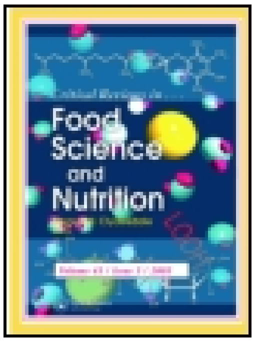

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Critical Reviews in Food Science and Nutrition

ASSESSMENT OF CADMIUM LEVELS IN HUMAN BREAST MILK AND THE AFFECTING FACTORS: A SYSTEMATIC REVIEW, 1971 -2014

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ABSTRACT:

Background: This is the first systematic review summarizing 43 years of research from 36 countries in the assessment of cadmium in breast milk; a suitable matrix in human biomonitoring.

Objectives: To report from the published literature the levels of cadmium in breast milk and the affecting factors causing the increase of cadmium concentrations; also to gather several quantitative data which might be useful to evaluate the international degrees of maternal and infant exposure.

Methods: we reviewed the literature for studies reporting quantitative data about cadmium levels in human breast milk in the world that have been published between 1971 and 2014 and that are available on Pubmed, Science direct and Google scholar. The aim of the study, country, period of samples collection, size of samples, sampling method, time of lactation, mother's age, area of residence, cadmium concentration and other information were extracted.

Results: 67 studies were selected and included in this systematic review, some concentrations greatly exceed the limit of the WHO, however about 50% of the studies had less than 1 µg/l cadmium concentration (the recommendation of the WHO); as well many factors have shown their implication in breast milk contamination.

Conclusion: Breast milk is a pathway of maternal excretion of cadmium. It's also a biological indicator of the degree of environmental pollution and cadmium exposure of the lactating women and the nourished infant. Therefore preventive measures and continuous monitoring are necessary.

Keywords

cadmium, breast milk, affecting factors

1. *INTRODUCTION:*

Heavy metals are toxic environmental contaminants and have no benefit for the human body. Among these heavy metals, cadmium (Cd), which requires careful attention because of its widespread use and high toxicity. Human population is exposed to this harmful metal from food water and air and may cause in many organs as kidney, liver, lungs, cardiovascular, immune and reproductive systems even cancer (Fowler 2009).

The human body can absorb cadmium via 3 ways: gastrointestinal, dermal and pulmonary (Godt et al. 2006); During pregnancy poisonous metals like cadmium can be transferred to the fetus due to placental transfer. This transfer could continue after birth in the lactation period through the transport from the body reserve and the maternal blood to the mammary glands of the lactating mothers (Jensen 1983). In this manner, it is secreted into breast milk which is the best and principal food for the newborn as it offers the ideal and optimal source of nutritional cognitive and immunological development of the nourished enfant in the short and long term (Lönnerdal 2003). However the existence of this element in breast milk could cause adverse effects in the infant's health and constitute a real hazard. Normal milk levels are reported to be < 1 μg/l (WHO 1989).

In this respect, the investigation and the evaluation of this environmental pollutant in breast milk is crucial for the promotion of mothers and children health.

The aims of this systematic review are to report data on cadmium concentrations in breast milk from published research around the world and to identify the affecting factors observed causing the increase of cadmium levels. Furthermore, to gather several quantitative data, this might be useful to assess the international level of maternal and infant exposure to cadmium to carry out public health research.

2. *REVIEW METHOD:*

2.1. Search strategy:

We conducted a worldwide search of studies reporting information about cadmium levels in human breast milk. From the published literature, we selected studies which provided quantitative data on cadmium concentrations in human milk samples.

Searches were conducted in databases such as Pubmed, Science direct and Google scholar, for studies published in English before December 2014 using the combination of the following keywords: cadmium, heavy metals, trace elements, human milk and breast milk. This was supplemented by manual searches in the reference lists within the retrieved articles to identify other suitable research.

We only considered studies in which cadmium levels were measured on human subjects and furnished numeric results. We excluded studies lacking quantitative data on cadmium exposure, results from reviews, reports, thesis and posters abstracts.

This strategy has lead to approximately 364 references. After screening studies for inclusion criteria and verified data, we selected 82 articles presenting quantitative data on cadmium in human milk, and because our review was limited to studies published in English we selected 69. For two old studies (found in the reference lists) we could not retrieve the full text even after requesting the copy from the author; So 67 papers were identified and included in this review. (Figure 1)

2.2. Data extraction:

The information was taken from each paper using an adapted data extraction table. The following details were obtained: aim of the study, country, period of samples collection, size of samples, sampling method, time of lactation, mother's age, subgroups, area of residence, cadmium concentration, analytic technique, limit of detection, certified reference materiel use, microwave digestion step, approval of the ethics committee, the calculated daily intake, other specimens measured and the affecting factors discussed. A second reviewer verified the accuracy of the information.

3. RESULTS:

3.1. Description of the study:

From the reviewed literature, we selected 67 full text studies reporting quantitative data on cadmium levels in human milk from 36 countries through 4 continents: Europe, Asia, America and Africa (figure 2), published between 1971 and 2014 in English. Several details of the reviewed studies are summarized in table 1.

In fact, the amount of researches concerning this topic increased over time especially since 2000. Figure 3 shows the progression of the number of studies published on cadmium levels from 1971 to 2014.

3.2. Studies design:

This review includes mostly cross sectional studies and longitudinal studies, the aim was mainly:

a) Determination and/or the evaluation of cadmium concentration in human milk;
b) changes in cadmium levels during the lactation period;
c) Influence of some factors (mother's age, diet, smoking, residence area, intake of supplementation…..) on cadmium levels;

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d) Test and develop analytic methods and techniques for determination of concentrations of cadmium and other metals (Coni et al. 1989; Coni et al. 2000; Elmastas et al. 2005; Khalid et al. 1987; Kosanovic et al. 2008; Spěváčková et al. 2005)

Actually, 11 Longitudinal studies were included in this review discussing the variation of cadmium concentrations during the lactation period (Chao et al. 2014; Friel et al. 1999; Kinsara et al. 2006; Krachler et al. 1998; Matos et al. 2014; Schulte-Löbbert and Bohn 1977; Stawarz et al. 2007; Sternowsky and Wessolowski 1985; Vuori et al. 1983) and two studies include both the cross sectional study and the longitudinal study (Gundacker et al. 2006; Spěváčková et al. 2005).

Two studies were published by the WHO. The first was a multinational study reporting levels from 6 countries: Guatemala, Sweden Hungary, Philippines, Nigeria, and Zaire (Parr et al. 1991). The second, a collaborative breastfeeding study from Swedish mothers (Larsson et al. 1981).

Indeed, 14 studies reported that they had also collected and measured cadmium concentrations in other human specimens: blood, umbilical cord blood, placenta tissue, maternal urine, new born urine and meconium (Abdulrazzaq et al. 2008; Ahmada et al. 2014; Hamzaoglu et al. 2014; Honda 2003; Kippler et al. 2009; Kippler et al. 2012; Klopov 1997; Kovar et al. 1984; Krachler et al. 1999; Nishijo et al. 2002; Radisch et al. 1987; Sakamoto et al. 2012; Schramel et al. 1988; Sharma and Pervez 2005). Other studies had collected animal milk specimens as well: buffalo, goat, cow, ewe and mare milk (Elmastas et al. 2005; Khalid et al. 1987; Rodriguez et al. 1999; Stasiuk et al. 2011; Tripathi et al. 1999). Significant cadmium levels were found in infant products and in several types of milk products (Khalid et al. 1987; Kippler et al. 2012; Murthy and Rhea 1971; Rodriguez et al. 1999; Tripathi et al. 1999; Ursinyova and Masanova 2005) as well as in water and soil (Cardoso et al. 2014).

The number of human milk samples varied from 5 (Khalid et al. 1987) to 344 (Al-Saleh et al. 2003) and 41 studies (61%) included less than 100 samples. 45 (67%) studies reported the mother's age, the range was from 15 to 51 years old.

In fact, between all types of milk, the mature milk was the most scrutinized, followed by colostrum and transitory milk. In 11 studies the lactation time was not indicated and the period of collection was not available in 29 studies. In regards to ethical consideration, 22 studies mentioned the approval of the ethic committee.

3.3 Analytical methodology:

The collection method of human milk was done manually or by a pump and it was stored in different types of containers most often in glass, polystyrene, polypropylene or polyethylene containers (pre-washed by nitric acid).

Within the 67 articles, the analytical technique most used was Atomic absorption spectrometry (AAS) in 64% of studies (Graphite Furnace AAS, Electrothermal AAS, Flame AAS, and flameless AAS). Next is the inductive coupled plasma (ICP) (Mass Spectrometry, Atomic Emission Spectrometry, Optical Emission Spectrometry, Quadrupole Mass Spectrometry) in18 studies, and 5 studies used Radiochemical Neutron Activation (ARNA) or Differential Pulse Anodic Stripping Voltammetry (DPASV).

