

## Effect of High Water Fluoride Concentration on the Intellectual Development of Children in Makoo/Iran

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### Abstract

**Objective:** Prolonged excessive intake of fluoride during child's growth and development stages has been associated with mental and physical problems.

The aim of this study was to investigate the effect of excessive fluoride intake on the intelligence quotient (IQ) of children living in five rural areas in Makoo/Iran.

**Materials and Methods:** In this cross-sectional study, 293 children aged 6-11 years were selected from five villages in Makoo with normal fluoride ( $0.8 \pm 0.3$  ppm), medium fluoride ( $3.1 \pm 0.9$  ppm) and high fluoride ( $5.2 \pm 1.1$  ppm) in their water supplies. The IQ of each child was measured by the Raven's test. Educational and residential information and the medical history of each child was recorded by a questionnaire completed by the parents. Data were analyzed by ANOVA test with a significance level of 0.05.

**Results:** The mean IQ scores decreased from  $97.77 \pm 18.91$  for the normal fluoride group to  $89.03 \pm 12.99$  for the medium fluoride group and to  $88.58 \pm 16.01$  for the high fluoride group ( $P=0.001$ ).

**Conclusion:** Children residing in areas with higher than normal water fluoride levels demonstrated more impaired development of intelligence. Thus, children's intelligence may be affected by high water fluoride levels.

**Key Words:** Intelligence Quotient; Fluoride; Drinking Water

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### INTRODUCTION

Prolonged excessive intake of fluoride has been associated with fluorosis [1, 2]. Fluorosis

is a degenerative and progressive disorder, which adversely affects several organs. Although dental fluorosis is the most obvious

clinical manifestation of increased fluoride intake, many other organs such as the bones, thyroid, kidney, liver, lung and brain may be affected by the increased fluoride level [1-8]. Due to the substantial role that neural health plays on the individual's quality of life, numerous studies have been conducted on the effect of excess fluoride on neurological development.

Most of these investigations, which support the neurotoxic effect of fluoride, have been performed in animals, demonstrating generation of free radicals and alterations in the level of neuro-transmitters in the brain [7-11]. These changes may interfere with normal development of the central nervous system (CNS) during the fetal and early childhood development. This period is the most critical phase in neuro-behavioral development, in which the brain is sensitive to absent or increased levels of certain elements.

Any cerebral impairment in this stage of the child's growth, leads to future cognitive and intellectual deficits [12-14].

Although human subjects are more vulnerable to excessive fluoride compared to animals, controversies exist among the data obtained from various studies on the effect of fluoride on human's intellectual abilities.

A major shortcoming in this area of research is the small pool of regions in which research has been carried out, with most of the data having been collected from China with various methodological limitations [13-19].

Geographically, Iran lies on one of the high fluoride belts, with endemic fluorosis existing in various regions including Makoo [1,20]. Makoo is located in the North West of Azarbaijan province, in the North West of Iran, between longitudes 44° 21' - 45° 10' and latitudes 39° 13' - 39° 34'. It is restricted between Turkey on the west and Aras river on the east. Geologically, this region is covered by basaltic lavas. The mean annual temperature varies between -16.2°C and 35.1°C and is considered as a cold climate region. Local groundwater is the chief source of water supply for its inhabitants [20]. This study investigates the effect of different levels of fluoride in drinking water on the intelligence quotient (IQ) of children living in five rural areas in Makoo/Iran from 2009 to 2010.

## MATERIALS AND METHODS

### Water sample collection and analysis:

Groundwater samples were collected in uniform clean plastic bottles from wells and springs distributed over the study area.

**Table 1.** Fluorosis Distribution in the Three Groups

Fluorosis	Normal		Very Mild		Mild		Moderate		Severe		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Normal</b>	71	78	8	8.8	12	13.2	0	0	0	0	91	100
<b>Medium</b>	0	0	0	0	19	17.9	53	50	34	32.1	106	100
<b>High</b>	0	0	0	0	12	12.5	24	25	60	62.5	96	100
<b>Total</b>	71	24.2	8	2.7	43	14.7	77	26.3	94	32.1	293	100

The fluoride and iodine in the drinking water were analyzed by SPADNS (Sulfophenylazo dihydroxynaphthalene-disulfonate) method, utilizing 4000 UV-Vis spectrophotometer (Hach Company, Germany) in the environmental health engineering laboratory of Public Health School of Tehran University of Medical Sciences.

According to the data obtained by water analysis, the villages were categorized into normal, moderate and high fluoride content groups.

