Dental amalgam risks in dental staff: systematic review

Abdelkarim Manyani[1,2,*], *Hanane* Chaou [2], *Naima* Rhalem[2], *Abdelmajid* Soulaymani[1], *and Rachida* Soulaymani Bencheikh[2,3]

[1] Department of Biology, Faculty of Sciences, IbnTofail University, Kenitra, Morocco
[2] Department of Toxicovigilance, Poison Control and Pharmacovigilance Center, Morocco
[3] Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco

Abstract. Mercury is an essential constituent of dental amalgams, several studies have shown that dental personnel who work with dental amalgams are chronically exposed to mercury vapors. The World Health Organization considers that inhaling mercury vapors can have harmful effects on the nervous, immune, pulmonary and renal systems. The objective of this review was to collect and analyze data relating to the exposure of dental personnel to mercury and the possible harmful effects on human health. All biomonitoring studies published between 2002 and 2019 measuring mercury in hair, blood, urine and nails were included. Dentists reported higher levels of mercury in their biomarkers compared to control groups. These levels reflected occupational exposures to chronic low levels of elemental mercury in dental amalgam fillings. Some studies have shown a high prevalence of neurological symptoms and memory deficit in dental staff compared to controls. Studies based on genes involved in mercury metabolism have shown associations between sources of mercury exposure and single nucleotide polymorphisms in these genes. It is important that preventive measures are strengthened to reduce exposure to mercury and that a biomonitoring program for dental professionals exposed to mercury vapors is implemented.

1. Introduction

Dental amalgam is used in dentistry as a restorative material [1]. It is a mixture of metallic mercury (about 50% of the weight of the powder / liquid mixture) and a set of powdered metals (silver 35%, tin 9%, copper 6% and traces of zinc) [2].

The problem is that when handling these dental amalgams, they release mercury vapour. However, since elemental mercury is absorbed by direct skin contact or by inhalation, the use of mercury in dental amalgam continues to be a controversial issue, as it can pose occupational risks to dentists and their assistants [3, 4]. Therefore, dental professionals, handling these amalgams, are exposed daily to this vapour. Indeed, several studies have shown that after the inhalation of this mercury vapour, approximately 80% of the inhaled vapours are absorbed by the pulmonary tissues and join the blood circulation [2, 5]. Once in the blood, elemental mercury (Hg^0) is easily distributed throughout the body and it will penetrate all tissues and organs. Mercury is easily converted to an organic form and causes destruction of proteins and DNA and also damage to cell membranes [6-11]. Long-term exposure to Hg^0 has also been associated with similar effects on the central nervous system (CNS), resulting in memory loss, depression and anxiety [12].

Over the past 20 years, many studies have been designed to measure the effects of mercury in many groups of dental professionals. The objective of this review was to collect and analyse the data, reported in the published scientific literature, relating to the exposure of dental staff to mercury and the risks to human health. It is expected that the exposure data collected here will provide information relevant to future work on the assessment of the association between the use of dental amalgams and occupational exposure to mercury among dental staff.

2. Materials and methods

In order to choose the studies to include in our analysis, we set a protocol for the research strategy with the following selection criteria:

- Articles evaluated by peers,
- Articles published in English or in French.
- All the original articles assessing the risks and health effects due to occupational exposure to mercury among dental professionals.
- All biomonitoring studies measuring mercury in urine, blood, head-hair, fingernail and saliva were included.
- Period: between January 2002 and December 2019.
- Search terms: dental amalgam, mercury, mercury toxicity, occupational exposures, have been combined with terms relating to dental personnel such as dentists, dental nurses, dental assistants.
- The Boolean operators (e.g. AND, OR and NOT) the truncation (*) were used.
- The searches were carried out using three electronic databases for the literature published in Science Direct, PubMed and Web of Science.
- Articles including dental students were excluded because dental students were not considered to have had time in clinical practice to be able to develop significant exposure to mercury or associated health symptoms.

- These articles were examined in several stages: first, the duplicated studies were deleted in order to avoid duplication, then the title and summary fields were searched to check their relevance, and the full text was examined on the articles deemed potentially relevant.

1. Results

The studies examined the levels of mercury detected in biological fluids (urine, whole blood and saliva) and tissues of dental personnel (hair and nails), personal characteristics and the impact of mercury exposure, both occupational and non-occupational, on the health of dental professionals. In total, we collected 247 scientific articles. The total sample population for these surveys, which sometimes span over several years, included 8,889 people, including 12,489 measurements of biomarker exposure to mercury (Figure 1). The studies represented dental staff from 14 countries. The exposed groups included dentists, dental nurses and dental assistants. Figure 2 represent a distribution of the articles selected by country of study. The percentage of cross-sectional studies was 74% while that of cohort studies was 26%.

The benchmarks for the biological exposure index were 35µg/g creatinine for urine and 15µg/L for blood, as set by the World Health Organisation and the American Conference of Governmental Industrial Hygienists (ACGIH) [13].

