Application of fingernail samples as a biomarker for human exposure to arsenic-contaminated drinking waters

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This study evaluated the relationship between arsenic uptake via drinking water ingestion and arsenic concentration in fingernails as a biomarker for human exposure. For this purpose, we collected fingernail samples from 40 healthy participants of arsenic-affected rural regions of Kaboudarahang County, the west of Iran. A total of 49 fingernail samples were also collected from individuals who lived in areas where contamination of drinking water sources with arsenic had not been reported. It was found that the fingernails arsenic contents in 50% and 4.08% of the samples collected from arsenic-contaminated and reference villages were higher than the normal arsenic values of nails (0.43–1.08 µg/g), respectively. Based on the results of adjusted multiple linear regression, a significant association was found between groundwater and fingernails arsenic concentration (p < 0.001). Moreover, a statistically significant association was shown between arsenic in the fingernail samples and gender (p = 0.037). Fingernails arsenic contents were not significantly affected by other variables including age, smoking habits, and BMI (p > 0.05). In light of the results of this study, the use of biological indicators such as fingernail tissues due to easier sampling and less risk of external contamination is suitable for assessing exposure to heavy metals in contaminated areas.

Arsenic is considered one of the dangerous metalloids occurring in drinking water sources through natural and anthropogenic activities. Anthropogenic activities such as the application of herbicides, pesticides, wood timber preservatives, and metal smelting industries, and natural sources of arsenic exposure including geothermal processes, volcanic eruptions, and weathering of mineral lead to widespread arsenic contamination in subsurface environments like sediment, soil, surface water, and groundwater sources1–3. This metalloid recognized as a human carcinogen by the International Agency for Research on Cancer (IARC) and the United States Environmental Protection Agency (USEPA) is found in organic and inorganic forms and with different oxidation states (−3, 0, +3, +5) in the environment4–7. Non-occupational exposure to inorganic arsenic (arsenite and arsenate) through the consumption of drinking water sources causes carcinogenic and non-carcinogenic health effects in the exposed human population8–10. Acute and chronic human health effects of arsenic exposure include skin lesions, cardiovascular disease, anemia, renal impairment, as well as respiratory disorders, and different types of cancers (lung, skin, liver, kidney, and bladder)11–13. Therefore, to ensure the health of water for drinking purposes, the maximum allowable level for arsenic has recommended by the World Health Organization is 10 µg/L14,15. In addition, due to the widespread occurrence of arsenic in the environment and its potential for adverse effects on human health, biological monitoring of pollutants is of great importance in toxicological studies for assessing human exposure through natural and anthropogenic sources. Biological monitoring usually involves collecting fluids and tissues from the human body and analyzing them to identify the chemicals or their metabolites16,17. There are several biomarkers to identify and evaluate human exposure monitoring to arsenic and its compounds. Blood, urine, hair, and nails have been identified as easily accessible biomarkers to assess arsenic exposure in epidemiological studies17. Among these bioindicators, the amount of arsenic measured in blood and urine samples indicates recent intake of arsenic, on the order of approximately four days in the urine samples and 2–6 h in the blood samples18. On the other hand, the need to freeze collected urine samples, the invasive nature of blood

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To achieve the precision of data, the arsenic levels in groundwater, fingernails, standard solutions (standard solution Fluka-51844, Sigma–Aldrich, Switzerland), and blank samples were examined in triplicate. In all repeated measurements, a relative standard deviation of 5–10% was achieved during the experiments. Furthermore, to further verify the results, no human fingernail-certified reference material was available for comparison.

**Statistical analysis.** In the present study, SPSS V.16.0 software was used to perform statistical calculations of the data with a significant level at $p < 0.05$. To check the normality of the data, the One-Sample Kolmogorov–Smirnov test was applied. Because the concentration of arsenic in fingernail samples was not normally distributed, non-parametric statistical tests such as Mann–Whitney U test were used to find significant differences between the groups of participants. The Chi-square test was applied to compare the distribution for...
the categorical variables such as BMI, gender, and smoking habits in the two reference and exposed groups. Also, an independent t-test was used to compare the age variable in the two reference and exposed groups. The association between arsenic concentration in groundwater and fingernail samples was evaluated using single and multiple linear regression models adjusted for age, BMI, gender, and smoking habits. Descriptive statistics including maximum, minimum, average, and standard deviation of arsenic concentration in fingernail samples were calculated using Excel 2013 Software (Microsoft Office).

