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REVIEW ARTICLE

Mercury level in biological samples of dentists in Iran: a systematic review and meta-analysis

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Abstract
Exposure to mercury is an important risk to dentists health. The aim of the present study was to assess the pooled mean mercury level (MML) in the urine, blood, nail, and hair of Iranian dentists (IDs) through the meta-analysis technique. Comprehensive and systematic searches were performed in main local databases including SID, Magiran, Iran medex, and ISC as well as internationally available databases including Embase, PubMed and Scopus for all the relevant studies up to 2018. In order to prevent bias in this study and identify eligible studies, various steps of the study was performed independently by two researchers. Out of 13 studies in the meta-analysis process which included 1499 IDs, the mean of the mercury level in the urine, nail, and blood was estimated to be 6.29 (95% CI: 2.61–9.97, I-square: 62.7%, P: 0.006), 3.54 (95% CI: 2.81–4.28, I-square: 0.0%, P: 0.968), 11.20 (95% CI: 2.28–20.13, I-square: 59.9%, P: 0.082), respectively. The mean mercury level (MML) in the biological samples of IDs was higher than the standard of World Health Organization (WHO). So, in accordance with Article 10 of the European Union Regulations (EUR), in the context of the Minamata Convention (MC) on Dental Amalgam (DA), in order to avoid the dangers of mercury exposure in dentists, it is necessary for Iran and other countries to approve laws and to implement a national plan to reduce mercury levels and replace the appropriate materials.

Keywords Occupational exposure · Mercury · Dentists · Iran

Abbreviations

BML	Blood Mercury Level
UML	Urine Mercury Level
HML	Hair Mercury Level
IDs	Iranian Dentists
MML	Mean Mercury Level
MC	Minamata Convention
SD	Standard Deviation
EMVs	Elemental Mercury Vapors
DA	Dental Amalgam

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Introduction

Metals are found in the crust of the Earth [1]. Out of the 35 natural metals available, 23 have specific density above 5 g/cm3 with the atomic weight more than Forty, which are commonly referred to as heavy metals [2–4]. Exposure to some of these metals such as mercury is extremely dangerous in very small amounts and can cause acute and chronic toxicity in humans [5]. Among the heavy metals, mercury has unique physicochemical properties, according to which human exposure to its various compounds has caused a great deal of environmental and health concerns worldwide [6–8]. Mercury is known to be the most dangerous element after arsenic and lead [9]; Agency for Toxic Substances and Disease Registry (ATSDR) has classified it as the third element of the highest priority pollutants [10]. Accordingly, mercury effects on health of human have extensively been studied by various authors and international agencies [11–23]. Mercury has three forms including elemental (or metallic), organic, and inorganic mercury [24]. It is widely introduced to the environment from natural and human resources [25, 26]. Liquid form of

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metallic mercury is poorly absorbed through the body. Elemental mercury enters the blood stream easily at the room temperature by inhaling the vapor. In general, Persons are exposed to mercury via diet, air inhalation, dental amalgam (DA), mercury-containing vaccines, and occupational exposure [26–28]. Mercury vapor inhalation through DA is the uppermost source of exposure with inorganic mercury for most humans around the world [29]. In addition, mercury can become one of the most toxic forms in the environment, namely methyl mercury, and via accumulating in the food chain (especially contaminated fish and seafood) and being consumed by humans, it causes serious toxicity and damage to various human organs [29]. Mercury mainly affects the central nervous system [30, 31], but can also damage other major organs such as the brain and kidneys [7]. It simply crosses the barriers of blood-brain and is rapidly converted to mineral mercury by the intracellular reaction and remains in the brain for many years [32]. behavior and toxic effects of mercury forms for humans depend on chemical structure, dose, exposure time, person age of exposed (most sensitive to the fetus), exposure modes (inhalation, ingestion, and skin contact), and health status of the exposed person [24, 32–35]. In general, the major complications of acute and chronic exposure to mercury in humans are severe disorders in various organs, especially the respiratory, reproductive, renal, hepatic, genetic and epigenetic, neurological, and cardiovascular systems [27, 28, 36–44]. Also, mercury-induced toxicity can cause symptoms such as impaired cognitive function, altered neurological response, headache, hypertension, tremor, and insomnia in humans [45–47]. Among the different pathways of mercury exposure, risks of occupational exposure are very important. Occupational exposure to inorganic mercury occurs more via the inhalation of elemental mercury vapors (EMVs) and may cause numerous disorders, especially in persons working in mines, factories, dentistry, and so on. Among the occupational groups, dentists have been in frequent contact with mercury because of its use with amalgam and their exposure is primarily via inhalation of vapors. The DA ingredients are a combination of several metals including mercury (about 50% by weight), silver, tin, copper, and zinc [48]. Based on the World Health Organization's (WHO) report [49], the highest exposure of dentists to mercury vapor is due to amalgam filling during dental restoration. Rate of mercury vapor release from amalgam depends on various parameters including tooth specification, rate of filling, and also amalgam age, surface area, and composition [29]. Approximately 80% of the mercury vapor of the element released from the amalgam is absorbed by inhalation [32]. Of course, eating foods such as fish and using DA by dentists are also among the most important ways of exposing them to mercury. Therefore, due to the toxicity of mercury in amalgam, WHO has recommended that the use of this material for dental restoration be gradually phased out and replaced with alternative materials [50]. However, due to the high cost of this option for low- and middle-income countries, use of dental amalgam is still widely used as the most important restorative of dental in various regions of the world [51]. Lower price than other materials, effective protection of the tooth structure, relatively long durability, excellent sealing and strong bonding with the teeth, usability at all ages, and ease of use by dentists are among the benefits that make it widely used in dentistry [52]. Due to the health and environmental effects of mercury, health authorities in some parts of the world have banned or reduced the use of this substance in dentistry. For example, the use of DA is banned in countries such as Norway [53] and Sweden [54] and, in other countries such as Japan and Switzerland [29], the use of fillers is banned. However, DA use in other countries such as Denmark, Finland, Estonia, and Italy accounts for less than 5% of the total dental restoration [29]. However, in Iran, there is still widespread use of this material in research as well as manufacturing of DA materials for dental filling by dentists, which poses serious health risks.

