



Review

The concentration of polycyclic aromatic hydrocarbons (PAHs) in mother milk: A global systematic review, meta-analysis and health risk assessment of infants



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ABSTRACT

Background: Bio-monitoring of polycyclic aromatic hydrocarbons (PAHs) contaminants in mother milk is essential to keep mothers and infants healthy against potential risks. The current study assesses the concentration of PAHs in mother milk through a meta-analytic and systematic review approach.

Methods: All the published studies up to December 2020 regarding the concentrations of various PAHs in mother milk were searched throughout major international databases such as PubMed, Scopus, and Web of Science. Moreover, the possible carcinogenic and mutagenic risks to infants were evaluated based on the BaP (benzo[a]pyrene) equivalent dose.

Results: According to the results of 13 articles included among 936 retrieved studies, the lowest and highest concentration of PAHs was (0.125 ng/g) and (76.36 ng/g) related to benz(a)anthracenem and 1-methylnaphthalene, respectively. The highest (9.830 ng/g) and lowest (0.009 ng/g) concentration of PAHs was related to Mexico and Japan, respectively. Besides, carcinogenic and mutagenic risk assessment of the PAHs indicated that risk pattern was different across countries. It can be concluded that the consumption of mother milk is safe and does not pose a risk due to the ingestion of PAHs to the health of infant consumers.

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1. Introduction

For decades, polycyclic aromatic hydrocarbons (PAHs) have been recognized as strong mutagenic, carcinogenic, and endocrine-disrupting toxic compounds in humans and animals (Cok et al. 2012). Due to their structural properties consisting of 2 or more fused aromatic rings, these compounds are lipophilic and have a high tendency for long persistence and transport in the environment (Santonicola et al. 2017). The most prominent physicochemical properties of PAHs have been widely mentioned in various scientific studies, and thus >100 different organic com-

pounds of PAHs have been identified as an environmental contaminant for human health (Pirsaheb et al. 2020). The United States Environmental Protection Agency (USEPA) considered 16 PAHs as potent carcinogens and mutagenic for humans (Olyaei et al. 2015). According to the number of aromatic rings, the PAHs are classified into two groups of light (2–3 rings) and heavy (4–6 rings). The heavy PAHs, such as benzo [g,h,i] perylene, benzo [a] pyrene, and indeno [1,2,3-c,d] pyrene, because of higher octanol-water partition coefficients (K_{ow}), are more toxic and stable compared to the light ones (Bandowe and Meusel 2017). The fate, transfer, and partitioning of PAHs between and within the environment part and eco-toxicological system depend on their different characteristics (Bandowe et al. 2014). Many different sources have been reported for the production of toxin PAHs compounds (Baali et al. 2016, Li et al. 2016, Acharya et al. 2019). They can be formed by the discharge of the electrical currents that occur in paint, insulation products, and glue (Lima et al. 2005). Also, the greatest amounts of PAHs released into the various environment types are produced by partial combustion of biomass (as wood) and

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fossil fuels such as coal and petroleum, anthropogenic emissions from vehicle exhaust, heat and power generation, tobacco smoke, and increases in urbanization and industrialization (Aguinaga et al. 2007, Asamoah et al. 2019). Human exposure to PAHs compounds can occur through the diet contaminated with water, soil, water, and food (Mahmood et al. 2013). The toxicity caused by the PAHs varies and is broadly related to duration, concentration, exposure route, age, health status, and the type of nutrition (Nwaichi and Ntorgbo 2016). Significantly, the health risks caused by the PAHs can be divided into two forms of acute or chronic effects. Other toxicities associated with these compounds include carcinogenicity of various tissues such as breast, prostate, and gonadal, metabolic disorders, and mutagenic (Ledesma et al. 2016). Various health agencies such as European Food Safety Authority (EFSA) and the World Health Organization (WHO) have approved the health risks of the PAHs (WHO 1998, Cancer 2010). PAHs residues in seafood and cooked, baked, fried, or grilled foods have been reported in various studies (Nieva-Cano et al. 2001, Duedahl-Olesen et al. 2006, Martorell et al. 2010). In addition to the mentioned studies, another important issue regarding PAHs is their residues in mother milk. Breast milk is the best nutrition source for babies a few months after birth due to its specific compounds. It is considered a complete food for infants' growth, development, and health (Cho and Shin 2012). Like other food sources, breast milk can be exposed to harmful environmental pollutants and pose a health risk to infants (Del Bubba et al. 2005). Various studies have shown that breast milk can be contaminated with pesticides, heavy metals, and mycotoxins (Perera et al. 2005, Mehri et al. 2020, Khazaei, Talebi Ghane et al. 2021). Breast milk due to conatinating lipophilic tissue and different lipids (such as triacylglycerols, phospholipids, fatty acids, and sterols) is susceptible to accumulation compounds with lipophilic nature like PAHs (Hegazy et al. 2020). Contaminations of milk mother with PAHs due to its high significance have been reported in numerous reviews and original research studies (Kishikawa and Kuroda 2009, Hunter et al. 2010, Karam 2019). Therefore, using a meta-analysis and systematic review, the current study investigated the concentration of PAHs in mother milk in different worldwide in order to examine their effects on infants' health. This may help to find useful interventions to monitor PAH levels in mother milk and recognize possible gaps. Our assessment of PAH in mother milk based on a meta-analysis study is indicated for the first time in the field.

2. Material and methods

In current study, the meta-analysis and systematic review was performed based on PRISMA statement for evaluate the prevalence and concentration of PAHs in mother milk in different parts of the world (Mehri et al. 2020, Khazaei et al. 2021).

2.1. Data sources and search strategy

Search strategies were done to search all articles in the association with PAHs in mother milk that met inclusion criteria. Two authors separately investigated studies published between 8/January/1991 and 28/ December /2020. The both internal databases include PubMed, Scopus, Web of Science, and references of published manuscripts were systematically searched. The following important keywords employed in title, abstract and keywords were included: (human milk OR mother milk OR breast milk) AND (polycyclic aromatic hydrocarbons OR PAHs OR contaminants, residual, concentration). The search was not limited to specific language.