Also 16 studies employed the Microwave digestion step, 28 studies indicated the limit of detection and 32 studies specified the use of certified reference materials powder milk.

3.4. Results reporting:

About 76% of the studies (51 studies) provided an arithmetic mean, most often with the standard deviation SD, others with or just by median, and Geometric mean was reported in 5 studies.

Furthermore, in the selected studies 14 units of measurement were used: Microgram per liter (μg/l), Microgram per deciliter (μg/dl), Microgram per milliliter (μg/ml), Nanogram per milliliter (ng/ml), Nanogram per liter (ng/l), Nanogram per cubic meter (ng/m3), Nanogram per gram (ng/g), Milligram per liter (mg/l), Milligram per kilogram (mg/kg), Microgram per kilogram (μg/kg), Microgram per gram (μg/g), Parts per million (ppm), Parts per billion (ppb) and Nanomole per liter (nmol/l). The microgram per liter (μg/l) was the most used (42 studies).

Twenty three studies calculated the provisional tolerable weekly intake (PTWI) or the provisional tolerable daily intake (PTDI) of cadmium by infants of different ages and weight, considering different quantity of human milk consumed per day (table 3). The WHO recommended 1μg/kg/day and 7μg/kg/week level of cadmium (WHO 1989).

*Limiting problems**:*** the principal difficulty is the multitude of protocols of samples preparation and pretreatment, further the units of measurement of the concentrations varied across studies which made comparison complicated, and for this reason we unified the units of measurements in μg/l (table 2).

4. DISCUSSION:

4.1. Cadmium Concentration in Human Breast Milk:

In this systematic review, 67 studies have been selected between 1971 and 2014 reporting quantitative data about cadmium concentration in human breast milk. Countries surveyed were: Austria, Bangladesh, Brazil, Canada, China, Croatia, Czech Republic, Egypt, Finland, Ghana, Germany, Greece, Guatemala, Hungary, India, Iraq, Iran, Italy, Japan, Nigeria, Pakistan, Philippines, Poland, Portugal, Russia, Saudi Arabia, Slovakia, Slovenia, Spain, Sweden, Taiwan, Turkey, UAE, UK, USA and Zaire.

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The concentrations of cadmium varied widely from continent to continent and from country to country, detailed results on levels of cadmium of those studies are presented in table 2 and figure 4.

4.1.1 Levels in Europe:

17 countries conducted 38 searches in cadmium levels in human milk samples in European countries from 1977 to 2014.

In turkey 6 studies were carried out (Cinar et al. 2011; Elmastas et al. 2005; Gurbay et al. 2012; Hamzaoglu et al. 2014; Orun et al. 2011; Turan et al. 2001).

4 studies in each of these countries: Italy (Abballe et al. 2008; Coni et al. 1989; Coni et al. 2000; Turconi et al. 2004), Germany (Radisch et al. 1987; Schramel et al. 1988; Schulte-Löbbert and Bohn 1977; Sternowsky and Wessolowski 1985), Sweden (Björklund et al. 2012; Hallén et al. 1995; Larsson et al. 1981; Parr et al. 1991) and Poland (Sikorski et al. 1989; Stasiuk et al. 2011; Stawarz et al. 2007; Winiarska-Mieczan 2014).

As well 2 studies in each of: Austria (Gundacker et al. 2006; Krachler et al. 1998), Finland (Kantola and Vartiainen 2001; Vuori et al. 1983), Spain (Garcia-Esquinas et al. 2011; Rodriguez et al. 1999) and Slovenia (Kosta et al. 1983; Krachler et al. 1999).

In UK, Greece, Portugal, Czech republic, Slovakia, Croatia, Hungary and Russia studies were performed by (Kovar et al. 1984); (Leotsinidis et al. 2005) ; (Matos et al. 2014) ; (Spěváčková et al. 2005) ; (Ursinyova and Masanova 2005); (Frković et al. 1997); (Parr et al. 1991); (Klopov 1997) respectively.

The highest mean concentrations of cadmium were reported by (Stasiuk et al. 2011) : 26.04 µg/l; (Sternowsky and Wessolowski 1985) : 24,6µg/l, in the city and 17.3µg/l in rural area, and

(Stawarz et al. 2007): 18µg/l. Lower values were measured by (Coni et al. 1989): 6µg/l, (Klopov 1997) :5.2µg/l in smokers, (Kosta et al. 1983) :3 µg/kg dry weight, (Rodriguez et al. 1999): 2.7 µg/l, (Turan et al. 2001): 2.8µg/l ; (Frković et al. 1997): 2.54µg/l, (Winiarska-Mieczan 2014): 2.114µg/l and (Turconi et al. 2004): 1.68µg/l.

(Sikorski et al. 1989) (Garcia-Esquinas et al. 2011) expressed the levels by geometric mean 2µg/l and 1.31µg/l respectively, (Vuori et al. 1983) by the median: 2µg/l in 1Mpp and for (Schulte-Löbbert and Bohn 1977) by the range: 3-35µg/l.

For the remaining studies, levels of cadmium were widely less than 1µg/l or even undetectable in Hungary and Sweden (Parr et al. 1991); while (Gurbay et al. 2012) found cadmium in one sample on 64 samples of breast milk.

<u>4.1.2 Levels in Asia:</u>

Extensive investigations were conducted throughout the Asian countries between 1983 and 2014. In India (Sharda et al. 1983; Sharma and Pervez 2005; Tripathi et al. 1999), Japan (Honda 2003; Nishijo et al. 2002; Sakamoto et al. 2012), Iran (Abdollahi et al. 2013; Goudarzi et al. 2013; Rahimi et al. 2009), Saudi Arabia (Al-Saleh et al. 2003; Kinsara et al. 2006) UAE (Abdulrazzaq et al. 2008; Kosanovic et al. 2008), Bangladesh (Kippler et al. 2009; Kippler et al. 2012), Pakistan (Ahmada et al. 2014; Khalid et al. 1987), Iraq (Nassir et al. 2012; Zaidan et al. 2013), china (Liu et al. 2013), Taiwan (Chao et al. 2014) and Philippines (Parr et al. 1991).

In fact, mean levels of cadmium in these countries were extremely high in Iran as discovered by (Zaidan et al. 2013) : 114640µg/l and relatively high in studies by (Sharda et al. 1983): 20µg/l in colostrum; (Abdollahi et al. 2013): 12.1µg/l;(Khalid et al. 1987) :6µg/l;(Kinsara et al. 2006) :5.6µg/l and (Nassir et al. 2012): 5.6µg/l. Lower concentrations were measured in Philippines by

(Parr et al. 1991): 2.67µg/l “median value”, (Rahimi et al. 2009): 2.44µg/l; (Sharma and Pervez 2005) 2.13 µg/l among workers of an industrial area); (Goudarzi et al. 2013): 1.92µg/l (Al-Saleh et al. 2003): 1.732µg/l and (Chao et al. 2014): 1.37µg/l in colostrum. In the other studies the values were well above 1µg/l.

<u>4.1.3 Levels in America and Africa:</u>

(Murthy and Rhea 1971) from USA were the first in the world to investigate and publish data on cadmium levels in human milk in 1971 and they found high mean concentrations: 19µg/l. In Brazil (Nascimento et al. 2005) reported 54.5 µg/l of cadmium in breast milk, but (Cardoso et al. 2014) measured quite low quantities similar to (Dabeka et al. 1986; Friel et al. 1999) et al from Canada. In Guatemala (Parr et al. 1991) it was undetectable.

Regarding Africa, 6 studies were conducted, according to (Adesiyan et al. 2011) Nigeria explored the highest concentration: 977.9 µg/l and lowest levels were reported by (Parr et al. 1991): 3.67µg/l “Median value.” In Egypt (Moussa 2011) found 2.56µg/l (the highest value among 3 cities examined),and in Ghana,(Bentum et al. 2010): 1,34µg/l and (Koka et al. 2011)below 0.035µg/l. finally in Zaire (Parr et al. 1991) it was undetectable.

4.2 Factors Affecting Cadmium Levels in Human Breast Milk

About 41 of the reviewed studies (61%) discussed the association between the level of cadmium and the following factors: lactation stage, age of mothers, parity, smoking, diet, supplement intake, interaction with other mineral elements, and other parameters. The findings are in some case contradictory between authors.