To minimize the effect of other factors, such as velocity of flowing water and the seasonal temperature, on the water-fluoride level during the last 12 years, the mean fluoride content of all seasons for this time period, as registered by the local health clinics, was calculated and set as the final fluoride concentration of that region [1,20].

The reported fluoride levels by the local clinics were in line with our findings of water fluoride analysis.

In addition to fluoride, the amount of iodine and lead in the regions' drinking water was determined using 4000 UV-Vis spectrophotometer (Hach Company, Germany) and polarograph with mercury electrode (Hach Lange, France), respectively.

### Study population:

Two-hundred ninety-three participants (142 boys and 151 girls) out of 314 children (6-11 year olds) living in five villages in Makoo were recruited for the study. The five selected rural areas were similar in their general demographic and geographic characteristics with the inhabitants having a comparable level of socioeconomic status and similar occupations. As fluoride excess toxicity is increased by iodine deficiency [7], we measured the amount of iodine in their drinking water and made sure that all households received iodine enriched salts for cooking and eating purposes. The villages (Babur, Panjarlu, Dizaj, Small Donalau and Large Donalau) were classified into three groups based on the fluoride content of their water supplies (normal, medium and high). According to WHO guidelines, the standard range for water fluoride concentration is 0.5-1 mgL<sup>-1</sup> and levels greater than that were classified as medium (3.1±0.9 ppm) and high (5.2±1.1 ppm) [1, 14, 21]. All participants were long-life residents of the villages under study, with their mothers having lived in the area during their pregnancies. The exclusion criteria included a history of genetic disease, systemic disorders or brain trauma in the family.

**Table 2.** Children's IQ in Five Rural Areas in Makoo

Groups	number	IQ(Range)	Mean±SD		
			Male	Female	Total IQ
Normal <sup>x,□</sup>	91	50-140	95.58±15.92	99.73±21.22	97.77±18.91
Medium <sup>x,o</sup>	106	59-120	87.29±12.75	90.9±13.12	89.03±12.99
High <sup>□,o</sup>	96	50-115	88.09±16.52	89.19±15.52	88.58±16.01
<b>Total</b>	293	50-140	89.93±15.93 <sup>β</sup>	93.37±17.44 <sup>β</sup>	91.6±16.48

X,□: P=0.001; o: P=0.995; β: P=0.07

A written informed consent was obtained from the parents of all eligible subjects after explaining the nature and aim of the study.

A detailed questionnaire was completed with the assistance of parents, including information about child's and parents' medical and residential history, their educational level and source of drinking water.

#### Dental examinations:

Following theoretical training for fluorosis, the examiner supervised by an experienced pedodontist examined 40 children who had been selected from the subjects previously. The examiner recorded the diagnosis about each child. If there was any doubt about the diagnosis, a decision was made after discussion. Four weeks later the examined subjects were re-examined in order to assess the intra-examiner reliability.

The dental examinations were carried out by a dentist according to the WHO- recommended Dean's index [1]. Following theoretical training for fluorosis, the examiner supervised by an experienced pedodontist examined 40 children who had been selected from the subjects previously. The examiner recorded the diagnosis about each child.

If there was any doubt about the diagnosis, a decision was made after discussion.

Four weeks later the examined subjects were reexamined in order to assess the intra-examiner reliability. All dental examinations were performed in the school's medical room using a mirror and cotton rolls under day light.

#### IQ evaluation:

The intellectual ability of each child was calculated using Raven's Color Progressive Matrices (RCPM). The RCPM is a non verbal multiple choice IQ test designed for 5 to 11-year-old children. The models were presented in the form of matrixes. In each test item, the child was asked to identify the missing part that completes the model. The test was administered in a convenient school classroom under the supervision of a trained psychologist, a teacher and an assistant in a blind manner, following the procedures laid down in the manual of Raven's Progressive Matrices [22]. The average time taken to complete the test was 30 minutes. The test comprised of 30 problems, beginning with easy problems and ending with difficult ones. Each question contained a matrix of geometric design with eight alternatives for one removed cell.

**Table 3.** IQ score Distribution for Children Living in Areas with Normal, Medium and High Water Fluoride Content

Group IQ	Normal		Medium		High		Total	
	N	%	N	%	N	%	N	%
Superior Intelligence	4	4.4	0	0	0	0	4	1.4
Above Average Intelligence	17	18.7	6	5.7	2	2.1	25	8.5
Normal or Average Intelligence	47	51.6	58	54.7	61	63.5	166	56.7
Dullness and Lower IQ	23	25.3	42	39.6	33	34.4	98	33.5
<b>Total</b>	91	100	106	100	96	100	293	100

Only one of the options fitted correctly. Each group consisted of 15 students, who worked independently.