In recent years, the dangers and concerns of mercury contamination and toxic effects have led to the Minamata Convention (MC) being implemented in 2013 with the aim of protecting the human health and environment against the release of mercury and its compounds. According to Article 19 of this Convention, parties to the Convention are required to endeavor and evaluate the impact of mercury and its compounds on the human health and environment, in particular in relation to vulnerable populations [55, 56]. Therefore, dentists as one of the most vulnerable and at-risk groups due to the frequent and prolonged exposure to mercury vapors present in DA should be regularly reviewed.

Exposure to mercury in dentists can be assessed by measuring the concentration of mercury in different types of biological samples such as the blood, urine, hair, and nails. Blood is the best specimen for evaluating MeHg. Although exposure to inorganic mercury or mercury vapor will raise blood levels. Urine is not useful for measuring methylmercury and determining urinary mercury level in dentistry is used to test exposure to metallic vapor and inorganic forms of mercury. Also, mercury levels in hair and nails are used as biomarker of chronic methylmercury exposure [57].

A tremendous number of research have been done so far; but, the findings are inconsistent. Specifically, the results of this study can be used to control global mercury pollution to assess the effectiveness of the MC [9]. Therefore, this work aims to determine the mercury level in the blood, urine, hair, and nail samples of Iranian dentists (IDs) using systematic review and meta-analysis.

Materials and methods

Study protocol

For search strategy and review processes in this systematic review, we followed the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines [58]. The ultimate population-exposure-comparator-outcome (PECO) statement was designed as the population: dentists; exposure: mercury; comparisons: specific to each study; outcomes: mercury level in the blood, urine, hair, and nail.

Search strategy

Comprehensive and systematic searches were performed in main local databases (SID, Magiran, Iran medex, and ISC), as well as internationally available databases(Embase, PubMed and Scopus) for all the relevant studies with mercury levels in biological samples of dentists in Iran.

The search was conducted up to December 31, 2018. Also, to access more information, sources of the articles were also reviewed for access to other related articles. The search strategy was performed using the following keywords: "occupational exposure", "occupational diseases", "mercury", "dentists", and "Iran" to select the related studies. For online electronic databases in the national and local scales, the equivalent Farsi keywords were employed.

Study criteria

Inclusion criteria

The inclusion criteria included all the studies in Farsi and English for determining the Mean Mercury Level (MML) in dentists' blood, urine, hair, and nails samples in Iran up to December 31, 2018.

Exclusion criteria

The exclusion criteria included all the studies aiming to determine MML in the blood, urine, hair, and nail samples, but not related to the population of IDs, having samples containing mean concentrations of heavy metals (other than mercury) in the blood, urine, hair, and nails of IDs, non-Farsi or English language studies, interventional studies, studies outside Iran, availability of information, duplicate articles, qualitative studies, case reports, review articles, letter to the editor, case series, and articles published after the said period**.**

Selecting studies

In general, in the initial search, 677 articles were found. After reviewing the entry and exit criteria and qualitative evaluation, finally, 13 eligible articles were entered into the meta-analysis. In order to prevent bias in this study and identify eligible studies, the research process, selection of articles, quality assessment, and data extraction were performed independently by two researchers. In case of disagreement between the results of the two researchers, the results were examined by the third researcher and, eventually, the final consensus group discussion. In this study, after removing the duplicates, the titles of all the articles were reviewed and the unrelated items were removed. In the next step, the remaining articles were studied. In this stage, the unrelated articles that did not meet the inclusion criteria were excluded. Finally, by reviewing the full text of the possible relevant articles, the final eligible articles were selected to enter the meta-analysis process and eliminate the unrelated cases.

A flow diagram of PRISMA for details of the review process is given in Fig. 1.

Data extraction

The required data were extracted using a pre-prepared checklist including name of first author, publication year, study place, sample size, type of study, age (mean ± SD), MML in biological samples of IDs (Mean ± SD), sample environment, and analytical technique.

Quality assessment and risk of bias

The quality assessment of eligible remained papers was conducted independently by two independent research experts (YM and NM) using the Newcastle-Ottawa Scale (NOS) [59, 60]. A NOS score of 7 or more can be considered as "good" [61].

Meta-analysis

STATA version 16.0 (Stata Corporation, College Station, TX, USA) was used for meta-analysis. The pooled estimate was calculated by random effect model (REF), because of the heterogeneity in the included studies were high. The reported mean and standard deviation (SD) were eligible for inclusion in the meta-analysis [62]. To assess the heterogeneity Cochran Q test and an I^2 statistic were used. Low, moderate, or high degrees of heterogeneity were approximated by I^2 values of 25%, 50%, and 75%, respectively. Heterogeneity was assessed by subgrouping the time of measures and study population. Publication bias was assessed by Egger test with the significance level set at p value <0.10.