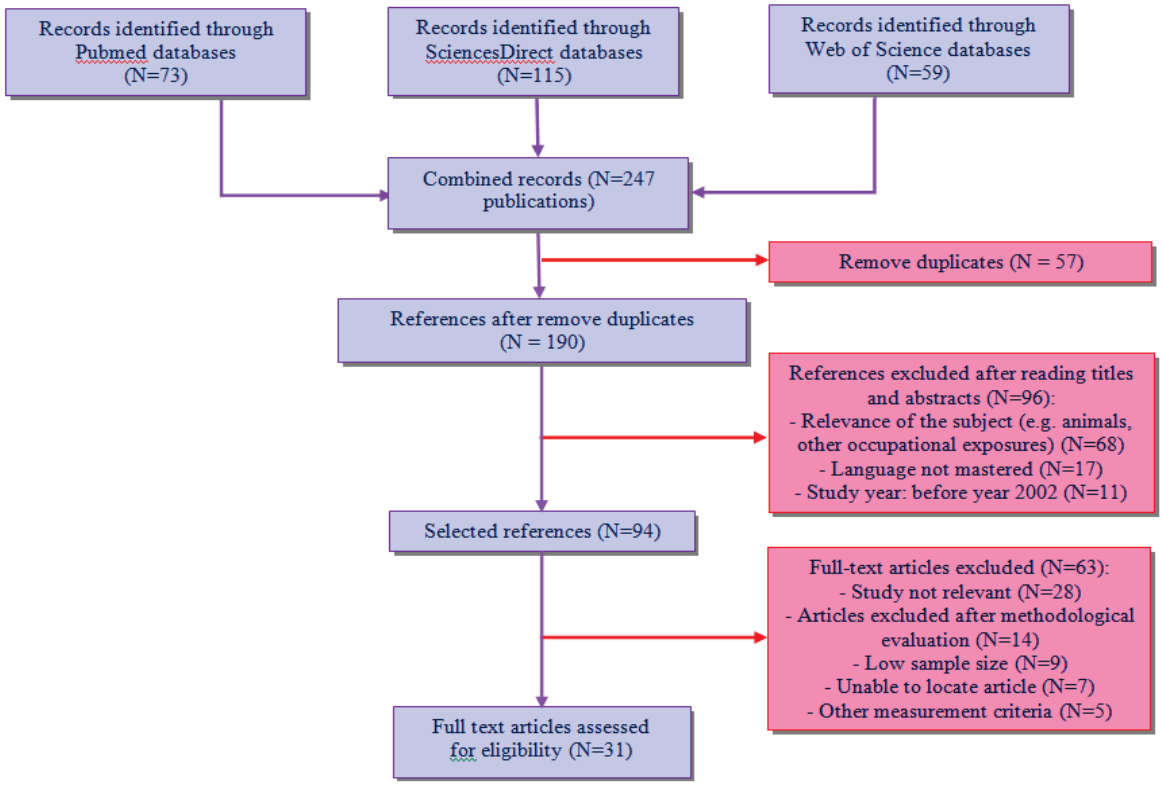

Fig.1. Flowchart showing the process of identifying, sorting and selecting articles included in the current review. Dental amalgam risks in dental staff: systematic review, 2002-2019.

2. Discussion

Mercury enters the human body through inhalation, skin contact, ingestion, and via the placenta. Whether exposure to the various forms of mercury will harm a person's health depends on a number of factors, such as the chemical form of mercury, the dose, the age of the person exposed, the duration of exposure, the route of exposure-inhalation, ingestion, dermal contact, and the health of the person exposed [13]. Dental staff is exposed to mercury through the handling of dental amalgam fillings. Biomonitoring of this exposure is possible by measuring the level of mercury in various body fluids (such as urine, blood, breast milk or saliva) or in body tissues (hair, nails or umbilical cord blood).

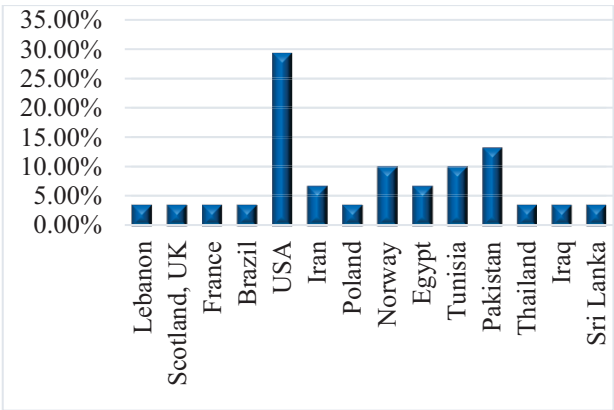

Fig. 2. Distribution of 31 articles selected according to the country of study. Dental amalgam risks in dental staff: systematic review, 2002-2019.

Data on exposure in dentists were obtained from cross-sectional or cohort biomonitoring studies, the distribution of selected articles by type of study is presented in Figure 3.

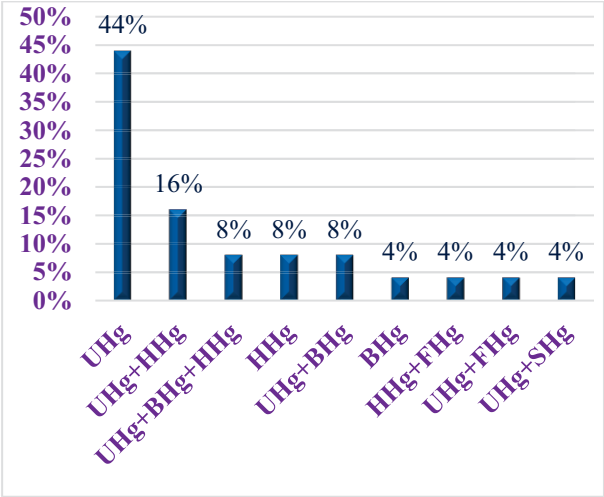

Fig. 3. Distribution of studies depending of biomarkers used. Dental amalgam risks in dental staff: systematic review, 2002-2019. Note: HHg: head-hair mercury concentrations. UHg: urinary mercury concentrations. BHg: blood mercury concentration. FHg: fingernails mercury concentration. SHg: saliva mercury concentration.

