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Assessment of risk factors for arsenicosis in Bangladesh

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STUDY SUPPORTED BY UNICEF, BANGLADESH

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Executive summary

Arsenic contamination of drinking water is a serious problem in Bangladesh. It is likely that many arsenicosis cases are as yet to be diagnosed. Risk factors for development of clinical arsenicosis, beyond ingestion of arsenic contaminated water, are poorly understood. Better understanding of the epidemiology of arsenicosis and of individual risk factors could help to target efforts to provide arsenic free water towards those most at risk, could indicate other means to reduce the risk in arsenic exposed populations, and may give clues to the mechanisms of toxicity. Active case detection in several upazilas in Bangladesh provided the opportunity to describe a series of cases in one upazila and to undertake a small case-control study, as described here.

Methods

Potential arsenicosis cases were identified by active case finding efforts by trained government health service providers in Shahrasti upazila, Chandpur district. These cases were sent to the upazila health complex (UHC), where trained doctors confirmed which were cases of arsenicosis and recorded some details about each case, including examination findings.

Trained interviewers providers visited the houses of 54 of those confirmed cases. They administered a questionnaire to the cases and to other household members over 10 years old. They also administered the questionnaire to members of a neighboring household that shared the same tube well water source with the case household.

Findings

Description of the arsenicosis cases

About 475 probable arsenicosis cases were identified by the trained service providers. All of them were sent to the Health Complex for confirmation. 415 of them were confirmed as arsenicosis cases by trained doctors in the Upazila Health Complex.

Among the 415 cases, about half (49%) were male. Males were older than females (mean age 37.9 years in males, 32.3 years in females). Some 27% of males and 33% of females had no education, while 52% of males and 38% of females had 6 years or more of education. A third of males were in service work or manual labour (32%) and 41% were unemployed. Most (80%) of the females were recorded as housewives.

Nearly all the cases (99.7%) used tube well water for drinking, but almost none used it for cooking (2%) or washing (2%). Nearly all had used the same tube well for ten years or more. Males reported drinking more tube well water than females (mean consumption: males 11.2 glasses per day, females 10.13 glasses per day).

Nearly half the cases (45%, 152/339) said they had an illness, with males less likely to report this than females. About a third reported another patient like them at home

(35%, 120/342). Nearly all (96%, 329/343) knew that drinking arsenic contaminated water is damaging to health.

On clinical examination: nearly half were clinically anaemic, but very few had oedema or enlarged liver or spleen. Blood pressure measurements (undertaken in about a quarter of the patients) were mainly in the normal range. The mean BMI was 19.14; it was slightly higher in females. Glcosuria was detected in 1.5% (6/413). Melanosis was nearly universal, with keratosis in over a half. Other skin manifestations were rare.

Further information was collected from 54 cases of arsenicosis, as well as 369 controls: 121 from within the same household and 248 from a different household.

Comparison of cases and controls

There was an apparent excess of males among cases. However, this was because there were only 37% males among the controls, probably because male household members who were not arsenicosis cases were at work and so were missed by the interviewers. The remaining analysis was undertaken after stratification by sex.

Cases of arsenicosis were more likely than controls to report poor general health. However, from this study it is not possible to determine if their perception of poor health came before or after their diagnosis of arsenicosis.

Cases did not report a higher consumption of tube well water at home, compared with controls. However, for the subgroup of people working outside the house, cases were more likely to report a high consumption of tube well water at work. The arsenic contamination status of the tube wells used at work is not known. As 99% of the tube wells in that Upazila are contaminated, if their working places are from the same Upazila area they are almost certainly contaminated.

Very few females smoked. Among males, there was no evidence of an excess of smokers among the cases.

Cases were more likely to report eating less than three meals a day. There was no excess of low Body Mass Index (BMI) among the cases compared with controls, but cases may have more subtle nutritional deficiencies.

There was no difference in reported pesticide use or reported consumption of pesticide treated vegetables between cases and controls. However, members of households with a case are more likely to report pesticide use and consuming pesticide treated vegetables than members of control households. Thus pesticide exposure may increase the risk of developing arsenicosis after ingestion of arsenic, with the balance being tipped by other factors in individual cases within the household.

