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Spatial variation and probabilistic risk assessment of exposure to fluoride in drinking water

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1. Introduction

About 80% of the world’s diseases are related to poor water quality, and contamination of drinking water to fluoride accounts for 65% of endemic fluorosis (Felsenfeld and Roberts, 1991; WHO, 2002; WHO, 2011; Karami et al., 2017; Miri et al., 2017; Mohammadi et al., 2017a). Fluoride can be dissolved in water through presence in the soil and increase its concentration in groundwater (Farooqi et al., 2007). The concentration of fluoride in water depends on numerous factors including pH, total solids, alkalinity and hardness (Subba Rao et al., 1998; Karthikeyan and Shunmugasundarraj, 2000; Baghani et al., 2017; Dehghani et al., 2017; Rostamia et al., 2017). A small amount of fluoride is necessary to form bones, enamel and to prevent tooth decay. On the other hand, too much fluoride can damage bones and teeth in children and adults (Petersen, 2004; Jones et al., 2005; Paudyal et al., 2012; Cai et al., 2015; Podgorny and McLaren, 2015; Khorsandi et al., 2016). Fluoride can have destructive effects on the structure, function, and metabolism of soft tissues such as the kidney, liver, lung and testicles (Barbier et al., 2010; Yang and Liang, 2011; Zhang et al., 2016). It is also responsible for reducing intelligence quotient (IQ) in children (Tang et al., 2008). High levels of fluoride have neurotoxicological effects as well as potential for skeletal cancer (Bassin et al., 2006; Choi et al., 2012). The World Health Organization has set the permissible fluoride in drinking water from 0.5 to 1.5 mg/l (Barathi et al., 2014; Cai et al., 2016). Although more than 200 million people in the world use fluorides in excess of 1.5 mg/l (Yadav et al., 2013). The US Public Health Service has set the optimum concentration of fluoride in drinking water at 0.7 mg/l (Kohn et al., 2001). Drinking fluoride-containing water and its potential health consequences continue to be a health problem, especially in developing countries (Huang et al., 2017). High concentrations of fluoride
have been reported in different countries of the world, such as China, India and parts of Africa (Sun et al., 2013; Vithanage and Bhattacharya, 2015). In Iran, high concentrations of fluoride are reported in some central and southern cities such as Bushehr, Khozestan and Poldasht where drinking water is supplied through groundwater (Battaleb-Looie et al., 2013; Mohebbi et al., 2013; Abtahi et al., 2015; Mohammadi et al., 2017b). Health risk is one of the assessment methods that perform risk assessment based on input data such as chemical concentration and other risk model parameters. This assessment method can examine the real risk, especially in areas where low risk is considered (Lonati and Zanoni, 2012; Alahabadi et al., 2017). The Monte Carlo simulation is one of the probabilistic approaches used for risk analysis with a realistic risk assessment approach for chemicals (Lonati et al., 2007; Miri et al., 2016b; Fallahzadeh et al., 2017). In Monte Carlo method, the random values of the range of variables are repeated in the calculation of risk, and ultimately the risk domain is defined in the output (Morisset et al., 2013). This method has been widely used in various studies to assessment the potential risk and evaluates the risk of contaminants in water and other environments (Wu et al., 2011; Niizuma et al., 2013; Peng et al., 2016; Huang et al., 2017).

Geographic Information System (GIS), and its application software ArcGIS, is one of the suitable tools for displaying the spatial and temporal distribution of drinking water quality parameters in the space between two points with specified values (Abokifa et al., 2016; Miri et al., 2016a; Mokhtari et al., 2016; Gholizadeh et al., 2017; Hajizadeh et al., 2017). In this study, fluoride concentration of drinking water supply wells in 6 cities of Yazd province were evaluated. After determining the concentration of fluoride, risk assessment, sensitivity analysis and uncertainty in tree age groups (children, teens and adults) were carried out for non-carcinogenic risk assessment and also the most important variable in determining non-
carcinogenic risk. The spatial analysis of fluoride concentration was performed to investigate spatial distribution of fluoride concentration in studied areas using GIS software.

2. Material and methods

2.1. Study area, sampling and analysis

Yazd province is located in the center of Iran. Yazd province has a hot-dry weather with an annual mean temperature of 18.9 °C. The counties studied included Ardakan, Ashkezar, Mehriz, Meybod, Yazd and Taft. Figure 1 shows the geographic location of the studied areas.