Urine mercury levels are generally considered the best measure of recent exposures to inorganic mercury or elemental mercury vapor, as urinary mercury most closely indicates levels of mercury present in the kidneys. Note that there is a strong correlation between elemental mercury in inhaled air and urinary mercury at medium and high concentrations [13]. The American Conference of Governmental Industrial Hygienists (ACGIH) set creatinine corrected urinary mercury (U-Hg) in spot urine samples, as the recommended biological monitor for workers exposed to metallic mercury and the level of 1–5 µg Hg/g creatinine was determined as a background level in persons not occupationally exposed to mercury. The level of 35 µg Hg/g creatinine is considered as Biological Exposure Index (BEI) that necessitates exclusion of the mercury exposed worker to another job where there is no mercury exposure until its level declines to baseline value. Therefore, using urinary mercury (U-Hg) was adopted in many studies investigating mercury load in dental personnel [3, 13]. In this review, we found 84% of studies measuring mercury in urine (Figure 3). When analysing these studies, we noticed that the mercury concentration was between a minimum of 0.70 µg Hg/L and a maximum of 1065 nmol/L (which corresponds to 120 µg Hg/L) as well as this concentration, depending on creatinine, was between a minimum of 0.44 µg Hg/g creatinine and a maximum of 19.76 µg Hg/g creatinine. In the majority of countries, urinary mercury concentrations in exposed subjects were at least twice as high as in controls. In agreement, 54.55% of the studies found a significant difference between dental personnel and control subjects. In addition, the urinary mercury level in dental personnel was much higher than in control subjects in three countries; Egypt (in 2009 and 2011), Tunisia (in 2009, 2015 and 2018) and Norway (in 2010) (Table 1; see also Figure 4). This can be explained by the fact that dental practitioners handle dental amalgam and use it as dental filling materials, which makes them exposed to the mercury vapours given off during this manipulation. A study in Poland (2007) found no significant difference in mean urinary Hg concentrations between dental professionals and control groups, except that the duration of dental practice showed a statistically significant influence on Hg-U total ($r = 0.3000$; $p = 0.024$) [2]. Another study in the United States (in 2012) found no significant difference in mean of urine Hg concentrations between dental professionals and control groups, apart from three out of a total of 504 subjects showed stable and statistically significant interaction of single nucleotide polymorphisms (SNPs) with mercury biomarkers [14].

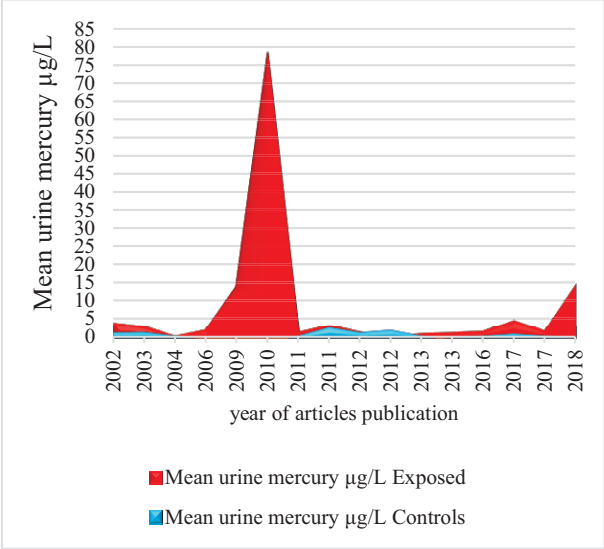

Fig. 4. The mean urinary mercury concentration (µg / L) in exposed and controls subjects according to the year of publication. Risks associated with dental amalgam fillings among dental personnel: systematic review, 2002-2019.

Blood mercury levels; As the blood mercury level reflects organic mercury as well as metallic and inorganic mercury (i.e., influenced by the consumption of fish contaminated with methylmercury), it is not recommended as reliable indicator of total body burden in longer-term exposures. It is useful primarily in cases of short-term, higher level exposures to metallic form, and the level of 15 µg/L is considered the Biological Exposure Index (BEI) [3, 13]. From the selected articles, it was noted that the blood mercury level in dental personnel was higher than in control subjects. The blood mercury concentration in exposed subjects, participants in the study which took place in Pakistan (2016), exceeds 15µg / L, the maximum mean concentration of which was recorded in dentists (29.835 µg / L), followed by dental assistants (22.798 µg / L), whereas the minimum concentration was recorded in Iraq (2017) in exposed subjects (1.241 ± 0.13 mg / L). Blood was used to assess mercury level in 20% of the selected studies (Table 1).

Table 1. Levels of mercury in biological markers, based on studies of occupational mercury exposure. Risks of dental amalgam among dental personnel: a systematic review. 2002- 2019.

