES), Jadavpur University, Kolkata. The inter-laboratory differences were within 5 %. The EPA water was also assessed to observe the recovery percentage of arsenic (99.22 %).

Measurement of carbon monoxide (CO) in exhaled breath

CO was measured in exhaled breath of all the 834 participants by portable CO monitor (Smoke Check SC01, Micro Medical, Kent, UK).

Collection of background data by personal interview

The interviewer was blind to original exposed/control status and administered a structured questionnaire in Bengali, the local language, to the participants. The questionnaire elicited information about age, education, family size, income, lifetime residential history, current and past water sources at home and at work sites, current and past (5 years prior) fluid consumption patterns, frequency of rice intake both in the form of boiled rice and *paanta bhat* (a common form of preserving cooked rice in water), smoking habits and type of cooking fuel used at home (biomass/LPG).

Prevalence of respiratory symptoms

Respiratory symptoms were ascertained from structured questionnaire based on the respiratory questionnaire of British Medical Research Council (Cotes 1987), American Thoracic Society (ATS 1995) and National Heart and Lung Institute Division of Lung Diseases questionnaire (Ferris 1978). Information sought were (i) the prevalence of upper respiratory symptoms like sinusitis, rhinitis (runny or stuffy nose), sore throat, common cold and fever in the past 3 months and preceding 1 year; (ii) the prevalence of lower respiratory symptoms such as dry or wet cough, wheeze, heaviness in chest or pain, disturbed sleep due to breathing difficulties (Pope and Dockery 1999). To minimize the seasonal variation and the observer bias, the survey was conducted by the same team of experienced researchers in control and arsenic-prone areas on consecutive days.

Dyspnea was assessed following the modified, six-point Medical Research Council (MRC) dyspnea scale that

consists of six questions about perceived breathlessness (Eltayara et al. 1996). The degree of dyspnea was classified into six categories: category 0, no dyspnea; category 1, slight dyspnea (shortness of breath when hurrying on the level or walking up a slight hill); category 2, moderate dyspnea (walks slower than people of the same age on the level because of breathlessness); category 3, moderately severe dyspnea (has to stop because of breathlessness when walking at own pace on the level); category 4, severe dyspnea (stops for breath after walking about 100 yards or after a few minutes on the level); category 5, very severe degree of dyspnea (too breathless to leave house or breathless when dressing or undressing).

The anthropometric indicators used in this study were height (m) and weight (kg) measured with shoes off, body mass index (BMI; weight in kg/height in m²), and mid-upper arm circumference (MUAC) in centimeters. MUAC values of 23.0 cm in men are useful cut-off points for simple screening of nutritional state in developing countries like India (James et al. 1994).

Measurement of lung function

Pulmonary function test (PFT) of the participants was done by electronic spirometer [Spirovit SP-1, Switzerland] (American Thoracic Society 1995). The age, standing height with shoe removed, and body weight of each participant were recorded prior to PFT. The individuals were subjected to spirometry while in a sitting position with nose closed by nose clips. The procedure was repeated several times so as to collect three acceptable attempts each with correct start and end of test criteria. The instrument was calibrated using a 2.0 lit syringe at the start of the day and after every 50 measurements. The data were then compared with predictive values based on age, sex, height and ethnic group and the following spirometric parameters were recorded for analysis: forced vital capacity (FVC), i.e. the volume of air in liters that can be maximally forcefully exhaled; forced expiratory volume at 1 s (FEV₁), i.e. volume of air (in liter) forcefully exhaled in 1 s; ratio of FEV₁ to FVC (FEV₁/FVC), expressed as percentage; forced expiratory flow at 25–75 % (FEF_{25–75} %) which is the average expiration flow rate during the middle 50 % of the FVC; and peak expiratory flow rate (PEFR): the peak flow rate during expiration. The collected data were checked independently by the respiratory scientist and the clinician. After collection of the spirometry data, the Global Lung Function Initiative (GLI) (2012) Desktop software for individual calculations was used for calculations of the predictive values.

Miller's prediction quadrant (Miller et al. 1956) was used to classify the type of lung function deficits into three categories: (i) restrictive type: FVC < 80 % of predicted value and FEV₁/FVC > 70 % of predicted; (ii) obstructive

type: FVC > 80 % of predicted and FEV₁/FVC < 70 % of predicted; and (iii) combined type: FVC < 80 % of predicted and FEV₁/FVC < 70 % of predicted.