2.2. Inclusion and exclusion criteria

Among different databases, the studies that determined the prevalence, concentration and residual f PAHs in mother milk were included. The manuscripts were included if they have following criteria: (1) indicated the level of PAHs in mother milk (2) research published studies (3) reported detail of size and number of positive samples (4) explained precise analytical method (5) manuscripts that full-text were accessible and (6) All studies have evaluated at least one PAH in mother milk were included in the study. The studies were excluded if they were: duplicated papers, case series, and review manuscript, letter to editor, case reports, salami publication and or studies that evaluated the effect of feeding, climate change, effect processing to remove of metals in PAHs in mother milk, studies that reported fate of PAHs in mother milk were excluded. It also should be noted that articles that did not find raw data, mean values, or standard deviations, authors, journal, year of publication, country of origin and type of PAHs, excluded from study.

2.3. Data extraction

The investigated parameters included titles, abstract and full text were screened independently by two researchers (ZK and FM). Following data were collected in pre-prepared form: first author's name, publication year, type of product, total sample size, mean and standard divisions and range of PAHs concentration, positive samples, prevalence of PAHs, method detection and countries. In order to unify the units, all units of concentration of PAHs including ppb, $\mu\text{g}/\text{kg}$, ppb and mg/kg were changed to ng/g milk, wet weight.

2.4. Meta-analysis and statistical analysis

The pooled concentration of PAHs in mother milk was assessed using via mean and standard error (SE). The SE of the level of PAHs was estimated using the Eq. (1) (Ghane et al. 2021):

$$SD/\sqrt{n} \quad (1)$$

In this current, SD and n show standard deviation and sample size, respectively. The subgroup analysis was separately performed according to PAHs type and country. Heterogeneity was investigated by I^2 and Q tests. I^2 statistic ($I^2 > 50\%$) shows a large heterogeneity and Cochran Q test (Q statistic, $p < 0.10$) indicate statistically significant heterogeneity and. Furthermore, meta-regression was performed to explore the year of study as a possible sources of heterogeneity. The data were investigated by the Stata software, version 14 (StataCorp, College Station, TX, USA). The significance level was considered to be < 0.05 .

2.5. Risk assessment

Carcinogenic and Mutagenicity risk for 7 PAHs compounds was determined using BaP equivalent dose of mutagenic or carcinogenic PAHs (BaPEQ) which considered by the (Asamoah 2017). BaPEQ value is dependent to TEQ_{BaP} (toxicity equivalent quotient) or MEQ_{BaP} calculated by the sum of mutagenic equivalent factor (MEF) or toxicity equivalent factor (TEF) multiplies each PAH concentration. TEQ_{BaP} or MEQ_{BaP} and also BaPEQ estimate using the equation (2, 3 as follows).

$$TEQ_{BaP} = \sum (TEF_i \times C_i) \quad (2)$$

$$MEQ_{BaP} = \sum (MEF_i \times C_i) \quad (3)$$

Where, C_i is the individual PAH concentration with its corresponding TEF_i or MEF_i value. Values of TEF_i for BaA, BaP, BbFlu, BkFlu, Chr, DahA and IndP are 0.1, 1, 0.1, 0.01, 0.001, 1 and 0.1, respectively (USEPA 1993). Also Values of MEF_i for BaA, BaP, BbFlu, BkFlu, Chr, DahA and IndP are 0.082, 1, 0.25, 0.11, 0.017, 0.290 and 0.310 respectively (Durant et al. 1996). The BaP equivalent dose calculate based on Eq as follows (4) as follows:

$$\text{BaPEQ} = (\text{TEQ}_{\text{orMEQ}}) \times \text{IR} \times \text{EF} \times \text{ED} / \text{BW} \times \text{AT} \quad (4)$$

Based on the mentioned equation, IR is ingestion rate of mother milk in g per day (700 g milk/day), EF show exposure frequency (350 days/year), ED states exposure duration (1 year), BW is body weight (5 kg), AT_n is the average life expectancy. (2 years). Mutagenic or cancer risk is calculated according to Eq. (5) as follows:

Risk carcinogenic or (mutagenic) = $\text{SF}_{\text{BaP}} \times \text{BaP}$ equivalent dose of mixture of PAHs (5) where SF_{BaP} is the oral carcinogenic slope factor for benzo[a]pyrene (7.3 per mg/kg/day). According to the USEPA guidelines, CR higher than 10^{-4} indicates risk; CR in the range of 10^{-6} to 10^{-4} is acceptable; CR lower than 10^{-6} indicates safe (Heshmati et al. 2020).

3. Results and discussion

3.1. Processing the systematic review

According to the PRISMA flow chart, a summary of the search process used in this study is shown in Fig. 1. In our study, 639 published articles were retrieved between 8/January/1991 and 28/December /2020 via searching international databases, including Scopus (310), PubMed (80), and Web of Science (279). At the beginning of the study, 296 articles were excluded because of repetition. Based on the titles, 343 articles were found to be appropriate. Subsequently, due to irrelevant titles, 174 articles were excluded from the analysis. Based on the abstracts, 169 articles were investigated, and 143 articles were excluded. Based on the Full texts, 26 articles were reviewed, and then 13 articles were excluded due to lack of full texts. Full texts of 13 articles were reviewed.

3.2. Characteristics of reviewed studies

The main characteristic of collected studies is shown in Table 1s. The studies were done all over the world. The following rank order was obtained for study zones, namely Europe including Italy, Japan, and Canada (5 studies, 39%) > (Kishikawa et al. 2003) (Del Bubba et al. 2005, Yu et al. 2011, Wheeler et al. 2014, Ilo et al. 2017), Asia including Turkey, China, and India (4 studies, 30.7%) > (Madhavan and Naidu 1995, Cok et al. 2012, Wang et al. 2018, Asamoah et al. 2019), America including Mexico, the USA, and Louisville, KY (3 studies, 20%) and Africa including (Kim et al. 2008, Hunter et al. 2010, Acharya et al. 2019) Egypt, (1 study, 7.2 %) (Hegazy et al. 2020). All articles were published between 1991 and 2020. The number of the reviewed samples in the studies ranged from 8 to 128, reporting 8796 cases with 6189 PAH positive samples.