Conclusions

Active case finding produced some 415 confirmed cases of arsenicosis, equally divided between males and females. Information from these cases confirmed the key role of drinking tube well water and the nearly universal presence of melanosis. The small case-control study confirmed an important role for ingestion of tube well water at work in increasing the risk of arsenicosis. This study did not support smoking as a risk factor for arsenicosis. It did provide some preliminary evidence to suggest that pesticide exposure might increase the risk of arsenicosis.

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Introduction

In 1993, arsenic contamination in shallow water was first detected in one of the northern districts of Bangladesh. The recent detection of high concentration levels of arsenic in water from numerous tube-wells in 61 out of 64 districts of the country poses serious problems for providing safe water. At present, a population of about 30 million people are likely to be affected through arsenic contamination of about 10 million shallow tube wells currently serving as sources of water for drinking and cooking. To date, more than twelve thousand arsenicosis patients have been identified and many more remain undiagnosed. The time to develop clinically evident effects from drinking arsenic contaminated water is generally thought to be about 10 years, but early manifestations are not uncommon and manifestations of the disease in children below 10 years have been reported. Clinical arsenicosis begins with hyper-pigmentation of the skin and mucous membranes and progresses to death from malignancies. The only way to save lives is to identify patients early before their condition becomes irreversible and to provide supportive management to all diagnosed cases.

The present knowledge about management of arsenicosis is far from satisfactory. The drugs used for chelating arsenic in acute poisoning have proved to be ineffective in chronic arsenicosis. The use of arsenic free water may prevent progression of effects, but it is not clear whether reversal of effects is possible. Supportive therapy with nutritional improvement may play some role in diminishing symptoms and may reverse some cases of melanosis. Recently, success in the treatment of arsenicosis with indigenous medicine 'Spirulina' has been claimed, but it is yet to be confirmed.

The individual factors that increase or decrease susceptibility to develop clinical arsenicosis after ingestion of arsenic-contaminated water are little understood. It has been suggested that there might be differences in susceptibility by sex, by nutritional status and by general health. It would be useful to know more about the factors that increase or decrease the risk of developing arsenicosis. It might indicate some empirical prevention and treatment options for those who have already ingested arsenic contaminated water. Evidence about factors increasing the risk of arsenicosis might throw light on mechanisms of development of clinical arsenicosis, potentially leading to development of specific, effective interventions.

This study took advantage of a process of active case detection in several upazilas. In one upazila, details about clinically-confirmed cases of arsenicosis were recorded and some of these cases were compared with non-cases using the same home water source, within the same household or in another household sharing the same water source. Thus some of the features of the arsenicosis cases were described and in a comparison with controls, some factors increasing the risk of arsenicosis were investigated.

Methods

Study population

Case finding

Active case finding in the selected upazila, as well as in several others, was undertaken by government health service providers. They first received training about arsenicosis, including the clinical features of arsenicosis. They visited each household and checked each individual whether having characteristic skin manifestation. All probable cases of arsenicosis identified by the health service providers were sent to the upazila health complex (UHC). All of those probable cases were examined by a trained doctor who decided which were confirmed arsenicosis cases. General information and arsenic related information including important clinical findings were recorded by the examining doctor from all confirmed cases in a pre-designed questionnaire/checklist. A sub-set of these confirmed cases were randomly selected to form “cases” for a subsequent case-control study.

Controls (referents)

The referents were people who shared the same water source with the cases but who did not show signs of clinical arsenicosis. The trained health service providers visited the households of the arsenicosis cases and identified as controls the other members of the household over ten years old. They also identified as controls the members of adjacent households sharing the same water source as the ‘case’ household. During interview, any other individual in the case or control households suspected of having arsenicosis were referred to the doctor in the upazila health complex for confirmation of status.

Data collection

Doctors in the UHC administered a short questionnaire to confirmed cases and recorded details of the features on clinical examination. Trained interviewers from the upazila administered a questionnaire to both cases and controls about personal characteristics, water consumption, diet and other factors that could be relevant to the development of clinical arsenicosis. They also weighed and measured the height of the cases and controls. Data of the ‘case series’ as well as of the ‘case-control series’ were collected during January and February 2002.

Data management and analysis

Data were entered using the Epi Info software package. This package was also used for the data analysis. Body mass index (BMI) was calculated as weight (Kg) / height (m) squared.

