

## 論文の内容の要旨

論文題目 Arsenic Exposure and Oral Cavity Arsenicosis in Bangladesh

バングラデシュにおける砒素曝露と口腔前庭黒色症との関連

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**Introduction:** Groundwater contamination by arsenic represents a major public health concern worldwide, affecting 150 million people in more than 70 countries. In Bangladesh, about 35-77 million people have reportedly been exposed to arsenic through drinking water. As a result, WHO described the arsenic problem in Bangladesh as “the largest mass poisoning of a population in history”.

Several epidemiological studies have reported the effects of environmental exposure to arsenic on the development of cancers. Regarding the effects on oral health, in a recent study in Bangladesh, 75.5% of participants showed swelled vallate papillae as an indication of arsenicosis. Therefore, arsenic exposure may also manifest buccal mucus membrane melanosis. However, research is needed to examine the impact of arsenic toxicity on oral health. To our knowledge, no study to date has measured the relationship between arsenic exposure and arsenical lesions of the oral cavity and the associated factors, particularly pertaining to lesions of the gums, lips, and tongue, in Bangladesh or elsewhere, at the population level.

Preventing arsenic exposure by health education programs is one of the vital mitigation approaches to be pursued. On the other hand, community-based awareness

programs might also have a positive role in decreasing urinary arsenic levels and arsenical lesions of the oral cavity. In this context, Health Effects of Arsenic Exposure Longitudinal Study (HEALS) data represents a unique opportunity for investigating toward the following objectives: 1) to assess the relationship between arsenic exposure and arsenical lesions of the oral cavity, and 2) to examine the reduction of urinary arsenic levels and arsenical lesions of the oral cavity after an arsenic mitigation process. The information uncovered through these research objectives might be useful in developing appropriate strategies to support arsenic-affected communities in Bangladesh.

**Methods:** The present study was conducted by utilizing the data from the HEALS. The HEALS is an ongoing population-based cohort study to investigate both the short-term and long-term health outcomes associated with arsenic exposure through drinking water in Araihasar, Bangladesh. Participants were 11,746 married individuals, aged 17-75 years, recruited during the period from October 2000 to May 2002. In the follow-up survey, 11,323 participants were recruited from June 2002 to June 2004. Trained study physicians and research assistants, blinded to the arsenic measurements, conducted in-person interviews and clinical evaluations, and collected spot urine samples from the participants in their homes using a structured process. Concentrations of arsenic in urine were measured using Graphite Furnace Atomic Absorption spectrometry (GFAA), with a detection limit of 2.0 $\mu$ g/L.

At baseline and follow-up interview, arsenical lesions of the gums, lips, and tongue

were ascertained by the trained study physicians. Study physicians had sufficient training for the detection and diagnosis of arsenicosis and recorded the presence or absence of arsenical lesions of the gums, lips, and tongue. In addition, the HEALS research team disseminated mitigation efforts in the study area during the baseline data collection. Mitigation efforts included health education, test results of wells, and well labeling.

In the analysis of available data, the prevalence of arsenical lesions of the gums, lips, and tongue were calculated. Further, multinomial logistic regression models were created, with adjustment for potential confounders, to determine the factors associated with arsenical lesions of the gums, lips, and tongue, respectively. We also used the same models in the sex stratified analysis.

**Results:** Out of 12,050 eligible participants, 11,746 were included in the HEALS cohort.

Among 11,746 participants, 42.9% (n=5,042) were males and 57.1% (n=6,704) were females.

The prevalence of arsenical lesions of the tongue was 0.7%, followed by lesions of the gums (0.3%) and lips (0.2%). Multinomial regression models showed that participants with higher urinary arsenic levels (286.1-5000.0 $\mu$ g/g) were more likely to develop arsenical lesions of the gums [multinomial odds ratio (M-OR 2.90; 95% CI=1.11-7.54)], and tongue (M-OR 2.79; 95% CI=1.51-5.15), compared with those with lower urinary arsenic levels (7.0-134.0 $\mu$ g/g).

Similar findings were also observed through the sex stratified analysis. Females were less likely to develop arsenical lesions of the gums (M-OR 0.35; 95% CI= 0.13-0.92) than were

males. Our results also showed that participant's age was significantly associated with presence of arsenical lesions of the tongue (M-OR 1.03; 95% CI=1.00-1.05).

Findings from this study also showed that, among participants with higher urinary arsenic levels (286.1-5000.0 $\mu$ g/g) decreased in the follow-up (24.0%), compared with the baseline phase (33.0%). In contrast, participants with lower urinary arsenic levels (7.0-134.0 $\mu$ g/g) increased in the follow-up (43.0%), compared with the baseline (33.0%). Similar findings were also observed for the lips and tongue.

**Conclusion:** In conclusion, a positive association was detected between arsenic exposure and the risk of arsenical lesions of the gums and tongue. This is the first study to show arsenic-induced symptoms of the gums and tongue due to arsenic exposure at the population level. The results of this study have an important public health message concerning arsenic-exposed populations in Bangladesh. Therefore, further investigation is necessary to determine whether arsenic exposure on the gums and tongue can further impact to the development of oral cancer. However, the mitigation efforts provided by HEALS helped to decrease the urinary arsenic levels and rates of oral cavity lesions. Thus, government and related agencies need to strengthen strategies that include health education programs and provide well test results to adequately address the health consequences linked to this enormous problem. Pursuing such strategies might help to reduce the risk of increased deaths which might otherwise result from extended exposure.