3.3. The concentration of various PAH in breast milk

Determining PAHs in mother milk is important to keep mothers and infants healthy against harmful effects related to this contamination. Mother milk is the best source of nutrition for babies, particularly in the first six months. As the World Health Organization recommends, it is best to breastfeed extensively during this time (WHO 2001). The results of Cochran's Q test and I² statistics suggested a significant heterogeneity among the included studies in

terms of PAHs ($Q = 47403.3$, $df = 41$, $p < 0.001$ and $I^2 = 99.9\%$). In order to reduce the heterogeneity, we performed subgroup analysis based on PAHs type and countries (Tables 1 and 2). As shown in Table 1, the ranking of different subgroups of PAHs according to their concentrations was in order of benz(a)anthracene (0.125 ng/g) < chrysene (0.254 ng/g) < dibenzo[a,h]anthracene (0.386 ng/g) < benzo(b)fluoranthene (0.551 ng/g) < benzo(a)pyrene (0.5520.552) < indeno[1,2,3-c,d]pyr (0.720 ng/g) < pyrene (0.822 ng/g) < fluoranthene (0.881 ng/g) < acenaphthene (1.660 ng/g) < benzo[k]fluoranthene (2.054 ng/g) < benzo[g,h,i]perylene (2.839 ng/g) < phenanthrene (3.124 ng/g) < fluorine (3.634 ng/g) < anthracene (3.734 ng/g) < naphthalene (3.874 ng/g) < 2-Methylnaphthalene (4.20 ng/g) < 1-methylnaphthalene (76.36 ng/g). Many studies investigated the content of PAHs in different samples of breast milk. Yu et al. (2014) reported that the concentration of PAHs including anthracene, fluoranthene, pyrene, benz[a]anthracene, chrysene, benzo [b]fluoranthene, and benzo[k]fluoranthene was 14.4, 50.9, 36.5, 3.97, 7.42, 20.5, and 8.62 ng/g in various samples of mother milk, respectively (Yu et al. 2015). In another study conducted by Wheeler et al. (2014) in Canada, the detected concentration of naphthalene in the mother milk was 7.75 ng/g (Wheeler et al. 2014). There are many differences between our results and other reports concerning the contamination of PAHs in breast milk samples, which can be related to critical factors such as physicochemical properties of individual PAHs, women-specific metabolic activity, age of mother, and type food consumed before milk collection (Forehand et al. 2000, Zanieri et al. 2007). According to the literature, PAH levels with low molecular weight (LMW) in human milk were higher than other PAHs, which can be related to their physical and chemical properties assisting their transport in the mammary cells (Cavret et al. 2005). In addition, LMW PAHs under metabolic mechanisms turn to hydroxyl and epoxy derivatives that have a higher inclination to water and are certainly eliminated by the urine (Oliveira et al. 2020). Moreover, in late pregnancy, the fat of the maternal body starts mobilizing to produce fat for breastfeeding, which can transfer the aggregated lipophilic contaminants as PAHs to mother milk (Fernández-Cruz et al. 2017). As mentioned in similar studies, one of the influential parameters in the differences observed between PAHs levels can be related to the body mass index (BMI) of a mother. For example, Acharya et al. (2019) investigated PAHs in the breast milk of obese vs. normal women. Their results indicated that the content of fluoranthene, pyrene, benz(a)anthracene, and chrysene in mothers with (BMI) > 30 vs. BMI 18.5–24.9 was 24.8, 19, 17.4, and 22.3 ng/g vs. 10.9, 7.7, 5, and 0 ng/g, respectively (Acharya et al. 2019). According to their results, PAHs with two or more aromatic rings are lipophilic and have a high tendency to store in adipose tissue, and therefore increases in the body fat lead to more lipophilic contaminants in the body (Heindel et al. 2015). The other reason that may influence the concentrations of PAHs found in breast milk is related to the mother's age. The studies indicated that the metabolism rate of environmental pollutants such as PAHs might reduce with an increase in age, and therefore aggregation of unmetabolized compounds may lead to the increase in their concentration in breast milk. Acharya et al. (2019) and Tsang et al. (2011) showed moderate associations between the mothers' age and content of PAHs in their milk (Tsang et al. 2011, Acharya et al. 2019) (see Table 3).

3.4. Content of PAHs in mother milk samples according to various countries

As detected in the present study, the content of PAHs in the mother milk samples was different among the countries. As shown in Table 2, the ranking of concentration of PAHs according to various countries was in the order of Japan < Louisville,

