

# Environmental and occupational exposure to chromium in Iran: A systematic review

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**Received:** April 13, 2017

**Accepted:** June 5, 2017

**Online Published:** July 3, 2017

**DOI:** 10.5430/jer.v3n2p31

**URL:** <https://doi.org/10.5430/jer.v3n2p31>

## ABSTRACT

**Background:** Chromium (Cr) is a heavy metal and trace mineral found in various forms. Cr III is an essential nutrient, that is normally found in human blood and urine; in contrast, Cr VI is listed in group I carcinogens and is hazardous for human health. Several studies have been done about measuring human Chromium levels in Iran and this review attempted to summarize these studies.

**Methods:** Electronic resources including SID, Magiran, PubMed, Web of Knowledge, and Google Scholar were searched; with phrases including “Exposure to Chromium, Chromium exposure, Chromium measuring, Occupational exposure to Chromium, Environmental exposure to Chromium, Chromium” and their Persian translations until December 2, 2016.

**Results:** From the 1,309 retrieved articles, 32 articles were selected. In welding, electroplating and cement companies, chromium concentrations in workers who dealt directly with Cr were higher than others employees. In the general population, people who lived near a factory or an industrial center, or people who had taken dental treatments especially with orthodontic appliances, had higher Cr levels. Cr deficiency was also investigated in several studies, for its possible relation to diabetes type 2.

**Conclusion:** Cr VI exposure should be under surveillance in Iranian industrial workers; and residential areas should be kept in a safe distance from Cr producing industries. Cr III deficiency might be related to diabetes type 2.

**Key Words:** Chromium, Environmental exposures, Heavy metals, Iran

## 1. INTRODUCTION

Chromium (Cr) is a shiny and silvery-gray, brittle and hard metal, that is resistant to oxidation, even at high temperatures.<sup>[1,2]</sup> Cr can be naturally found in rocks, plants and soil,<sup>[3]</sup> and from a public health perspective, it is one of the toxic heavy metals.<sup>[4]</sup> According to an Agency for Toxic Substances and Diseases Registry (ATSDR) report, in the US environment, the median concentrations of Cr in ambient air is < 20 ng/m<sup>3</sup> and for indoor air with smoking it can be 100-400 times higher. The mean level of Cr in soil is 37.0 mg/kg, and in drinking water is less than 5 µg/L.<sup>[3]</sup>

Cr can be found in various forms Cr (II) to Cr (IV) and it is stable in the form of Cr III.<sup>[4]</sup> Cr VI is listed in group 1 carcinogens by International Agency for Research on Cancer (IARC)<sup>[5]</sup> and is a human carcinogen.<sup>[6]</sup> Cr (III) is an essential nutrient<sup>[7]</sup> that is normally found in human blood and urine<sup>[3]</sup> and is classified by IARC<sup>[5]</sup> in group 3, which means there is no sufficient evidence about its carcinogenesis.<sup>[6]</sup> The Institute of Medicine of the National Academy of Sciences considers, 20-45 µg of Cr III intake<sup>[3]</sup> (21-25 micrograms per day for women and 25-35 micrograms per day for men),<sup>[8]</sup> adequate and enough for adults and adolescents.<sup>[3]</sup> Cr III

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deficiency may cause, heart diseases, metabolic disorders and diabetes, and its high intake can cause skin irritation.<sup>[1]</sup>

The general population may be exposed to Cr through breathing, eating and drinking food or water and skin contact.<sup>[1]</sup> ATSDR reported that, in the US general population, the mean concentration of Cr in human serum and urine is, 0.16-0.10  $\mu\text{g/L}$  and 0.22  $\mu\text{g/L}$ , respectively.<sup>[3]</sup> Cr is widely used in various industries, including plating, welding, dyes and pigments, leather and wood products.<sup>[1-4]</sup> According to the report of Occupational Safety and Health Administration (OSHA), in general and in construction industries, the permissible air borne exposure limit (PEL) based on time-weighted average (TWA) for Cr II, Cr III and Cr VI is 0.5  $\text{mg/m}^3$ , 0.5  $\text{mg/m}^3$  and 1 $\text{mg/m}^3$ , respectively.<sup>[9]</sup>

Cr VI is hazardous for human health and can cause health problems including, respiratory complications (lung irritation, nasal and lung problems), digestive complications (inflammation and ulceration of the stomach and small bowel lesions), hematological complications (anemia hypochromic and microcytic) as well as adverse reproductive effects (reducing sperm count and epididymal damages).<sup>[3]</sup>

Several studies have been performed, in different groups and cities in Iran about human levels of Chromium. This paper attempts to summarize these studies and make an overall estimation about the situation of this contaminant in humans, in Iran.