Study details	Study population	Biomonitoring results	Refe-rence
- Steve Harakeh et al (2002) Lebanon - Cross-sectional study	- Dentists : n=96 - Controls: n=0 (no controls recorded)	- H-Hg (Overall mean) : 4.11 µg/g - Number of amalgams in the dentist's teeth (Nr Amlg) : (H-Hg ; Mean ± SD) (P = 0.302): ♠ Nr Amlg ≤ 5 **:** 3.83 ± 2.84 µg/g ♠ Nr Amlg >5 **:** 4.40 ± 4.26 µg/g	[15]
- K A Ritchie et al (2002) Scotland - Cross-sectional study	- Dentists:n = 180 - Control : n=180	- U-Hg (Mean ± SD) (nmol Hg / mmol creatinine): ♠ Dentists: 2.58 ± 2.76 ♠ Controls: 0.67 ± 0.68 - U-Hg (Mean ± SD) (µgHg/L): ♠ Dentists: 3.61 ± 3,87 ♠ Controls: 0.94 ± 0.95 - F-Hg (Mean ± SD) (mass Hg/g): ♠ Dentists: 5.25 ± 20.60, ♠ Controls: 0.32 ± 0.30	[16]
- B. Bouard et al (2003) France - Cross-sectional study	- Dental assistants: n=71 - Control : n=71	- U-Hg (Mean ± SD) (µg/l) (p = 0,000002): ♠ Dental assistants: 2,64 ±3,5 range (0,25 - 22,5) ♠ Control: 1,05 ±1,3 range (0,2 - 7,9)	[17]
- Heyer NJ et al (2004) USA - Cohort study	- Dentists: n=193 - Dental assistants : n=230 - Controls: n=0	- U-Hg (Mean ± SD): 2.32µg/l ± 1.49	[12]
- L. Canto-Pereira et al (2005) Brazil - Cross sectional study	- Dentists : n= 15 - Control : n=13	- U-Hg (Mean ± SD) (µg/g creatinine) (p = 0.0235): ♠ Dentists: 1.97±1.61 ♠ Controls: 0.75±0.40	[4]
- Nicholas J. Heyer et al (2006) USA -Cohort study	- Dentists : n = 80 - Dental assistants : n = 98 females - Controls: n=0	- U-Hg (Mean ± SD) (µg/l) (p= 0.03) : ♠ Male dentists: 1.9±1.8, ♠ Dental assistants: 1.4±1.6	[18]
- G. Zolfaghari et al (2007) Iran - Cross-sectional study	- Dentists : n=100 - Dental nurses : n = 25 - Control : n=50	- H-Hg (Mean ± SD ; range) (mg/kg dry wt) (p = 0.06) ♠ Dentists: 2.84 ± 0.47 (0.09- 25.43) ♠ Controls: 0.61 ± 0.07 (0.10–2.56). ♠ Dental nurses: 0.92± 0.23; (0.12–4.56) - F-Hg (Mean ± SD ; range) (mg/kg dry wt): ♠ Dentists: 3.56 ± 0.53 (0.10–7.27) ♠ Controls: 0.39 ± 0.06 (0.01– 0.55) ♠ Dental nurses: 1.77 ± 0.51 (0.01–8.68)	[19]
- Małgorzata Trzcinka-Ochocka et al (2007) - Poland - Cross-sectional study	- Dentists and dental nurses : n = 51 - Control : n=16	- U-Hg (Mean ± SD) (µg/g creatinine): ♠ Exposed: 0.44±0.44, ♠ Controls: 0.57 ± 0.27	[2]
- S. Farahat et al (2009) Egypt - Cross-sectional study	- Dental staff : n = 39(21 dentists and 18 dental nurses) - Control : n=42	- U-Hg (Mean ± SD) (µg Hg/g creatinine) (P < 0.001) : ♠ Dental staff: 19.76 ± 1.37, ♠ Controls: 5.44 ± 1.18 - B-Hg (Mean ± SD) (µg/L) (p< 0.001) : ♠ Dental staff: 7.82 ± 0.97, ♠ Controls: 4.82 ± 0.75	[3]
- N. Chaari et al (2009) Tunisia - Cross-sectional study	- Dental staff : n = 52 - Controls : n= 52	- U-Hg (Mean ± SD) (µg/l) (p = 0.001) : ♠ Dental staff: 13.8 ± 22.7 ♠ Controls: 0.03 ± 0.2	[20]
- K. Svendsen et al (2010) Norway - Retrospective cohort study (1960 - 1990)	- Dental nurses : n =143 - Dentists : n =130 - Controls: n=0	- U-Hg (Mean ± SD) (nmol/l): ♠ Dentist and dental nurses 74 ± 91.4 [from Norwegian National Institute of Occupational Health] - U-Hg (nmol Hg/l) (p < 0.005) : ♠ Dental nurses: max = 1065 ♠ Dentists: max = 305	[21]
- Jaclyn M. Goodrich et al (2011) USA - Cross-sectional study	- Dental staff : n=515 ♠Dentists: n=243 ♠Non-dentists: n= 268 - Controls: n=0	- U-Hg total population (Mean ± SD): 1.04 ± 1.18 µg/l - U-Hg (Mean ± SD) µg/l (p < 0.001) : ♠ Dentists: 1.37 ± 1.3 ♠ Non-dentists: 0.75 ± 0.97 - H-Hg total population (Mean ± SD) : 0.49 ± 0.63 µg/g - H-Hg p < 0.001 (Mean ± SD) µg/g: ♠ Dentists: 0.69 ± 0.81 ♠ Non-dentists:0.31 ± 0.33	[22]
- Aicha Samir et al	- Dental staff :	- U-Hg (Mean ± SD) (µg Hg /mg creatinine) (p < 0.001):	[10]