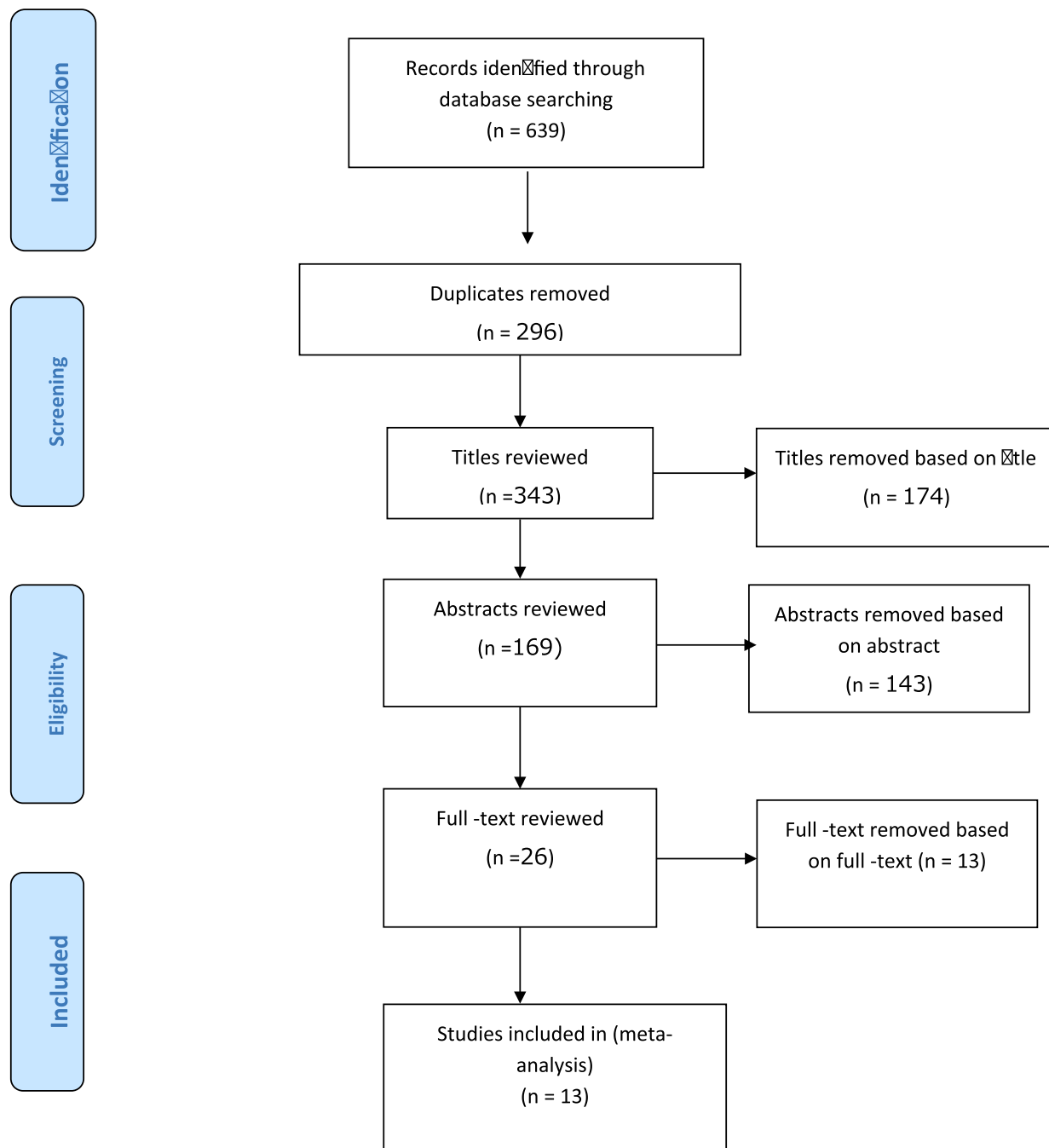


Fig. 1. Selection process evidence searches and inclusion.

KY < India < Northwest China < Turkey < Egypt < China < Italy < Mexico. According to the results (Table 2), the highest (9.830 ng/g) and lowest (0.009 ng/g) levels of PAHs were related to Japan and Mexico, respectively. Obviously, the concentration of PAHs is different in breast milk samples according to previous studies conducted in various countries. For example, Santonicola et al. (2017) conducted a comparative study on the occurrence of PAH in the breast milk of Italian mothers. Their study indicated that the mean concentrations of total PAHs were (114.93 ng/g). Furthermore, the most identified foundation was related to benzo(a)pyrene (BaP), chrysene, Benzo(a,h)anthracene, and Benzo(b)fluoranthene (Santonicola et al. 2017). Madhavan et al. (1995) reported the content of PAH in Indian mothers. They detected Benzo(a) pyrene (0.26 ng/g), dibenzo(a,c) anthracene (0.28 ng/g),

and chrysene (0.09 ng/g) in all samples (Madhavan and Naidu 1995). Kishikawa et al. (2003) detected the presence of 12 kinds of PAHs with a mean concentration of (0.75 ng/g) in Japanese mothers' milk (Kishikawa et al. 2003).

The difference between these observations could be associated with food habits and environmental exposures during breastfeeding to infants. For example, Zanieri et al. (2007) studied the effect of smoking and residential region on PAHs level of Italian mothers' milk. Their findings showed that mothers living in rural areas had lower PAH content than those living in urban areas. They supposed that the living area of the mother affects PAH content in milk. They also suggested that other factors influencing PAH levels in breast milk are environmental sources, including motor vehicle emission, industrial or vehicular activities emissions, asphalt particles, tire

Table 1
Meta-analysis of concentration of different sub-groups of PAH in breast milk based on PAHs type.

Study	N of studies	ES (95% CI)	Heterogeneity				
			weight	Statistics	df	P.Value	I ² (%)
Acenaphthene	9	1.660 (1.445, 1.875)	5.21	266.91	8	<0.001	96.6
Anthracene	10	3.734 (2.988, 4.480)	4.28	1945.71	9	<0.001	99.7
Benz(a)anthracene	7	0.125 (0.081, 0.169)	9.32	343.44	6	<0.001	98.3
Benzo(a)pyrene	7	0.552 (-0.144, 1.248)	10.05	6278.63	6	<0.001	99.9
Benzo(b)fluoranthene	6	0.551 (0.204, 0.899)	6.58	347.71	5	<0.001	98.8
Benzo(g,h,i)perylene	5	2.839 (2.034, 3.645)	6.67	1392.22	4	<0.001	99.6
Benzo(k)fluoranthene	7	2.054 (0.610, 3.498)	7.62	35645.66	6	<0.001	100.0
Chrysene	5	0.254 (0.187, 0.321)	11.01	533.06	4	<0.001	98.7
Dibenzo[a,h]anthracene	8	0.386 (0.222, 0.550)	4.20	288.19	7	<0.001	99.0
Fluoranthene	4	0.881 (0.734, 1.027)	5.15	1868.25	3	<0.001	99.5
Fluorene	10	3.634 (1.476, 5.791)	2.81	679.79	9	<0.001	99.4
Indeno[1,2,3-c,d]pyr	5	0.720 (0.512, 0.927)	8.47	2366.10	4	<0.001	99.7
1-methylnaphthalene	1	76.36 (72.376, 80.344)	0	–	0	<0.001	–
2-Methylnaphthalene	1	4.20 (3.854, 4.546)	0.42	–	0	<0.001	–
Naphthalene	4	3.874 (1.691, 6.057)	2.60	842.61	5	<0.001	99.4
PAH	7	20.327 (17.929, 22.725)	5.30	5801.40	8	<0.001	99.9
Phenanthrene	6	3.124 (2.662, 3.586)	4.60	1021.77	7	<0.001	99.3
Pyrene	8	0.822 (0.661, 0.983)	5.73	991.61	9	<0.001	99.1

Table 2
Meta-analysis of concentration of various sub-groups of PAH in breast milk based on country.