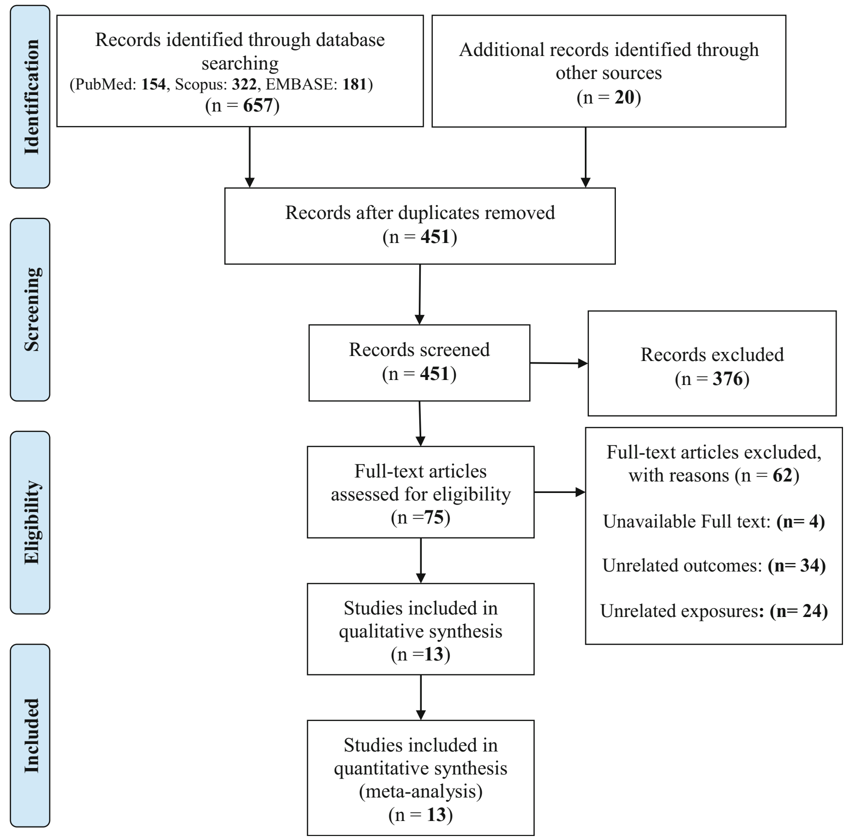

Fig. 1 PRISMA flow diagram

Results

Search results and studies description

After searching the databases, 677 articles were retrieved (PubMed; 154, Scopus; 322, EMBASE; 181). Upon removing 226 duplicate articles and excluding 376 articles according to their titles and abstracts, 75 full texts were reviewed. Based on the inclusion and exclusion criteria and qualitative evaluation, 62 were excluded from the full texts due to inaccessibility and irrelevant results. Finally, 13 eligible studies were entered into the meta-analysis (Fig. 1).

Based on the results presented in Table 1, among the 13 articles, in the study of Neghab et al. (2011), MML in the urine was reported; therefore, mean and SD of this study were calculated using Hozo et al. [63]. 13 eligible studies were selected. Of these, 3, 9, 1 and 2 studies were related to the level of mercury in blood, urine, hair and nails, respectively (Table 1).

From the 13 eligible studies, in the ones by Shirkhanloo et al. (2017) and Zolfaghari et al. (2007), mercury levels in the biological sample of IDs were reported in two biological samples, the data of which are presented separately in Table 1.

All studies entered into the meta-analysis process were analytical cross-sectional (7 articles) and cross-sectional (6 articles). Studies were conducted in 6 provinces of Iran, including Tehran, Hamedan, East Azerbaijan, Khuzestan, Fars, and Khorasan Razavi. The total sample size entered into the meta-analysis process was 1499 IDs. The lowest and highest numbers of samples in meta-analysis process were related to Khamverdi et al. (2004) with the sample size of 30 and Mousavi et al. (2009) with the sample size of 280, respectively (Table 1). Overall, the risk of bias in primary studies was low (Table 1).

Quantitative synthesis (meta-analysis) and subgroup analysis

MML in blood, urine, hair, and nail of IDs

In this study, 13 eligible studies, which were conducted in Iran up to December 31, 2018, entered the meta-analysis process. The pooled standardized mean difference of mercury in IDs was 3.96 (95% CI: 3.03–5.90, I-square: 61.6%, P: 0.001) (Fig. 2).

Publication bias

The results of Eggers test showed that confidence interval was not zero (coefficient: 1.63, T: 4.67, P: 0.001, 95% CI: 0.87–2.37). The funnel plot is represented in (Fig. 3). A significant bias occurred in the publication of the results. So, the result of

Table 1 The details of literature studies in biological samples (blood(μg/l), urine(μg/l), hair(μg/g), nail(μg/g)) of IDs (2000-2018)

Study/ Year	Place (Province)	Sample Size	Study Type	Age Average (Mean ± SD/ Rang)	Mean of Mercury Level (Mean ± SD/Rang)	Biological samples	Analytical Technique	NOS Score
Shirkhanloo et al. [64], 2017	Tehran	50 (25 male, 25 female)	Analytical Cross-sectional	31 ± 4.21	16.40 ± 4.97 (Range: 6.23–27.80)	Blood	FI-CVAAS	6
Kasraei, et al. [65], 2010	Hamadan	43 (35 Male, 8 Female)	Cross-sectional	37.30 ± 9.60 (Range: 27–73)	6.30 ± 1.31 (Range: 4.15–8.93)	Blood	CV-AAS	7
Sadeghneiat et al. [66], 2007	Tehran	50 (24 mail, 26 femail)	Analytical Cross-sectional	29.42 ± 8.72	21.9 ± 14	Blood	CV-AAS	7
Shirkhanloo et al. [64], 2017	Tehran	50 (25 male, 25 female)	Analytical Cross-sectional	31 ± 4.21	19.41 ± 5.18 (Range: 5.43–32.53)	Urine	FI-CVAAS	7
Ostadi, et al. [67], 2017	East Azerbaijan	47 (36 male, 11 female)	Analytical Cross-sectional	36.85 ± 7.11 (Range: 27–54)	20.9 ± 6.71	Urine	AAS	7
Daghayeghi et al. [68], 2014	Khuzestan	37	Cross-sectional	42.5 ± 7.5 (Range: 27–59)	3.4 ± 2.2	Urine	F-AAS	6
Akbari et al. [69], 2013	Khorasan Razavi	45	Cross-sectional	–	9.26 ± 2.7	Urine	HGS-F-AAS	6
Neghab et al. [70], 2011	Fars	106	Analytical Cross-sectional	38 ± 8 (Range: 27–59)	5.95 ± 5.25 (Range: 0.01–18.1)	Urine	CV-AAS	7
Mousavi, et al. [71], 2009	Tehran	280 (145 male, 135 femail)	Analytical Cross-sectional	(Range: 20–50)	3.4 ± 0.10	Urine	CV-AAS	6
Zolfaghari et al. [72], 2007	Tehran	100 (54 male, 46 femail)	Analytical Cross-sectional	(Range: 25–28)	2.84 ± 0.47 (Range: 0.09–25.43)	Hair	AMA-S-PAAS	6
Zolfaghari et al. [72], 2007	Tehran	100 (54 male, 46 femail)	Analytical Cross-sectional	(Range: 25–28)	3.53 ± 0.53 (Range: 0.1–27.27)	Nail	AMA-S-PAAS	7
Hasani Tabatabaei et al. [73], 2007	Tehran	211	Cross-sectional	36.62 ± 6.96 (Range: 23 ± 52)	3.11 ± 3.96 (Range: 0–30)	Urine	CV-AAS	6
Esmaili Sari A et al. [74], 2007	Tehran	100 (54 mail, 46 femail)	Analytical Cross-sectional	–	3.56 ± 0.53 (Range: 0.11–27.27)	Nail	AMA-S-PAAS	7
Khamverdi et al. [75], 2004	Hamedan	30	Cross-sectional	–	31.62 ± 17.88 (Range: 7.69–64.46)	Urine	AAS	7
Nasiri et al. [76], 1993	Tehran	250 (190 males, 60 female)	Cross-sectional	(Range: 20–65)	57.2 ± 36.4	Urine	AAS	6