Frequencies for features of the cases in the case series were generated. A case-control analysis was performed to compare potential risk factors between cases and controls, with stratification by sex. The Mantel-Haenszel procedure was used to calculate the Odds Ratio and 95% confidence interval from 2 by 2 tables. For continuous variables, the significance of differences between means was tested by the t-test.

Findings

The case series

There were 415 confirmed arsenicosis cases. Almost half (49%, 203/415) were male. Almost all were Muslim (98%, 408/415). Most were married (82%, 338/414). Some 17% (69) were unmarried and just 2% (7) were widowed.

Age, education, occupation and income

Table 1 shows mean age, years of education, occupation and mean monthly household income for all the cases and for the males and females separately.

Table 1. Education, occupation and household income in the case series

Feature	Males	Females	All cases
<i>Age (n=415)</i>			
Mean age (yr)	37.91	32.25	35.02
<i>Education (yrs) (n=394)</i>			
No education	27% (51)	33% (66)	30% (117)
1-5 years	21% (40)	29% (59)	25% (99)
6 years plus	52% (99)	38% (76)	44% (175)
Non-formal edn	1% (2)	1% (1)	1% (3)
<i>Occupation (n=409)</i>			
Service	11% (22)	1% (2)	6% (24)
Labour	21% (42)	0	10% (42)
Agriculture	7% (13)	0	3% (13)
Unemployed	41% (81)	1% (2)	20% (83)
Student	20% (40)	18% (39)	19% (79)
Housewife	0	80% (168)	41% (168)
<i>Income (n=404)</i>			
Mean income (Tk)			2872.15

The age range was 7-85 years. The mean age of the males was significantly higher than the mean age of the females ($p=0.000012$).

Source of water

Almost all the cases who answered the question reported tubewell as their main source of drinking water (99.7%, 364/365). For cooking, nearly all the cases who answered reported they used pond water (98%, 347/355). Similarly, nearly all who answered reported they used pond water for washing (98%, 336/342).

Most of those who responded said they had used the same tubewell water for at least 10 years (96%, 306/320), with no difference between males and females.

About two thirds of those who responded said they drank at least 10 glasses of tubewell water per day (63%, 208/329). Males were twice as likely to report drinking

10 glasses of tubewell water per day, compared with females¹. The mean consumption of tubewell water was significantly higher among males (males 11.21 glasses per day (SD3.32) vs females 10.13 glasses per day (SD3.72), p=0.006)

Health perceptions and knowledge

Of those who answered the question, nearly half said they had an illness (45%, 152/339). Males were less likely than females to say they had an illness².

Of those who responded, a third said there was another patient “like them” in their household (35%, 120/342). There was no difference between males and females in the number reporting another similar patient in the household.

Nearly all the patients who responded to the question said they knew that drinking arsenic contaminated water is damaging for health (96%, 329/343). There was no difference between males and females in this knowledge. It is not surprising that there was a high level of awareness in this group as they had been sent for examination to confirm if they were cases of arsenicosis and has already had contact with the health service providers undertaking the case finding exercise.

Clinical examination

Anaemia

About half the cases were considered to be clinically anaemic (48%, 197/415). Males were slightly more likely than females to be considered anaemic³.

Oedema

Pitting oedema was rarely seen (3%, 12/414). The frequency of oedema was the same in males and females.

Organomegaly

In only three cases was a palpable liver recorded (0.7%, 3/415). And in only one case was a palpable spleen recorded.

Blood pressure

The blood pressure was randomly recorded for only 140 of the patients. Among these, the mean systolic blood pressure was recorded as 123 mmHg (range 90-180), with no difference between males and females. The mean diastolic blood pressure among these 140 patients was recorded as 74 mm Hg (range 60-110), again with no difference between males and females.

¹ 115/155 males (74%) drank at least 10 glasses of tube well water daily, compared with 93/174 (53%) of females. Odds Ratio 2.50 (95% CI 1.52-4.13)

² 61/161 (38%) of males said they had an illness, compared with 91/178 (51%) of females. Odds Ratio 0.58 (95% CI 0.37-0.92)

³ 107/203 (53%) of males were clinically anaemic, compared with 90/212 (43%) of females. Odds Ratio 1.51 (95% CI 1.00-2.28)

Height and weight

The mean height in metres (among 413 patients) was 1.53 m (range 1.20-1.83 m). As expected, males were taller than females on average (1.59 m vs 1.47 m, p0.000000).