4.2.1 <u>Age of mothers:</u>

According to (Nascimento et al. 2005; Nassir et al. 2012; Parr et al. 1991; Winiarska-Mieczan 2014) a positive correlation has been reported between maternal age and cadmium levels in breast milk, however for (Nascimento et al. 2005) it was not statistically significant. In fact (Nassir et al. 2012; Rahimi et al. 2009; Ursinyova and Masanova 2005) observed that older mothers had higher cadmium levels in their milk; in contrary (Frković et al. 1997; Honda 2003), showed higher concentrations in the milk of younger mothers, stating however that the differences were not statistically significant.

Whereas studies by (Abdulrazzaq et al. 2008; Al-Saleh et al. 2003; Garcia-Esquinas et al. 2011; Kantola and Vartiainen 2001; Leotsinidis et al. 2005; Liu et al. 2013; Matos et al. 2014; Nishijo et al. 2002; Orun et al. 2011; Sikorski et al. 1989; Turconi et al. 2004; Zaidan et al. 2013) did not find any significant correlations neither relationship between the level of this contaminant in breast milk and the mother's age.

4.2.2 <u>Diet and eating habits:</u>

The frequency of the consumption of fish has significant effects on the levels of cadmium in breast milk. Moreover (Al-Saleh et al. 2003; Kantola and Vartiainen 2001) had observed higher cadmium in mothers who did not eat fish. while positive influence of cadmium levels in breast milk of mothers who ate fresh vegetables and dry nuts (Leotsinidis et al. 2005), cereals (Gundacker et al. 2006) and liver (Hallén et al. 1995).

Furthermore (Chao et al. 2014; Garcia-Esquinas et al. 2011; Turconi et al. 2004) did not reveal any statistically significant differences between dietary habits and breast milk cadmium, conversely to (Abdollahi et al. 2013).

(Nassir et al. 2012) demonstrated significant low concentrations of cadmium in the milk of mothers who used to drink bottled water as compared to mothers who drank river or tap water.

4.2.3 <u>Education and work:</u>

Milk cadmium levels were higher in educated mothers as per (Abdulrazzaq et al. 2008) in contrast to studies of (Al-Saleh et al. 2003; Garcia-Esquinas et al. 2011; Leotsinidis et al. 2005; Liu et al. 2013; Orun et al. 2011).

Likewise cadmium was higher in the breast milk of unemployed mothers than the working mothers (Liu et al. 2013; Orun et al. 2011). Although (Nassir et al. 2012) noticed otherwise; in his study, the working conditions were positively associated with the presence of high levels of cadmium in breast milk. Furthermore (Abdulrazzaq et al. 2008; Al-Saleh et al. 2003; Leotsinidis et al. 2005; Turconi et al. 2004) have reported that it did not affect the Cd level.

Actually, breast milk cadmium increased with the decreasing of the socioeconomic status (Kippler et al. 2009; Kippler et al. 2012).

4.2.4 <u>Intake of vitamin and mineral Supplement :</u>

(Liu et al. 2013; Orun et al. 2011) confirmed that the milk of mothers who did not take vitamin and iron supplements at the 2nd month postpartum contained higher levels of Cd than mothers who took supplements. Similarly, findings have been registered (Gundacker et al. 2006) which observed lower breast milk levels in non smokers taking supplements. In discordance (Leotsinidis et al. 2005; Matos et al. 2014) noticed no significant effect of supplementation on milk cadmium.

4.2.5 <u>Interaction with other mineral elements:</u>

Breast milk cadmium was positively correlated with manganese (Mn) (Kippler et al. 2009; Kippler et al. 2012; Krachler et al. 1998) as well as iron (Fe) (Kippler et al. 2009; Kippler et al. 2012) and molybdenum (Krachler et al. 1998).

In addition, a negative correlation existed between calcium and cadmium concentrations in breast milk (Björklund et al. 2012; Honda 2003; Kippler et al. 2009) in contrast to (Stawarz et al. 2007) who found a strong positive correlation.

Whilst (Murthy and Rhea 1971) reported that the metabolism of cadmium follows that of zinc, been its antagonist, (Stawarz et al. 2007) also remarked a strong correlation between zinc and cadmium in human milk.

4.2.6 Lactation stage:

The studies conducted by (Chao et al. 2014; Krachler et al. 1998; Leotsinidis et al. 2005; Rodriguez et al. 1999; Schulte-Löbbert and Bohn 1977; Sternowsky and Wessolowski 1985; Vuori et al. 1983) have confirmed higher cadmium concentration in colostrum than in transitory and mature milk and that it decreases with the stage of lactation. However others have observed the opposite (Matos et al. 2014; Winiarska-Mieczan 2014). The lowest value was contained in the first months of lactation. Even so (Sharda et al. 1983) has remarked no change from colostrum to mature milk.

4.2.7 Parity and parturition:

Several studies have shown that no statistical significant difference exists between cadmium concentrations in milk of primiparous vs multiparous mothers (Al-Saleh et al. 2003; Frković et al. 1997; Garcia-Esquinas et al. 2011; Honda 2003; Kantola and Vartiainen 2001; Leotsinidis et al. 2005; Liu et al. 2013; Matos et al. 2014; Nascimento et al. 2005; Nishijo et al. 2002; Orun et al. 2011; Rahimi et al. 2009; Sharda et al. 1983; Ursinyova and Masanova 2005).

However (Kippler et al. 2009) had reported that multiparous women had significantly higher Cd compared to primiparous women.

Concerning delivery some studies mentioned that there were no significant differences in breast milk cadmium of women with or without caesarean operation (Honda 2003; Leotsinidis et al. 2005; Nishijo et al. 2002; Turconi et al. 2004).

4.2.8 <u>Residence area:</u>

On this item, many studies confirmed the influence of the living area with the presence of cadmium in breast milk, (Al-Saleh et al. 2003; Hallén et al. 1995), thus (Cinar et al. 2011; Sikorski et al. 1989) pointed that rural populations had higher levels than urban populations. Conversely, others found the opposite in urban women (Abdollahi et al. 2013; Nassir et al. 2012; Sternowsky and Wessolowski 1985).

(Hamzaoglu et al. 2014; Nassir et al. 2012) have detected high concentration in industrialized areas. While (Frković et al. 1997; Garcia-Esquinas et al. 2011; Kantola and Vartiainen 2001; Leotsinidis et al. 2005; Turconi et al. 2004) have reported no significant difference between residence area and cadmium in breast milk.

Indeed (Dabeka et al. 1986) noticed a significant association of age of the house and the increase of milk cadmium levels.

4.2.9 <u>Smoking habits:</u>

The effect of smoking on cadmium concentration in breast milk is the most scrutinized researched, several studies confirm that smoking increases cadmium concentration in breast milk

(Abdollahi et al. 2013; Chao et al. 2014; Frković et al. 1997; Gundacker et al. 2006; Hallén et al. 1995; Klopov 1997; Koka et al. 2011; Nassir et al. 2012; Nishijo et al. 2002; Rahimi et al. 2009; Sikorski et al. 1989; Winiarska-Mieczan 2014; Zaidan et al. 2013). Even smoking before, during and/or after pregnancy, at home (Liu et al. 2013; Orun et al. 2011; Ursinyova and Masanova 2005) or the smoking of the father (Dabeka et al. 1986) affect the cadmium levels in breast milk. But only the studies of (Chao et al. 2014; Dabeka et al. 1986; Gundacker et al. 2006; Koka et al. 2011; Liu et al. 2013; Orun et al. 2011; Radisch et al. 1987; Sikorski et al. 1989; Ursinyova and Masanova 2005; Winiarska-Mieczan 2014) have shown significant differences of this fact.

Furthermore (Garcia-Esquinas et al. 2011; Radisch et al. 1987) observed a significant increase of cadmium levels with the increase of cigarette consumption and (Gundacker et al. 2006) remarked that the infants of smokers were significantly shorter and tended to have a lower birth weight.

Whereas (Kantola and Vartiainen 2001; Leotsinidis et al. 2005; Nascimento et al. 2005; Turan et al. 2001; Turconi et al. 2004) did not find any variation between cadmium content in milk of smokers and non smokers.

5. CONCLUSION:

Breast milk is a good biological indicator of the nutritional status, the degree of environmental pollution and cadmium exposure of both mother and her child.

To sum up, some concentrations greatly exceed the limit of the WHO, however about 50% of the studies had less than 1 µg/l cadmium concentration, in addition many other factors are implicated in contamination of breast milk and findings are diverse and frequently conflicting by others.

Notwithstanding, breastfeeding must be encouraged. Furthermore, as breast milk is an excellent matrix in biomonitoring the body, periodic program for the analysis of breast milk is recommended.