Statistical evaluation of data

Results are expressed as mean \pm SD (standard deviation). The statistical significance between arsenic-exposed and control groups was determined using the Student's *t* test, Fisher's χ^2 test and Odd's ratio (OR). Correlation coefficients between the lung function measurements and arsenic exposure parameters were carried out using Spearman's correlation test. One-way ANOVA followed by Dunnett *t* test, where significance level was set at 0.05, was used to check the statistical difference between groups. Dunnett *t* test treats one group as a control and treats all other groups against it. All results were computed and analyzed using the SPSS statistical software package 10.0 (SPSS, Chicago, IL). $p < 0.05$ was considered significant. Multivariate logistic regression analysis was done to find association between As exposure and other parameters after controlling potential confounders. Correlation was done by Spearman's rank correlation test.

Results

Socio-economic and demographic characteristics of the study population

The control and As-exposed subjects were comparable in age, BMI, MUAC, education, religion, tobacco smoking and chewing, food habit and family income. However, they differed significantly ($p < 0.05$) with respect to occupation and type of cooking fuel used at home (Table 1). Agricultural activities (landowner/farmer/agricultural laborer) and use of unprocessed solid biomass (wood, cow dung and agricultural wastes like jute stick, hay, bamboo, dried leaves, paddy husk) were more prevalent among As-exposed subjects.

Arsenic levels in drinking water

We had collected 25 groundwater samples from tube wells of Narayanpur, 8 from Saguna and 14 from Majher Char villages, and the As content was determined by AAS-VGA method. The results showed that As concentration in groundwater of Narayanpur had a mean of 22.93 ± 10.1 (SD) $\mu\text{g/L}$ and the median value was $23.94 \mu\text{g/L}$. In Saguna and Majher Char, the mean As levels were 3.61 ± 1.5 and $5.4 \pm 4.7 \mu\text{g/L}$, respectively. The median values were 4.03 and $3.09 \mu\text{g/L}$, respectively. The mean value of the groundwater As contamination at Narayanpur was significantly higher ($p < 0.0001$; Fig. 1) than the mean As levels of areas Saguna and Majher

Table 1 Socio-demographic characteristics of the participants (India 2014)

Characteristics	Control (<i>n</i> = 388)	Arsenic exposed (<i>n</i> = 446)	<i>p</i> value
Age in years (mean \pm SD)	36.2 \pm 13.4	35.3 \pm 11.3	0.293
Body mass index (kg/m ² ; mean \pm SD)	22.2 \pm 2.9	21.9 \pm 3.1	0.1513
Mid-upper arm circumference (cm; mean \pm SD)	25.4 \pm 2.8	25.3 \pm 2.4	0.5788
Marital status, married (%)	98.4	98.9	0.9601
Occupation (%)			
Agricultural work	77.6	87.4	0.9601
Office job/trader/self- employed	22.4	12.5	0.0365
Years of formal schooling (%)			
<5 years	6.9	7.8	0.729
5–10 years	79.9	77.3	0.7772
>10 years	13.1	14.8	0.6390
Tobacco smoking/chewing history (%)			
Current smoker	0	0	
Ex-smoker	7.4	6.7	0.7972
Smoker in family	10.8	13.9	0.3455
Tobacco/betel quid chewer	11.8	15.4	0.2947
Biomass used as cooking fuel at home (%)	63.1	82.5	0.0145
Alcohol consumption, yes (%)	4.9	5.6	0.7518
Religion (%)			
Hindu	82.5	85.2	0.7667
Muslim	17.5	14.8	0.5189
Food habit (%)			
Vegetarian	7.2	5.8	0.6019
Non-vegetarian/mixed	92.8	94.2	0.8847
Family income per month in Rupees ^a (mean \pm SD)	3,528 \pm 736	3,587 \pm 832	0.2816

n number of participants

p value calculated with Students' *t* test and Chi-square test

^a 56 Indian Rupees = 1 US \$

Char taken together. Thus, from here onwards we would refer the areas with $\leq 10 \mu\text{g/L}$ of As level in groundwater as control areas and the subjects enrolled from these places as control subjects. Similarly, the area with $11\text{--}50 \mu\text{g/L}$ of As level as chronically low As-exposed area and subjects enrolled from this area as exposed group.

