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The Relationship between Exposure to Arsenic in Drinking Water and the Prevalence of Diabetes Mellitus in Two Urban Populations in the Southeastern Areas of Iran

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ABSTRACT

Introduction: Chronic exposure to Arsenic (As) can increase the risk of *diabetes mellitus*. This study aims to determine the relationship between exposure to the As by drinking water and the prevalence of diabetes mellitus in two urban populations of Rafsanjan and Kashkuyeh, Iran, in 2020.
Materials and Methods: In this research, 120 participants from Rafsanjan and Kashkuyeh were recruited and divided into four groups. The first two groups have lived in Rafsanjan and Kashkuyeh for the past 10 years, and the second two groups have lived in these two cities for less than a year. Individuals with two episodes of fasting blood glucose (FBG) ≥ 126 mg/dl were considered to have diabetes.
Results: As was found in high levels in all samples (10 samples) in Rafsanjan and 55% of samples (10 samples) in Kashkuyeh. The prevalence of diabetes was significantly higher in people with a residence duration of more than 10 years ($p = 0.038$). The analysis of Multiple Logistic Regression model demonstrated that the chance of developing diabetes in people who had lived in either city for more than 10 years was almost 5.7 times higher than others (OR = 5.79; P = 0.003). Also, the chance of developing diabetes was 91% higher in people who had lived in Rafsanjan compared with Kashkuyeh, and 91% higher in men than in women (OR = 1.915; P = 0.215).
Conclusion: Chronic exposure (≥ 10 years) to high levels of As by drinking water can increase the risk of diabetes, and future research is needed in this regard.

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Introduction

Nowadays, pollution of water resources with heavy metals due to natural geological changes and human activity (such as agriculture, industry, and mining) has become a major problem in most countries [1, 2]. Arsenic (As) is one of the most toxic heavy metals and an important pollutant of water resources [3]. As contamination of water resources

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has been reported in many parts of the world, especially in Southeast Asian countries, such as India, Bangladesh, Taiwan, and Iran [4-6]. Exposure to As occurs mainly by drinking and eating contaminated water and food [7], and more than 200 million people worldwide are exposed to As-contaminated drinking water [6]. Long-term exposure to As can have adverse carcinogenic and non-carcinogenic effects on human health [8]. The most important non-carcinogenic effects of long-term exposure to As by drinking water include adverse health effects on the nervous system and the reproductive system, cardiovascular disease (CVD), hypertension, and diabetes [9-11]. As triggers gluconeogenesis, apoptosis, and destruction of pancreatic beta cells. It also reduces insulin secretion, and inhibits insulin-dependent glucose uptake, which corresponds to the pathogenesis of diabetes mellitus [12, 13]. In addition, acute As poisoning can cause complications such as general muscle weakness, loss of appetite, nausea, inflammation of the mucosal membranes of the eyes, nose, and larynx, and skin lesions [14].

Diabetes mellitus is a metabolic disease, which occurs due to insufficient production of insulin by the pancreas or insulin resistance and leads to chronic hypoglycemia [15]. This disease can cause symptoms such as frequent urination, overhydration, and weight gain or weight loss, and could lead to complications such as diabetic ketoacidosis, hyperosmolar coma, major vascular disorders such as kidney failure, heart disease, stroke, diabetic foot ulcer, and vascular disorders such as retinopathy and neuropathy [15, 16]. Therefore, diabetes mellitus is a major global public health concern and an important cause of death [17]. The prevalence of diabetes and its associated complications depend on various factors and vary in different parts of the world. Due to its rapid increase in Iran, its prevalence is estimated to double during 2011-2030 [18]. The best way to prevent any further increase in the prevalence of this disease and its subsequent complications is to change people's lifestyle, in such ways as proper nutrition and regular exercise [19]. Factors related to this disease include age, obesity [20], place of residence, and economic and cultural factors [21]. Although most cases of diabetes in western countries are reported in old age, the prevalence of this disease in Iran is higher in middle-aged people, who are active productively and economically [20].

One of the most important factors associated with diabetes is environmental exposures such as air pollution, and drinking water pollution [22]. Prolonged consumption of As-contaminated drinking water increases the risk of diabetes and its complications [13, 23]. Therefore, due to the importance of regional research in this area, this study was conducted to investigate the relationship between As in drinking water and prevalence of diabetes in two urban populations of Rafsanjan and Kashkuyeh in the southeastern region of Iran. The results can help control this factor in this area and prevent an increase in diabetes by providing accurate results.