(2011) Egypt - Cross-sectional study	n=32 - Controls: n =37	♠ Exposed: 10.02 ± 1.36 ♠ Control: 4.74 ± 0.84	
- Masoud NEGHAB et al (2011) Iran - Cross-sectional study	- Dentists : n=106 - General practitioners (GPs) : n =94	- U-Hg (Median and range) (µg/l) (p = 0.02) ♠ Dentists: 2.86 (0.01–18.1) ♠ GPs: 2.26 (0.21–5.6) - U-Hg (Median and range) (µg/g creatinine) (p = 0.049) ♠ Dentists: 3.16 (0.01–30) ♠ GPs: 2.18 (0.33–5.08)	[23]
- Yi Wang et al (2012) USA - Cross-sectional study	- Dental professionals : n=515 - Controls: n=0	- Dental professionals: Mean U-Hg : 1.06 µg/l ; Mean H-Hg : 0.51 µg/g - US general population : Mean U-Hg : 0.95 µg/l; Mean H-Hg : 0.47µg/g	[14]
- Alfred Franzblau et al (2012) USA - Cohort study (1997–2006)	- Dental professionals: n=2656 - Controls: n=0	- U-Hg ($p < 0.001$) ♠ Dental professionals (Mean ± SD): 3.46 ± 3.35 µg/l range (0.14 to 49.3) ♠ NHANES: 1.55 µg/l	[24]
- Jaclyn M. Goodrich et al (2013) USA - Cohort study	- Dental staff : n=131 - Controls: n=0	- H-Hg (geometric mean, 95% CI): 0.37 µg/g (0.31–0.44) - U-Hg (geometric mean, 95% CI): 0.70 µg/l (0.60–0.83)	[7]
- Jaclyn M. Goodrich et al (2013) USA - Cohort study	- Dental staff : n=284 - Controls: n=0	- H-Hg (Mean ± SD): 0.45 ± 0.53 µg/g range (0.02–5.18) - U-Hg (Mean ± SD) : 0.94 ± 0.99 µg/l range (0.03–5.54)	[25]
- Somsiri Decharat et al (2014) Thailand - Cross-sectional study	- Dental staff: n=124 - Controls :n=124	- U-Hg (Mean ± SD) (µg/g creatinine) ($p < 0.001$): ♠ Exposed: 8.24 ± 1.89 ♠ Unexposed : 2.00 ± 0.11	[26]
- Neila Chaari et al (2015) Tunisia - Cross-sectional study	- Dentists: n= 64 - Non exposed subjects: n= 64	- U-Hg (Mean ± SD) (µg/g creatinine) ($p < 0.05$): ♠ Dentists: 21.1 ± 19.6 ♠ Unexposed : 0.05 ± 0.9	[27]
- Nadia Jamil et al (2016) Pakistan - Cross- sectional study	- Dentists : n=37 - Dental assistants : n=31 - Controls : n=30	- B-Hg (Mean) (µg/L) ($p < 0.05$): ♠ Dentists: 29.8 ♠ Dental assistants : 22.7 ♠ Controls : 3.2769	[28]
- Rajendra Parajuli et al (2016) USA - Cohort study (2012)	- Dental staff: n=380 - Controls: n=0	- H-Hg (Mean ± SD): 0.62 ± 1.01 µg/g range (0.01–7.45) - B-Hg (Mean ± SD): 3.75 ± 3.96 µg/L range (0.2–25.3) - U-Hg (Mean ± SD): 1.32 ± 1.76 µg/L range (0.14 – 11.5)	[29]
- Enas Sultan Al-Zubaidi et al (2017) Iraq - Cross-sectional study	- Dentists and dental assistants : n=30 - Controls: n=05	- U-Hg (Mean ± Standard Error (SE)) (µg/L) ($p< 0.05$): ♠ Exposed group : 4.30 ± 0.51 ♠ Controls: 0.57 ± 0.26 - B-Hg (Mean ± SE) (µg/L) ($p< 0.05$): ♠ Exposed group : 1.241 ± 0.13 ♠Controls: 0.192 ± 0.12	[30]
- Jaclyn M. Goodrich et al (2017) USA - Cross-sectional study	- Dental staff : n=630 - Controls: n=0	- Geometric means (GM, 95% CI) range: ♠ H-Hg: 0.60 µg/g (0.54–0.67) range (0.02 - 7.45) ♠ U-Hg: 1.28 µg/l (1.19–1.37) range (0.13–13.1) ♠ B-Hg: 3.67 µg/l (3.37–3.98) range (0.16 to 25.3)	[31]
- N. Chaari et al (2018) Tunisia - Cross-sectional study	- Dental staff : n=52 - Controls: n =52	- U-Hg (Mean ± SD) (µg/l) ($p = 0.001$): ♠ Exposed group: 13.8 ± 22.7 ♠ Controls : 0.03 ± 0.2 - S-Hg (Mean ± SD) (µg/l) ($p < 0.0001$): ♠ Exposed group: 10.6 ± 13 ♠ Controls : 0	[32]
- Lumbini A. Wijesekara et al (2018) Sri Lanka - Cross-sectional study	- Dentists : n=50 - Controls: n=50	- H-Hg (Mean ± SD) (ppb) ($p < 0.05$): ♠ Dentists: 5.36 ± 2.64 ♠ Control groups : 3.1 ± 1.99	[33]

Note: SD: Standard Deviation. H-Hg: head hair mercury concentrations. U-Hg: urinary mercury concentrations. B-Hg: blood mercury concentration. F-Hg: Finger nails mercury concentrations. S-Hg: saliva mercury concentration. dry wt: dry weight. ppb: parts per billion (ppb corresponds to µg/L). NHANES: National Health and Nutrition Examination Survey.

Head-hair mercury levels; Hair sequesters methylmercury during its formation, providing an accurate and reliable method for measuring methylmercury levels in the body. Once incorporated into the hair, mercury does not return to the blood, so it is a good marker for long-term exposure to methylmercury. The normal level of mercury in the hair is 1 to 2 ppm (or 1 to 2 µg/g), but people who consume fish once or more times a day may have levels of Hg in the hair exceeding 10 ppm. The United States Environmental Protection Agency (USEPA) reference dose is approximately 1 ppm of mercury in the hair for people who consume little fish. Hair grows approximately 1cm per month and can be graded along the stem to provide an exposure profile over time; previous exposures remain unchanged for up to 11 years

[13, 22]. We analysed the studies, which used the hair to measure mercury; we found that the average level ranged from a minimum of 0.35 µg Hg/g to a maximum of 5.36µg/g (Figure 6).