For this study, 269 drinking water supply wells in 6 counties in Yazd province were sampled in 4 cycles (1 sample each season) from 23 March 2015 to 23 March 2016. Sampling information is given in Table 1. The samples were collected from all wells that used as supply of drinking water in study area. For this aim a 1 L polyethylene container washed twice with distilled water and used for water sampling. Then samples were labeled and transferred to the lab in 4 C° for analyses. Samples were analyzed within 24 h after collection at the School of Public Health laboratory, using a flame atomic absorption spectrometer (FAAS, Spectra model AA-20, Varian, Australia). For this aim firstly 8 standard of fluoride concentration (rage from 0.01 to 5 mg/l) were made and injected to FAAS for calibration it. After that every sample injected to FAAS three times and the results which have a standard division (SD) more than 1, repeated again. The limit of detection (LOD) of fluoride was 0.01 mg/l , and all samples have concentration more than LOD.

2.2. Health risk assessment
In this study, three populations of 3 to 10 years old, 11 to 20 years old and 21 to 72 years old were selected to evaluate the health risks of the population in the studied cities and the health risk potential for these three groups was investigated.

In this study, the daily exposure to fluoride by drinking water was estimated using the equations 1 and 2 introduced by USEPA (1989)(EPA, 1989).

\[ EDI_{\text{ing}} = \frac{C_w \times IR_w \times EF \times ED}{BW \times AT} \]  

(1)

\[ EDI_{\text{durm}} = \frac{C_w \times SA \times K_p \times F \times ETs \times EF \times ED \times 10^{-3}}{BW \times AT} \]  

(2)

In this regard, \( EDI_{\text{ing}} \) estimates daily intake of fluoride consumed per day by drinking water and \( EDI_{\text{durm}} \) estimates the amount of fluoride received by skin absorption based on mg/kg/day. \( C_w \) is the concentration of fluoride in drinking water in mg/l, \( IR_w \) is the drinking water ingestion rate based on L/day, \( EF \) is the exposure frequency based on Day/year, \( ED \) is the exposure duration in terms of years, \( BW \) is the body weight in Kg, \( AT \) is the averaging time in days, \( SA \) is the surface area of skin in terms of Cm\(^2\), \( K_p \) is the coefficient of skin permeation (Cm/h), \( F \) is the fraction of the contact surface of the skin with water (without unit) and \( ETs \) is the exposure time when showering (h/day).

The Hazard quotient (HQ) of the non-carcinogenic risk estimate for fluoride exposure through drinking water and dermal exposure is calculated using equation (3).

\[ HQ = \frac{EDI}{RfD} \]  

(3)

\( RfD \) in this equation expresses the reference fluoride dose by a specific exposure pathway in mg/Kg/day. Based on the USEPA’s Integrated Risk Information System (IRIS) database, the amount of \( RfD \) through oral contact and drinking water consumption is 0.06 mg/kg/day(Huang et
There is no a dose reference available for fluoride skin exposure, but USEPA has introduced a method for converting a drinking reference dose into a reference dose of skin exposure. RfD_{derm} can be calculated from the following equation (Staff, 2001):

\[ RfD_{derm} = RfD_0 \times ABS_{gi} \]  

In this equation, the RfD_{derm} is the dermal reference dose, RfD_0 is the drinking reference dose (mg/kg/day), and ABS_{gi} indicates the digestive absorption factor.

Also HQ_{overall} was calculated as follow:

\[ HQ_{overall} = HQ_{ing} + HQ_{derm} \]  

### 2.3. Monte Carlo simulation and sensitivity analysis

When using a single-point value of a variable in the assessment of risk for a population, the probability of interference and error, and eventually the uncertainty of the result, is achieved. Therefore in this study, Monte Carlo simulation was used to minimize uncertainty (Huang et al., 2017). In Monte Carlo simulation, instead of using a single-point value of a variable, a range of variable value is used, and the calculation is repeated several times, and finally, the results achieved with different degree of assurance between 1 to 99 percent. In the Monte Carlo simulation, sensitivity analysis is also performed to determine the variable that has the greatest impact on the outcome of the risk assessment. In this study, Crystal Ball (version 11.1.1.1, Oracle, Inc., USA) was used to simulate Monte Carlo and perform sensitivity analysis with 1000 trails. The variables used in the model were based on previous studies for three age groups of children, teens and adults (Table 2).