CO in exhaled breath

In the control group, 385 participants (99.2 %) had normal CO (0–6 ppm) and 3/388 (0.8 %) had mild-to moderately

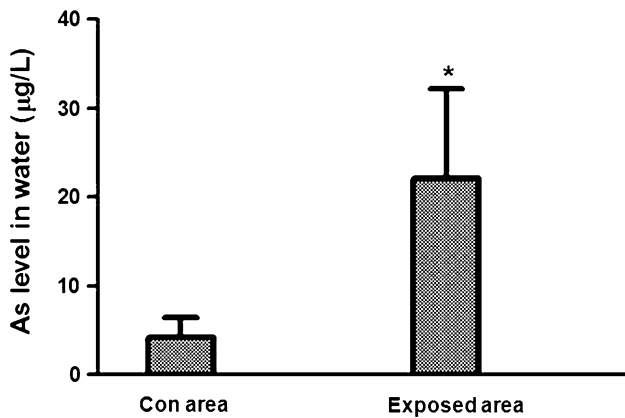


Fig. 1 Comparison of the concentration of arsenic in groundwater of endemic (Narayanpur) and control [Saguna and Majher Char] areas showing significantly higher arsenic level ($p < 0.0001$) in the endemic area (India 2014)

high CO (7–10 ppm) in expired air. In contrast, 421/446 (94.4 %) of arsenic-exposed subjects had 0–6 ppm of CO while 25 (5.6 %) had 7–10 ppm of CO in expired air ($p < 0.05$).

Prevalence of respiratory symptoms

Self-reported respiratory symptoms prevalence data are presented in Table 2. During personal interview 50.4 % of villagers from Narayanpur (exposed area) declared that they had experienced one or more URS in the past 1 month. In contrast, 37.6 % of age-matched and never-smoking control subjects from Saguna and Majher Char (control area) complained of URS ($p < 0.001$). Similarly, LRS were more prevalent among As-exposed subjects (Table 2). Sore throat and runny or stuffy nose were common URS while breathlessness on exertion was the common LRS among exposed subjects. Dyspnea was also four times more prevalent ($p < 0.001$) and the degree of dyspnea was more severe among As-exposed subjects (Table 3). Exhaled CO (7–10 ppm) showed strong positive association with dyspnea (Odds ratio [OR] = 2.83, 95 % confidence interval [95 % CI] 1.32–3.97). After controlling exhaled CO, indoor air pollution due to cooking with biomass and agricultural occupation as potential confounders, exposure to 11–50 µg/L As was positively associated with URS (OR = 1.14, 95 % CI 1.03–1.26), LRS (OR = 1.23, 95 % CI 1.06–1.44) and dyspnea (OR = 1.88, 95 % CI 1.17–2.68).

Prevalence of asthma and other symptoms

Compared with controls, persons chronically exposed to ground water arsenic had higher prevalence of asthma (7.8

Table 2 Prevalence (%) of upper and lower respiratory symptoms among control and arsenic-exposed subjects (India 2014)

Type of symptom	Control (<i>n</i> = 388)	Arsenic exposed (<i>n</i> = 446)	<i>p</i> value
URS (%)			
Sinusitis	11.8	14.8	0.3827
Sore throat	19.8	37.9	0.0000
Runny or stuffy nose	11.3	22.0	0.0014
Sneezing	5.7	12.3	0.0057
URS, overall	37.6	50.4	0.0370
LRS (%)			
Dry cough	13.4	34.1	0.0000
Cough with phlegm	11.8	31.6	0.0000
Wheeze	3.6	7.8	0.0268
Chest discomfort	11.6	25.8	0.0000
Breathless on exertion	14.9	37.2	0.0000
LRS, overall	34.0	57.8	0.0000

Results are expressed in percentage of individuals; more than one symptom were present in many individuals

n number of subjects, URS upper respiratory symptom, LRS lower respiratory symptom

p values are in comparison to control in Ch-square test

Table 3 A comparison of the prevalence (%) of dyspnea between control and arsenic-exposed subjects (India 2014)

	Control (<i>n</i> = 388)	Arsenic exposed (<i>n</i> = 446)	<i>p</i> value
Dyspnea, overall prevalence (%)	14.3	58.4	0.0000
Severity (%)			
Slight (MRC1)	11.3	22.9	0.0005
Moderate (MRC 2)	1.8	14.6	0.0000
Moderately severe (MRC 3)	1.2	3.4	0.0446
Severe (MRC 4)	0.0	0.6	

n number of subjects

p values are in comparison to control in Chi-square test

vs 2 %), headache (26.6 vs 13.9 %), eye irritation (28.7 vs 8.2 %), dizziness (25.2 vs 9.8 %), muscle pain (25.1 vs 10.3 %) and tingling and/or numbness of the extremities (27.8 vs 6.4 %) which were highly significant $p < 0.001$ in Chi-square test.