Materials and Methods

Study area and sample collection

In this cross-sectional study conducted in Rafsanjan and Kashkuyeh in the southeast of Iran in 2020, 120 participants were selected and divided into four groups. The sampling size for comparing the prevalence of diabetes in two urban populations of Rafsanjan and Kashkuyeh was based on the following equation:

$$n = \frac{2(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \bar{P}(1-\bar{P})}{(P_1 - P_2)^2}; \ \bar{P} = \frac{P_1 + P_2}{2}$$

where, P_1 is the prevalence of diabetes in Rafsanjan according to a previous study [24], which reported a prevalence of 24%; P_1-P_2 is the difference of diabetes rates in the two investigated areas, which is equal to 0.18. Finally, the sample size for each region was calculated as 60 people with a confidence level of 95% and statistical power of 80%.

The first two groups have lived in Rafsanjan and Kashkuyeh (with similar living conditions, but different As concentration in drinking water compared to Rafsanjan) for the past 10 years, and the second two groups have lived in these two cities for less than a year and have migrated to these cities from other provinces. Their age range was ≥ 45 years. They had no history of special diseases, and

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they were selected randomly at 12-16 o'clock on three different days with a three-day interval from among people who were walking in the central roundabout of the city. Also, in order to equalize the living conditions and lifestyle, people were interviewed; those who had similar living conditions, lifestyle, and eating habits were selected.

Sample containers (polyethylene bottles) were washed with 1% nitric acid and double-distilled water. For drinking water sampling, 30 seconds after opening the water tap, 5 samples were collected from the beginning of the water distribution network and 5 samples from the end of the distribution network in both cities (totally 20 samples). Water storage bottles were filled to the brim and had no space for air.

Diabetes and As detection

Blood samples were taken from all subjects after 8 to 10 hours of fasting between 7 and 9 am. Individuals with diabetes mellitus with or without fasting blood glucose (FBG) ≥ 126 mg/dl were considered to be diabetic [25]. They were instructed not to take blood sugar medications during the month leading to sample collection. FBS was measured by Medisign MM1100 device, which was calibrated before starting the tests.

For As detection, one mLof 1% nitric acid was added to every 100 mL of water sample to stabilize the pH below 3. After stabilizing the pH, 20 final samples were transferred to the Laboratory of Valiasr University of Rafsanjan, Iran, for As analysis by graphite furnace Atomic Absorption spectrophotometry (990 AAS NORDANTEC, China).

Statistical analysis

Data were analyzed by SPSS software (version 18). Quantitative data were reported as mean and standard deviation, and qualitative data were expressed as a percentage. Using a cut-off point of 126 for FBS, the participants with values above this level were considered diabetic, and the number of diabetic patients was reported as low and high in terms of the duration of residence, and gender was reported as a graph. Furthermore, blood glucose levels in the two regions were compared using an independent t-test. Multiple Logistic Regression was used to evaluate the effect of various factors such as gender and place of residence on the incidence of diabetes. The significance level in all tests was set at 0.05.

Ethical Issues

This article is a graduate degree thesis, with the code of ethics: IR.PNU.REC.1399.030.

Results

In this study, 30 participants from each group were randomly selected with an equal gender distribution. In terms of age, 56.7% were in the age group 45-50 years, 20.8% were in the age group 50-55 years, 12.5% were in the age group 55-60 years, and 10.0% were in the age group ≥ 60 years. Mineral water consumption was low among the participants, and almost all of them used tap water (Table 1).

Table 1: Demographic information of the participants

Groups	TRM	TRF	NRM	NRF	TKM	TKF	NKM	NKF
Number	15	15	15	15	15	15	15	15
Age								
45-50	9	7	7	8	10	9	10	8
50-55	5	3	5	4	1	2	4	1
55-60	0	2	1	3	4	1	1	3
≥ 60	1	3	2	0	0	3	0	3
Bottled mineral water consumption								
Always	0	0	0	0	0	0	0	0
Minimum 5 days/week	0	0	0	0	0	0	0	0
Minimum 3 days/week	0	0	0	0	0	0	0	0
Minimum once a day	1	1	0	1	0	0	1	0

TRM*: Men living in Rafsanjan for more than 10 years; **TRF***: Women living in Rafsanjan for more than 10 years; **NRM***: Men living in Rafsanjan for less than 1 year; **NRF***: Women living in Rafsanjan for less than 1 year; **TKM***: Men living in Kashkuyeh for more than 10 years; **TKF***: Women living in Kashkuyeh for more than 10 years; **NKM***: Men living in Kashkuyeh for less than 1 year; **NKF***: Women living in Kashkuyeh for less than 1 year