### 2.4. Fluoride Spatial Distribution
In this study, ArcGIS 10.4.1 software (Esri, Berkeley, CA, USA) was used for spatial and
temporal distribution of fluoride in the studied areas. The inverse distance weighting (IDW)
method was used to prepare a fluoride zoning map. IDW is an algorithm that uses interpolation
of data in a spatial form to predict the value of a variable based on the weighted mean of each
parameter and the distance between the points (Mokhtari et al., 2016; Gholizadeh et al., 2017;
Hajizadeh et al., 2017).

3. Results and Discussion

3.1. Fluoride concentration

Table 3 indicated the fluoride concentrations in study area. The range of fluoride concentration
were from 0.02 mg/l to 1.96 mg/l and the mean ± SD of it was 0.658 ± 0.321 mg/l, which is
lower than the standard value determined by the WHO (1.5 mg/l) (Barathi et al., 2014; Cai et al.,
2016). However, the average concentration of fluorine in the Ardakan, Ashkezar and Meybod
cities is higher than the optimum value set by the US Public Health Service(Kohn et al., 2001).
The highest concentration of fluoride with 1.96 mg/l is related to Meybod and the lowest
concentration with 0.02 mg/l is related to Mehriz. In general, 740 (68.77%) of the samples were
in the WHO standardized range of 0.5-1.5 mg/l, compared to WHO (Barathi et al., 2014),
European Union (DECLG and (Department of the Environment, 2014) and Canada guidelines
(Toft et al., 1987) 0.4 percent of cases were more than 1.5 mg/l. The cities of Ashkezar and
Meybod with 43.33 and 10 percent of cases had the highest and the lowest number of cases
outside the WHO standard, respectively. Figure 2 is a box plot chart that shows the concentration
of fluoride and its distribution range in the studied areas. Based on this chart, the highest
distribution of fluoride concentration was in the city of Ashkezar and the lowest is in Meybod,
Mehriz and Yazd, respectively. In other study in rural area of Khuzestan, the fluoride
concentration reported range from 0.5 to 1.5 mg/l (Abtahi et al., 2015). Also Mohebbi et al (2013) (Mohebbi et al., 2013) reported the fluoride concentration in drinking water of 31 provinces of Iran is ranged from 0.5 to 1.5 mg/l.

3.2 Spatial variation

Spatial variation of fluoride in groundwater of Ardakan, Ashkezar, Mehriz, Yazd, Meybod and Taft is shown in Figure 3. Generally, the north and west of study area have higher concentration of fluoride and south areas have lower fluoride concentration, which maybe the main reason is due to soil texture. The city of Ashkezar, located in the western region of Yazd-Ardakan plain, has the highest concentration of fluorine in terms of spatial extent. Groundwater in the southern and western parts of the Mehriz and Taft cities has a fluoride concentration lower than 0.5 mg/l, which is less than the WHO guidelines (WHO, 2004). According to previous studies, reducing the concentration of fluoride from 0.5 mg/l in drinking water leads to increased tooth decay (Dissanayake, 1991; Jones et al., 2005; Ozsvath, 2009).

3.3 Health Risk Assessment:

In this study, non-carcinogenic risk was used to evaluate the health risks assessment of fluoride in groundwater used for drinking. EDI is presented in Table 4 for populations with different age groups in three groups of children, teens and adults exposed to fluoride through drinking water and dermal exposure. Table 5 shows the mean value and 95th percentile of the estimated HQ value for contact by fluoride in the ground water with drinking-dermal exposure. The average non-carcinogenic risk value for all age groups except children in Meybod is estimated to be less than 1 and negligible. The HQ value for the 95th percentile in both teens and adults was less than 1 and for children in all studied regions is higher than 1, indicating a high non-carcinogenic risk.
for the children age group. The reason for the high risk of non-carcinogens for children is the low BW for this group compared to other age groups (Huang et al., 2017). The initial signs of acute fluoride intoxication occur at a dose of 0.3 mg F kg\textsuperscript{-1} BW (Akinbla, 1997). No age group receives this dose in this study. The highest mean and 95 percentile for the calculated HQ in the studied areas in Meybod city are 1.14 and 2.48 for children group respectively, indicating high non-carcinogenic risk in this city.