## 2. METHODS

### 2.1 Databases and searching strategy

Iranian/Persian electronic resources including SID, Magiran and international databases including PubMed, Web of Knowledge and Google Scholar were searched; with phrases including “Exposure to Chromium, Chromium exposure,

Chromium measuring, Occupational exposure to Chromium, Environmental exposure to Chromium, Chromium” and their Persian translations until December 2, 2016.

### 2.2 Data extraction and Inclusion criteria

All articles were reviewed by two authors separately. Among them, studies that investigated occupational or environmental exposures to Chromium in Iran and measured Chromium concentration in human tissues, were included in this study.

Studies done outside Iran, those that were not performed on humans, or did not report an estimate for chromium contamination in humans were excluded. Therefore, articles which measured chromium levels in animals, plants, air (including workers breathing zone), water and soil were excluded.

Information including first author, year of data collection, population, sample size, mean and standard deviation of Cr levels, location of sampling and *p*-values of subgroup comparisons, were retrieved from each article.

## 3. RESULTS

Finally, 32 articles were selected from 1,309 retrieved articles. The population under study in these articles and the method of reporting was very heterogeneous across studies and therefore pooled results were not calculated. The process of article selection has been shown in Figure 1.

Studies except one<sup>[10]</sup> showed that people who had taken dental treatments especially orthodontic appliances for some time, had higher Cr levels in their body tissues than others (see Table 1).

All studies except one<sup>[21]</sup> showed that Cr concentrations in patients with diabetes type 2 was lower than healthy controls and suggested a probable relation between Cr deficiency and diabetes (see Table 2).