Consent to participate. All of the authors in this paper are acknowledged and listed as contributors, and they confirm the final version of the manuscript.
Results
In the present study, the fingernail samples were used as a biomarker to assess human exposure to arsenic via drinking water consumption in individuals who lived in the arsenic-contaminated areas. It should be pointed that the individuals were allocated into the reference group (areas D, E, and F) with levels of 0.179 μg/L arsenic and the exposed group with different concentrations of arsenic in groundwater sources (region A = 200 μg/L, region B = 76.6 μg/L, and region C = 74.5 μg/L). To do this research, we collected 89 fingernail samples, of which 40 samples were from the participants living in arsenic-contaminated villages and the rest from those having no exposure to arsenic. Table 1 represents arsenic levels (μg/g) in the fingernail samples of the participants collected from exposed and reference villages of Kaboudrahang County. According to the results, the mean values of arsenic in fingernail samples of 1.78 μg/g with a range of 0.13–10.33 μg/g was observed in the exposed regions of the area studied compared to those from the reference areas (0.43 μg/g, with a range of 0.1–1.21 μg/g). This means that the average, minimum, and maximum concentrations of arsenic in the fingernail samples were higher in the participants living in arsenic-contaminated areas than in those living in areas without arsenic exposure. According to the results of the present study, in the villages exposed to arsenic via drinking water, 85% of the fingernail samples contained arsenic above the normal level, while in the villages without arsenic exposure, 28.57% of the fingernail samples had arsenic concentration higher than normal value.

The general properties of the participants studied, including age, gender, BMI, and smoking habits have been summarized in Table 2. As can be seen, the age average in the arsenic exposure group (34.8 ± 10.39 years) was significantly higher than that in the reference group (29.51 ± 10.8 years) (p = 0.022). Also, there was no significant difference between the two groups in terms of variables such as gender, smoking, and BMI (p > 0.05). A significant difference was shown between arsenic levels in drinking water and the fingernail samples in two exposed and reference groups of the area (p < 0.001) (Table 2).

The results of the association between arsenic levels in drinking water sources and fingernail samples by using crude linear regression models have been depicted in Table 3. In the simple linear regression model, a significant relation was shown between the concentration of arsenic in fingernail samples with variables including gender (p = 0.019) and oral intake of arsenic through contaminated drinking water (p < 0.001). The results showed that females had significantly lower concentrations of arsenic in the fingernail samples (β = −0.248, 95% CI = −0.843,

Table 1. Summary statistics for arsenic concentrations (μg/g) in fingernail samples. *Normal level of arsenic in nail samples ranges from 20 to 500 μg/kg22.

| Variable       | Exposed area | Reference area |
|----------------|--------------|----------------|
| Minimum        | 0.13         | 0.10           |
| Maximum        | 10.33        | 1.21           |
| STDEV          | 2.21         | 0.23           |
| Average        | 1.78         | 0.43           |

Table 2. The studied variables in the two exposed and referenced groups. SD standard deviation.

| Variables       | Exposed participants | Reference participants | p-value |
|-----------------|-----------------------|-------------------------|---------|
| Age (Mean ± SD) | 34.8 ± 10.39          | 29.51 ± 10.8            | 0.022a  |
| BMI, N (%)      | 5 (12.5)              | 7 (14.4)                | 0.66b   |
| < 18.5          | 21 (52.5)             | 21 (42.8)               |         |
| 18.5–24.9       | 14 (35)               | 21 (42.8)               |         |
| Gender, N (%)   | 23 (57.5)             | 28 (57)                 | 0.973b  |
| Female          | 17 (42.5)             | 21 (43)                 |         |
| Smoking, N (%)  | 7 (17.5)              | 7 (14.3)                | 0.679b  |
| Yes             | 33 (82.5)             | 42 (85.7)               |         |
| No              | 1.78 ± 2.21           | 0.43 ± 0.23             | < 0.001c|