At the end of FBS tests, 6 out of 15 (40%) men living in Rafsanjan for more than 10 years had high FBS, which was a very large number for any population. For women living in Rafsanjan for more than 10 years, this rate was 4 out of 15 (26%), which was a similarly large number and higher than the predictions. In both groups of men and women living in Rafsanjan for less than 1 year, this rate was much smaller and was about 13% in men and 6% in women. The diabetes rate was 26% in men and 20% in women living in Kashkuyeh for more than 10 years. These statistics may be lower than those of Rafsanjan, but they are still high compared to national and global rates. Men and women living in Kashkuyeh for less than 1 year were among those with the lowest number of diabetes, which was only one case in the first group (6%) and zero case in the second group (Table 2). The results show, that people with more than 10 years domicile have a higher incidence of diabetes. In contrast, residents who have lived in these cities for less than a year have the lowest incidence of diabetes (Table 2).

Table 2: Comparison of diabetes rates in the areas by different groups

Blood glucose	TRM	TRF	NRM	NRF	TKM	TKF	NKM	NKF
< 126 mg/dl	9	11	13	14	11	12	14	15
≥ 126 mg/dl	6	4	2	1	4	3	1	0

Significance level $p < 0.05$

Arsenic was found in the water samples of both cities, which was 100% in Rafsanjan and 55% in Kashkuyeh. The highest level of contamination (41 μg/L) was obtained in Rafsanjan, which is four times greater than the World Health Organization (WHO) standard (10 μg/L). Also, the mean concentration of As was about twice greater than the standard level, indicating severe As contamination in the drinking water of Rafsanjan. Kashkuyeh had not good condition in terms of water health, as the mean concentration of As was 12 μg/L. In the highest detection rate, As contamination was 22 μg/L, which is twice greater than the standard level. These results showed that drinking water in both cities is severely contaminated with As, and this contamination rate is higher in Rafsanjan. All diabetic samples also live in As-contaminated areas (Table 3).

Table 3: Comparison of As contamination rates in Rafsanjan and Kashkuyeh

Variables	Rafsanjan	Kashkuyeh
Mean As concentration (μg/L)	18	12
Maximum As concentration (μg/L)	41	22
Number of samples above allowable limit (%) (10 μg/L)	100%	55%

Significance level: $p < 0.05$

The independent t-test was used to compare the amount of As and FBS. Long years of residence in the As-contaminated areas showed a significant difference ($p = 0.038$). In other words, there was a significant relationship between years of residence and As contamination (Table 4).

Table 4: The relationship between As levels and the number of diabetic people in each city

Variables	Rafsanjan	Kashkuyeh
Number of diabetic people living in As-contaminated areas	13	8
Mean FBG level of diabetic people living in As-contaminated areas mg/dl	139	137

Significance level: $p < 0.05$

The analysis of Multiple Logistic Regression model is provided in Table 5. According to the results of this model, the chance of developing diabetes in people who were in Rafsanjan was 91% higher than those who lived in Kashkuyeh (OR = 1.915; P = 0.215). The chance of developing diabetes in people who have lived in both cities for more than 10 years is almost 5.7 times higher than people who have lived less than a year (OR = 5.79; P = 0.003). Also, the chance of developing diabetes in men was 91% higher than the chance in women (OR = 1.915; P = 0.215).

Table 5: The analysis of Multiple Logistic Regression model

Variables	B	SE	OR	P-value
City of residence (Rafsanjan compared to Kashkuyeh)	0.650	0.519	1.915	0.210
Duration of residence (more than 10 years compared to less than a year)	1.756	0.600	5.790	0.003
Gender (men compared to women)	.650	0.519	1.915	0.210
Constant	-3.379	0.705	0.034	0.000

Discussion

Presence of As in the water resources, especially in the southeastern areas of Iran, is relatively higher than the WHO standard level (10 µg/L). This can be due to various reasons such as the geological properties, use of As-containing pesticides and herbicides, and lack of sewage treatment systems for metal and non-metal industries [2]. Arsenic is present in the environment and the human body as inorganic and organic compounds and can lead to DNA damage, lipid peroxidation, and reduced antioxidant defenses [26]. Arsenic can also increase cancer in some organs and cause non-cancerous side effects [27]. Non-cancerous effects of oral As include clinical manifestations in the gastrointestinal, cardiovascular, pulmonary, immunological, neurological, endocrine, and dermal systems [28].