The children's IQ scores were divided according to the Stanford-Binet classification in eight groups: Genius (164 and over), very superior (148-164), superior (132-148), above average (116-132), average (84-116), dullness (68-84), borderline (52-68) and mental deficiency (below 58)[23].

### Statistical analysis

All analyses were performed by SPSS version 11.5 for Windows (SPSS Inc., Chicago, Ill, USA) . The data were subjected to ANOVA, Post Hoc test and Kruscal-Wallis. The significance level was fixed at 0.05.

### RESULT

The villages were classified as normal, medium and high fluoride content according to their water fluoride concentrations.

The mean level of fluoride in medium and high groups was approximately 3 and 5 times higher than WHO standards, respectively [1].

A concentration of 0.08-0.1 mg/l for iodine and 0-0.5 mg/l for lead was found by the water content analysis.

Two hundred and ninety three 6 to 11-year-old children 6 to 11 took part in this study. Kappa coefficient for intra- examiner reliability was acceptable (0.92). Dental examination revealed that all children in medium and high-fluoride groups demonstrated mild to severe fluorosis. In comparison, only 22% of the subjects in the normal group showed very mild and mild fluorosis and the remaining 78% were unaffected (Table 1). An increase in water fluoride content above the standard level was associated with the incidence of more severe dental fluorosis ( $P < 0.001$ ). IQ evaluation results from the three groups are shown in table 2. Although IQ scores for children with normal fluoride content were significantly higher than the medium and high fluoride level ( $P = 0.001$ ), there was no statistically significant difference between the IQ of children residing in medium and high fluoridated areas ( $P = 0.995$ ). Furthermore, we did not observe any significant difference between the scores of girls and boys in any of the groups examined ( $P = 0.07$ ). IQ scores of children living in areas with various water fluoride content (normal, medium and high) have been demonstrated in table 3, exhibiting that nearly half of the children residing in the normal fluoride area showed normal IQ levels.

**Table 4.** Factors Influencing IQ Scores

Variable	$\beta$ - Value	P- Value
Age	0.02	0.7
Gender	0.148	-0.082
Child's Educational Level	0.31	0.595
Mother's Educational Level	0.09	0.129
Father's Educational Level	0.008	0.891
Fluorosis Intensity	-0.160	0.014
Water Fluoride Content	-3.865	<0.001

We investigated the influence of the child's age, gender, parent's and child's educational level on the child's IQ scores. There was no difference between the intellectual ability of pre-school children (6 years) and school children in the present study, indicating that the child's educational level had no impact on the IQ scores. In addition, a relationship between the child's age, gender, parent's educational level and the IQ scores was also not observed (Table 4).

## DISCUSSION

Fluoride in small amounts is essential for the child's development [1,20]. Although excessive fluoride ingestion may result in visible side effects, some effects may go unnoticed if unchecked [1, 8]. In this study, we investigated the consequence of high fluoride content water on children's intelligence in Iran, a country lying on one of the geographical fluoride belts [1].

Here we demonstrated that the average IQ of children living in the area with a high fluoride content in the drinking water was significantly lower than children with standard water fluoride levels. Since all potentially confounding factors were adjusted, the difference in IQ scores may reveal the potential effect of high fluoride exposure on the intellectual development of children. These results are consistent with findings reported by Xiang et al., who confirmed a decrease in children's neurobehavioral ability when exposed to elevated fluoride levels [18]. However, no adjustment was made to remove the confounding factors in their investigation and the water fluoride content in the control area was lower than the standard water fluoride concentration. This may be important, as a reduced level of fluoride content may also give rise to adverse neurological impacts [3, 13,18,24,25]. In a similar study, Xiang et al. reported an inverse concentration-respond relationship between the fluoride content of drinking water and the IQ

scores of children [18]. In contrast, we could not find any significant difference between the intellectual ability of children residing in locations with medium and high-fluoride water. Most of the assessments on the influence of water-fluoride content have been performed in China. The fluoride concentration in our investigation was higher than previous studies in China [1, 13,14,18]. Furthermore, we compared two fluoride levels above the normal limits to evaluate the effect of different concentrations of fluoride on children's IQ and dental fluorosis. In addition, our results demonstrated a higher percentage of children with above the normal IQ range in the standard fluoride group compared to medium and high-fluoride groups. This was in line with the findings of Trivedi et al., who reported that an elevated fluoride level would affect the higher levels of intelligence more vigorously than normal and low intelligence levels [26]. Hong and colleagues demonstrated that although an elevated fluoride level in drinking water lowers the IQ, the amount of iodine in the water of the investigated area was a more significant factor influencing the average IQ [14] We found a concentration of 0.08-0.1 mg/l for iodine and 0-0.5 mg/l for lead, which were in accordance to standard levels for these two elements [27, 28], which may accuse the high level of fluoride for the decreased IQ scores in the present study.