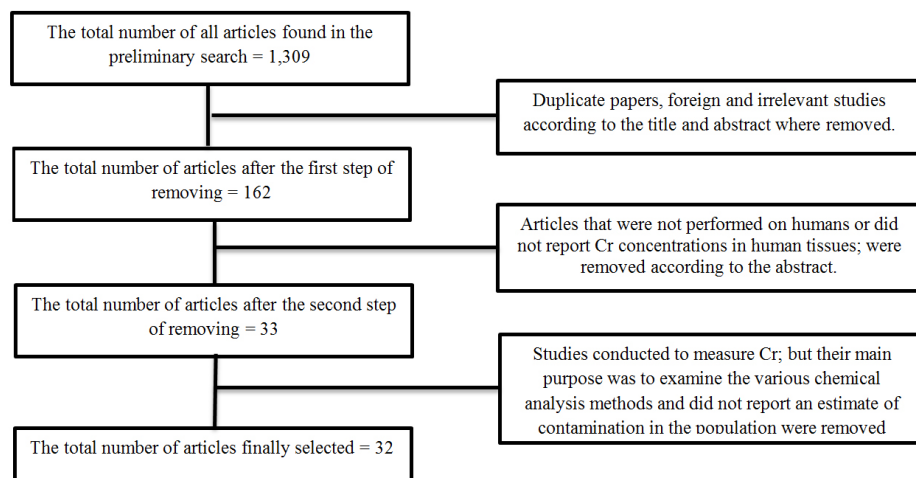


Figure 1. Process of article selection

**Table 1.** Summary of studies measuring Cr in orthodontic patients in Iran

	First Author and year of data collection (Ref)	Population	Location	Sample	Mean ± SD of Cr	p-value of comparison
1	Amini, 2013-2014 [10]	30 orthodontic patients 11-26 years old: The patients were divided into two groups of experimental (metal-injection molding (MIM) brackets) and control (Conventional brackets), n = 15 in each group.	Department of Orthodontics, Dental Branch, Islamic Azad University, Tehran	Saliva	Brackets used: Baseline (pretreatment): -Controls = 0.25 ± 0.56 µg/l -MIM brackets = 0.42 ± 0.48 µg/l  60 <sup>th</sup> day: -Controls = 0.35 ± 0.62 µg/l -MIM brackets = 0.26 ± 0.57 µg/l (decreased)  Regardless of the brackets used: Baseline (pretreatment) = 0.34 ± 0.52 µg/l 60 <sup>th</sup> day = 0.3 ± 0.59 µg/l	After six months: In controls > .05  In MIM brackets = .0438 but ↓  .110
2	Amini, 2013-2014 [11]	24 patients with orthodontics (12 males and 12 females)	The Orthodontics Department of Azad University, Tehran	Hair	Baseline: Females = 0.1440 ± 0.0760µg/g Males = 0.1469 ± 0.0812µg/g Total = 0.1455 ± 0.0769µg/g  6 months later: Females = 0.1652 ± 0.0692µg/g Males = 0.1713 ± 0.0752µg/g Total = 0.1683 ± 0.0707µg/g  Increase in Cr in all patients happened 6 months after orthodontic treatment = 0.0229 ± 0.0266 µg/g	.0002
3	Amini, the sampling was performed 16 ± 2 months after the start of treatment with fixed orthodontic appliances, year of data collection not reported [12]	56 Subjects, 28 subjects with fixed appliances in both arches (16 females and 12 males) and 28 controls (a same-gender sister or brother) without any orthodontic appliance	Tehran	Saliva	With appliance = 2.6 ± 1.6 ng/ml Without appliance = 2.2 ± 1.8 ng/ml	.03
4	Amini, 2011-2012 [13]	24 patients with only the maxillary arch stainless steel brackets treatment (12 male and 12 female)	Department of Orthodontics, Dental Branch, Islamic Azad University, Tehran	Gingival Crevicular Fluid (GCF)	Pretreatment (baseline) = 1.978 ± 0.721 mg/g of GCF  1 month after the initiation of treatment = 4.135 ± 1.591 mg/g of GCF  6 month after baseline = 13.760 ± 3.555 mg/g of GCF	Baseline vs Month one < .001  Baseline vs Month six < .001
5	Khane Masjedi, 2014-2015 [14]	24 female and 22 males fixed orthodontic patients: Conventional brackets (control) and Metal injection molding (MIM) brackets (experimental) (A total of 60 patients were assessed until 46 patients were included)	Orthodontics Department of Ahvaz University of Medical Sciences, Ahvaz	Hair	Before treatment= 0.1657 ± 0.0884 µg/g After 6 months = 0.3066 ± 0.1362 µg/g Difference = 0.1409±0.1131 µg/g	.305