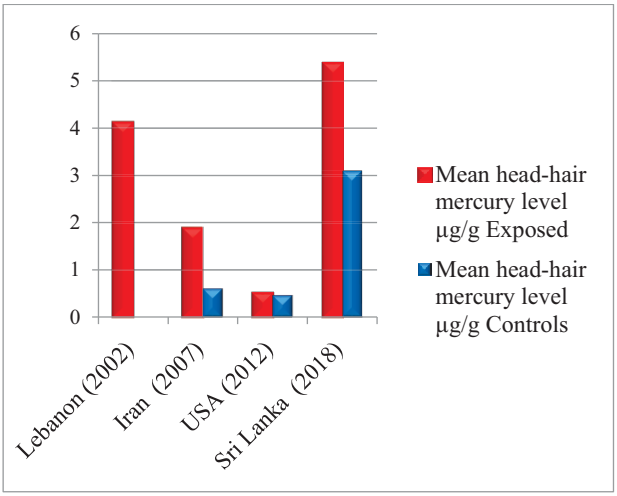

Fig. 6. The mean concentration of head-hair mercury (µg/g) in exposed and controls subjects. Risks associated with dental amalgam among dental personnel: systematic review, 2002-2019.

From the selected articles, it was noted that the level of mercury in the hair of dental workers exceeded the reference dose (1µg/g) in three countries Lebanon (2002) (4.1µg/g), Iran (2007) (1.88µg/g) and Sri Lanka (2018) (5.36µg/g) (Table 1).

Finger nails mercury levels; Only two studies used nails as a biological sample to measure mercury level, one of which analyzed nails and urine and the other analyzed nails associated with hair (Figure 3). It was noted that there is a significant difference between dental staff and control subjects; Scotland, United Kingdom (2002): dentists (5.25 ± 20.60 mass Hg / g), controls (0.32 ± 0.30 mass Hg / g) and Iran (2007): dentists (3.56 ± 0.53 mg / kg dry weight), controls (0.39 ± 0.06 mg / kg dry weight) (Table 1).

Mercury vapour airborne in dental clinics; During the amalgam preparation and tooth restoration process, the mercury vapor is emitted into the air [26]. Studies that determined the concentration of mercury vapor in the air at dental clinics found that mercury vapor concentrations were higher and exceeded the baseline in all dental clinics. In agreement, Enas Sultan Al-Zubaidi et al (2017) conducted a study in Iraq and found that mercury vapor concentrations (µg/m3) from the four sites within dental clinics: S2 (above the work surface) and S3 (around the patient chair) had the highest values of mercury vapor concentrations in all dental clinics [30] (Table 2).

Symptoms related to occupational exposure to mercury; During the handling (installation or removal) of dental amalgams, they release a vapor of mercury, thus dentists and their assistants are exposed daily to this vapor, in fact studies show that after inhalation of this vapor of mercury, approximately 80% of inhaled vapors are absorbed by lung tissue and enter the bloodstream [2, 5]. Typically mercury vapor is absorbed by the body and oxidized to ionic mercury (mercuric form Hg^{2+}), which can covalently bind with cell proteins. This means almost any protein can be damaged if sufficient levels of mercury are present [34]. Mercury is cytotoxic, neurotoxic, immunotoxic, and nephrotoxic, as occupational exposure to high doses of elemental mercury has been shown to affect the immune, renal and nervous system [35]. The central nervous system (CNS) is a sensitive and critical target organ due to the ability of elemental mercury to cross the blood brain barrier and access the CNS. Mercury has a high affinity for selenoproteins, which are important for decreasing oxidative stress [22, 35]. The effects of mercury on neural tissue are diverse at these levels of exposure and can include mood changes, memory and concentration problems, headache, fatigue, reduction in hand steadiness, and manual dexterity [35]. As demonstrated by BE Moen et al (2008) that dental assistants reported markedly and significantly more neurological symptoms, psychosomatic symptoms, memory loss, concentration difficulties, fatigue and sleep disturbance than a reference group of assistant nurses. The memory loss seemed to be most important. The possible exposure to mercury among the dental assistants during their work with filling material might be an explanatory factor for this finding, as this exposure was not likely among the referents [36]. According to a study conducted by Aicha Mohamed Samir and Wael Mohamed (2011), dental staff exposed to elemental mercury showed higher levels of urinary and blood mercury compared to their control group. They also concluded that oxidative stress is an important molecular mechanism for renal dysfunction upon exposure to mercury in dental personnel, manifest ed by decreased activity of antioxidant enzymes; glutathione peroxidase (GPX) and superoxide dismutase (SOD) [10]. The results of a study conducted by Masoud NEGHAB et al (2011), indicate that occupational exposure to mercury, even at low levels, is associated with a significant increase in the prevalence of intoxication symptoms such as hyper-pigmentation, breathing problems, irregular heartbeat, hand tremors, upper limb spasms, mood swings, nervousness, anxiety, insomnia, erethism, memory deficit, depression and chronic fatigue, these symptoms were significantly more

Table 2: Mercury levels in dental office air, based on studies of occupational mercury exposure. Risks of dental amalgam among dental personnel: a systematic review. 2002- 2019.