The mean weight was 44.58 Kg (range 19.00-85.00). On average, males weighed more than females (47.79 vs 41.52 Kg, p0.000000).

The mean body mass index was 19.14 (range 11.43-45.29). The small difference between males and females (18.97 vs 19.31) did not approach statistical significance (p=0.34).

Glycosuria

On urine testing, some 1.5% (6/413) of the cases had glycosuria. The proportion was about the same in males (2%, 4/202) and females (1%, 2/211).

Skin manifestations

Table 2 shows the recorded skin manifestations. Nearly all cases had melanosis and over half had keratosis. Other manifestations were more rare.

Table 2. Skin manifestations in the arsenicosis cases

Feature	Males	Females	All cases
Melanosis	98% (199/203)	95% (201/212)	96% (400/415)
Keratosis	63% (128/203)	57% (120/212)	60% (248/415)
Hyper-keratosis	10% (20/202)	11% (24/212)	11% (44/414)
Leukomelanosis	5% (11/203)	7% (14/212)	6% (25/415)
Skin ulcers	4% (8/202)	3% (7/211)	4% (15/413)

Case control analysis for risk factors

Sex and age

The trained health service providers collected information from 54 cases, as well as 369 controls: 121 from the same households as the cases and 248 from neighbouring households sharing the same water source as the case households.

The sex and age of the cases and controls are summarized in Table 3.

Table 3 Sex and age of arsenicosis cases and same water-source controls

Characteristic	Cases N=54	Same house controls N=121	Other house controls N=248	All controls N=369
% Male	54% (29/54)	39% (47/120)	35% (87/247)	37% (134/367)
Mean age (yrs)	36.7 (SD 15.24)	35.3 (SD19.80)	33.2 (SD 18.41)	33.9 (SD 18.87)
Males	37.1 (SD 17.70)	39.5 (SD21.86)	36.4 (SD20.85)	37.5 (SD 21.18)
Females	36.2 (SD12.11)	32.9 (SD18.03)	31.2 (SD16.62)	31.7 (SD17.05)

There is an excess of males among the cases compared with the controls⁴, both controls within the same household⁵ and controls in a different household⁶. However, this is because of a relative lack of males among the controls, both in the same household and in neighbouring households. The most likely explanation is that males who were not ill were out at work and were not present in the houses at the time of the visits, so were not included among the controls. The apparent excess of males among the cases is therefore an artefact. The remaining analysis is carried out for males and females separately.

The mean age of the cases is higher than the mean age of the controls. However, this higher age among cases is confined to females. The differences in age are not statistically significant.

Body mass index

Table 4 Mean BMI in cases and same water-source controls

Sex	Cases N=54	Same house controls N=121	Other house controls N=248	All controls N=369
Male	19.52 (SD3.12)	18.80 (SD2.70)	18.67 (SD3.40)	18.71 (SD3.17)
Female	19.62 (SD3.21)	19.68 (SD3.19)	18.88 (SD2.91)	19.13 (SD3.02)

As shown in Table 4, among both males and females there is no difference in mean BMI between cases and controls.

⁴ 29/54 (54%) of cases were male, compared with 134/367 (37%) of all controls. Odds Ratio 2.02 (95% CI 1.09-3.75)

⁵ 29/54 (54%) of cases were male, compared with 47/120 (39%) of same household controls. Odds Ratio 1.80 (95% CI 0.89-3.65)

⁶ 29/54 (54%) of cases were male, compared with 87/247 (35%) of different household controls. Odds Ratio 2.13 (95% CI 1.12-4.06)

Perceived health

When asked for a self-rating of their health, both male and female cases are more likely to rate their health as ‘bad’ compared with all controls⁷, and compared separately with same household controls⁸ and with other household controls⁹.

Consumption of tube well water

The questionnaire administered to cases and controls included questions about the source of their drinking, cooking and washing water at home and in their workplace (if relevant). Respondents were also asked about how much water and tea they drank per day, at home and at work.

Consumption of tube well water at home

Virtually all cases (98%, 53/54) and nearly all controls (97%, 359/369) reported drinking water from a tube well at home. Most cases (78%, 42/54) and controls (71%, 260/368) reported drinking water from the same tube well at home for at least ten years.