6	Amini, year of data collection not reported [15]	20 patents with fixed orthodontics (12 female and 8 male)	The Orthodontics Department of Azad University, Tehran	Saliva	Immediately before initiation of treatment (baseline) = 3.86 ± 1.34 µg/L  6 months after orthodontic treatment= 4.60 ± 6.11 µg/L  12 month after orthodontic treatment= 2.04 ± 1.66 µg/L	Baseline vs Month 6 = .360  Baseline vs Month 12 = .0038  Month 6-Month 12 = .046
7	Amini, year of data collection not reported (during 3 years) [16]	60 dental patients (30 cases with fixed orthodontic appliances and 30 controls without any type of orthodontic appliances or metal restoration in their mouth)	The Orthodontics Department of Azad University, Tehran	Mucosa cell	Cases = 4.24 ± 1.82 ng/mg Controls = 3.46 ± 1.65 ng/mg	.09
8	Arash, year of data collection not reported* [17]	11 fixed orthodontic patients (7 females and 4 males)	Babol	Saliva	Before treatment = 0.483 ± 0.324 mg/dl 1 day later = 0.471 ± 0.238 mg/dl 1 week later = 0.685 ± 0.624 mg/dl 1 month later = 0.741 ± 0.414 mg/dl 2 months later = 1.240 ± 1.244 mg/dl 6 months later = 3.244 ± 0.777 mg/dl T1: before appliance placement= 2.6 ± 3.14 µg/L T2: 20 days after appliance placement= 3.68 ± 3.95 µg/L T3: 3 months after appliance placement= 3.41 ± 3.36 µg/L T4: 6 months after appliance placement= 3.39 ± 3.41 µg/L	.013
9	Yassaei, year of data collection not reported [18]	32 patients 11 to 24 years old who visited the orthodontic clinic	Yazd	Saliva	1st time (before orthodontics) = 4.1 ± 2.3 µg/L 2nd time (3 months later) = 4.4 ± 3.2 3rd time (5 min following the induction of stress) = 4.8 ± 3.3 µg/L 4th time (30 min following the induction of stress) = 5.1 ± 3.3 µg/L First time (before orthodontics) = 5.2 ± 3.38 µg/L Second time (3 months later and before stress) = 5.42 ± 2.44 µg/L Third time (after stress) = 6.27±2.68 µg/L	.168  The mean amount of salivary Cr was not significantly different between the four time points (p > .05)
10	Amini, 2012 [19]	30 patients with fixed orthodontics	The Orthodontics Department of Azad University, Tehran	Saliva	1st time (before orthodontics) = 4.1 ± 2.3 µg/L 2nd time (3 months later) = 4.4 ± 3.2 3rd time (5 min following the induction of stress) = 4.8 ± 3.3 µg/L 4th time (30 min following the induction of stress) = 5.1 ± 3.3 µg/L First time (before orthodontics) = 5.2 ± 3.38 µg/L Second time (3 months later and before stress) = 5.42 ± 2.44 µg/L Third time (after stress) = 6.27±2.68 µg/L	The mean amount of salivary Cr was not significantly different between the four time points (p > .05)
11	Amini, 2012-2013 [20]	10 patients with fixed orthodontics	The Orthodontics Department of the Azad University, Tehran	Saliva	First time (before orthodontics) = 5.2 ± 3.38 µg/L Second time (3 months later and before stress) = 5.42 ± 2.44 µg/L Third time (after stress) = 6.27±2.68 µg/L	> .05