Study details	Study population	Outcomes	Refer ence
- Somsiri Decharat et al (2014) Thailand - Cross-sectional study	- Dental staff: n=124 - Controls: n=124	- 17.6% (n= 32/182) of the air samples were higher than the occupational exposure limit (OEL).	[26]

- M. Khwaja and M. Abbasi (2014) Pakistan - Cross-sectional study	- n = 34 dental sites - Controls: n=0	- Dental sites with air mercury levels > reference level of 300 ng/m^3 : ♠ Teaching institutions (Max – Min) ng/m^3 : 44,067-109 ♠ Hospitals (Max – Min) ng/m^3: 17,172 - 174 ♠ Private clinics (Max – Min) ng/m^3: 1800 - 333	[37]
- Khwaja Mahmood .A et al (2016) Pakistan - Cross-sectional study	- Dental staff : n=131 - Controls: n=30	- Highest mercury levels was in Abbottabad :49,807 ng/m^3 - High mercury levels (5289 ng/m^3) observed in the adjacent corridors.	[38]
- Enas Sultan Al-Zubaidi et al (2017) Iraq - Cross-sectional study	- dental staff : n=30 - Controls: n=05	-Mean ± Standard Error (SE) of the mercury vapor concentrations (µg / m^3) in the ambient air of four dental clinics varied between: 84.7 ± 18.67 and 609.3 ± 238.90.	[30]

prevalent in dentists than in the control groups ($p < 0.05$). In addition, there was a significant association between the number of amalgam fillings per day and neuropsychological and muscular disorders ($p \leq 0.001$) [23]. Jaclyn M. Goodrich et al (2013) report significant associations between diastolic blood pressure (DBP) and capillary mercury ($n = 262$, $p = 0.02$). Exposure to elemental mercury was associated with a significant decrease in systolic blood pressure (SBP) ($n = 262$, $p = 0.04$) [25]. However, Neila Chaari et al (2015) found that mean urinary mercury levels were significantly higher in the dentist group than in the controls, with values of 21.1 ± 19.6 µg/g creatinine and 0.05 ± 0.9 µg/g creatinine, respectively. In nine dentists with urinary mercury levels greater than 35 µg/g creatinine, neurological examination showed an intentional bilateral and symmetrical tremor in both upper limbs. In the exposed group, neuropsychological manifestations and urinary mercury levels were significantly correlated. In the exposed group, scores for neurological symptoms, memory impairment and anxiety were found to be significantly higher than those in controls ($p < 0.01$) [27]. Julia Anglen et al (2015) suggest a positive association between Hg^0 exposure and tremor [39]. Rajendra Prasad Parajuli et al (2016) found that there is an association between sources of Hg exposure and single nucleotide polymorphisms (SNPs) with respect to Hg biomarker concentrations; 38 SNPs had significant main effects and/or gene–Hg exposure source interactions. Twenty-five, 23, and four SNPs showed significant main effects and/or interactions for H-Hg, B-Hg, and U-Hg levels, respectively ($p < 0.05$), and Six SNPs [in Glutamate-Cysteine Ligase Catalytic (GCLC), Metallothionein1M (MT1M), metallothionein 4 (MT4). The findings suggest that polymorphisms in environmentally responsive genes can influence Hg biomarker levels. Hence, consideration of such gene–environment factors may improve the ability to assess the health risks of Hg more precisely [29].

3. Conclusion

This Review reveals that dental practitioners have higher levels of mercury in their biomarkers (urine, blood, head hair, fingernails, saliva) compared to control groups. These levels reflected occupational exposures to chronic low levels of elemental Hg contained in dental amalgams (urine) and to methylmercury through the consumption of fish (hair, blood). Some studies have reported a high prevalence of neurological symptoms and memory deficit among dentists and dental staff compared to controls. Studies based on genes involved in Hg metabolism have shown the associations between sources of Hg exposure and Single nucleotide polymorphisms in these genes. These results obtained in many parts of the world are consequences of the exposure of dental personnel to mercury due to the continued use and handling of dental amalgam, dental professionals must step up preventive measures to reduce exposure to Hg and a biomonitoring program for dental professionals exposed to mercury vapors must be implemented.

4. Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this article.

References

1. Needleman HL, JAMA J. Am. Med. Assoc **295**, 1835–1836 (2006)
2. M. Trzcinka-Ochocka, A. Gazewski, R. Brodzka, Int. J. Occup. Med. Environ. Health **20**, 147–153 (2007)
3. S. A. Farahat, L. A. Rashed, N. H. Zawilla, S. M. Farouk, Toxicol. Ind. Health **25,** 159–167 (2009)
4. L. H. M. Canto-Pereira, M. Lagoa, M. F. Costa, A. R. Rodrigues, C. A. Saito, L. C. L. Silveira, D. F. Ventura, Environ. Toxicol. Pharmacol **19**, 517–522 (2005)
5. WHO, Elemental mercury and inorganic mercury compounds: human health aspects, http://www.who.int/ipcs/publications/cicad/en/cicad50.pdf?ua=1. accessed on december 2020 (2003)
6. L. Bensefa-Colas, P. Andujar, A. Descatha. Rev. Med. Interne **32**, 416–424 (2011)
7. J. M. Goodrich, N. Basu, A. Franzblau, D. C. Dolinoy, Envir. Mol. Mutagen **54**, 195–203 (2013)
8. T. Kea, F. M. Gonçalvesa, C. L. Gonçalvesa, A. A dos Santosa, J. B.T. Rochab, M. Farinac, A. Skalnyd,g,h, A. Tsatsakise, A. B. Bowmanf, M. Aschner, Biochim. Biophys. Acta - Mol. Basis Dis **865**, 2068–2081 (2019)
9. S. A. Farahat, L. A. Rashed, N. H. Zawilla, S. M. Farouk, T. Ind Health **25**, 159–167 (2009)
10. A. M. Samir, W. M. Aref, Toxico Indus Health **27**, 779–786 (2011)