*Independent-samples T-test. bChi-square test. cMann–Whitney U test.
some areas. According to the results of the present study, the average, minimum, and maximum concentrations of arsenic in toenail samples and drinking water supplies, which is consistent with the findings of our study. The geological structure of the study area, which comprised limestone, Jurassic sandstone, marl, metamorphic rocks, and shale. Also, most portions of the area belong to the northwestern part of the Sanandaj-Sirjan zone and the southwestern part of the Zagros thrust belt. Another reason for arsenic contamination in drinking water sources is the proximity of the area to Kurdistan Province, where the presence of arsenic in drinking water sources has been reported in some areas. According to the results of the present study, the average, minimum, and maximum concentrations of arsenic in the fingernail samples were higher in the participants living in arsenic-contaminated areas than those living in areas without arsenic exposure. Spatial variations and regional distribution of arsenic contents in toenail samples and drinking water supplies of Nova Scotia in Canada were examined by Dummer et al. They also assessed the geological and environmental characteristics related to high concentrations of arsenic in drinking water sources. Based on the findings of this study, the levels of arsenic in drinking water samples were less than the detection limit of the method (478 µg/L). In their research, they stated that the contamination of drinking water sources with arsenic originated from the geological structure of the study area. Also, in this research close associations were observed between the high levels of arsenic in toenail samples and drinking water supplies, which is consistent with the findings of our study. According to the results, in the villages exposed to arsenic, 85% of the fingernail samples contained arsenic above the normal level, while in the villages without arsenic exposure, 28.57% of the fingernail samples had arsenic concentration higher than normal value. The observations of a study by Chakraborti et al., who analyzed the concentration of arsenic in 176 biological samples (hair, urine, and nail), indicated that 69 participants had skin lesions caused by arsenic exposure, and the rest did not have arsenical skin lesions. In this study, normal arsenic levels in hair, nail, and urine samples were reported to be 20–200 µg/kg, 20–500 µg/kg, and < 100 µg/L, respectively. They found that 100% of the biological samples had an arsenic concentration above normal values. In the multivariate linear regression model adjusted for age, gender, BMI, smoking, and exposure to arsenic, the variables including gender and arsenic levels in drinking water were significantly associated with fingernail sample arsenic (p < 0.05). Moreover, in this stage, a 1% increase in groundwater arsenic was associated with a 56% increase of arsenic in the fingernail samples. The arsenic concentration in the fingernail samples of the female participants was lower than those in male participants (β = − 0.248). Also, no statistically significant relationship was found between arsenic concentration in the fingernail samples and variables like age, BMI, and smoking. However, similar to the findings achieved in simple linear regression, with increasing age (β = 0.199), smoking (β = 0.152), and decreasing BMI (β = − 0.125), the arsenic concentration of the fingernail samples increased.

### Discussion

In recent decades, the study on biological monitoring in epidemiological and toxicological research to assess the risk of human exposure to pollutants from different routes has been of great importance. In this regard, due to the widespread occurrence of arsenic in the environment and drinking water sources, as well as its potential for adverse effects on human health, biological monitoring is used as a valuable tool to assess exposure to arsenic through natural and anthropogenic pathways.

The main source of groundwater contamination with arsenic could be attributed to the geological structure of the study area, which comprised limestone, Jurassic sandstone, marl, metamorphic rocks, and shale. Also, most portions of the area belong to the northwestern part of the Sanandaj-Sirjan zone and the southwestern part of the Zagros thrust belt. Another reason for arsenic contamination in drinking water sources is the proximity of the area to Kurdistan Province, where the presence of arsenic in drinking water sources has been reported in some areas. According to the results of the present study, the average, minimum, and maximum concentrations of arsenic in the fingernail samples were higher in the participants living in arsenic-contaminated areas than those living in areas without arsenic exposure.