In a study that conducted by Guissouma et al, found that consumer of drinking water in 5 areas where the HQ is higher than the guidelines suffer from dental fluorosis (Guissouma et al., 2017). For all study areas, the non-carcinogenic risk of fluoride was categorized as Adults> Teens> Children for three groups of exposed subjects. According to the results of health risk assessment, the population at potential risk is the children age group which is consistent with the study of Huang et al (2017) (Huang et al., 2017) and Guissouma et al. (2017) (Guissouma et al., 2017). Given that the estimated non-carcinogenic risk for the children age group at the 95th percentile was more than 1, so children health is highly at risk in these areas. Some guidelines have been suggested for preventing and controlling fluorosis for populations at risk. Firstly, a defluoridation project that meets the environmental conditions must be done to improve water quality for regions where the concentration of fluoride is high endemically (Lian-Fang and Jian-Zhong, 1995). The use of low concentration fluoride sources such as deep wells is recommended for areas where surface water or shallow wells have a high concentration of fluoride (Huang et al., 2017).

3.4. Sensitivity Analysis

Sensitivity analysis was performed to determine the most influential variable on the health risk assessment. Figure 4 shows the results of the sensitivity analysis to assess the non-carcinogenic
risk for three age groups of children, teens and adults exposed to fluoride. In the adult age group, in all cities other than Meybod, fluoride concentration in drinking water (C) is the most important variable affecting the health risk values. In Meybod, the drinking water ingestion rate (IR) is the most important variable affecting the amount of health risk in adult age group. In the teens group, the drinking water ingestion rate (IR) is the most effective variable on the value of health risk assessment in all studied cities. In the age group of children, for every city except Taft, the drinking water ingestion rate (IR) is the most effective variable on the value of health risk assessment. And for Taft, the most important influencing factor on the health risk in the children age group is the concentration of fluorine in drinking water (C). The factors affecting the consumption of drinking water are the weather conditions. As the temperature increases, water consumption increases too in order to drink and the individual is exposed to higher fluoride levels (Sohn et al., 2001; Craig et al., 2015). Fluoride can also penetrate by other forms of contact, such as consumption of various foods (Erdal and Buchanan, 2005).

Figure 5 shows the results of the sensitivity analysis for the various variables involved in calculating health risk for different age groups based on the type of contact (dermal and ingestion). The HQ value for dermal contact is lower than the HQ level by consumption water containing fluoride for drinking. The most important variables affecting the value of HQ-ing in three age groups are drinking water ingestion rate (IR) and fluoride concentration in water (C), and the most important variables in the value of HQ-derm in dermal contact including both concentration fluoride in water and the fraction of skin in contact with water (F). Overall HQ contains total HQ-derm and HQ-ing. Due to the higher impact of HQ-ing and its higher value, the HQ-ing variables have the highest impact on HQ-overall calculations, so the most important
variables affecting HQ-overall contains drinking water ingestion rate (IR) and fluoride concentration in drinking water (C).

3.5. Uncertainty analysis

The Monte Carlo technique were used to quantify of the uncertainty of the exposure to fluoride in drinking water. Based on this technique a range of each parameter input to exposure equation randomly, then the process completed many time, finally a range of predicted values results that indicate overall uncertainty in the inputs to the calculation (Assessment, 1992). Moreover, Monte Carlo technique for quantify the uncertainty, other uncertainties were considered in fluoride risk assessment process, especially for input parameters which known by the sensitivity analysis.

Fluoride concentration measured based on collecting sampling water from all deep-wells, Qanat and other groundwater that used as drinking water resources in study area. In addition, atomic absorption spectrometer used as most accurate method to calculate fluoride with three time repeat for each sample. Also the samples were collected in four season. Because, ingestion rate may change in different season. The water consumption rate in warm season is much higher than cooler season (Craig et al., 2015; Huang et al., 2017). For F parameter, more time and frequency of taking a shower can increase health risk of exposure to fluoride. While drinking water is the most common resources for daily intake of fluoride, other sources such as fluoride supplements, tea and foods may also significantly help to daily fluoride intake (Erdal and Buchanan, 2005; Huang et al., 2017).