Pulmonary function

The spirometric data of pulmonary function test of As-exposed and corresponding control group are presented in

Table 4 Comparison of pulmonary function tests between control and arsenic-exposed subjects (India 2014)

Lung function parameters	Control (n = 388)	Arsenic exposed (n = 446)	% Change from control
FVC (L)			
Measured	3.2 ± 0.4	2.7 ± 0.6*	-16
% Predicted	94.1 ± 8.9	81.8 ± 11.2*	-13
FEV₁ (L)			
Measured	2.8 ± 0.5	2.3 ± 0.6*	-18
% Predicted	95.4 ± 5.9	79.3 ± 9.8*	-17
FEF₂₅₋₇₅ % (L/s)			
Measured	2.6 ± 0.3	2.2 ± 0.4*	-15
% Predicted	92.9 ± 18.7	82.7 ± 24.4*	-11
PEFR (L/s)			
Measured	4.6 ± 0.8	3.7 ± 0.9*	-20
% Predicted	88.5 ± 13.9	72.6 ± 18.9*	-18

Results are expressed as mean ± SD

N number of the participants, FVC forced vital capacity, FEV₁ forced expiratory volume at 1 s, FEF₂₅₋₇₅ % forced expiratory flow at 25-75 % which is the average expiration flow rate during the middle 50 % of the FVC, PEFR peak expiratory flow rate

* $p < 0.0001$ in Student's *t* test compared with control

Table 4. The As-exposed subjects had 500 ml lower mean FVC than the control subjects who were minimally exposed to As in drinking water ($p < 0.001$). The percent predicted value of FVC in the As-exposed was also appreciably lower than the control level. Similarly, the mean FEV₁ value of As-exposed subjects was 18 % lower than the control. Reductions in FEV₁ values indicate obstruction in the airways, whereas decline in FVC underlines reduction in lung volume and consequent lower volume of air intake. Due to the change in FVC and FEV₁ values, the FEV₁/FVC ratio showed a modest decline from 0.87 in control to 0.85 in arsenic-exposed subjects. The PEFR value was also appreciably lower than the control in subjects who were drinking arsenic containing water 5 years or more (Table 4).

Overall, 15 % lower FEF₂₅₋₇₅ % value was recorded in As-exposed subjects compared with the control group. FEF₂₅₋₇₅ % value lower than 80 % of the predicted value (an indication of small airway obstruction) was present in 44 (11.3 %) of control and 165 (37.0 %) of arsenic-exposed subjects. Mild reduction in FEF₂₅₋₇₅ % (60-79 % of predicted) was lower in As-exposed group than control [90.0 vs 78.8 %; $p = 0.237$]; moderate reduction (40-59 % predicted) was higher in exposed group than control [18.8 vs 91.1 %; $p = 0.000$] and severe FEF₂₅₋₇₅ % reduction (FEF₂₅₋₇₅ % < 40 % of predicted) was observed with similar higher trend [0 vs 3.6 %]. The reduction of FEF₂₅₋₇₅ % in exposed subjects was progressive with increasing lifetime exposure to As in drinking water,

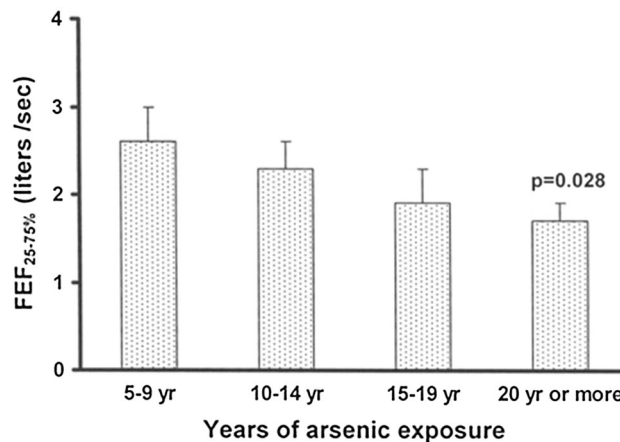


Fig. 2 Changes in measured FEF₂₅₋₇₅ % values in arsenic-exposed subjects in relation to years of exposure to arsenic. Bars represent standard deviation of mean. The FEF₂₅₋₇₅ % after 20 years of chronic arsenic exposure exhibited a significant decrement ($p < 0.05$) than 5-9 years of arsenic exposure (India 2014)

indicating a positive association between small airway obstruction and years of exposure to As. The FEF₂₅₋₇₅ % after 20 years of chronic arsenic exposure exhibited a significant decrement ($p = 0.028$) than 5-9 years of As exposure (Fig. 2).