\* The results of this study were contradictory and we did not receive any answer from the corresponding author to clarify the situation. The results presented in this review are from the article's Table 1.

**Table 2.** Studies measuring Cr in diabetic patients and their controls in Iran

First Author and year of data collection (Ref)	Population	Location	Sample	Mean ± SD of Cr	p-value
12 Nourmohammadi, year of data collection not reported [21]	40 subjects (20 diabetic patients who attended the diabetic clinic and were taking insulin and 20 controls from university staff with no complications and not receiving any medication)	Semnan	Hair	Diabetic Patients = 2.418 ± 2.089 µg/g Controls = 0.3625 ± 0.23 µg/g	.001
13 Basaki, year of data collection not reported [22]	40 female subjects referred to Dr. Saeb's specialized hormone lab (20 patients with type 2 diabetes and 20 nondiabetics doing a checkup)	Shiraz	Blood (Serum)	Nondiabetic controls = 0.27 ± 0.15 (unit?) Patients with type 2 diabetes = 0.16 ± 0.07 (unit?)*	< .05
14 Rafiei, 2012 [23]	132 pre-diabetic patients (but 24 patients were not included in the final statistical analyses because they did not complete their laboratory studies)	Shariati Hospital, Isfahan	Blood	The mean and standard deviation of serum Cr was 1.08 ± 1.06 µg/L. Thirty-four (31.5%) patients had Cr deficiency and 74 (68.5%) patients had normal Cr. There was no significant difference in Cr between men and women, between the investigated age groups (< 50 years and ≥ 50 years), and between patients with and without a family history of diabetes. No significant differences in age, BMI, FBS or insulin were observed between Cr deficiency and Cr normal groups. In the group with a normal level of Cr, there was a significant reversed correlation between Cr levels and age. (r = -0.276)	> .05  .017
15 Saburi, 2008-2009 [24]	30 type 2 diabetes patients referred to Sina Hospital (15 males and 15 females) and 30 healthy individuals	Tabriz	Blood (Serum)	Diabetic Patients = 0.80 ± 0.28 µg/dl Controls = 1.19 ± 0.33 µg/dl	< .001
16 Palizban, year of data collection not reported [25]	-47 patients with both metabolic syndrome and type 2 diabetes (30 females and 17 males) and -45 patients with metabolic syndrome and without type 2 diabetes (33 females and 12 males) and -35 healthy individuals as a control group (23 females and 12 males)	Isfahan	Blood	Patients with both metabolic syndrome and type 2 diabetes: 11.60 ± 14.73 µg/L Patients with metabolic syndrome and without type 2 diabetes: 18.83 ± 22.82 µg/L Control: 28.02 ± 19.28 µg/L	p-value for one way ANOVA = .002
17 Parsaeian, year of data collection not reported [26]	370 participants: 108 patients with type 2 diabetes (57 males and 51 females) and 47 patients with type 1 diabetes (21 males and 26 females) and also 108 individuals with (IGT) impaired glucose tolerance (56 males and 51 females) and 108 controls (54 males and 54 females)	Yazd	Blood (Serum)	Controls: -Total = 0.24 ± 0.023 µg/L Impaired glucose tolerance (IGT): -Total = 0.17 ± 0.025 µg/L Type 1 diabetes: -Total = 0.090 ± 0.028 µg/L Type 2 diabetes: -Total = 0.097 ± 0.021 µg/L	p-value for one way ANOVA = .004
18 Tadayon, 2009-2010 [27]	250 women 33-35 years old: 142 controls and 108 diabetes patients type 2	Tehran	Hair	Patients = 0.777 ± 1.8 µg/g Controls = 1.505 ± 1.33 µg/g	p-value not reported
19 Abdolsamadi, 2009-2011 [28]	70 pregnant women: 35 gestational diabetes mellitus and 35 non-diabetic pregnant women	Hamadan	Saliva	Patients = 6.63 ± 5.48 µg/100ml Controls = 8.30 ± 6.95 µg/100ml Hair: -Patients = 1.21 ± 0.97 µg/g -Control = 4.36 ± 1.03 µg/g	< .05
20 Nasli-Esfahani, year of data collection not reported [29]	301 participants: diabetic patients (n=150) and healthy controls (n=151).	Dr Shariati Hospital, Tehran	Hair Urine Nail Serum	Urine: -Patients = 0.010 ± 0.006 µg/ml -Control = 0.009 ± 0.007 µg/ml Nail: -Patients = 1.10 ± 0.34 µg/g -Control = 2.37 ± 0.64 µg/g Serum: -Patients = 0.0013 ± 0.0004 µg/ml -Control = 0.0018 ± 0.0014 µg/ml	> .05  < .05  < .05
21 Yousefi Rad, year of data collection not reported [30]	30 (15 male and 15 female) diabetes patients and 30 (15 male and 15 female) healthy people	Sina Hospital, Tabriz	Serum	Diabetes patients = 0.80 ± 0.258 µg/dl Healthy people = 1.19 ± 0.33 µg/dl	< 0.001
22 Makhloogh, 2010-2011 [31]	70 patients with type 2 diabetic nephropathy (macro and micro-albuminuria) and 70 healthy individuals	Sari, Mazandaran	Blood (Serum)	Approximate values based on Figure 1 are: Cases: Patients with diabetic nephropathy: Cr = 0.28 µgr/L Controls: Healthy Group: Cr = 0.6 µgr/L Approximate values based on figure 2 are: Cases with Micro Albuminuria: Cr = 0.28 µgr/L Cases with Macro Albuminuria: Cr = 0.27 µgr/L	Cases vs. Controls < .001  Comparing cases with macro vs. micro Albuminuria > .05
23 Tadayon, year of data collection not reported [32]	100 women between 35 to 70 years of age	Tehran	Hair	Approximate values based on Figure 2 are: Diabetic patients = 0.6 µg/g Healthy Group = 1.3 µg/g	< .05

\* The unit was not reported and we did not receive any answer from the corresponding author.

In industrial jobs, such as welding, electroplating and cement companies, Cr VI concentrations were higher in workers who dealt directly with Cr than others employees of the same industry. In the general population, the Cr concentration was various in different groups. One study showed Cr levels of

serum were significantly higher in bladder cancer cases than healthy controls<sup>[33]</sup> and the other showed Cr was lower in tinnitus patients.<sup>[34]</sup> Also, one study showed Cr was significantly higher in matured boys with normal weight than low weight (see Table 3).<sup>[35]</sup>