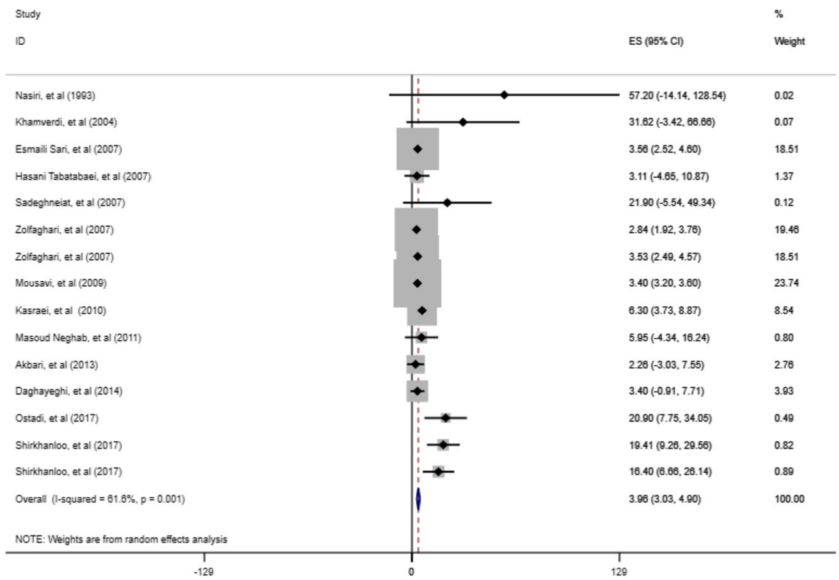

Fig. 2 Pooled standardized mean of mercury in Iranian densities (random effect model)

the Eggers test shows that the outcome influenced the decision of whether to publish.

Mean of mercury level in Iranian densities based on subgroup analysis

The results of the subgroup analysis of pooled mean of mercury in dentists in Iran based on type of studies, technique, and sample environment are showed in Table 2.

Mean of mercury level in Iranian densities based on sample environment Subgroup analysis in this meta-analysis was conducted based on sample Environment and technique for detecting source of heterogeneity. Results showed that pooled mean of mercury in dentists by sample environment in the urine, nail, and blood was 6.29 (95% CI: 2.61–9.97, I-square: 62.7%, P: 0.006), 3.54 (95% CI: 2.81–4.28, I-square: 0.0%, P: 0.968), 11.20 (95% CI: 2.28–20.13, I-square: 59.9%, P: 0.082), respectively (Fig. 4). Based on Table 1, the lowest and highest mean urine mercury level (UML) in IDs were 3.11 μg/l and 57.2 μg/l, respectively. Also, the lowest and highest mean blood mercury level (BML) of the IDs was reported as 6.30 μg/l and 21.9 μg/l, respectively.

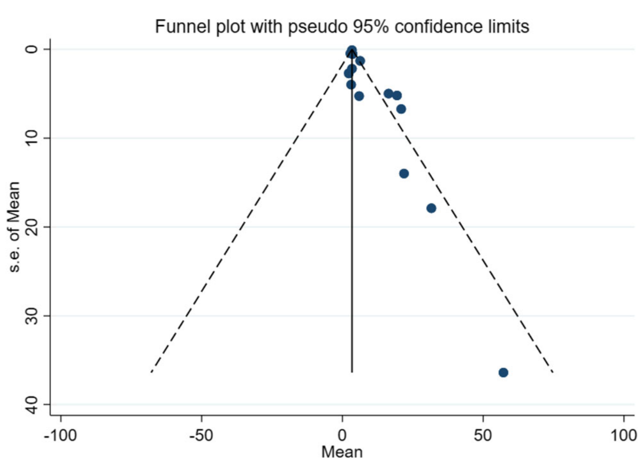

Fig. 3 Publication bias; Mean of mercury in Iranian densities

According to the WHO guidelines, the mean urinary mercury levels in the four studies were higher than the normal limit recommended by the WHO. Mercury levels in all blood and hair studies were higher than the WHO standard.

To better highlight mercury levels in the blood, urine, hair, and nail of IDs according to the WHO standard, the map of spatial distribution of mean mercury concentrations was generated by using geographic information system (GIS) (Fig. 5).

Mean of mercury level in Iranian densities based on analytical technique Also, the mean of mercury based on technique was various and, in AAC method, higher than other techniques (Fig. 6). Results showed that pooled means of mercury in dentists by analytical technique in CV-AAS, AMA-S-PAAS, AAS, and FI-CVAAS were 4.51 (95% CI: 2.36–6.65, I-square: 41.6%, P: 0.144), 3.27 (95% CI: 2.70–3.85, I-square: 0.0%, P: 0.502), 23.24 (95% CI: 11.10–35.37, I-square: 0.0%, P: 0.546), 17.84 (95% CI: 10.81–24.87, I-square: 0.0%, P: 0.675), respectively (Fig. 6).

Generally, blood samples of IDs (4-5 cc of venous blood) were collected and, then, stored in polyethylene (one study) and polypropylene (one study) containers. In Shirkhanloo et al.'s (2017) and Sadeghneiat et al.'s (2007) studies, the retention temperature of the samples has been −20 °C prior to the analysis, but was not reported in Kasraei et al. (2010).