Study	N of studies	ES (95% CI)	Heterogeneity				
			weight	Statistics	df	P.Value	I ² (%)
Egypt	5	0.480 (0.391, 0.569)	17.81	7012.05	4	<0.001	99.9
Ghana	4	0.523 (0.249, 0.797)	8.13	105.61	3	<0.001	97.2
India	1	0.090 (-0.050, 0.230)	1.91	–	0	–	–
Italy	8	2.767 (0.745, 4.789)	14.14	23924.08	7	<0.001	100.0
Japan	7	0.009 (0.004, 0.015)	24.85	182.31	6	<0.001	96.7
Louisville, KY	3	0.038 (-0.003, 0.080)	10.20	22.07	2	<0.001	90.9
Mexico	6	9.830 (2.694, 16.966)	1.52	180.06	5	<0.001	97.2
Northwest China	1	0.283 (0.262, 0.304)	3.59	–	0	–	–
Turkey	7	0.437 (0.298, 0.575)	17.84	237.10	6	<0.001	97.5

Table 3
Carcinogenic risk assessment based on BaP equivalency for human breast milk.

Country	BaA	BaP	BbFlu	BkFlu	Chr	DahA	IndP	Total
Egypt	1.960E-10	1.029E-06	2.646E-09	–	1.274E-11	–	1.588E-08	1.05E-06
Ghana	–	–	–	3.920E-10	1.470E-10	1.441E-06	2.940E-08	1.47E-06
India	–	–	–	–	4.410E-11	–	–	4.41E-11
Italy	2.011E-08	3.969E-07	3.822E-08	3.102E-08	4.116E-10	2.136E-06	3.807E-07	3.00E-06
Japan	2.254E-10	1.274E-09	2.038E-08	3.234E-11	3.234E-11	3.430E-09	1.764E-10	2.56E-08
Louisville, KY	4.900E-10	2.450E-08	–	–	2.940E-11	–	–	2.50E-08
Mexico	5.733E-07	4.900E-08	7.595E-07	3.871E-08	5.831E-09	–	6.076E-07	2.03E-06
China	–	–	–	–	–	–	1.387E-08	1.39E-08
Turkey	2.818E-08	1.210E-07	2.244E-08	1.024E-09	7.267E-10	4.704E-08	2.607E-08	2.47E-07
Total	6.22E-07	1.62E-06	8.43E-07	7.12E-08	7.23E-09	3.63E-06	1.07E-06	7.87E-06

Chr = chrysen, BaA = benzo[a]anthracene, BaP = benzo[a]pyrene, BkF = benzo [k]fluoranthene, BbF = benzo[b] fluoranthene BghiP = benzo[g,h,i]perylene, DahA = dibenz[a,h]anthracene, IndP = indeno[1,2,3,c,d]pyrene

wear debris, and waste incineration (Zanieri et al. 2007). In another study, a high level of the PAHs in this area was related to consumption of fossil fuels, more traffic volumes, and less dispersion of contaminants due to the meteorological conditions (Rengarajan et al. 2015). The other factor that may influence the concentrations of PAHs in breast milk is the eating habits of mothers. According to previous studies, eating habits and food preparation is significantly different across countries. PAHs were found as contaminants in various foods, including fruits, meats, vegetables, oils, cereals, milk, etc. In a study by Xia et al. (2010) on concentrations of PAHs in food samples in Taiwan, the content of PAHs in meat products was higher than the one in vegetables, milk, and wheat (Xia et al. 2010). Pirsahab et al. (2018) reported processing methods of foods such as baking, barbecuing, roasting, and frying and found that

grilling and barbecuing are other sources of PAH contamination (Pirsahab et al. 2020). Since eating habits are different across countries (for example, in some countries, vegetarian and meat-eating diets are common), PAHs level in breast milk can vary depending on eating different foods.

3.5. Health risk assessment

Mother milk provides all the nutrients and energy necessary for the suitable cognitive and development of infants and defends them against chronic diseases and infections, especially in the first six months of life. Contamination of mother milk with toxic substances such as PAHs can lead to health risks for infants (Perera et al. 2005). Exposure of infants to PAHs by consuming mother

Table 4
Mutagenic risk assessment based on BaP equivalency for human breast milk.

Country	BaA	BaP	BbFlu	BkFlu	Chr	DahA	IndP	Total
Egypt	1.607E-10	1.029E-06	6.615E-09	—	2.166E-10	—	4.922E-08	1.09E-06
Ghana	—	—	—	4.312E-09	2.499E-09	4.178E-07	9.114E-08	5.16E-07
India	—	—	—	—	7.497E-10	—	—	7.50E-10
Italy	1.649E-08	3.969E-07	9.555E-08	3.412E-07	6.997E-09	6.196E-07	1.180E-06	2.66E-06
Japan	1.848E-10	1.274E-09	5.096E-08	3.557E-10	5.498E-10	9.947E-10	5.468E-10	5.49E-08
Louisville, KY	4.018E-10	2.450E-08	—	—	4.998E-10	—	—	2.54E-08
Mexico	4.701E-07	4.900E-08	1.899E-06	4.258E-07	9.913E-08	—	1.884E-06	4.83E-06
China	—	—	—	—	—	—	4.299E-08	4.30E-08
Turkey	2.310E-08	1.210E-07	5.611E-08	1.127E-08	1.235E-08	1.364E-08	8.081E-08	3.18E-07
Total	5.10E-07	1.62E-06	2.11E-06	7.83E-07	1.23E-07	1.05E-06	3.33E-06	9.53E-06