Possible mechanisms for the neurotoxic effect of fluoride may be explained by several animal studies [7-10]. Fluoride can pass through the placenta by maternal exposure to elevated fluoride levels during the prenatal period or it may be ingested through the child's diet. High levels of absorbed fluoride in children (80-90%) and adults (60%) are retained in the body [1,15]. Once absorbed in the blood, fluoride forms lipid soluble complexes which cross the blood-brain barrier and accumulate in cerebral tissues [1, 8,11]. The penetrated fluoride complexes adversely affect the CNS develop-

ment by different neurotoxic and exciotoxic mechanisms, such as free radical generation, inhibition of anti-oxidant and mitochondrial energy enzymes and inhibition of glutamate transporters [29].

The structural and functional alterations in CNS, specifically in the fetal period and the first 8 years of life, may lead to learning and intellectual deficits and cognitive dysfunctions [7-10,29]. In addition, fluoride interferes with the activity of the thyroid gland, which has a deleterious effect on brain development and function in children [5].

Our findings showed that the prevalence and severity of dental fluorosis was greater among children with a higher water fluoride content. As a probable result of "the halo effect", we found a 22% prevalence of fluorosis in children living in the village with a standard fluoride level, which was in accordance with WHO guidelines explaining that at an optimal fluoride level (1 ppm), about 20% of the population demonstrate fluorosis [1,4]. However, in villages with a higher than standard fluoride level, all children demonstrated dental fluorosis with a severity index of moderate to severe. In this study, we administrated Raven's Colored Progressive Matrices (RCPM) test to evaluate the child's intellectual development, a validated test for basic cognitive abilities and widely used to evaluate the normal development of brain functions [12,30]. It consists of problems containing a matrix of geometrical design, with a part removed. The child has to select the missing cell from 6-8 given alternatives [30,31]. Owing to the high correlation of this test in evaluating children's IQ (ranging from 0.7-0.92) of this test in evaluating children's IQ (ranging from 0.7-0.92) compared to the conventional IQ test, RCPM is recommended for measuring the intellectual and conceptual ability of young children (5 to 10.5 years). Furthermore, due to the non-verbal characteristics of the test, it is successfully administrated in pre-school children, as it does

not require any verbalization or reading skills [30-32].

Based on the general concept that intellectual development is a consequence of different neurological and environmental factors, we have evaluated some of the environmental factors on the child's intellectual ability. Our finding showed that child's age and educational stage had no correlation with IQ scores, this was in line with studies performed by Li et al. and Seraj et al., indicating that the fetal and early childhood periods are the most susceptible stages in brain development and any induced neurological impairments are not reversible [12,18,33].

As it is well accepted, the neurobehavioral development may be influenced by many genetic, socioeconomical and geographical factors [12]. Thus, we have recruited our samples from a homogenous rural population in Makoo, diminishing the effect of some environmental and inherited factors, yet it is obvious that complete exclusion of such factors is impossible. In a study, the urinary fluoride level was implemented as the basic indicator for the child's fluoride exposure [16]. However, since urinary fluoride excretion may vary from one subject to the other or even in the same person and because drinking water was typically the greatest single contributor to daily fluoride intake in this area, we have evaluated the effect of different amounts of fluoride in drinking water [1,20]. In the present study, the effect of fluoride concentration on the child's IQ was assessed; however, it is possible that other trace elements in drinking water may have some neurological side effects [16,34]. Thus, further studies are required to investigate the effect of other environmental or geological contaminants.

The data from this research may support the hypothesis that excess fluoride in drinking water has neurological toxic effects. Therefore, a close monitoring of fluoride levels in local water-supplies from areas with endemic fluorosis

and implementing public health measures to reduce the fluoride exposure levels in high fluoridated regions seem necessary.

## CONCLUSION

Within the limitation of this cross-sectional study, these conclusions may be drawn:

1. The IQ scores of children living in areas with above the standard water fluoride levels were lower compared to children living in normal fluoride level regions.
2. The proportion of children with above the normal intelligence in the group with the standard level of fluoride in their drinking water was greater than those with medium and high fluoride content.
3. Age, gender, child's and parent's educational level had no significant impact on the IQ scores.

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