In this study, As was found in all water samples of Rafsanjan and in 55% of water samples of Kashkuyeh, indicating that Kashkuyeh has better conditions than Rafsanjan both in terms of As contamination and diabetes. In previous studies conducted in the southeast of Iran, As contaminated water resources were confirmed [2, 29]. This can be due to geological properties, weathering, and oxidation of mineral rocks, and release of heavy metals, especially As, in this region [2]. Also, mining activities, such as cooper industries, and agricultural activates in this area can release As into the water resources [30].

This study also indicated that the prevalence of diabetes was higher in people who lived in the area for more than ten years and drank As-containing water, indicating the chronic effect of As on diabetes. These results are consistent with those of many domestic and international studies on human and non-human samples. In an experimental study by Sertorio et al. on mice with diabetes in 2019, the prevalence of diabetes was 6.8% in the As-contaminated group, and 5.8% in the non-contaminated group [31]. On the other hand, Chen et al. evaluated the relationship between Arsenic exposure through drinking water and blood pressure using data from 10,910 participants in Bangladesh. They concluded that the effect of low As exposure on blood pressure was nonlinear and might be more pronounced in people with lower food intake related to As metabolism and cardiovascular health [32]. Navas et al. also conducted cross-sectional studies to evaluate the association between oral As exposure through oral consumption and the prevalence of type II diabetes in urinary specimens of adults in the United States. They evaluated 788 adults aged 20

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years and older and reported urinary levels of 1.7, 0.3, and 0.9 mg/l for total As, dimethyl arsenate, and arsenobetaine, respectively. The prevalence of type II diabetes was 7.7%. After moderating the risk factors for diabetes and seafood consumption markers, the total As level was 26% higher in participants with type II diabetes than in non-diabetic participants. Dimethyl arsenate level was 10% higher in diabetic participants than in non-diabetic participants. Arsenobetaine levels were also similar in both groups [33]. Moreover, in a study evaluating the association of urinary As concentration with the incidence of diabetes in Native Americans, Kim Hee Nan et al. compared 150 non-diabetic subjects aged 25 years and older, who subsequently developed type II diabetes, with 150 subjects who remained non-diabetic for 10 years or more. They found that a moderate increase in exposure to inorganic As might be a predictor of type II diabetes in Native Americans [34].

In addition, the results of some studies suggest that several risk factors for diabetes in individuals may be similar to risk factors for As-induced diabetes. In a study by Eick et al. in Chile in 2019, the prevalence of As-induced diabetes was higher in people with lower socioeconomic status [32]. In another study in this country, exposure to As increased the incidence of diabetes, which has a significant relationship with increased Body Mass Index (BMI) [35]. Another factor is the type of nutrition. In a study by Grau-Perez et al. in Spain, serum and urinary Arsenic levels in the general population, especially in those who consumed seafood, were directly correlated with the prevalence of diabetes [36]. Another link between As and diabetes was found in a study by Khan et al. in Bangladesh, as exposure to As and the presence of As in the urine of pregnant women increased the risk of gestational diabetes by a factor of 9.4, which highlights the importance of the relationship between these two factors in pregnant mothers [37]. Despite studies confirming the association between As and diabetes, several studies have reported results that are inconsistent with the results of the present study. Sripaoraya et al. reported no significant relationship between the As level of drinking water and the prevalence of diabetes in Thailand in 2017, though diabetes was found to be directly correlated with age and BMI [38]. In addition, in the study of Akinloye et al., although serum cadmium and lead levels were significantly higher in diabetic patients than in healthy individuals, this relationship was not significant for As [39].

In general, it can be argued that the prevalence of diabetes has been increasing in recent decades, and this trend is expected to continue [22]. The results of the present study and many other studies have indicated the relationship between As levels and the prevalence of diabetes. Since the study area in the present research is exposed to As-containing groundwater, further studies are required to provide more accurate results and strategies to prevent an increase in the prevalence of As-induced diabetes.

Conclusion

The findings of the present study showed that the drinking water of Rafsanjan and Kashkuyeh cities contains As, and the prevalence of diabetes is higher in the residents who have used the drinking water of these areas for a longer period. The chance of developing diabetes in people who have lived in both cities for more than 10 years is almost 5.7 times higher than others (OR = 5.79; P = 0.003). Therefore, it is important to provide appropriate solutions to reduce the prevalence of As-induced diabetes in this region.

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Conflict of interest

The authors declare that they have no conflict of interest.

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