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Table 1: Summary of the literature studies on cadmium levels in human breast milk with main characteristics (1971-2014)

Authors/Year/ Country	Period of samples collection	Sample size	Sampling method	Lactation Time	Age of mothers	Note	Cadmium Concentration		Analytical technique	L
							Arithmetic mean ± SD	Median & range		
Murthy, G. and U. Rhea (1971) USA	April-may 1968	22 (13w)					0.019±0.027 Ppm		AAS	
Schulte-Löbbert, F. and G. Bohn (1977) Germany[LONG I]		95 (5w)		1to16 & 18,19,23 Dpp	24-36			3-35 ppb	fAAS	
Larsson, B., et al. (1981) Sweden	1978-1979	41		3-6Mpp	21-35			0.1 µg/kg	fAAS	0 µ g
Kosta, L et al. (1983) slovenia			manual	1-14Dpp (Morning/ Formilk)			3	1 -5 µg/kg dry weight	RNA	
Sharda, B., et al. (1983). India		178 50 43 85	manual	2-5Dpp 6-10Dpp After 11D to 6 Mpp (Morning/ Foremilk)			2±0.71 1.5±0.43 1.6±0.19to 1.7±0.13 µg/dl	1-3.2 1-2.9 1.2-3.0 1.0-3.0 µg/dl	AAS	
Vuori, E., et		20	manual			Smokers			EAAS	

al. (1983) Finland [LONGI]		**(7w) 7 7 6**		**1Mpp 3Mpp 6Mpp (Foremilk & Hindmilk over 24h)**		**& non smokers**		**2.0 (1.7-3.1) 1.5 (1.3-2.5) 1.6 (1.2-2.0) µg/l**		
Kovar, I., et al. (1984) UK	**September-November 1980**	**28**	**manual**	**5Dpp (morning/5minute after feeding)**	**29,2[Mean] 24-37**	**Urban population Smokers & non smokers**	**0.4±0.275 µg/l**	**0.3-1.2 µg/l**	**GFAAS**	**< µ**
Sternowsky, H. J. et al (1985). Germany[LONGI]	**May-June 1983**	**(20w)**	**Manual & Pump**	**2 to 90Dpp morning**	**>20**	**10city 10rural**	**24.6±7.3 17.3±4.9 µg/l**		**AAS**	**6**
Dabeka, R., et al. (1986) Canada	**1981**	**210**					**0.08 0.063[GM] ng/g**	**0.06 (<0.002-4.05) ng/g**		**0 5 n**
Khalid, N., et al. (1987). Pakistan	**May-June 1984**	**5**		**Transitory milk**		**Urban**	**6±0.3 ng/g**		**EAAS**	
Radisch, B., et al. (1987). Germany		**71**	**manual**	**>1Wpp**	**17-40**	**NonSmoker:15 Smoker : 56**		**0.07 0.16 <0.05-0.41 µg/l**	**fAAS**	**0 µ**
Schramel, P., et al. (1988). Germany (munich-bavaria)		**34**	**pump**	**Colostrum & mature milk**			**0.88±0.37 ng/l**		**DPASV**	

Sikorski, R., et al. (1989). Poland		**110 90 20**	**Manual & Pump**	**4Dpp Hindmilk**	**26.7 Mean 15-44**	**overall Urban Rural Smoker:66 NonSmoker:44**	**0.002 GM 0.0019 0.0024 0.0017 0.0025 mg/kg**	**(0.0007-0.0050)**	**FAAS**	
Coni, E., et al. (1990). Italy		**36**	**Glass aspirating seringue**			**(urban smokers /not smokers) & (rural smokers /non smokers)**	**0.006µg/l**	**0.002 (0.001-0.005) 25-75 0.001-0.065 Min-Max**	**ICP AES**	
Parr, R. M., et al. (1991). Guatemala Huangary Nigeria Philippines Sweden Zaire		**13 11 9 15 13 15**	**pump**	**3Mpp Noontime (4h after last feeding)**				**ND ND 3.67 ±2.03 2.67±0.50 ND ND µg/l**	**RNAA**	
Hallén, I. P., et al. (1995). Sweden	**March 1990-March 1992**	**73 15 58**	**Electric pump**	**6Wpp (2-3 h after last feeding)**	**29 Mean**	**overall Smoker: Non smoker:**	**0.06±0.04 0.07±0.04 0.06±0.04 µg/l**		**GFAAS**	
Frković, A., et al. (1997). Cratia	**September 1995-january 1996**	**29**	**manual**	**2-12 Dpp**	**28.9 Mean 27 median 17-45**	**Industrial city**	**2.54±2.06 µg/l**	**1.80 0.45-9.10**	**GFAAS**	**0 µ**
Klopov, V. P. (1997) Russian arctic	**Februry-March 1995**	**42**		**First 3Dpp**		**Smoker Non smoker (Industrialized arctic zone)**	**5.2 1.2 µg/l**		**fAAS**	**0 µ**
Krachler, M.,& rossipal al. (1998)Austria LONGI	**1995-1996**	**55 (46w)**	**Electric pump**	**1 to 293Dpp/ morning before feeding**		**overall C = 13 T = 18 M1 = 8 M2 = 8**	**0.5 1.3 0.3 0.2 0.1**	**0.3(<0.18-5.0) 1.1(<0.18-5.0) 0.3(<0.18-**	**ICP MS**	**0 µ g**

				1-3Dpp 4-17Dpp 42-60Dpp 66-90Dpp 97-293Dpp		M3 = 8	0.3 µg/kg	0.8) <0.18(<0.18-0.6) <0.18(<0.18-0.3) 0.2(<0.18-0.5)		
Friel, J. K., et al. (1999). Canada LONGI	**Sep 1988-Oct 1993**	**288 (43w) 152 (24w) 136 (19w)**	**Electric pump**	**2Dpp to 12 Wpp Morning / during feeding (1time per week for 8 weeks & in 12th week)**	**20-35**	**PRT24 (premature) FT19 (full term) (95% of the mothers were of European origin)**		**<1 µg/l**	**ICPMS**	
Krachler, M., et al. (1999).Slovenia	**1996-1997**	**27**	**manual**	**1-3Dpp**	**27** Mean		**0.6±0.5µg/l**	**0.6 <0.18-1.9** Min-max **0.2-0.8** 25-75	**ICPMS**	
Rodriguez, E. R et al. (1999). Spain	**1994-1996**	**55 (12w)**	**pump**	**2W-6Mpp**	**21-35**		**2.70±2.40 µg/l**	**0.59-11.34** Min-Max	**EAAS**	
Tripathi, R., et al. (1999). India		**(30w)**					**0.09±2.76** GM **µg/l**		**DPADV**	
Coni, E., et al. (2000). Italy		**(30w)**	**Manual suckers**	**2Mpp**			**0.8±0.2 ng/ml**		**Q ICPMS**	**0 n l**
Kantol, M.		**256**	**manual**	**4Wpp**					**ETAA**	**0**

and T. Vartiainen (2001) .Finland	**1987 1993-1995**	**175 81**		**during 2 weeks morning & afternoon after 5min of feeding**	**27.7^{Mean} 28.8^{Mean}**	**Urban 82 & rural 83: Urban 18 & rural 56:**	**0.095±0.12 0.04±0.06 µg/l**	**0.058 0.040**	**S**	**0 µ**
Turan, S., et al. (2001).Turkey	**Dec 1995-Febr 1996**	**30**	**pump**	**48Hpp**	**18-33**	**urban city**	**2.8±1.7 µg/l**	**1.2-9,00**	**ETAAS**	**0 µ**
Nishijo, M., et al. (2002). Japan	**Mar-Aug 1999**	**(57w) 45 12**		**5-8Dpp**	**28 $.5^{Mean}$ (<2µg /g Cr) 33^{Mean} (≥2µg /g Cr)**	**Smoker & Non smoker**	**2.8±1.7 nmol/l 4.6±2.5 nmol/l**		**fAAS**	
Al-Saleh, I., et al. (2003). Saudi Arabia	**1999-2000**	**344 150 194**			**15-51 29.8^{Mean}**	**overall riadh region Al ehssa region**	**1.732±1.691 1.182±1.142 2.157±1.912 µg/l**	**1.131 (<0.123-11.672) 1.011 <0.123-11.672 1.483 <0.123-9.224 µg/l**	**ETAAS**	**0 3 µ**
Honda, R. et al (2003). Japan		**68**		**5 --8Dpp**	**19-38**	**Non Industrial area**	**0.28 ^{GM}±1.82 µg/l**	**0.07-1.22 $_{Min-Max}$**	**fAAS**	
Turconi, G., et al. (2004) Italy	**March-July 2000**	**143**	**pump**	**3-4dpp**	**18-42**	**Urban and mountains Smoker & Non smoker**	**1.68±2.37 µg/l**	**1(1-1) $1\text{-}20^{Min-Max}$ µg/l**	**GFAAS**	**2**
Elmastas, M., et al. (2005). Turkey		**32**	**pump**	**2Mpp (morning Between**			**0.097-0.007 µg/l**		**FAAS**	