The estimated of health risk of exposure to fluoride in Yazd province inhabitants could be underestimated, because Yazd province has a hot-dry weather and drinking water ingestion rate maybe is more the value that used in this study. Also only the exposure to fluoride from drinking water was investigated. In addition, because of the limited data, fluoride exposure via inhalation
during water use was not investigated. So, more fluoride data of different exposure pathway are
needed to calculate the accurate and precise health risk estimate of exposure to fluoride in Yazd
province inhabitant's that should be considered in future studies.

4. Conclusion

In this study, fluoride concentration and its health risk were investigated in 269 drinking water
supply wells in 4 seasons. Of the 1076 samples taken from these wells, 68.77% were within the
standard range set by the WHO guidelines. The results showed that HQ was less than 1 for all
age groups except for children, indicated that children in study area are highly at the risk.
Therefore, defluoridation projects should be done. According to the results of sensitivity
analysis, the most important factor affecting the increase of non-carcinogenic risk in children is
the drinking water ingestion rate. According to the results of spatial distribution performed with
GIS software, the city of Ashkezar has the highest concentration of fluoride distribution. The
southern and western parts of Mehriz and Taft cities contain water with fluoride concentration
less than 0.5 mg/l as determined by the WHO guidelines. It is suggested that in future studies, the
amount of fluoride received through other ways of contact, such as food and its health risk
should be investigated.

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References


Mohammadi, A., Nemati, S., Mosaferi, M., Abdollahnejad, A., Almasian, M., Sheikhmohammadi, A., 2017a. Predicting the capability of carboxymethyl cellulose-stabilized iron nanoparticles for the


Zhang, S., Niu, Q., Gao, H., Ma, R., Lei, R., Zhang, C., Xia, T., Li, P., Xu, C., Wang, C., 2016. Excessive apoptosis and defective autophagy contribute to developmental testicular toxicity induced by fluoride. Environmental Pollution 212, 97-104.

Figure caption:

Figure 1: Geolocation of studied regions

Figure 2: Fluoride concentration and distribution status in studied regions

Figure 3: Spatial distribution of fluoride in groundwater in the studied areas

Figure 4: Sensitivity analysis results for age groups of children, teens and adults in studied regions.

Figure 5: Sensitivity analysis based on the type of contact (skin, oral) for different age groups.
Figure 1:

Figure 2:
Figure 3:

<table>
<thead>
<tr>
<th>City</th>
<th>Adults</th>
<th>Teens</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardakan</td>
<td><img src="chart1.png" alt="Graph" /></td>
<td><img src="chart2.png" alt="Graph" /></td>
<td><img src="chart3.png" alt="Graph" /></td>
</tr>
<tr>
<td>Ashkezar</td>
<td><img src="chart4.png" alt="Graph" /></td>
<td><img src="chart5.png" alt="Graph" /></td>
<td><img src="chart6.png" alt="Graph" /></td>
</tr>
<tr>
<td>Mehriz</td>
<td><img src="chart7.png" alt="Graph" /></td>
<td><img src="chart8.png" alt="Graph" /></td>
<td><img src="chart9.png" alt="Graph" /></td>
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</table>
Figure 4:

<table>
<thead>
<tr>
<th>Age group</th>
<th>HQ_{mg}</th>
<th>HQ_{derm}</th>
<th>HQ overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 5:
### Table 1: Specifications of studied regions and collected samples

<table>
<thead>
<tr>
<th>City</th>
<th>Latitude</th>
<th>Longitude</th>
<th>Population (person)</th>
<th>Area (km²)</th>
<th>Number of Wells</th>
<th>Number of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardakan</td>
<td>32.3082° N</td>
<td>54.0086° E</td>
<td>56776</td>
<td>2505</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Ashkezar</td>
<td>32.0002° N</td>
<td>54.2075° E</td>
<td>31000</td>
<td>5552</td>
<td>30</td>
<td>120</td>
</tr>
<tr>
<td>Mehriz</td>
<td>31.5778° N</td>
<td>54.4452° E</td>
<td>44391</td>
<td>6776</td>
<td>38</td>
<td>152</td>
</tr>
<tr>
<td>Meybod</td>
<td>32.2487° N</td>
<td>54.0079° E</td>
<td>82333</td>
<td>1330</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Taft</td>
<td>31.7590° N</td>
<td>54.2047° E</td>
<td>45357</td>
<td>6048</td>
<td>88</td>
<td>352</td>
</tr>
<tr>
<td>Yazd</td>
<td>31.8974° N</td>
<td>54.3569° E</td>
<td>486152</td>
<td>2397</td>
<td>78</td>
<td>312</td>
</tr>
<tr>
<td>Sum</td>
<td>-</td>
<td>-</td>
<td>746009</td>
<td>45768</td>
<td>269</td>
<td>1076</td>
</tr>
</tbody>
</table>