For studies related to the determination of mercury levels in urinary, in two studies by Shirkhanloo et al. (2017) and Mousavi et al. (2009), 24-h urine samples were obtained from

Table 2 Subgroup analysis of pooled mean of mercury in dentists in Iran based on type of studies, technique, and sample environment (fixed effect model)

Outcomes	Subgroup		No. of studies	Mean of mercury (95% CI)	Between studies		
					I^2	$P_{heterogeneity}$	Q
Mean of Mercury	Sample Environmental	Blood (μg/l)	3	11.20 (2.28–20.13)	59.9%	0.089	3.78
		Hair (μg/g)	1	------	------	------	------
		Nail (μg/g)	2	3.54 (2.81–4.28)	0.0%	0.986	1.42
		Urine (μg/l)	9	6.29 (2.61–9.97)	62.7%	0.006	6.38
	Analytical technique	CV-AAS	5	4.51 (2.36–6.65)	41.6%	0.144	3.62
		AMA-S-PAAS	3	3.27 (2.70–3.85)	0.0%	0.502	11.16
		AAS	3	23.24 (11.10–35.37)	0.0%	0.546	3.75
		FI-CVAAS	2	17.84 (10.81–24.87)	0.0%	0.675	4.98
	Type of Studies	Cross Sectional Analytical	9	4.62 (1.74–7.51)	29%	0.218	5.33
		Cross Sectional	6	3.57 (2.77–4.73)	70.1%	0.001	7.37

IDs who had a number of months of steady exposure at the end of a working week. In these two studies, all the sampling vessels were of polypropylene type and retention temperature for all the samples was −20 °C prior to the analysis. In the study of Ostadi et al. (2017), urine samples were taken before mid-week. Also, 20 cc of urine samples was prepared in polyethylene bottles. In Daghayeghi et al. (2014), Akbari et al. (2013), and Khamverdi et al. (2004), urine samples (120-125 cc, polyethylene bottles) have been taken in the first morning of a working day. However, the sample collection in Hasani Tabatabaei et al.'s (2007) research was at the end of the working day.

Hair samples were collected from the scalp area of IDs. The quantity of hair needed for mercury analysis was 1 g (1 to 3 cm). Hair samples were cut by the stainless steel scissors and, then, stored in labeled plastic bags.

Also, the amount of nail needed for mercury analysis was 1 g. The nail samples were entered into an electric oven at 60 °C for 12 h and, then, powdered.

In the selected studies, MML in the blood and urine of IDs was reported in μg/L and, in the hair and nail, in μg/g, respectively.

Overall, the mercury level in the biological samples of IDs was obtained using flow-injection cold vapor atomic absorption spectrometry (FI-CVAAS), atomic absorption spectrometry (AAS), cold vapor atomic absorption spectrometry (CVAAS), and advanced mercury analyzer, single-purpose atomic absorption spectrometer (AMA-S-PAAS).

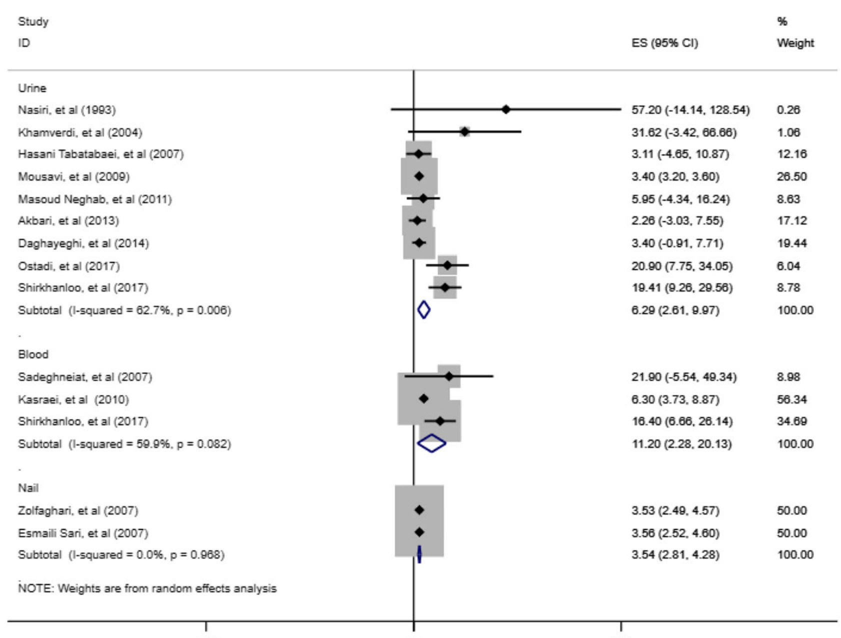

Fig. 4 Subgroup analysis: Standardized mean difference of mercury in Iranian densities based on sample environment (random effect model)