Overall prevalence of lung function deficits

Overall, 92 out of 446 As-exposed subjects (20.6 %) had reduced lung function. In contrast, 53 of 388 control subjects (13.6 %) had reduced lung function ($p < 0.0001$ in Chi-square test; Fig. 3a).

Types of lung function deficits

Restrictive type of lung function deficit was present in 71 (15.9 %) As-exposed subjects compared with 35 (9.0 %) of control ($p < 0.001$). On the other hand, 9 exposed (2.0 %) and 12 control subjects (3.1 %) had obstructive type of lung function deficits. Combined type of lung function deficits (FVC < 80 % and FEV₁/FVC < 70 %) was present in 12 As-exposed (2.7 %) against 6 (1.5 %) of age- and sex-matched control ($p < 0.001$, Fig. 3b). Therefore, As-exposed subjects had 1.5-times more instances of reduced lung function (with the prevalence of restrictive and combined type) than control.

Association between lifetime exposure to arsenic through drinking water and lung function

With years of As exposure, the Rho values and p values for FVC (L) [-0.258; 0.015], FEV₁ (L) [-0.254, 0.016]; FEF₂₅₋₇₅ % (L) [-0.246, 0.017] and PEFR (L) [-0.244;

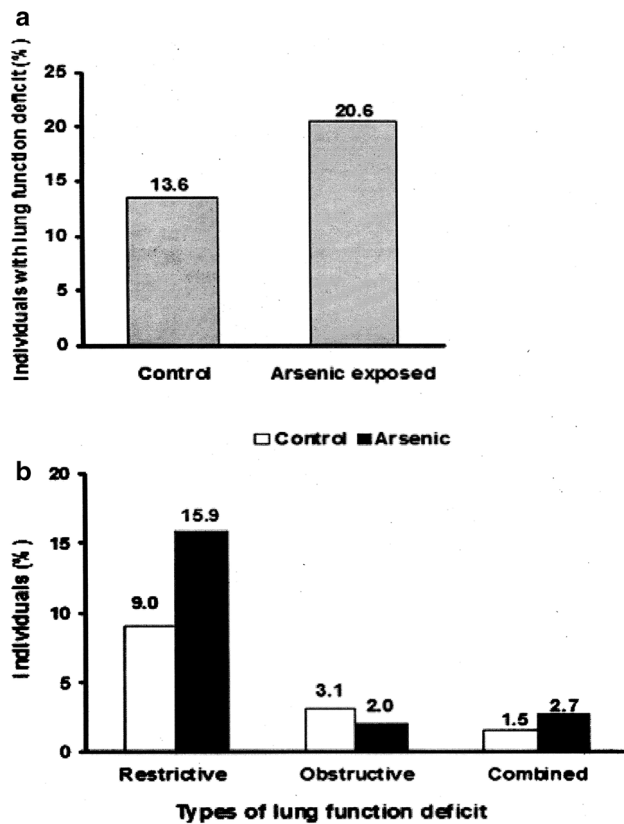


Fig. 3 Prevalence of reduced lung function (a) and the type of lung function deficits (b) among arsenic-exposed and control subjects (India 2014)

0.017] exhibited a strong negative correlation in Spearman's rank correlation test.

After controlling the influences of confounders such as biomass fuel use at home and agricultural activities as occupation in multivariate logistic regression analysis, 11–50 $\mu\text{g/L}$ of As in drinking water was found to be independently associated with reduction of FVC below 80 % of the predictive value (OR = 1.37, 95 % CI 1.10–1.96). Similarly, chronic 11–50 $\mu\text{g/L}$ of As exposure was positively associated with FEV₁ below 80 % of predicted level (OR = 1.22, 95 % CI 1.04–1.72), FEF_{25–75} % < 80 % of predicted (OR = 1.18, 95 % CI 1.14–1.88), and PEF_R < 80 % predicted (OR = 1.13, 95 % CI 1.02–1.57).