### Table 2: Parameters used for the probabilistic risk model.

<table>
<thead>
<tr>
<th>Parameters (units) (References)</th>
<th>Distribution type</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Children (kg)</td>
</tr>
<tr>
<td>Skin surface area (cm²)(34)</td>
<td>Lognormal</td>
<td>7422±1.25</td>
</tr>
<tr>
<td>Body weight (kg)(34)</td>
<td>Lognormal</td>
<td>16.68±1.48</td>
</tr>
<tr>
<td>Ingestion rate (L/day)(23)</td>
<td>Normal</td>
<td>1.25±0.57</td>
</tr>
<tr>
<td>Average time (days)(23)</td>
<td>Fixed value</td>
<td>2190</td>
</tr>
<tr>
<td>Exposure frequency (day/year)(39)</td>
<td>Triangular</td>
<td>Min:180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mode:345</td>
</tr>
<tr>
<td>Exposure duration (year)(23)</td>
<td>Fixed value</td>
<td>6</td>
</tr>
<tr>
<td>Dermal permeability constant (cm/h)(40)</td>
<td>Fixed value</td>
<td>1×10⁻³</td>
</tr>
<tr>
<td>Exposure time in the shower (h/day)(41)</td>
<td>Lognormal</td>
<td>0.13±0.0085</td>
</tr>
<tr>
<td>Fraction of skin in contact with water*(41)</td>
<td>Uniform</td>
<td>Min:0.4</td>
</tr>
<tr>
<td>Fraction of fluoride absorbed in gastrointestinal tract*(40)</td>
<td>Fixed value</td>
<td>1</td>
</tr>
<tr>
<td>Oral reference dose (mg/kg/day)(42)</td>
<td>Fixed value</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*unit less

### Table 3: Fluoride concentration in studied regions

<table>
<thead>
<tr>
<th>City</th>
<th>Fluoride concentration in samples (mg/l)</th>
<th>Compared to the WHO standard (Number(percent))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardakan</td>
<td>Mean(SD): 0.832±0.315 Min: 0.19 Max: 1.22</td>
<td>12(20.00) 0(0.00) 48(80.00)</td>
</tr>
<tr>
<td>Ashkezar</td>
<td>Mean(SD): 0.734±0.416 Min: 0.17 Max: 1.90</td>
<td>48(40.00) 4(3.33) 68(56.66)</td>
</tr>
<tr>
<td>Mehriz</td>
<td>Mean(SD): 0.562±0.209 Min: 0.02 Max: 1.35</td>
<td>56(36.84) 0(0.00) 96(63.15)</td>
</tr>
<tr>
<td>Meybod</td>
<td>Mean(SD): 0.911±0.323 Min: 0.15 Max: 1.96</td>
<td>45(5.00) 45(5.00) 72(90.00)</td>
</tr>
<tr>
<td>Taft</td>
<td>Mean(SD): 0.601±0.329 Min: 0.04 Max: 1.50</td>
<td>136(38.63) 0(0.00) 216(61.36)</td>
</tr>
<tr>
<td>Yazd</td>
<td>Mean(SD): 0.642±0.259 Min: 0.16 Max: 1.50</td>
<td>72(23.07) 0(0.00) 240(76.92)</td>
</tr>
<tr>
<td>Yazd Province</td>
<td>Mean(SD): 0.658±0.321 Min: 0.02 Max: 1.96</td>
<td>328(30.48) 8(0.74) 740(68.77)</td>
</tr>
</tbody>
</table>
Table 4: EDI for different age groups in the studied areas