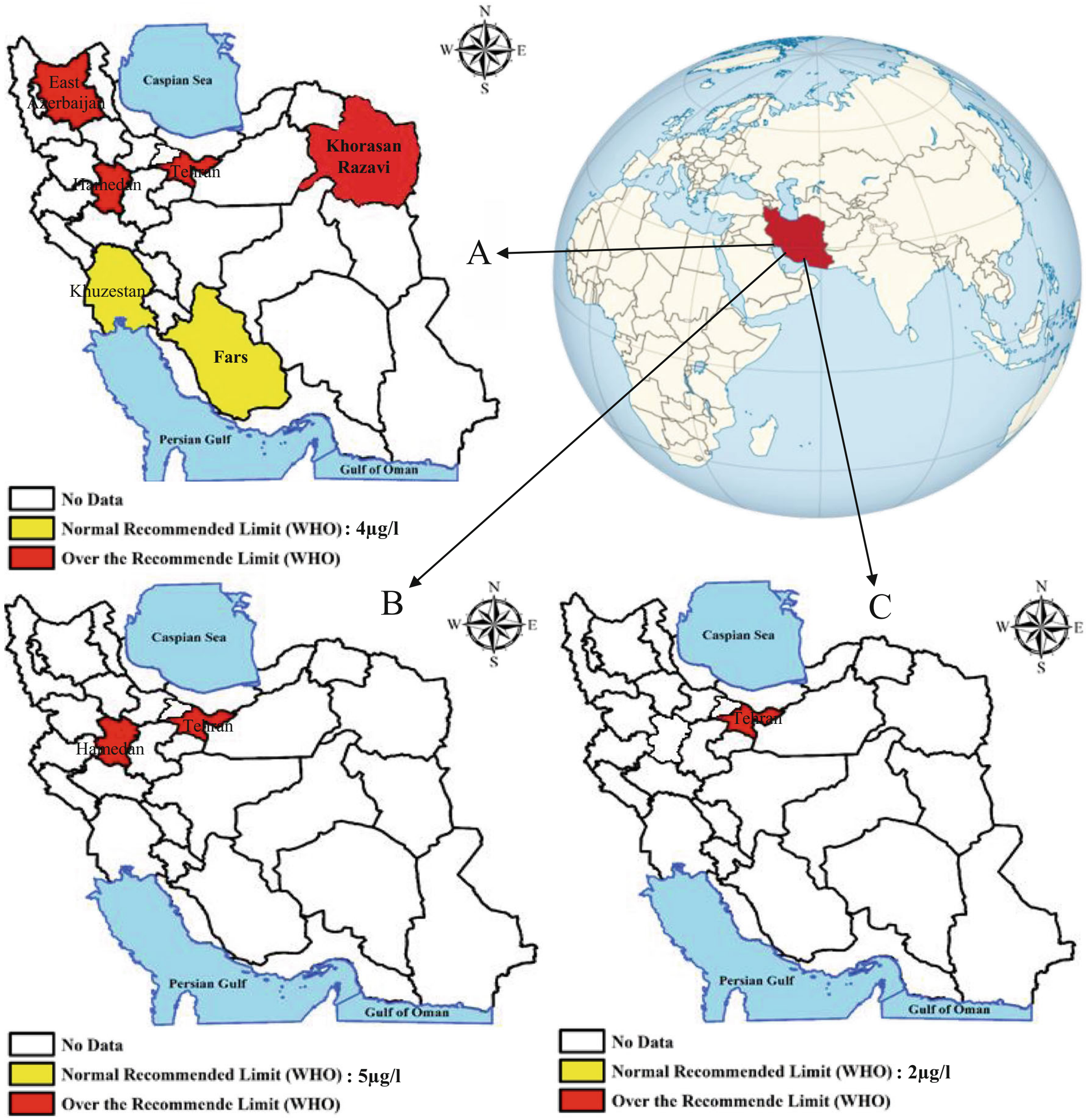

Fig. 5 Geographical distribution of mercury levels in urine (**a**), blood (**b**), and hair (**c**) of IDs according to WHO standard

Among the analytical methods mentioned above, the BML of IDs was obtained using FI-CVAAS and CVAAS. The urine mercury content was obtained by FI-CVAAS, CVAAS, and AAS. Also, AMA-S-PAAS method was employed to measure mercury level in the hair and nail.

Mean of mercury level in Iranian densities based on study type The mean of mercury in cross-sectional studies was higher than that in the analytical cross-sectional works (Fig. 7).

Meta-regression

Meta-regression was used to discover the sources of between-study heterogeneity, including study sample size and age of the participants. Based on the results, the mean of mercury did not have a relationship with sample size (*p* value >0.10) and age of individual (p value >0.10).

Discussion

In occupational exposure, dentists are one of the most important at-risk groups to mercury due to the frequent use of DA (containing approximately 50% mercury) during work activities. Therefore, it is expected that the health of such specialists will be at serious risk due to repeated exposure to this highly toxic element [77]. Also, the European Union approved the MC by law on May 17, 2017 in the European Parliament and the Council. Article 10 of the Regulation stipulates the law

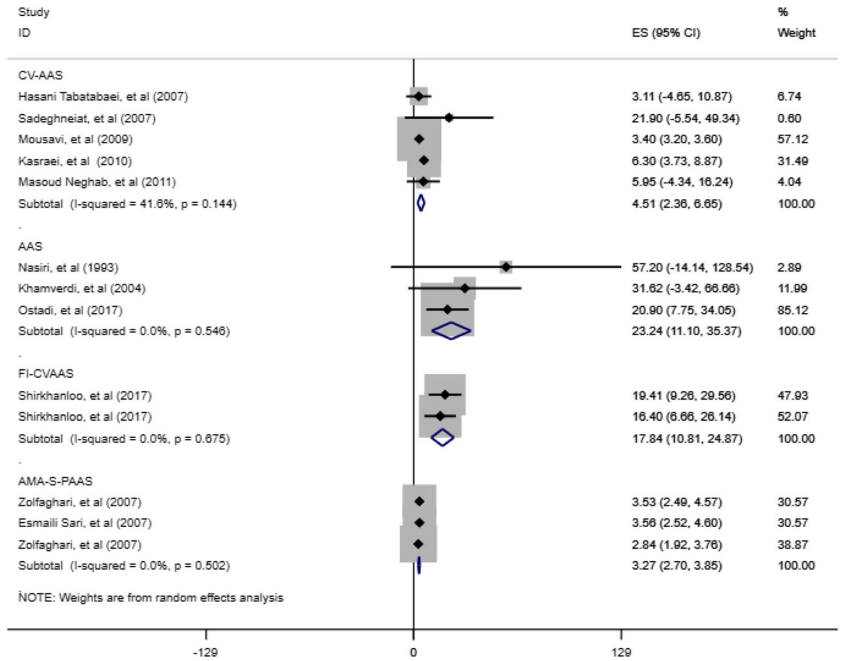

Fig. 6 Subgroup analysis: Standardized mean difference of mercury in Iranian densities based on analytical technique

concerning DA and its management [78]. Since the global treaty of MC (specifically for mercury) was signed by the Iran and over one hundred countries in October 2013 [79], it is necessary that the researchers of the country, through scientific research on the modeling and geographical monitoring of mercury and mercury compounds in vulnerable populations, under Article 19 of this Convention (research, development, and monitoring), strive to successfully manage and enforce the MC [55]. So, for the prevention, protection, and promotion of dentists' health in the face of mercury, we need a overall understanding of the current situation for planning and formulation of appropriate policies for the future [9]. Generally, studies have been performed on mercury levels in different biological samples of IDs; but, the results of some studies are different. Therefore, the present meta-analysis was performed to determine the MML in biological samples of IDs and compare it with WHO standard. According to WHO's guideline, the mercury levels of 5 μg/l, 4 μg/l, and 2 μg/g were considered as "reference values" in the blood, urine, hair, and nail of humans, respectively [12, 49]. But, few researches have been done on nails and there is no standard limit for at least one of the available studies.