Very few cases (8%, 4/53) or controls (7%, 27/268) reported using tube well water for cooking. They mostly used other sources of water for cooking. Similarly, very few cases (6%, 3/54) or controls (2%, 7/368) reported using tube well water for washing at home.

The average consumption of tube well water per day was reported as 11.76 glasses. The reported average consumption was higher among females than males (12.21 glasses (SD 3.42) vs 10.98 glasses (SD 4.57)). High consumption of tube well water at home was defined as drinking at least ten glasses of water per day from a tube well source. This was commonly reported (77%, 327/423), and there was no difference between cases (76%, 41/54) and controls (77%, 285/368).

Table 5 Mean consumption of tube well water at home in cases and same water-source controls (number of glasses)

Sex	Cases N=54	Same house controls N=121	Other house controls N=248	All controls N=369
Male	12.35 (SD6.25)	11.13 (SD3.98)	10.52 (SD4.16)	10.66 (SD4.04)
Female	12.76 (SD4.12)	12.51 (SD3.24)	12.06 (SD3.59)	12.20 (SD3.49)

The differences in consumption between cases and controls were not statistically significant among males or females (Table 5).

⁷ 23/54 (43%) of cases rate their health as bad, compared with 77/367 (21%) of all controls. After stratifying by sex, Odds Ratio 2.80 (95% CI 1.53 – 5.10)

⁸ 23/54 (43%) of cases rate their health as bad, compared with 27/121 (22%) of same household controls. After stratifying by sex, Odds Ratio 2.38 (95% CI 1.19-4.77)

⁹ 23/54 (43%) of cases rate their health as bad, compared with 50/246 (20%) of different household controls. After stratifying by sex, Odds Ratio 3.10 (95% CI 1.64-5.84)

About a quarter (27%, 113/424) of respondents reported drinking two or more cups of tea at day at home. This level of tea consumption at home was the same in cases (30%, 16/54) and controls (26%, 96/369). Tea drinking was not different between males and females.

About a third (35%, 90/261) of respondents who answered a question about eating *panta vat* (soaked rice) said they ate this rice soaked in tube well water. This was not different between cases (39%, 13/33) and controls (34%, 77/227).

Consumption of tube well water at work

Overall, just over a third (39%, 164/423) of the respondents reported working outside the house. Men were much more likely than women to report working outside the house¹⁰. There was no difference between cases (39%, 21/54) and controls (39%, 143/368) in the proportion that reported working outside the house. This lack of difference between cases and controls was not changed after stratifying by sex.

Those who worked outside the house nearly all reported they used tube well water for drinking at work (98%, 155/159), with no difference between cases and controls. Among those who worked outside the home, about a quarter (24%, 37/154) reported drinking at least ten glasses a day of tube well water.

The average consumption of tube well water at work among cases and controls is shown in Table 6.

Table 6. Mean consumption of tube well water at work in cases and same water-source controls (number of glasses)

Sex	Cases N=54	Same house controls N=121	Other house controls N=248	All controls N=369
Male	8.00 (SD4.82)	6.03 (SD3.77)	7.11 (SD5.41)	6.77 (SD4.96)
Female	7.50 (SD5.80)	3.73 (SD1.75)	3.53 (SD2.59)	3.59 (SD2.36)

The mean consumption of tube well water at work is significantly higher ($p=0.025$) among cases (7.92 glasses, SD4.86) than controls (5.66 glasses, SD4.47), considering both males and females together. Considering only males, the difference is not significant at the 5% level. But considering only females, the difference is significant ($p=0.006$) (Table 6).

Cases of arsenicosis were more likely to report drinking at least ten glasses a day of tube well water at work, compared with all controls¹¹. A similar excess of high consumption of tube well water at work was found among cases compared separately with same household controls¹² and different household controls¹³.

¹⁰ 106/163 (65%) of men worked outside the home, compared with 57/258 (22%) of women. Odds Ratio 6.56 (95% CI 4.13-10.45)

¹¹ 10/21 (48%) of cases reported drinking at least ten glasses a day of tube well water at work, compared with 27/133 (20%) of all controls. Stratified by sex, Odds Ratio 2.67 (95% CI 1.03-6.91)

¹² 10/21 (48%) of cases reported drinking at least ten glasses a day of tube well water at work, compared with 6/38 (16%) of same household controls. Odds Ratio 4.85 (95% CI 1.22-20.14)

¹³ 10/21 (48%) of cases reported drinking at least ten glasses a day of tube well water at work, compared with 21/95 (22%) of different household controls. Odds Ratio 3.20 (95% CI 1.07-9.67)

Smoking and alcohol consumption

Only 15% (65/424) of the respondents reported being a smoker. Among the men, 39% (64/163) reported smoking, while almost none among women smoked (1/259).