<table>
<thead>
<tr>
<th>Location</th>
<th>Adults</th>
<th></th>
<th>Teens</th>
<th></th>
<th>Children</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95th</td>
<td>Mean</td>
<td>95th</td>
<td>Mean</td>
<td>95th</td>
</tr>
<tr>
<td>Ardakan</td>
<td>5.47E-3</td>
<td>1.05E-2</td>
<td>2.35E-2</td>
<td>4.98E-2</td>
<td>5.11E-2</td>
<td>1.07E-1</td>
</tr>
<tr>
<td>Ashkezar</td>
<td>4.80E-3</td>
<td>1.09E-2</td>
<td>2.05E-2</td>
<td>5.15E-2</td>
<td>4.35E-2</td>
<td>1.08E-1</td>
</tr>
<tr>
<td>Mehriz</td>
<td>3.74E-3</td>
<td>7.21E-3</td>
<td>1.53E-2</td>
<td>3.20E-2</td>
<td>3.50E-2</td>
<td>7.68E-2</td>
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<tr>
<td>Yazd</td>
<td>4.22E-3</td>
<td>8.71E-3</td>
<td>1.76E-2</td>
<td>3.74E-2</td>
<td>4.00E-2</td>
<td>8.97E-2</td>
</tr>
<tr>
<td>Meybod</td>
<td>6.05E-3</td>
<td>1.19E-2</td>
<td>2.48E-2</td>
<td>4.98E-2</td>
<td>6.86E-2</td>
<td>1.49E-1</td>
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<tr>
<td>Taft</td>
<td>4.02E-3</td>
<td>8.89E-3</td>
<td>1.69E-2</td>
<td>3.96E-2</td>
<td>3.71E-2</td>
<td>8.96E-2</td>
</tr>
<tr>
<td>Overall</td>
<td>4.52E-3</td>
<td>9.57E-3</td>
<td>1.91E-2</td>
<td>4.43E-2</td>
<td>4.45E-2</td>
<td>1.02E-1</td>
</tr>
</tbody>
</table>

Table 5: Mean and percentile 95 HQ values for different age groups in studied regions

<table>
<thead>
<tr>
<th>Location</th>
<th>Adults</th>
<th></th>
<th>Teens</th>
<th></th>
<th>Children</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95th</td>
<td>Mean</td>
<td>95th</td>
<td>Mean</td>
<td>95th</td>
</tr>
<tr>
<td>Ardakan</td>
<td>9.11E-2</td>
<td>1.11E-1</td>
<td>3.91E-1</td>
<td>8.29E-1</td>
<td>8.51E-1</td>
<td>1.79</td>
</tr>
<tr>
<td>Ashkezar</td>
<td>8.01E-2</td>
<td>1.82E-1</td>
<td>3.41E-1</td>
<td>8.59E-1</td>
<td>7.25E-1</td>
<td>1.81</td>
</tr>
<tr>
<td>Mehriz</td>
<td>6.23E-2</td>
<td>1.20E-1</td>
<td>2.55E-1</td>
<td>5.33E-1</td>
<td>5.83E-1</td>
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<tr>
<td>Yazd</td>
<td>7.03E-2</td>
<td>1.45E-1</td>
<td>2.93E-1</td>
<td>6.24E-1</td>
<td>6.67E-1</td>
<td>1.50</td>
</tr>
<tr>
<td>Meybod</td>
<td>1.01E-1</td>
<td>1.99E-1</td>
<td>4.14E-1</td>
<td>8.30E-1</td>
<td>1.14</td>
<td>2.48</td>
</tr>
<tr>
<td>Taft</td>
<td>6.58E-2</td>
<td>1.45E-1</td>
<td>2.81E-1</td>
<td>6.61E-1</td>
<td>6.18E-1</td>
<td>1.49</td>
</tr>
<tr>
<td>Overall</td>
<td>7.53E-2</td>
<td>1.59E-1</td>
<td>3.18E-1</td>
<td>7.38E-1</td>
<td>7.42E-1</td>
<td>1.7</td>
</tr>
</tbody>
</table>
HIGHLIGHTS

- Fluoride concentration was measured in 6 counties of Yazd province.
- Probabilistic risk assessment of exposure to fluoride and spatial analysis were applied.
- The HQ in children age group was more than 1 in all counties.
- The most important variable in calculating the HQ was IR, C and F parameters.