				10am and 15pm)						
Leotsinidis, M., et al. (2005) Greece	2000- 2002	180 95	manual	3Dpp 14Dpp (Mornin g 2h after last feeding)	16-39 25[Mean]	Colostru m Transitor y milk	0.190±0.1 52 0.142±0.1 21 µg/l	0.130 0.062-0.270 0.127 0.062-0.199	ETAA S	0 0 µ
Nascimento, L. F. C., et al. (2005). Brazil	Septem ber- Novem ber 2003	58	manual	24Hpp After feeding	25[Mean] 15-45	Urban area	54.50± 381.0 µg/l	0.13-2904	GFAA S	
Sharma, R. and S. Pervez (2005) India	Januar y- Decem ber 2001	120 40 45 35	pump	<1Wpp	20-45	overall Industriel Workers: Non workers: (but township residents) Unconta mined	 2.13±0.94 * 1.56±0.74 * ≤0.3* µg/l	0.1-3.8 2.30*(0.6- 3.8) 1.7*(0.3- 2.3) <LOD-0.3* µg/l	AAS	
Spěváčková, V., et al. (2005). Czech republic LONGI+CROSS SECT	2002	49 (7w) 200		1,2,3,4,1 0,20 &30 Dpp ND		Prague (2 industrial & 2rural areas)	< 0.3 < 0.3 µg/l		EAAS	0 µ
Ursinyova, M. and V. Masanova (2005). Slovakia		158 49 111	Manua l & pump	4Dpp	18-39 25.6[M] ean	overall Smoking at home: Non Smoking at Home:	0.43±0.27 0.522±0.3 92 0.408±0.2 39 µg/kg	0.36 ND- 1.70	GFAA S	0 2 µ g
Gundacker, C., et al. (2006). Austria LONGI+CROSS SECT	Februr y 1999 Januar y 2000 2002- 2004	124 (8w)		2-14Dpp 1.3.5.7 &9 Wpp	28[Mean] 31 Mean	Urban, rural and Indus areas Urban & indus	0.086±0.0 85 µg/l	0.063 (CI:0.07- 0.1)	GFAA S	0 1 µ

						areas (smokers and non-smokers)				
Kinsara, A. and S. Farid (2006). Saudi Arabia LONGI		**156 (11w)**	**manual**	**1to7Dpp Morning &Afternoon before feeding**	**25**	**overall Morning afternoon**	**5,6 2.03±0.01 4.6±0.1 ppb**		**GFAAS**	
Stawarz, R., et al. (2007) Poland LONGI		**210 (5w)**	**pump**	**90Dpp (14d period /3time/day)**	**18-28**	**industrial**	**0.018±0.011 mg/kg**	**0.001-0.06** min-max	**DPASV**	
Abballe, A., et al. (2008). Italy	**1998-2001**	**39**		**4-8 Mpp**	**21-40**	**Urban primiparous**	**< 0.5ng/ml**		**AAS**	
Abdulrazzaq, Y. M et al. (2008). UAE	**2004**	**205**	**pump**	**4-80 Wpp**	**18-50**		**0.003±0.008 µg/l**	**0.002 -0.004-0.115** Min-Max	**ICPMS**	
Kosanovic, M., et al. (2008). UAE		**120**	**manual**				**0.27 ±0.04 µg/l**	**0.023-1.19 µg/l**	**ICPMS**	**0 9 p**
Kippler, M. et al. (2009) Bangladesh	**January-December 2002**	**123**	**manual**	**2Mpp**	**27** Median	**Rural area**		**0.14 <0.050--1.0 µg/kg**	**ICPMS**	**0 µ g**
Rahimi, E., et al. (2009). Iran	**August 2006-March 2007**	**(44w) 11 33**	**pump**	**1-6 Wpp**	**≤30 ≥30**	**overall Industrial area**	**2.44±1.47 µg/L**	**0.62-6.32 µg/l**	**GFAAS**	**0 8 µ**
Bentum, J., et al. (2010). Ghana		**20**	**manual**		**<25**	**Primiparous**	**1.34± 2.914 µg/l**	**<0.001-12.301 µg/l**	**AAS**	**0 1 p**
Adesiyan, A., et al. (2011). Nigeria		**80 100**	**manual**		**26-45**	**Hormoral Contraseption Not**	**94.78±29.42 97.79 ±21.73**		**AAS**	

						Usning	μg/dl			
Cinar, N., et al. (2011) Turkey		26 26 23	manual	1Mpp		industrial City center Rural area	0.022±0.026 0.031±0.055 0.044±0.067 μg/l	0.000-0.102 0.000-0.203 0.000-0.272 Min-Max	ICP OES	
Garcia-Esquinas, E., et al. (2011). Spain	October 2003-May 2004	100	pump	3Wpp After feeding	30.6 Mean	city	1.31 GM CI: 1.15-1.48 μg/l	1.41 0.25-2.8 Min-Max μg/L	GFAAS	0 μ
Koka, J., et al. (2011). Ghana	January-March 2007	24 24	manual			Acca Tema (Industriel areas/Smoker&Non smoker)	0.0246±0.0116 0.0329±0.1263 μg/l	0.0085-0.0500 0.0122-0.0644 μg/l	FAAS	
Moussa, W. (2011) Egypt		30	Pump	End of 5 Mpp	25-35 30 Mean	Modern area Industrial area Industrial area	0.638± 0.032 1.842±0.092 2.56±0.12 μg/l	0.0485-0.865 1.02-2.54 1.25-3.86 μg/l	GFAAS	0 5 μ
Orun, E., et al. (2011) Turkey		144	manual	2Mpp Morning 2h after last feeding	25 Mean 17- 41	Suburban		0.67 <0.2- 1.26 25-75 < 0.2-43 Min-Max μg/l	ICPMS	
Stasiuk, E., et al. (2011). Poland		40 (10w)		5 to 9Dpp	19-41		26.04±46.69 μg/l	3.42 0.45-128 μg/l	GFAAS	
Björklund, K. L., et al (2012). Sweden	2000-2002 2009	60	Pump or manual	14-21Dpp	29 median 29.4 Mean	primiparous	0.086±0.045 μg/l	0.075 0.028-0.27 μg/l	ICPMS	0 2 /l
Gurbay, A., et al. (2012) Turkey	October 2007-March	64	manual	2-5Dpp morning			just in one sample:		GFAAS	0 μ

	2008						4,62µg/l			
Kippler, M., et al (2012). Bangladesh	Aug2003-Mar2004	76	manual	2Mpp	27 Mean 18-43	Rural		0.13 <0.05-0.41 5-95% µg/l	ICPMS	
Nassir, I. M., et al (2012). Iraq	Februry-April 2012	68	pump	1-6Wpp	26.1 Mean		5.6±1 .77 µg/l		GFAAS	
Sakamoto, M., et al. (2012). Japan		9		3Mpp	30.4 Mean 22-36			0.14 0.06-0.22 ng/ml	ICPMS	0 1 µ
Abdollahi, A., et al. (2013). Iran		100				Urban & rural	0.0121 ppm		FAAS	
Goudarzi, M. A., et al. (2013). Iran	Sep2010-janu 2011	37	pump	1-6Wpp		Industrial area	1.92 + 1.04 µg/l	0.45--5.87 µg/l	GFAAS	0 1 µ
Liu, K.-s., et al. (2013) China	November2009-December 2010	170		2Mpp morning	26 Mean 18-42	Suburban		0.67 <0.2-1.26 25-75 < 0.2-43 Min-Max µg/l	ICPMS	
Zaidan, H. K., et al. (2013). Iraq		70	pump	1-51Wpp	20-42		114,64±0.027 µg/ml		fAAS	
Ahmad, N., et al. (2014). Pakistan		134	manual			Morning noon	0.038±0.019 0.037±0.036 µg/l	0.027µg/l < BDL-0.062 0.025 (< BDL-0.139) µg/l	AAS	
Cardoso, O. O., et al. (2014). Brazil		58	manual	1Mpp	>21	Non smokers		0.770 < 0.050-6.57 µg/l	ICPMS	
Chao, H. H., et al. (2014). Taiwan LONGI	March-August 2008	180 (45w)	manual	First 2 Mpp Morning formilk	29.8 Mean 22-39	1-4d C 5-10d T 30-35d M1	1.37± 0.94 0.65± 0.36 0.49± 0.25 0.34± 0.19		GFAAS	