Discussion

This study has assessed the impact of chronic low-level As exposure (11–50 $\mu\text{g/L}$) from drinking water on the prevalence of respiratory symptoms, dyspnea and lung function. We found an inverse association between As concentration in drinking water and spirometric lung function measurements. In

addition, As exposure showed positive association with the prevalence of upper and lower respiratory symptoms, especially the latter. Since respiratory symptoms indicate the presence of underlying respiratory illness, the findings may suggest increased risk of respiratory diseases among arsenic-exposed subjects. This is in conformity with a Bangladesh report that showed deleterious respiratory effects of a wide range of As exposure (0.1–761 $\mu\text{g/L}$) from drinking water among non-smokers (Parvez et al. 2008). Likewise, studies from Chile have shown high prevalence of respiratory illness (Zaldivar and Ghai 1980) and mortality from COPD due to As (Smith et al. 2006). Intervention measure by providing As-free water resulted in drastic reduction of the prevalence of common respiratory illnesses from 23 to 7 % (Borgono et al. 1977).

Chronic low-level As-induced lung function decrement was mainly of restrictive and combined nature measured by Miller's prediction quadrant (Miller et al. 1956). However, recommendations of the American Thoracic Society/European Respiratory Society suggest using a percentile-based approach to define an abnormal test [less than the fifth or greater than the 95th percentiles] (ATS/ERS 2005). A study showed that results obtained by both the methods were similar and can be interchangeably used for interpretation of lung function tests (Pakhale et al. 2009). Several studies have shown that a large amount of As is deposited and stored in the lung, especially in the epithelium Gerhardtsson et al. 1988; Saady et al. 1989). It is possible that the deposited As in the lung acts like some other metals by enhancing tissue inflammation or increasing pulmonary fibrosis, leading to impaired respiratory function (Nemery 1990). Chronic As poisoning renders the respiratory tract more susceptible to infection (Hotta 1989). Consequent inflammation (De et al. 2004) and oxidative stress-mediated cellular injury in the lung (Lantz and Hays 2006) may cause fibrosis and decline in lung function (von Ehrenstein et al. 2005).

Earlier investigators have shown that smokers are at a higher risk of developing respiratory illness following As exposure (von Ehrenstein et al. 2005; Mazumder et al. 2005). Our study has illustrated that respiratory effect of As exposure may be significant among never-smokers.

However, this investigation has some limitations. Being a cross-sectional study, it limits our inference on the causal direction. We did not measure the personal exposure of As by analyzing the nail and urine samples. Even the contribution of arsenic from the food chain has not been done. It is also likely that factors other than ground water As have influenced the respiratory changes observed among exposed subjects. Environmental risks like household air pollution have been reported to contribute a major share of the global disease burden (Lopez 2013). For example, high level of indoor air pollution due to cooking with unprocessed biomass fuels (practiced in 82.5 % of exposed vs. 63.1 % of control households) adversely affects the lung

function (Fullerton et al. 2011). Likewise, agricultural activities and resultant exposure to agricultural pesticides could also be harmful to the lung (Peiris-John et al. 2005). Since agricultural activities and use of unprocessed solid biomass were more prevalent among As-exposed subjects vis-à-vis the control group, the reduction in lung function in the former could be partly attributed to these factors. Fourth, we relied on self-reported symptoms that could be biased, and lung function tests that usually detect disease with relatively late-stage lung damage.

Despite these shortcomings, however, the sample size of this study was large enough to conclude that the connection between chronic consumption of 11–50 µg/L of As-contaminated water and reduced lung function, dyspnea, headache, chronic cough and related symptoms in rural never-smoking men was empirically observed. This conclusion is further supported by the finding that As concentration in the range of 11–50 µg/L showed negative association with spirometric lung function parameters even after controlling cooking with biomass and agricultural occupation as potential confounders. Moreover, we did not find any difference in the percentage of individuals having a MUAC value of <23 cm between the control and exposed groups, eliminating the possibility of nutritional deficiency as a contributor to respiratory toxicity. For the detection of early lung changes, invasive techniques like bronchoscopy or bronchoalveolar lavage are needed which are rarely available in rural India. In contrast, lung function test and questionnaire surveys represent a convenient tool for investigating large sample population due to low cost, easy to use by the investigator, and good compliance of the participants (Liard et al. 2000). In essence, the study underscores breathing problems and lung function deficits in association with 11–50 µg/L of arsenic in drinking water. Since millions of rural people of West Bengal and adjoining Bangladesh are chronically exposed to this dose, the finding is important from public health perspective.

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Conflict of interest None declared.

Ethical standards The experiments comply with the current laws of India where they were performed. The work was approved by Institutional Ethics Committee, Chittaranjan National Cancer Institute, Kolkata.

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