Chr = chrysen, BaA = benzo[a]anthracene, BaP = benzo[a]pyrene, BkF = benzo[k]fluoranthene, BbF = benzo[b]fluoranthene, BghiP = benzo[g,h,i]perylene, DahA = dibenz[a,h]anthracene, IndP = indeno[1,2,3-c,d]pyrene

milk can lead to various diseases, including pulmonary diseases, growth retardation, low IQ, changes in child behavior, and a higher talent to create allergies (Kamal et al. 2015, Drwal et al. 2019). The weight of the child at birth is another effective factor. Oliveira et al. (2020) indicated that the health risk associated with PAHs was higher in the child born with a weight lower than 3.0 kg, which can be related to un-metabolized and metabolized PAH in them (Oliveira et al. 2020). Based on a previous study, there is no acceptable guideline for assessing PAHs concentration in mother milk. Infant exposure to PAHs is evaluated based on benzo[a]pyrene (BaP) as an indicator. Tables 2 and 4 present the risk of carcinogenic or mutagenic PAHs by consuming mother milk in infants based on aP equivalent [ng/g milk] in different countries. The ranking of countries according to carcinogenetic risk was in the following order: Italy > Mexico > Ghana > Egypt > Turkey > Japan > Louisville > China > India. In addition, according to mutagenic risk, it was in the following order: Mexico > Italy > Egypt > Ghana > Turkey > Japan > China > Louisville > India. Differences in carcinogenetic and mutagenic risk of PAHs in infants across different countries are mainly attributed to their concentration in mother milk. Based on the data, approximately cancer and other non-cancer risks related to PAHs in infants were lower than 10⁻⁶; therefore, consuming mother milk posed no health risk to infants.

4. Conclusion

This systematic review was conducted to estimate the concentration of the PAHs in mother milk based on different sub-groups of PAHs and countries in the world. Cancer and carcinogenetic and mutagenic risks of PAHs were also assessed based on the consumption of mother milk and PAHs concentration in different countries. The results of 13 papers indicated that the lowest and highest concentration of PAHs was 0.125 ng/g and 76.36 ng/g related to benz(a)anthracene and 1-methylnaphthalene, respectively. The ranking of concentration of PAHs according to various countries was in the order of Japan < Louisville, KY < India < Northwest China < Turkey < Egypt < China < Italy < Mexico. Physicochemical characteristics of PAHs, women-specific metabolic activity, age of mother, and the type of food consumed before milk collection, and residential exposures have essential roles in the differences observed regarding the level of PAHs in mother milk. The carcinogenetic and mutagenic risks of PAHs indicated a different risk pattern in various countries. However, the consumption of mother milk is safe and does not pose any risks to infants' health.

CRediT authorship contribution statement

Shima Khanverdilu: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Project administration. **Elaheh Talebi-Ghane:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Ali Heshmati:** Conceptu-

alization, Methodology, Investigation, Writing – review & editing. **Fereshteh mehri:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sjbs.2021.07.066>.

References

- Acharya, N., Gautam, B., Subbiah, S., Rogge, M.M., Anderson, T.A., Gao, W., 2019. Polycyclic aromatic hydrocarbons in breast milk of obese vs normal women: Infant exposure and risk assessment. *Sci. Total Environ.* 668, 658–667.
- Aguinaga, N., Campillo, N., Viñas, P., Hernández-Córdoba, M., 2007. Determination of 16 polycyclic aromatic hydrocarbons in milk and related products using solid-phase microextraction coupled to gas chromatography-mass spectrometry. *Analytica Chimica Acta* 596 (2), 285–290.
- Asamoah, A., 2017. "Assessment of the Contamination Level of Persistent Organic Pollutants in Breast Milk of Ghanaian Women from a polluted Area in Accra."
- Asamoah, A., Fini, M.N., Essumang, D.K., Muff, J., Sogaard, E.G., 2019. PAHs contamination levels in the breast milk of Ghanaian women from an e-waste recycling site and a residential area. *Sci. Total Environ.* 666, 347–354.
- Baali, A., Kammann, U., Hanel, R., El Qoraychi, I., Yahyaoui, A., 2016. Bile metabolites of polycyclic aromatic hydrocarbons (PAHs) in three species of fish from Morocco. *Environ. Sci. Eur.* 28 (1), 1–6.
- Bandowe, B.A.M., Bigalke, M., Boamah, L., Nyarko, E., Saalia, F.K., Wilcke, W., 2014. Polycyclic aromatic compounds (PAHs and oxygenated PAHs) and trace metals in fish species from Ghana (West Africa): bioaccumulation and health risk assessment. *Environ. Int.* 65, 135–146.
- Bandowe, B.A.M., Meusel, H., 2017. Nitrated polycyclic aromatic hydrocarbons (nitro-PAHs) in the environment—a review. *Sci. Total Environ.* 581, 237–257.
- Cancer, I. A. f. R. o. 2010. "Agents classified by the IARC monographs, vol 1-100." <http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf>.
- Cavret, S., Feidt, C., Le Roux, Y., Laurent, F., 2005. Study of mammary epithelial role in polycyclic aromatic hydrocarbons transfer to milk. *J. Dairy Sci.* 88 (1), 67–70.
- Cho, Hyoun-Kyoung, Shin, Han-Seung, 2012. Evaluation of polycyclic aromatic hydrocarbon contents and risk assessment for infant formula in Korea. *Food Sci. Biotechnol.* 21 (5), 1329–1334.
- Cok, I., Mazmanci, B., Mazmanci, M.A., Turgut, C., Henkelmann, B., Schramm, K.W., 2012. Analysis of human milk to assess exposure to PAHs, PCBs and organochlorine pesticides in the vicinity Mediterranean city Mersin, Turkey. *Environ. Int.* 40, 63–69.