				through feeding and hindmil k		60-65 d M2	ng/ml			
Hamzaoglu, O., et al. (2014 Turkey	**october 2009-april 2011**	**56**	**Manua l**	**1-4 Dpp**	**19-35 27 Mean**	**Indus area Non Indus**	**2.68±3.25 0.82±0.72 ng/m3**	**0.10-17 0.12-2.10**	**ICPM S**	**< 0 /g**
Matos, C., et al. (2014) Portugal LONGI		**155 31w**	**Manua l & pump**	**1to 16Wpp Foremil k &hindm ilk Over 24h**	**21-39 30.9 Mean**	**1 Wpp 4 wpp 8wpp 12wpp 16wpp**	**0.027±0.0 98 0.060±0.0 75 0.023±0.0 79 0.055±0.1 2 0.060±0.0 73 µg/kg**	**-0.0044 (-0.081&0.29) 0.050 (-0.026&0.22) 0.024 (-0.12& 0.17) 0.031 (-0.079& 0.32) 0.050 (-0.044& 0.21)** Min-Max	**ICPM S**	
Winiarska-Mieczan, A. (2014) Poland	**August - Decem ber 2010**	**320w**	**manual**	**1-12Mpp (7 days samplin g)**	**20-40**		**2.114±2.1 12 µg/l**	**1.260 0.215-7.355** Min-Max **0.557-3.017 25-75 µg/l**	**GFAA S**	**0 n K**

Dpp :day post partum ; Mpp : month postpartum ; Wpp: week postpartum; W: women ; LONGI :longitudinal study ; CROSS SECT :cross sectional study ; Cr: Creatinine; GM: Geometric mean; CI : confidence interval; LOD: limit of detection; CRM: certified reference material; * Mean calculated from the averages

GFAAS: Graphite Furnace Atomic Absorption Spectrometry; ETAAS: Electrothermal Atomic Absorption Spectrometry; FAAS: Flame Atomic Absorption Spectrometry, fAAS: flameless Atomic Absorption Spectrometry, ICP MS: Inductive Coupled Plasma Mass Spectrometry, ICP AES: Inductive Coupled Plasma Atomic Emission Spectrometry, ICP OES: Inductive Coupled Plasma Optical Emission Spectrometry, Q-ICP-MS: Quadrupole Mass Spectrometry; hRNA: Radiochemical Neutron Activation; DPASV: Differential Pulse Anodic Stripping Voltammetry

Table 2: Cadmium concentrations in breast milk in µg/l

Authors/Year / Country		Note	Cadmium Concentration			
			Arithmetic mean ± SD	Median & range	Arithmetic mean ± SD (µg/l)	Median & range (µg/l)
Murthy, G. and U. Rhea (1971) USA			0.019±0.027 ppm		19±27	
Schulte-Löbbert, F. and G. Bohn (1977) Germany				3-35 ppb		3-35
Larsson, B., et al. (1981) Sweden				0.1 µg/kg		0.1
Kosta, L et al. (1983) slovenia			3 µg/kg dry weight	1 -5		
Sharda, B., et al. (1983). India		2-5Dpp 6-10Dpp After 11D to 6M	2±0.71 1.5±0.43 1.6±0.19to 1.7±0.13 µg/dl	1-3.2 1-2.9 1.2-3.0to 1.0-3.0 µg/dl	20±7.1 15±4.3 16±1.9to 17±1.3	10-32 10-29 12-30to 10-30
Vuori, E., et al. (1983) Finland		1Mpp 3Mpp 6Mpp				2.0 (1.7-3.1) 1.5 (1.3-2.5) 1.6 (1.2-2.0)
Kovar, I., et al. (1984) UK					0.4±0.275	0.3-1.2
Sternowsky, H. J. et al (1985) Germany		10city 10rural			24.6±7.3 17.3±4.9	
Dabeka, R., et al. (1986) Canada			0.063 GM 0.08 ng/g	0.06 (<0.002-4.05)	0.063GM 0.08	0.06 (<0.002-4.05)

				ng/g		
Khalid, N., et al. (1987). Pakistan			6±0.3 ng/g		6±0.3	
Radisch, B., et al. (1987). Germany		Non Smokers:15 Smokers:56				0.07 0.16 (<0.05-0.41)
Schramel, P., et al. (1988). Germany (munich-bavaria)			0.88±0.37 ng/l		0.00088± 0.00037	
Coni, E., et al. (1989). Italy			0.006 μg/g	0.002 (0.001-0.005)[25-75] 0.001-0.065[min-max]	6	2 (1-5) (1-65)
Sikorski, R., et al. (1989). Poland		overall Urban Rural Smoker:66 Non smoker:44	0.002 [GM] 0.0019 0.0024 0.0017 0.0025 mg/kg	(0.0007-0.0050)	2[GM] 1.9 2.4 1.7 2.5	(0.7-5)
Parr, R. M., et al. (1991). Guatemala Huangary Nigeria Philippines Sweden Zaire						 ND ND 3.67 ±2.03 2.67±0.50 ND ND
Hallén, I. P., et al. (1995). Sweden		overall Smoker: Non smoker:			0.06±0.04 0.07±0.04 0.06±0.04	
Frković, A., et al. (1997). Cratia					2.54±2.06	1.80 (0.45-9.10)
Klopov, V. P. (1997) Russian arctic		Smoker Non smoker			5.2 1.2	

Krachler, M.,& rossipal al. (1998)Austria		**1 to293Dpp(overall) 1-3Dpp 4-17Dpp 42-60Dpp 66-90Dpp 97-293Dpp**	**0.5 1.3 0.3 0.2 0.1 0.3 µg/kg**	**0.3(<0.18-5.0) 1.1(<0.18-5.0) 0.3(<0.18-0.8) <0.18(<0.18-0.6) <0.18(<0.18-0.3) 0.2(<0.18-0.5) µg/kg**	**0.5 1.3 0.3 0.2 0.1 0.3**	**0.3(<0.18-5.0) 1.1(<0.18-5.0) 0.3(<0.18-0.8) <0.18(<0.18-0.6) <0.18(<0.18-0.3) 0.2(<0.18-0.5)**
Friel, J. K., et al. (1999). Canada						**<1**
Krachler, M., et al. (1999).Slovenia					**0.6±0.5**	**0.6 (<0.18-1.9)**
Rodriguez, E. R et al. (1999).Spain					**2.70±2.40**	**(0.59--11.34)**
Tripathi, R., et al. (1999). India					**0.09±2.76GM**	
Coni, E., et al. (2000). Italy			**0.8±0.2 ng/ml**		**0.8±0.2**	
Kantol, M. and T. Vartiainen (2001).Finland		**1987 1993-1995**			**0.095±0.12 0.04±0.06**	**0.058 0.040**
Turan, S., et al. (2001).Turkey					**2.8±1.7**	**(1.2-9,00)**
Nishijo, M., et al. (2002). Japan		**(<2 µg/g Cr) (≥2µg/g Cr)**	**2.8±1.7 4.6±2.5 nmol/l**		**0.308±0.187 0.506±0.275**	
Al-Saleh, I., et al. (2003). Saudi arabia		**overall riadh region Al ehssa**			**1.732±1.691 1.182±1.142 2.157±1.912**	**1.131 (<0.123-11.672)**

		region				1.011 (<0.123-11.672) 1.483 (<0.123-9.224)
Honda, R. et al (2003). Japan					0.28 GM ±1.82	(0.07-1.22) MIN-MAX
Turconi, G., et al. (2004) Italy					1.68±2.37	1(1-1) (1-20)min-max
Elmastas, M., et al. (2005). Turkey					0.097-0.007	
Leotsinidis, M., et al. (2005) Greece		Colostrum Transitory milk			0.190±0.152 0.142±0.121	0.130 (0.062-0.270) 0.127 (0.062-0.199)
Nascimento, L. F. C., et al. (2005).Brazil					54.50± 381.0	(0.13-2904)
Sharma, R. and S. Pervez (2005)India		Industriel area Workers Non workers (township residents) Uncontamined	Moyenne ponderée calculée à partir des moyennes :		2.13±0.94* 1.56±0.74* ≤0.3*	0.1-3.8 2.30*(0.6-3.8) 1.7*(0.3-2.3) <LOD-0.3*
Spěváčková, V., et al. (2005). Czech republic		Prague 2 industrial & 2 rural areas			< 0.3 < 0.3	
Ursinyova, M. and V. Masanova (2005). Slovakia		overall Smoking at home Non Smoking at Home	0.43±0.27 µg/kg 0.522±0.392 0.408±0.239 µg/kg	0.36 (ND-1.70)	0.43 0.522±0.392 0.408±0.239	0.36 (ND-1.70)