**Table 3.** Summary of studies measuring Cr exposure in industrial workers or other groups in Iran

	First Author and year of data collection (Ref)	Population	Location	Sample	Mean ± SD of Cr	p-value of comparisons
24	Nazarpour, year of data collection not reported <sup>[36]</sup>	100 mothers attending clinics were sampled four to eight weeks after delivery	Varamin	Breast milk	3 ± 2.7 µg/ml	---
25	Hashemian, years of enrollment 2004-2008 (Golestan Cohort Study) <sup>[37]</sup>	30 nail samples from the participants of Golestan Cohort Study (GCS) who had died in accidents during the first 7 years of follow-up	Golestan	Toenail	0.25 ± 0.63 µg/g	---
26	Eskandary, 1999-2000 <sup>[38]</sup>	30 head injury patients	Bahonar Hospital, Kerman	Blood (Serum)	Severe head injury patients = 1.42 ± 0.23 mg/L Moderate head injury patients = 1.58 ± 0.23 mg/L Mild head injury patients = 1.41 ± 0.2 mg/L	the concentration of Cr in serum had no significant relation to the degree of head injury during the first 4 hours
27	Alirezace, year of data collection not reported <sup>[35]</sup>	45 premature male pupils (primary schools' children with average age of 10 years) and 49 mature male pupils (high school children with average age of 17 years) were randomly selected from 2 schools in the Fifth Education District of Mashhad	Mashhad	Nail	Premature: -Normal weight (n = 9) = 0.00012 ± 0.00001 percent/100gr nail -Low weight (n = 35) = 0.00014 ± 0.00001 percent/100 gr nail Matured: -Normal weight (n = 32) = 0.00020±0.00002 percent/100gr nail -Low weight (n = 14) = 0.00017 ± 0.00003 percent/100gr nail	.42 .043
28	Mazdak, 2006-2008 <sup>[33]</sup>	51 bladder cancer patients and 58 healthy individuals	Isfahan	Blood (Serum)	Patients = 128.82 ± 16.99 µg/L Controls = 121.93 ± 16.67 µg/L	< .05
29	Mozaffarinia, year not reported <sup>[34]</sup>	55 patients with tinnitus and 47 healthy volunteers	Isfahan	Blood (Serum)	Patients = 26.71 ± 5.39 µg/dl Controls = 30.57 ± 4.75 µg/dl Male = 27.62 ± 5.13 µg/dl Female = 29.40 ± 5.58 µg/dl	< .001 .100
30	Golbabaee, 2011 <sup>[39]</sup>	119 People (94 welders of natural gas pipes, 6 back welders, 29 assistants and 25 controls)	Brujen (Chaharmahal and Bakhtiari)	Urine	Welders= 3.36 ± 3.74 µg/L Back welders = 12.67 ± 4.50 µg/L Assistants = 1.98 ± 1.05 µg/L Control = 1.04 ± 0.56 µg/L	Welders vs Control=0.004 Back welders vs Control<0.001
31	Pournourmohammadi, year of data collection not reported <sup>[40]</sup>	90 volunteer male workers from a cement factory	Darab, Fars	Serum	Healthy control (n = 30) = 3.2 ± 0.5 µg/L Indirect-exposed (n = 28) = 3.6 ± 0.3 µg/L Direct-exposed (n = 60) = 5.2 ± 0.4 µg/L	Directly exposed vs Healthy controls = .009 Directly exposed vs. Indirectly exposed = .009
32	Golbabaee, year of data collection not reported <sup>[41]</sup>	45 Chromium plating workers and 40 Zinc plating workers as a control group	Isfahan	Urine	Chromium plating workers: Cr=9.798±7.554 µg/g Creatinine Zinc plating workers: Cr = 1.811 ± 0.699 µg/g Creatinine	< .001

#### 4. DISCUSSION

Several studies have shown that Cr is involved in glucose and lipid metabolism and has antioxidant functions.<sup>[42]</sup> Researchers think Cr improves glucose metabolism and insulin sensitivity in type two, type one and gestational diabetes,<sup>[43]</sup> and it may play a small role in human weight control.<sup>[44]</sup> It is also an essential trace element for proper protein, carbohydrate and lipid metabolism.<sup>[8]</sup> Studies have also shown associations between Cr deficiency and diabetes and cardio-

vascular diseases.<sup>[45]</sup>

Some studies have mentioned that polycystic ovarian syndrome (PCOS) that may cause infertility in women, can be treated by using Cr supplements.<sup>[46,47]</sup>