- Del Bubba, M., Zanieri, L., Galvan, P., Donzelli, G.P., Checchini, L., Lepri, L., 2005. Determination of polycyclic aromatic hydrocarbons (PAHs) and total fats in human milk. *Annali di Chimica* 95 (9–10), 629–641.
- Drwal, E., Rak, A., Gregoraszcuk, E.L., 2019. Polycyclic aromatic hydrocarbons (PAHs)—Action on placental function and health risks in future life of newborns. *Toxicology* 411, 133–142.
- Duedahl-Olesen, L., White, S., Binderup, M., 2006. Polycyclic aromatic hydrocarbons (PAH) in Danish smoked fish and meat products. *Polycyclic Aromat. Compd.* 26 (3), 163–184.
- Durant, J.L., Busby Jr, W.F., Lafleur, A.L., Penman, B.W., Crespi, C.L., 1996. Human cell mutagenicity of oxygenated, nitrated and unsubstituted polycyclic aromatic hydrocarbons associated with urban aerosols. *Mutation Research/Genetic Toxicology* 371 (3–4), 123–157.
- Fernández-Cruz, T., Martínez-Carballo, E., Simal-Gándara, J., 2017. Perspective on pre-and post-natal agro-food exposure to persistent organic pollutants and their effects on quality of life. *Environ. Int.* 100, 79–101.
- Forehand, J.B., Dooly, G.L., Moldoveanu, S.C., 2000. Analysis of polycyclic aromatic hydrocarbons, phenols and aromatic amines in particulate phase cigarette smoke using simultaneous distillation and extraction as a sole sample clean-up step. *J. Chromatogr. A* 898 (1), 111–124.
- Ghane, E.T., Poormohammadi, A., Khazaei, S., Mehri, F., 2021. Concentration of Potentially Toxic Elements in Vegetable Oils and Health Risk Assessment: a Systematic Review and Meta-analysis. *Biol. Trace Elem. Res.*, 1–10
- Hegazy, A.M., Fakhreldin, A.R., Nasr, S.M., 2020. Monitoring of carcinogenic environmental pollutants in women's breast milk. *Biomedical and Pharmacology Journal* 13 (1), 119–125.
- Heindel, Jerrold J., Newbold, Retha, Schug, Thaddeus T., 2015. Endocrine disruptors and obesity. *Nature Reviews Endocrinology* 11 (11), 653–661.
- Heshmati, A., Mehri, F., Karami-Momtaz, J., Khaneghah, A.M., 2020. The concentration and health risk of potentially toxic elements in black and green tea—both bagged and loose-leaf. *Quality Assurance and Safety of Crops & Foods* 12 (3), 140–150.
- Hunter, S., Myers, S., Radmacher, P., Eno, C., 2010. Detection of polycyclic aromatic hydrocarbons (PAHs) in human breast milk. *Polycyclic Aromat. Compd.* 30 (3), 153–164.
- Ilo, C.E., Oritsemuelebi, B., Santonicola, S., De Felice, A., Cobellis, L., Passariello, N., Peluso, A., Murru, N., Ferrante, M.C., Mercogliano, R., 2017. Comparative study on the occurrence of polycyclic aromatic hydrocarbons in breast milk and infant formula and risk assessment. *J Health Pollut* 175, 383–390.
- Kamal, Atif, Cincinelli, Alessandra, Martellini, Tania, Malik, Riffat Naseem, 2015. A review of PAH exposure from the combustion of biomass fuel and their less surveyed effect on the blood parameters. *Environ. Sci. Pollut. Res.* 22 (6), 4076–4098.
- Karam, F.F., 2019. Evaluation PAHs contamination level in the breast milk of women in al-diwanayah city, Iraq- a case study. *Journal of Global Pharma Technology* 11 (7), 79–84.
- Khazaei, S., Talebi Ghane, E., Bashirian, S., Mehri, F., 2021. The concentration of potentially toxic elements (PTEs) in fruit juices: a global systematic review, meta-analysis and probabilistic health risk assessment. *Int. J. Environ. Anal. Chem.*, 1–13
- Kim, Sung R., Halden, Rolf U., Buckley, Timothy J., 2008. Polycyclic aromatic hydrocarbons in human milk of nonsmoking U.S. women. *Environ. Sci. Technol.* 42 (7), 2663–2667.
- Kishikawa, Naoya, Kuroda, Naotaka, 2009. Evaluation of organic environmental pollutants detected in human milk. *J. Health Sci.* 55 (1), 1–10.
- Kishikawa, Naoya, Wada, Mitsuhiro, Kuroda, Naotaka, Akiyama, Syuzo, Nakashima, Kenichiro, 2003. Determination of polycyclic aromatic hydrocarbons in milk samples by high-performance liquid chromatography with fluorescence detection. *J. Chromatogr., B: Anal. Technol. Biomed. Life Sci.* 789 (2), 257–264.
- Ledesma, E., Rendueles, M., Díaz, M., 2016. Contamination of meat products during smoking by polycyclic aromatic hydrocarbons: Processes and prevention. *Food Control* 60, 64–87.
- Li, G., Wu, S., Wang, L., Akoh, C.C., 2016. Concentration, dietary exposure and health risk estimation of polycyclic aromatic hydrocarbons (PAHs) in youtiao, a Chinese traditional fried food. *Food Control* 59, 328–336.
- Lima, Ana Lúcia C., Farrington, John W., Reddy, Christopher M., 2005. Combustion-derived polycyclic aromatic hydrocarbons in the environment—a review. *Environ. Forensics* 6 (2), 109–131.
- Madhavan, N.D., Naidu, K.A., 1995. Polycyclic aromatic hydrocarbons in placenta, maternal blood, umbilical cord blood and milk of Indian women. *Hum. Exp. Toxicol.* 14 (6), 503–506.
- Mahmood, S., Eghtesadi Araghi, P., Mashinchian, A., Fatemi, M., Riazi, G., 2013. Evaluation of lysosomal stability and red blood cell membrane fragility in mudskipper (*Boleophthalmus dussumieri*) as a biomarker of poly aromatic hydrocarbons. *Iranian scientific fisheries journal* 22 (2), 65–76.