Gundacker, C., et al. (2006). Austria		**2-14Dpp 1.3.5.7 &9 Wpp**			**0.086 ±0.085**	**0.063 (0.07-0.10) (0.1-0.55)**
Kinsara,et al (2006). Saudi Arabia		**overall Morning afternoon**	**5,6 2.03±0.01 4.6±0.1 ppb**		**5,6 2.03±0.01 4.6±0.1**	
Stawarz, R., et al. (2007) Poland			**0.018±0.011 mg/kg**	**(0.010-0.060)min-max**	**18±11**	**(10-60)min-max**
Abballe, A., et al. (2008). Italy			**< 0.5 Ng/ml**		**<0.5**	
Abdulrazzaq, Y. M et al. (2008).UAE					**0.003±0.008**	**0.002 (-0.004-0.115) Min &Max**
Kosanovic, M., et al. (2008). UAE					**0.27 ±0.04**	**0.023-1.19**
Kippler, M. et al. (2009)Bangladesh				**0.14 (0.050--1.0) µg/kg**		**0.14 (0.050--1.0)**
Rahimi, E., et al. (2009). Iran					**2.44±1.47**	**(0.62-6.32)**
Bentum, J., et al. (2010). Ghana					**1.34± 2.914**	**<0.001-12.301**
Adesiyan, A., et al. (2011).Nigeria		**Hormoral contraseption Not usning**	**94.78±29.42 97.79±21.73 µg/dl**		**947.8±294.2 977.9±217.3**	
Cinar, N., et al. (2011) Turkey		**Industrial area City center Rural area**			**0.022±0.026 0.031±0.055 0.044±0.067**	**0.000-0.102 0.000-0.203 0.000-0.272**
Garcia-Esquinas, E.,					**1.31 GM CI (1.15-**	**1.41 (0.25-**

et al. (2011). Spain					**1.48)**	**2.8)min- max**
Koka, J., et al. (2011). Ghana		**Indus a Acca Indus a Tema**			**0.0246±0.011 6 0.0329±0.126 3**	**0.0085- 0.0500 0.0122- 0.0644**
Moussa, W. (2011) Egypt		**Modern area Industrial area Industrial area**			**0.638± 0.032 1.842±0.092 2.56±0.12**	**(0.0485- 0.865) (1.02- 2.54) (1.25-3.86)**
Orun, E., et al. (2011) Turkey						**0.67 (<0.2- 1.26)25-75 (< 0.2-43) Min-Max**
Stasiuk, E., et al. (2011). Poland					**26 .04±46.69**	**3.42 (0.45-128)**
Björklund, K. L., et al.(2012). Sweden					**0.086±0.045**	**0.075 (0.028-0.27)**
Gurbay, A., et al. (2012) Turkey					**in one sample: 4,62**	
Kippler, M., et al. (2012). Bangladesh						**0.13 (<0.05- 0.41) 5/95%**
Nassir, I. M., et al (2012). Iraq					**5.6±1 .77**	
Sakamoto, M., et al. (2012). Japan				**0.14 (0.06-0.22) ng/ml**		**0.14 (0.06-0.22)**
Abdollahi, A., et al. (2013). Iran			**0.0121 ppm**		**12.1**	
Goudarzi, M. A., et al. (2013). iran					**1.92 + 1.04**	**(0.45--5.87)**
Liu, K.-s., et						**0.67**

al. (2013) China						**(<0.2-1.26) 25-75 < 0.2- 43$^{Min-Max}$**
Zaidan, H. K., et al. (2013). Iraq			**114,64±0.027 µg/ml**		**114640 ±27**	
Ahmad, N., et al. (2014). Pakistan		**Morning Noon**			**0.038±0.019 0.037±0.036**	**0.027 (< BDL-0.062) 0.025 (< BDL-0.139)**
Cardoso, O. O., et al. (2014). Brazil						**0.770 (< 0.050-6.57)**
Chao, H. H., et al. (2014). Taiwan		**1-4d C 5-10d T 30-35dM1 60-65 dM2**	**1.37± 0.94 0.65± 0.36 0.49± 0.25 0.34±0.19 ng/ml**		**1.37± 0.94 0.65± 0.36 0.49± 0.25 0.34± 0.19**	
Hamzaoglu, O., et al. (2014 Turkey		**Indus area Non Indus**	**2.68±3.25 0.82±0.72 ng/m3**	**(0.10-17) (0.12-2.10)**	**$2.68.10^{-6}$ $\pm 3.10^{-6}$ $0.82.10^{-6} \pm 0.72.10^{-6}$**	**(0.10-17) 10^{-6} (0.12-2.10) 10^{-6}**
Matos, C., et al. (2014) Portugal		**1 Wpp 4 wpp 8wpp 12wpp 16wpp**	**0.027±0.098 0.060±0.075 0.023±0.079 0.055±0.12 0.060±0.073 µg/kg**	**-0.0044 (-0.081&0.29) 0.050 (-0.026&0.22) 0.024 (-0.12& 0.17) 0.031 (-0.079& 0.32) 0.050 (-0.044& 0.21)**	**0.027±0.098 0.060±0.075 0.023±0.079 0.055±0.12 0.060±0.073**	**-0.0044 (-0.081&0.29) 0.050 (-0.026&0.22) 0.024 (-0.12& 0.17) 0.031 (-0.079& 0.32) 0.050 (-0.044& 0.21)**

				Min-max		Min-max
Winiarska-Mieczan, A. (2014)Poland					**2.114±2.112**	**1.260 (0.215-7.355)Min-Max (0.557-3.017)**$^{25-75\%}$

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Table 3: Estimated daily or weekly intakes calculated by some studies

Authors/Year/ Country	Daily or weekly intake of Cd		Note
	mean±SD	Median range	
Murthy, G. and U. Rhea (1971) USA	0.008 mg per day	0.006-0.01 mg/day	615 ml BM day
Larsson, B., et al. (1981) Sweden		0.1*µg/kg BW (39 of the 41 samples was 0.4 µg/kg or less) (0.07-2.3)	3Mpp
Vuori, E., et al. (1983) Filand(longi)	2.7 µg/Kg 1.5µg/Kg		1Mpp 3Mpp
Kovar, I., et al. (1984) UK	0.14 µg/Kg/ day		3kg baby weight 150ml BM/kg/day
Sternowsky, H. J. et al (1985). Germany		1.6-2.2(city) 1.2-1.8 (rural) µg/kg/day	5.5kg baby weight 850ml BM/day
Khalid, N., et al. (1987). Pakistan		0.31 to 0.39 µg/kg BW/day	1 to 6 Mpp
Sikorski, R., et al. (1989). Poland		0.13 0.05-0.87 µg/kg BW	3,130g baby weight 210g of milk
Coni, E., et al. (1990). Italy		1.3 0.7-3.3µg/day	
Parr, R. M., et al. (1991).		<0.6(<0.6-1.2)	
Guatemala		<0.7(<0.7-1.2)	
Huangary		2.4(<0.6-1.8)	
Nigeria		1.7(0.5-2.7)	
Philippines		<0.8(<0.8-2.0)	
Sweden		<0.5(<0.5-0.5)µg/day	
Zaire			
Rodriguez, E. R et al. (1999). Spain	2.3 µg/day	$(0.44\text{-}8.51)^{\text{min-max}}$	750ml of BM
Tripathi, R., et al. (1999). India	0.06 µg/day		700ml BM/day
Al-Saleh, I., et al. (2003). Saudi Arabia	µg/kg		5-6 kg infant Body weight 850ml BM/day

Turconi, G., et al. (2004) Italy		**1.4% >PTWI = 7µg/kg BW**	**300 g of milk at the 6th lactating day**
Leotsinidis, M., et al. (2005) Greece		**0.098* (0.042-0.175)25-75 (ND-0.315) 10-90 0.182* (0.091-0.315)25-75 (0.008-0.518)10-90**	**0.1 liter/kg/day of colostrum 0.150 liter/kg/day of transitory milk**
Nascimento, L. F. C., et al. (2005). Brazil	**33µg/day 11µg/kg/day**		**600ml BM/day**
Ursinyova, M. and V. Masanova (2005). Slovakia		**0.5* (0.02-1.99) µg/kg BW/week**	
Gundacker, C., et al. (2006). Austria	**0.014µg/kg/day max value 0.119**		**3070g baby weight 500ml BM/day**
Kinsara, et al (2006).Saudi Arabia	**2.8 µg/kg**		**500ml BM/day**
Bentum, J., et al. (2010). Ghana	**1.05 µg/day 0.11µg/kg/day 0.08µg/kg/day**		**9kg BW 13kg BW**
Koka, J., et al. (2011). Ghana	**Acca: 0.0015µg/kg/day 0.019µg or 0.002µg Tema: 0.0020 µg/kg/day 0.026µg or 0.003**		**For mean weight of 9kg or 13 kg**
Stasiuk, E., et al. (2011). Poland	**28*µg**		**4kg BW 700ml BM/day (456% PTWI)**
Kippler, M., et al. (2012). Bangladesh		**<0.04 to 0..3 µg 0.007--0.061 µg/kg BW/day**	**860 ml**
Winiarska-Mieczan, A. (2014) Poland	**72..72***		**1Mpp**
	67.7*		**3Mpp**
	84.84*		**6Mpp**
	32.84* µg/kg BW/ week		**12Mpp**