Cr toxicity is mainly caused by the hexavalent form and can cause respiratory, dermal, cardiovascular, gastrointestinal, renal and carcinogenic effects.<sup>[48]</sup> However, there is no clear evidence that shows acute inhalation of chromium or

its compounds can cause immediate death.<sup>[49]</sup>

In Iran, many studies were performed to investigate and measure Cr concentration in water, soil, air, breathing zone of workers in related industries, or in food including rice, tea, cans, and also fishes and even in toys. Among the studies that evaluated Cr levels in human tissues in Iran, a large number of studies were performed in the general population and were more than the studies performed to investigate occupational exposures (29 from 32 articles). Also, one third of these studies were performed in the capital city of Iran, Tehran; and among patients who were under dental treatments especially with fixed orthodontic appliances (11 from 32 articles). Other studies were performed in big cities including Isfahan, Kerman, Yazd, Shiraz, Mashhad and Tabriz (8 from 32 articles) and in diabetes type 2 patients (11 from 32 articles).

#### 4.1 Environmental exposure to Cr

Chromium waste products are made during industrial process or mining.<sup>[50]</sup> These toxic waste products can create vast environmental problems<sup>[50]</sup> that affect human health by chromium toxicity and carcinogenicity.<sup>[51]</sup> It seems necessary to run environmental monitoring programs by considering all routes of chromium exposure<sup>[51]</sup> in Iran.

Higher than normal Cr exposure may result in elevated Cr levels in blood, urine, hair and nails. The most reliable tissues for measuring Cr exposure are blood and urine.<sup>[3]</sup>

Alirezaee et al. in Mashhad, investigated Cr concentrations in nails and showed that there was no significant relation between Cr concentration in nails before and after puberty in boys.<sup>[35]</sup> Authors have commented that variations in trace elements intake such as Cr may affect growing during the pre-mature and maturing periods.<sup>[35]</sup> Also, it seems that chromium supplementation can increase muscle accretion (increasing muscle area and percentage of muscle) and fat loss.<sup>[52]</sup>

Nazarpour et al. in Varamin, showed that Cr concentration of breast milk were higher in women with a smoking partner and women who lived near a factory or an industrial area.<sup>[36]</sup> The results of a study by Interdonato et al. in Italy also showed, adolescents living in the industrialized areas of northern Sicily had higher concentration of heavy metals including Cr in their body, although it was not significant.<sup>[53]</sup>

A case-control study from Isfahan, showed that Cr concentration in patients with bladder cancer was significantly higher than controls.<sup>[33]</sup> Other studies have also shown a probable relation between exposure to Cr and lung cancer.<sup>[54]</sup> The reaction of Cr VI with genetic matter can probably cause carcinogenicity<sup>[48,55]</sup> and significant relations between exposure to Cr VI and lung and airways cancers have been reported.<sup>[48,55,56]</sup>

Oxidative stress may play a role in the pathogenesis of tinnitus.<sup>[54,57,58]</sup> Meanwhile, Cr III has antioxidant effects<sup>[59,60]</sup> and it seems that Cr III deficiency can cause tinnitus. Mozafari Nia et al. in Isfahan showed a significant reduction in serum concentration of Cr in people with tinnitus compared to the control group.<sup>[34]</sup>

Chromium is a common component in the arch-wires of orthodontic appliances (fixed orthodontics) and is an element used in the alloy steel (17%-22%) used in fixed and conventional orthodontic appliances (brackets).<sup>[61]</sup> Studies have shown that Cr concentrations have increased in hair samples,<sup>[11,14]</sup> and in the Gingival Crevicular Fluid (GCF) of orthodontic patients.<sup>[13]</sup> Therefore, a longer duration of treatment with fixed orthodontics may lead to increased Cr concentrations. The result of a study by Ağaoğlu et al. in Turkey also showed, fixed orthodontic appliances can significantly increase Cr concentration in blood and urine; but this increased did not exceed toxic levels.<sup>[62]</sup> The results of a study by Singh et al. in India showed, Cr concentration of saliva after treatment with fixed orthodontic appliances significantly increased, especially in the first week after treatment.<sup>[63]</sup> However, the results of the study by Kocadereli et al in Turkey showed, there was no significant difference between Cr concentration of saliva at baseline time (before treatment) and after two months of treatments in patients with fixed orthodontics.<sup>[64]</sup>