### Table 3. Variables associated with the concentration of arsenic in fingernails. CI confidence interval.

| Variables          | β   | Lower  | Upper  | p-value | Variables          | β   | Lower  | Upper  | p-value |
|--------------------|-----|--------|--------|---------|--------------------|-----|--------|--------|---------|
| Age                | 0.199 | 0.00   | 0.035  | 0.062   | Age                | 0.152 | 0.007  | 0.033  | 0.2     |
| BMI                | −0.125 | −0.069 | 0.018  | 0.242   | BMI                | −0.152 | 0.077  | 0.015  | 0.184   |
| Gender             | −0.248 | −0.843 | −0.078  | 0.019*  | Gender             | −0.208 | −0.748 | −0.023 | 0.037*   |
| Smoking            | 0.192 | 0.043  | 1.011  | 0.071   | Smoking            | 0.002 | 0.513  | 0.525  | 0.982   |
| Exposure to arsenic| 0.595 | 0.781  | 1.413  | <0.001* | Exposure to arsenic| 0.558 | 0.709  | 1.348  | <0.001*   |

*p-value < 0.05.*
present study. The concentration of arsenic in biological samples was lower in females, which is consistent with the findings of others. Also, they reported that females had a higher methylation capacity than males, so the concentration of arsenic in biological samples was higher in males, older, and participants with skin lesions.

The results of their investigation represented that the concentration of arsenic in nail samples in different studies are reported in Table 4.

To study exposure to environmental pollutants is on the rise. It should be noted that the levels of measured arsenic in nail samples in different studies are reported in Table 4.

Table 4. The concentration of arsenic in nail samples collected from different studies.

| Arsenic in nail samples | Range (µg/kg) | References |
|------------------------|---------------|------------|
| Ganga plain, India     | 1254–202.20   | 22         |
| Hetao Basin, Inner Mongolia | 84–1290      | 24         |
| Shahpur block, Bihar state, India | 469–36,520 | 24         |
| Nadia district, West Bengal, India | 80–36,840 | 23         |
| Middle and Lower Ganga plain | 6.1–24       | 25         |
| Majuli, Assam, India   | 426–11,725    | 26         |
| Present study          | 0.13–10.33    |            |

Conclusion

The present study results showed that the use of the fingernail samples as a biomarker to evaluate arsenic exposure through ingestion of drinking water was appropriate. Nail samples contain high amounts of scleroproteins (like keratin) and sulfhydryl groups; it should be pointed out that arsenic has a strong affinity for binding to these sulfhydryl groups. Also, due to the feeding of germinal nail matrix from a rich blood source, arsenic deposition in nail samples occurs shortly after consumption. It can be concluded that because of the slow growth rate, less probability of external pollution compared to other biomarkers (like hair samples), easier collection, and non-invasive properties, the use of nail samples (fingernail and toenail samples) as a suitable biomarker to study exposure to environmental pollutants is on the rise. It should be noted that the levels of measured arsenic in nail samples in different studies are reported in Table 4.

Study limitations. There are several major limitations in the current study that should be noted. First, due to financial constraints, the number of fingernail samples analyzed was small, thereby reducing the accuracy of our analysis. Second, we did not investigate the relationship between arsenic concentrations in drinking water sources and other biomarkers such as hair, urine, blood, and agricultural products. Third, we only measured the values of total arsenic in fingernail samples and did not specify the values of organic and inorganic arsenic separately. The present study attempted to investigate the relationship between arsenic concentrations in drinking water sources and fingernail samples as biomarkers, but future studies with more samples size are required.
to investigate the relation of arsenic bioaccumulation (accumulation in hair, urine, saliva, and blood samples), diet and health.

Data availability
All of the data have been reported in the main manuscript body.

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**Author contributions**

R.S.: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, and Writing—original draft, Writing - review & editing, Supervision, Funding acquisition, Project administration. Mo.K.: Methodology, Validation, Formal analysis, Writing—review & editing. Ma.K.: Methodology, Validation, Formal analysis, Writing—review & editing. A.S.: Writing—review & editing. S.K.: Formal analysis, Writing—review & editing. Z.T.: Conceptualization, Methodology, Validation, Formal analysis, Resources, Writing—original draft, Writing - review & editing. All authors reviewed the manuscript.

**Competing interests**

The authors declare no competing interests.

**Additional information**

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