***Weekly intake; BM: breast milk; BW: body weight**

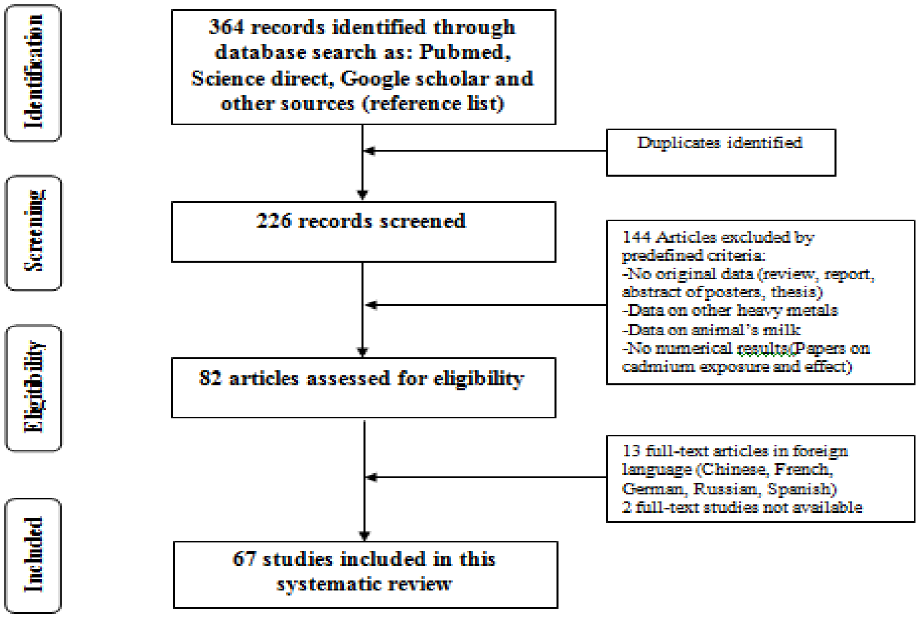

Figure 1: Flow diagram of the literature search process

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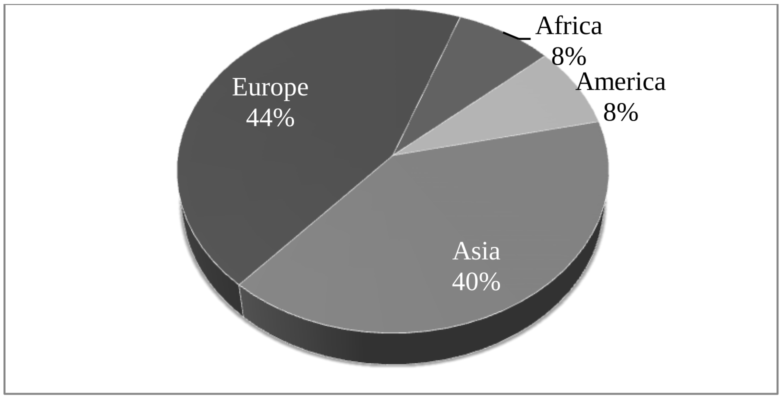

Figure 2: Proportion of the studies published in each continent

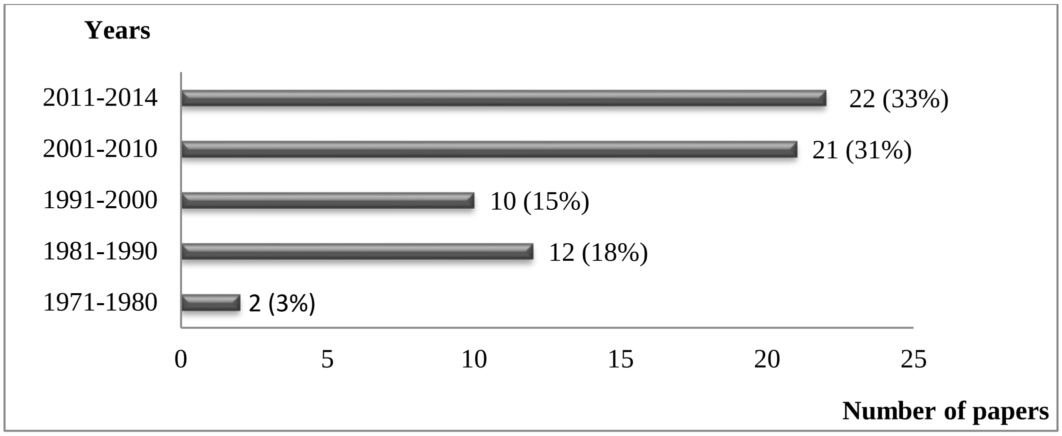

Figure 3: Number of articles published per year (1971-2014)

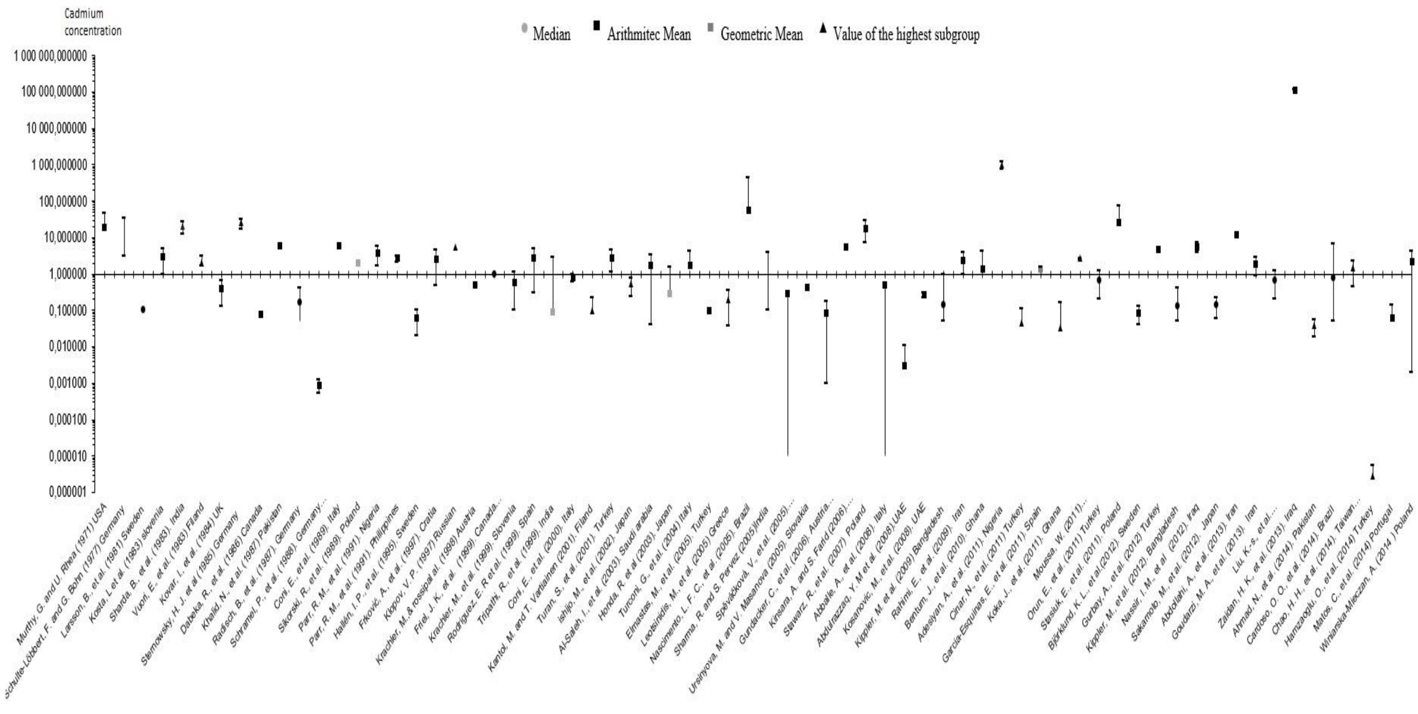

Figure 4: Total cadmium levels (μg/l) in human breast milk (1971-2014)