Overall, among cases of arsenicosis, 20% (11/54) were smokers, compared with 15% (54/369) among controls. A difference of this magnitude could easily have occurred by chance and the difference did not persist when sex was taken into account by stratification. Considering only males (since only one female was a smoker), the rate of smoking among cases (38%, 11/29) was the same as that among controls (40%, 53/134). Thus there was no evidence of an increased risk of arsenicosis associated with smoking.

Only four people reported drinking alcohol (two cases and two controls).

Diet

Most respondents (85%, 359/424) reported eating three full meals a day. The remainder ate a full meal once or twice a day. Cases of arsenicosis are less likely to eat a full meal three times a day, compared with all the controls¹⁴. The difference between cases and controls was less marked for same household controls¹⁵ than for different household controls¹⁶.

Exposure to pesticides

Overall, nearly half the respondents (41%, 174/423) said that pesticides were used by their household. There was no difference between cases (43%, 23/54) and controls (41%, 150/368). But households in which there was a case of arsenicosis were more likely to use pesticides (as reported by individual household members) than households without any case of arsenicosis¹⁷.

Similarly, 41% (174/422) of respondents reported eating vegetables treated with pesticides. There was no difference between cases (43%, 23/54) and controls (41%, 150/367). But again, there was a suggestion of more consumption of pesticide treated vegetables in households with a case of arsenicosis, compared with control households¹⁸.

¹⁴ 39/54 (72%) of cases ate a full meal three times a day, compared with 319/369 (86%) of all controls. After stratifying by sex, Odds Ratio 0.47 (95% CI 0.24-0.92)

¹⁵ 39/54 (72%) of cases ate a full meal three times a day, compared with 97/121 of same household controls. Odds Ratio 0.64 (95% CI 0.29-1.46)

¹⁶ 39/54 (72%) of cases ate a full meal three times a day, compared with 222/248 (90%) of different household controls. Odds Ratio 0.30 (95% CI 0.14-0.67)

¹⁷ 82/175 (47%) members of case households reported pesticide use in the household, compared with 92/248 (37%) members of control households. Odds Ratio 1.50 (95% CI 0.99-2.27)

¹⁸ 79/175 (45%) members of case households reported eating pesticide treated vegetables, compared with 95/247 (39%) members of control households. Odds Ratio 1.32 (95% CI 0.87-2.00)

Discussion

The active case finding exercise provided an opportunity to document some features of arsenicosis cases in one upazila. The equal division between males and females does not suggest any important differential susceptibility by sex. The role of drinking water, as opposed to cooking water, is emphasized as almost none of the cases used tube well water for cooking. Melanosis was virtually always present and is an important diagnostic marker. In this series anaemia was common and apparently somewhat more common among the males.

The small case-control study allowed examination of several potential risk factors. The volume of water ingested is important. This was not apparent when comparing cases and controls for water ingestion in the household but among those who went to work, those with higher water consumption had an increased risk of arsenicosis. It has been suggested that smoking might be a risk factor for the development of arsenicosis but this study does not provide support for this suggestion.

Poor general health might increase the risk of arsenicosis in people exposed to arsenic. In this case, the cases were more likely to consider their health poor compared with controls, but this might well be because they were aware of their diagnosis. In this study we are not able to examine what they thought about their health before they developed apparent arsenicosis.

There is some suggestion that poor nutritional status might contribute to the risk of developing arsenicosis. In this study, the BMI of the cases was not lower than that of the controls, but BMI is a crude indicator of nutritional status. In this case, the arsenicosis were more likely not to eat three meals a day and this may be associated with some more subtle nutritional deficiencies.

This study provides some preliminary evidence to support the possibility that exposure to pesticides might increase the risk of developing arsenicosis. If confirmed in other studies, this could be important for efforts towards prevention of development of arsenicosis among people exposed to arsenic contaminated water.

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