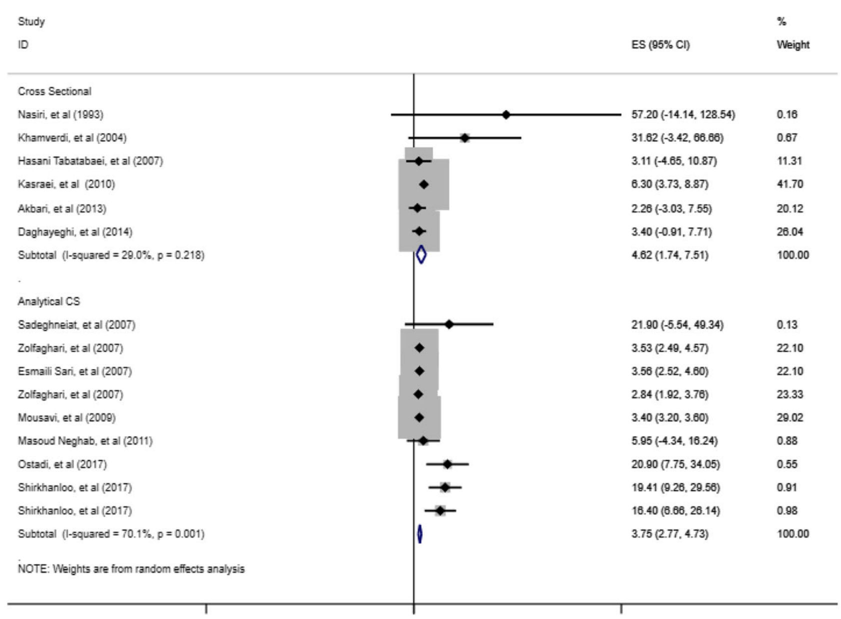

Fig. 7 Subgroup analysis: Standardized mean difference of mercury in Iranian densities based on study type

Blood, urine, hair, and nail were considered as appropriate bio-indicators of mercury contamination for determining the human risk factors in studying toxic metals [9]. Mean of BML was estimated to be 11.20 μg/l for IDs. Results of this study showed that the mean BML in IDs was higher than the WHO standard. According to WHO's report, contact with EMVs in dentistry is the most important source of high inorganic mercury in biological samples of dentists [49]. Although this may have occurred due to exposure to personal amalgam fillings in dentists' mouth [70, 80, 81], but high concentrations of mercury in the blood may be due to unprofessional exposure (for example, fish consumption). Blood mercury may reflect inorganic mercury exposure in recent weeks, but this amount is also affected by the consumption of organic mercury in food [82]. So, increased BML can occur after prolonged exposure to inorganic mercury [7]. Although it is difficult to distinguish between occupational and non-occupational exposure to mercury in human biological samples, in the study by Sadeghneiat et al. [66], via removing the effect of seafood consumption, the reason for high levels of mercury in dentists was found to be directly by inhalation of EMVs while working with DA. Also, in the work by Kasraie et al. [65], it was reported that BML in dentists was significantly correlated with higher working hours and number of amalgam restorations per day. Some studies have reported inconclusive evidence with no correlation or relatively weak correlation between the number of amalgam fillings and mercury levels [83–85]. In this work, the mean of BML was reported to be higher than the allowable limit of WHO in all relevant studies, which was consistent with the results of other studies in the world. This rate varies in different countries of the world: Egypt (7.74 μg/l) (86), Pakistan (29.83 μg/l) [81], Turkey (9.03–45.02 μg/l) [87], Turkey (35.7 μg/l) [88], Singapore (9.8 μg/l) [89], and USA (8.2 μg/l) [90]. However, results of studies in other countries, such as USA (3.75 μg/l) [91], Turkey (3.76 μg/l) [92], Denmark (4 μg/l) [93], and USA (3.67 μg/l) [80], are below the WHO reference value. The mean BML in dentists varies worldwide and, in the present study, was within the range of 6.30–21.9 μg/l. Various factors could be the cause of these changes in the BML of dentists in different countries. Probably, the reason of difference in BML in dentists, as well as occupational exposure to DA (poor and inadequate protective equipment), may be other factors such as type of nutrition, age, long working experience, exposure time, and geographic area [94]. However, factors such as the analysis method of samples and contaminated samples might influence the final results. In general, most of the health effects of organic mercury and metallic mercury compounds are related to the central nervous system, so increasing exposure to mercury can impair brain function and lead to tremors, shyness, irritability, memory problems and changes. Be in hearing or sight. [3, 7]. But, because these symptoms are also common in other diseases or conditions, it can be difficult to diagnose mercury poisoning in such cases [95]. However, pregnant dentists should be careful about this, because mercury exposure in pregnant women can affect the fetus and fetus may suffer from mental retardation, cerebellar symptoms, retention of primitive reflexes, malformations, and other abnormalities [32].