- Martorell, Isabel, Perelló, Gemma, Martí-Cid, Roser, Castell, Victòria, Llobet, Juan M., Domingo, José L., 2010. Polycyclic aromatic hydrocarbons (PAH) in foods and estimated PAH intake by the population of Catalonia, Spain: temporal trend. *Environ. Int.* 36 (5), 424–432.
- Mehri, F., Esfahani, M., Heshmati, A., Jenabi, E., Khazaei, S., 2020. The prevalence of ochratoxin A in dried grapes and grape-derived products: a systematic review and meta-analysis. *Toxin Reviews* 1–10.
- Nieva-Cano, M., Rubio-Barroso, S., Santos-Delgado, M., 2001. Determination of PAH in food samples by HPLC with fluorimetric detection following sonication extraction without sample clean-up. *Analyst* 126 (8), 1326–1331.
- Nwaichi, E., Ntorgbo, S., 2016. Assessment of PAHs levels in some fish and seafood from different coastal waters in the Niger Delta. *Toxicol. Rep.* 3, 167–172.
- Oliveira, M., Duarte, S., Delerue-Matos, C., Pena, A., Morais, S., 2020. Exposure of nursing mothers to polycyclic aromatic hydrocarbons: Levels of un-metabolized and metabolized compounds in breast milk, major sources of exposure and infants' health risks. *Environ. Pollut.* 266, 115243.
- Olyaei, S., Riahi Bakhtiari, A., Sharifpour, I., 2015. Pyrene's bioaccumulation in muscle, gill and liver tissues of common carp (*Cyprinus carpio*): in vitro study. *Iranian journal of health and environment* 8 (2), 191–202.
- Perera, F.P., Rauh, V., Whyatt, R.M., Tang, D., Tsai, W.Y., Bernert, J.T., Tu, Y.H., Andrews, H., Barr, D.B., Camann, D.E., Diaz, D., Dietrich, J., Reyes, A., Kinney, P.L., 2005. A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures. *Neurotoxicology* 26 (4), 573–587.
- Pirsaheb, Meghdad, Irandost, Mozghan, Asadi, Fateme, Fakhri, Yadolah, Asadi, Anvar, 2020. Evaluation of polycyclic aromatic hydrocarbons (PAHs) in fish: a review and meta-analysis. *Toxin Reviews* 39 (3), 205–213.
- Rengarajan, Thamaraiselvan, Rajendran, Peramaiyan, Nandakumar, Natarajan, Lokeshkumar, Boopathy, Rajendran, Palaniswami, Nishigaki, Ikuo, 2015. Exposure to polycyclic aromatic hydrocarbons with special focus on cancer. *Asian Pacific Journal of Tropical Biomedicine* 5 (3), 182–189.
- Santonicola, S., De Felice, A., Cobellis, L., Passariello, N., Peluso, A., Murru, N., Ferrante, M.C., Mercogliano, R., 2017. Comparative study on the occurrence of polycyclic aromatic hydrocarbons in breast milk and infant formula and risk assessment. *Chemosphere* 175, 383–390.
- Tsang, Hin L., Wu, Shengchun, Leung, Clement K.M., Tao, S., Wong, Ming H., 2011. Body burden of POPs of Hong Kong residents, based on human milk, maternal and cord serum. *Environ. Int.* 37 (1), 142–151.
- USEPA, 1993. "Provisional Guidance for Quantitative Risk Assessment of PAH." United States Environmental Protection Agency EPA/600/R-93/089.
- Wang, Li, Liu, Aiping, Zhao, Yuan, Mu, Xi, Huang, Tao, Gao, Hong, Ma, Jianmin, 2018. The levels of polycyclic aromatic hydrocarbons (PAHs) in human milk and exposure risk to breastfed infants in petrochemical industrialized Lanzhou Valley, Northwest China. *Environ. Sci. Pollut. Res.* 25 (17), 16754–16766.
- Wheeler, Amanda J., Dobbin, Nina A., Héroux, Marie-Eve, Fisher, Mandy, Sun, Liu, Khoury, Cheryl F., Hauser, Russ, Walker, Mark, Ramsay, Tim, Bienvenu, Jean-François, LeBlanc, Alain, Daigle, Éric, Gaudreau, Eric, Belanger, Patrick, Feeley, Mark, Ayotte, Pierre, Arbuckle, Tye E., 2014. Urinary and breast milk biomarkers to assess exposure to naphthalene in pregnant women: an investigation of personal and indoor air sources. *Environmental Health* 13 (1). <https://doi.org/10.1186/1476-069X-13-30>.
- WHO, 2001. "The optimal duration of exclusive breastfeeding. Report of an Expert Consultation. World Health Organization, Geneva." Switzerland.
- WHO, I. 1998. "Environmental Health Criteria 202: Selected Non-heterocyclic Polycyclic Aromatic Hydrocarbon." World Health Organization: Geneva.
- Xia, Zhonghuan, Duan, Xiaoli, Qiu, Weixun, Liu, Di, Wang, Bin, Tao, Shu, Jiang, Qiuqing, Lu, Bin, Song, Yunxue, Hu, Xinxin, 2010. Health risk assessment on dietary exposure to polycyclic aromatic hydrocarbons (PAHs) in Taiyuan, China. *Sci. Total Environ.* 408 (22), 5331–5337.
- Yu, Y., Li, Q., Wang, H., Wang, B., Wang, X., Ren, A., Tao, S., 2015. Risk of human exposure to polycyclic aromatic hydrocarbons: a case study in Beijing, China. *Environ. Pollut.* 205, 70–77.
- Yu, Yanxin, Wang, Xilong, Wang, Bin, Tao, Shu, Liu, Wenxin, Wang, Xuejun, Cao, Jun, Li, Bengang, Lu, Xiaoxia, Wong, Ming H., 2011. Polycyclic aromatic hydrocarbon residues in human milk, placenta, and umbilical cord blood in Beijing, China. *Environ. Sci. Technol.* 45 (23), 10235–10242.
- Zanieri, L., Galvan, P., Checchini, L., Cincinelli, A., Lepri, L., Donzelli, G.P., Del Bubba, M., 2007. Polycyclic aromatic hydrocarbons (PAHs) in human milk from Italian women: influence of cigarette smoking and residential area. *Chemosphere* 67 (7), 1265–1274.