Nour Mohammadi et al. in Semnan showed that, Cr levels of hair samples in diabetes type 2 patients was significantly higher than controls (20 healthy volunteers).<sup>[21]</sup> In contrast, studies from Tehran,<sup>[29,32]</sup> Shiraz, and Tabriz,<sup>[22,24]</sup> showed Cr in diabetic type 2 patients were significantly lower than controls. Likewise, Kazi et al. in Pakistan showed, Cr concentrations of hair and blood samples in diabetes type 2 patients were significantly lower than controls.<sup>[65]</sup> Some researchers have stated that Cr is an essential element for the human body and necessary for insulin functioning and glucose metabolism.<sup>[43,66]</sup> Palizban et al. in Isfahan showed, low Cr blood concentration was associated with diabetes and metabolic syndrome; and therefore suggested taking this element as a supplement.<sup>[25]</sup> A study by Rafiei et al. in Isfahan showed that Cr deficiency was common in prediabetes patients and suggested that patients with diabetes and prediabetes should be screened for Cr; and Cr deficiency should be eliminated in these patients.<sup>[23]</sup>

#### 4.2 Occupational exposure to Cr

Chromium can be released into the atmosphere through commercial and residential activities, such as combustion of gas, oil and coal or industrial activities including, chromium electroplating and steel production.<sup>[1-3]</sup> About one third of the

chromium released into atmosphere is Cr VI.<sup>[3]</sup> A considerable amount of Cr has been released to surface waters by electroplating, and the leather and textile industries.<sup>[3]</sup>

Cr VI is a toxic form of chromium and its compounds are used in many different industries as corrosion inhibitors, for production of pigments, metal finishing and plating, stainless steel production, leather tanning, and wood protection.<sup>[67,68]</sup> Industrial employees can be exposed to Cr VI through inhaling airborne Cr VI as dust, fume or mist during the different parts of production.<sup>[67]</sup>

Pour Nour Mohammadi et al. showed that Cr contamination was significantly higher in workers of a cement company in Darab who dealt with Cr directly, in comparison to administration employees in the same industry and controls.<sup>[40]</sup> Another study by Golbabaie et al. in Borujen showed Cr VI concentration in the breathing zone and urine of welders who directly dealt with Cr was higher than controls.<sup>[39]</sup> And in another study showed that Cr and N-Acetylglucosamine (NAG) concentration in urine samples of Cr plating workers was significantly higher than plating workers.<sup>[41]</sup> NAG is an enzyme that initially originates in the lysosomes of tubular cells. This marker does not get filtered by the renal glomerular system<sup>[41]</sup> and because of this, NAG may increase in subjects exposed to substances toxic for the renal tubular cells. In humans, its increased excretion is probably because of the dysfunction of renal tubular epithelial cells due to increased proteins in the tubular lumen.<sup>[69]</sup> Likewise, Wang et al. in China showed Cr (VI) concentration and NAG of urine samples in exposed Cr workers was significantly higher than

controls.<sup>[70]</sup>

A study by Kalantari and Farokhi on 24 platers from 8 workplaces in Isfahan showed that exposure to Cr VI in these workers was higher than the authorized amount by the National Institute for Occupational Safety and Health (NIOSH) for air in workplaces, and workers who dealt with Cr VI directly and worked near tubs of Cr, were exposed to Cr VI more than other workers working in other parts in the same industry.<sup>[71]</sup> Likewise, Gibb et al. in USA showed a strong dose-response relation between cumulative exposure to Cr VI in a chromate production plant and lung cancer.<sup>[56]</sup>

## 5. CONCLUSIONS

In industrial jobs, including welding, plating and cement, Cr VI concentrations were higher in workers who directly dealt with Cr than others employed in the same industry. Therefore, in Iran, exposure to Cr VI should be under surveillance in these occupations and unnecessary exposure should be prevented.

In the general population of Iran, people who lived near a factory or an industrial center, and who had taken dental treatments with orthodontic appliances, had higher concentration of Cr than others. Likewise, in several studies, Cr III deficiency was investigated in relation to diabetes type 2 and shows the probable necessity of this element in glucose metabolism.

## CONFLICTS OF INTEREST DISCLOSURE

The authors have no competing interests.

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