Among the methods of measuring mercury levels in biological samples of dentists, the most practical and sensitive method of measuring mercury in the body is urine mercury testing. Determining urinary mercury level in dentistry is used to test exposure to metallic mercury vapor and inorganic forms of mercury. A review of UK dentists data for the control of low-level occupational exposure to inorganic mercury also confirms this issue [96]. The results showed that the mean urinary mercury level was estimated to be 9.94 μg/L for IDs. Overall, the mean urinary mercury level in IDs was within the range of 3.11–57.2 μg/l. The mean of urinary mercury level in IDs compared with the reference value of WHO was higher, which was consistent with the results of other works in countries of Turkey (6.29 μg/L) [97], Egypt (10.02 μg/L) [86], the Netherlands (12.40 μg/L) [98], Tunisia (neuropsychological effects) (21.1 μg/g) [99], and Tunisia (20.4 μg/g) [100]. However, the results of studies in other countries, such as USA (3.22 μg/L (males), 1.98 μg/L (females)) [101], USA (1.32 μg/l) [91], Mexico (3.16 μg/l) [102], USA (1.28 μg/l) [80], USA (1.06 μg/L) [103], United Kingdom (1.73 μmol/mol) [96], and Scotland (2.58 nmol/mmol) [104], are below the WHO reference value. Although, for researchers, it is very difficult to determine the mercury level in biological samples of dentists through the consumption of fish or other food sources, inhaling inorganic mercury vapors in dental practice, or individual's own amalgam restorations, various studies have considered different factors to be effective for mercury concentration of dentists. However, the amount of mercury exposure depends on various factors such as personal status of the dentist (age, work history, and number of repairs per week) as well as exposure to mercury during preparation, placement, and removal of amalgam restorations [105, 106]. Amalgamator type, ventilation, and compliance with health standards such as washing and cleaning the equipment and manipulating spilled droplets are effective in exposure [107, 108]. In the study by Khamverdi et al. [75], there was significantly positive correlation between UML and number of daily amalgam restorations as well as how to clean amalgam-contaminated utensil used by IDs; the number of daily amalgam restorations was reported as the most important factor in increasing the urinary mercury level of IDs. The study of Nasiri et al. confirmed this [76]. In Khamverdi et al. [75], the researchers reported that relationship between urinary mercury level and how to clean amalgam-contaminated devices can be attributed to the release of mercury vapors during the various sterilization stages of amalgam-contaminated devices, which is linked to the ventilation condition and sterilization place. In this regard, Nixon et al. [109] demonstrated that increased ventilation would reduce the amount of mercury vapor in the air and, ultimately, reduce the amount of mercury in the body. However, in the study of Shirkhanloo et al. [64], no significant correlation was found between UML of IDs and manner of cleaning amalgam-contaminated utensil and air conditioning. In Hasani Tabatabaei et al. [73], there was a significant relationship between daily and weekly work hours, age, number of amalgam fillings, work history, and type of amalgam consumed (capsular or bulk), on the one hand, and urinary mercury level of dentists, on the other hand. But, there was no significant relationship between urinary mercury level and other factors such as how to remove excess mercury, storing stiff amalgam, crude amalgam storage, and presence and absence of ventilation. In the study by Akbari et al. [69], duration of work, type of amalgam consumed, and number of amalgam restorations per week had no effect on dental UML. But, type of ventilation system and type of amalgam discharge were effective for urinary mercury levels. Daghayeghi et al. [68] found no statistically significant relationship between urinary mercury levels and variables such as age, work experience, and number of teeth restored with amalgam. In the study by Ostadi et al. [67], there was a significant relationship between work experience and type of amalgam consumed with urinary mercury level; but, there was no relationship between amalgam waste disposal, washing equipment, mercury storage, and ventilation type. In various studies, the results of dentists' UML may be inconsistent, which could make interpretation and analysis difficult. So, regarding the low level of mercury in IDs in some studies, except for non-occupational exposure (fish consumption, etc.), it may be argued that adherence to health principles when working with amalgam, reducing the incidence of tooth decay, using composite for posterior teeth restoration, application of capsular amalgam, and increased use of tooth-colored restorative materials are causes of low mercury in dentists' urine samples.

In the only study on hair mercury level (HML) in IDs, mean was assessed to be 2.84 μg/g. The results of this work showed that the mean HML in IDs compared with the allowable limit of WHO was higher, which was consistent with the results of other studies in countries of Lebanon (5.58 μg/g) [110] and USA (4.11 μg/g) [111]. However, the results of studies in other countries, such as Sri Lanka (0.005 μg/g) [112], USA (0.60 μg/g) [80], USA (0.62 μg/g) [91], the Netherlands (1.88 μg/L) [98], USA (0.51 μg/L) [103], CZECH (0.51 μg/L) [113], United Kingdom (0.71 μg/g) [96], and Scotland (1 μg/g) [104], were below the WHO reference value. Also, mean nail mercury levels (MNM) in IDs was estimated to be 3.54 μg/g. This rate differs in countries of the world: United Kingdom (1.42 μg/g) [96], Scotland (5.25 μg/g) [104], and Sweden (0.12–2.80 μg/g) [114]. Nail and hair analyses are useful for estimating mercury bioavailability, especially in estimating long-term historical exposure [96]. While mercury levels in the hair and nail are used as a biomarker of chronic MeHg exposure, this is not regarded reliable for inorganic Hg levels, since external contamination may be an error source [96]. Also, although fish consumption and occupational exposure are effective factors for increasing the mercury concentration in IDs, use of other sources such as cosmetics or chemical shampoos can potentially affect the amount of mercury in the hair [115, 116].

Limitations

An heterogeneity of mercury measurement units between different studies in the blood, urine, hair, and nail of IDs has been observed in the present study. Therefore, the subgroup analysis was performed separately for pooled mean of mercury in IDs. In many studies, mercury levels in biological samples of IDs have not been reported based on gender, age, and work experience; this makes it impossible to provide statistics for meta-analysis. Another limitation of the present study was the non-representativeness of the study population. Therefore, our results are an overview of the evidence on MML in the blood, urine, hair, and nail of Iranian densities and it does not necessarily show the level of mercury exposure in all the population groups in Iran.

Conclusion

This study outlined and justified the need for a well-structured Iran mercury exposure dataset. In this study, studies on mercury concentrations in the blood, urine, hair, and nail of IDs were studied. The concentration values of these materials were also compared with the WHO standards. Mean of total mercury levels in the blood, urine, hair, and nail of IDs were greater than the WHO standard. So, it is important to manage and monitor mercury levels in IDs in different cities amongst the country. It is also essential to identify all potential risk factors for mercury exposure. According to the MC, Article 10 of European Union of the Regulation stipulates the law concerning DA and its management. So, according to the regulations adopted, from 1 July 2018, DA shall not be used for dental treatment of deciduous teeth, of children under 15 years old, and of pregnant or breastfeeding women, except when deemed strictly necessary by the dental practitioner based on the specific medical needs of the patients. Therefore, in order to avoid the dangers of mercury exposure in dentists, it is necessary, in agreement with the law enacted in Article 10 of these Regulations, in Islamic republic of Iran and other countries to approve the necessary laws and to implement a national plan in order to reduce mercury levels and replace suitable substances with it.

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Compliance with ethical standard

Conflict of interest The authors of this article declare that they have no conflict of interests.

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