11. T. Syversen, P. Kaur, J. Trace Elem. Med. Biol **26**, 215–226 (2012)
12. N. J. Heyer, D. Echeverria, A. C. Bittner, F. M. Farin, C. C. Garabedian, J. S. Woods **363** 354–363 (2004)
13. UNEP DTIE Chemicals Branch and WHO Department of Food Safety, Zoonoses and Foodborne Diseases, https://www.who.int/foodsafety/publications/risk-mercury-exposure/en/ accessed on april 2020 (2008)
14. S. Harakeh, N. Sabra, K. Kassak, B. Doughan, Sci. Total Environ **297**, 153–160 (2002)
15. K. A. Ritchie, W. H. Gilmour, E. B. Macdonald, FJT. Burke, D. A. McGowan, I. M. Dale, R. Hammersley, R. M. Hamilton, V. Binnie, D. Collington, Occup. Environ. Med **59**, 287–293 (2002)
16. J. D. D. B.Bouard, B. Sawicki, P. Choucroun, G. Durand, R. Baron, "études et enquêtes Exposition professionnelle au mercure des assistantes dentaires," Doc. pour le Médecin du Trav, https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&cad=rja&uact=8&ved=2ahUKEwijkPyt_YzwAhVcShUIHTWKDeUQFjAAegQIAxAD&url=https%3A%2F%2Fwww.inrs.fr%2Fdms%2Finrs%2FCataloguePapier%2FDMT%2FTI-TF-121%2Ftf121.pdf&usg=AOvVaw2o_WzZvzrfcNzvhOiEfca3 accessed on october 2020 (2003)
17. N. J. Heyer, A. C. Bittner, D. Echeverria, J. S. Woods, Toxicol. Lett **161,** 159–166 (2006)
18. G. Zolfaghari, A. Esmaili-Sari, S. M. Ghasempouri, and S. Faghihzadeh, Sci. Total Environ **381**, 59–67 (2007)
19. N. Chaari, A. Kerkeni, S. Saadeddine, F. Neffati, T. Khalfallah, M. Akrout, Rev Stomatol Chir Maxillofac **110**, 139–144 (2009)
20. K. Svendsen, T. Syversen, I. Melø, B. Hilt, Scand. J. Work. Environ. Heal **36**, 231–241 (2010)
21. J. M. Goodrich, Y. Wang, B. Gillespie, R. Werner, A. Franzblau, N. Basu, Toxicol. Appl. Pharmacol **257,** 301–308 (2011)
22. M. Neghab, A. Choobineh, J. H. Zadeh, E. Ghaderi, Ind. Health **49**, 249–254 (2011)
23. Y. Wang, J. M. Goodrich, R. Werner, B. Gillespie, N. Basu, A. Franzblau, Sci Total Env **23**, 1–7 (2012)
24. A. Franzblau, H. d'Arcy, M. B. Ishak, R. A. Werner , B. W. Gillespie, J. W. Albers, C. Hamannd, S. E. Gruninger, H. Chou, D. M. Meyer, Neurotoxicology **33**, 299–306 (2012)
25. J. M. Goodrich, Y. Wang, B. Gillespie, R. Werner, A. Franzblau, N. Basu, Int. J. Hyg. Environ. Health **216**, 195–201 (2013)
26. S. Decharat, P. Phethuayluk, S. Maneelok, P. Thepaksorn, J. Toxicol 2014, (2014)
27. N. Chaari, S. Chebel, I. Merchaoui, A. Kerkeni, F. Neffati, F. Najjar, M. Akrout, Recent Pat. Inflamm. Allergy Drug Discov **9**, 151–158 (2015)
28. N. Jamil, M. Baqar, S. Ilyas, A. Qadir, M. Arslan, M. Salman, N. Ahsan, H. Zahid, Biomed Res. Int., **2016**, 9 (2016)
29. R. P. Parajuli, J. M. Goodrich, H. Chou, S. E. Gruninger, D. C. Dolinoy, A. Franzblau, N. Basu, Environ. Res **149**, 247–258 (2016)
30. E. S. Al-zubaidi, A. M. Rabee, Inhal. Toxicol **0** 397–403 (2017)
31. J. M. Goodrich, H. N. Chou, S. E. Gruninger, A. Franzblau, N. Basu, J Expo Sci Environ Epidemiol **26**, 78-85 (2016)
32. N. Chaari, A. Kerkeni, S. Saadeddine, F. Neffati, T. Khalfallah, M. Akrout, Rev Stomatol Chir Maxillofac **110**, 139–144 (2018).
33. L. A. Wijesekara R. Usoof, S. T. Gamage, R. Jayasinghe, N. Gamage, D. De Silva, J. Investig. Clin. Dent **9**, e12302 (2018)
34. J. Mutter, J. of Occup Med Tox **7**, 614–614 (2011)
35. J. D. Zwicker, D. J. Dutton, J. C. H. Emery, Environ. Heal. A Glob. Access Sci. Source **13**, 1–11 (2014)
36. M. A. Khwaja, M. S. Abbasi, Rev Environ Health **29**, 29–31 (2014)
37. M. A. Khwaja, S. Nawaz, S. W. Ali, Rev Environ Health, 1–7 (2016)
38. B. E. Moen, B. E. Hollund, T. Riise, J. Occup. Med. Toxicol **3**, 1–7 (2008)
39. J. Anglen, S. E. Gruninger, H. Chou, J. Weuve, Mary E. Turyk, S. Freels,, J. Am. Dent. Assoc **146**, 659-668 (2015)