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Review Article

Lactational exposure of human infants to metal(loid)s in Sub-Saharan Africa and Mediterranean Europe: A systematic review and meta-analysis

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ABSTRACT

Breast milk, a fundamental component of infant nutrition, may serve as a reservoir for various metal(loid)s, which could pose significant health risks to infants of mothers exposed to toxic metals. Human exposure levels to metal(loid)s vary across regions, influenced by differences in diet, lifestyle, and environmental factors. This systematic review compares metal(loid) concentrations in breast milk from Sub-Saharan Africa (SSA) and Mediterranean Europe (Med. Europe), identifying key determinants of exposure. PubMed, Scopus, and Google Scholar were searched for articles reporting metal concentrations in human breast milk samples from SSA and Med. Europe. Weighted mean concentrations were estimated and compared between the two regions. Twenty-five studies from SSA and seventeen from Med. Europe were included in the review. Mean concentrations of cadmium (12.38 ± 1.21 μg/L vs 0.22 ± 0.51 μg/L; $p < 0.0001$), lead (14.96 ± 8.10 μg/L vs 1.16 ± 4.00 μg/L; $p < 0.0001$), and mercury (2.01 ± 1.37 μg/L vs 0.95 ± 4.32 μg/L; $p = 0.008$) were higher in breast milk samples from SSA than Med. Europe. Conversely, breast milk samples from SSA had lower concentrations of selenium (7.38 ± 2.67 μg/L vs 13.09 ± 16.89 μg/L; $p < 0.0001$) and iron (138.78 ± 106.33 μg/L vs 371.97 ± 446.74 μg/L; $p < 0.0001$) than those from Med. Europe. Key determinants of metal(loid)s levels in breast milk included maternal smoking, dietary patterns, and environmental exposure. There is an urgent need for effective interventions and policies to reduce metals exposure, particularly in SSA, to safeguard maternal and infant health.

1. Introduction

Breast milk is crucial to infant nutrition, providing a comprehensive array of nutrients and bioactive components essential for growth and development (Nuzzi et al., 2021). It contains numerous bioactive factors, including multi-potent stem cells, immunoglobulins, hormones, beneficial bacteria, and complex oligosaccharides, all of which contribute to the immune system and the development of a healthy gut microbiome in infants (Caba-Flores et al., 2022; Dessì et al., 2018; Nuzzi et al., 2021). Moreover, human breast milk influences biological metabolism during early infancy, particularly the antioxidant system (Lee and Ra, 2021). The World Health Organisation recommends exclusive breastfeeding for the first six months, with complementary breastfeeding extending up to two years (World Health Organization, 2024). Breastfeeding is associated with reduced infant morbidity and mortality, as well as a lower incidence of gastrointestinal, respiratory, inflammatory, and allergic diseases (Shoji and Shimizu, 2019).

However, despite being the optimal source of nutrition, breast milk

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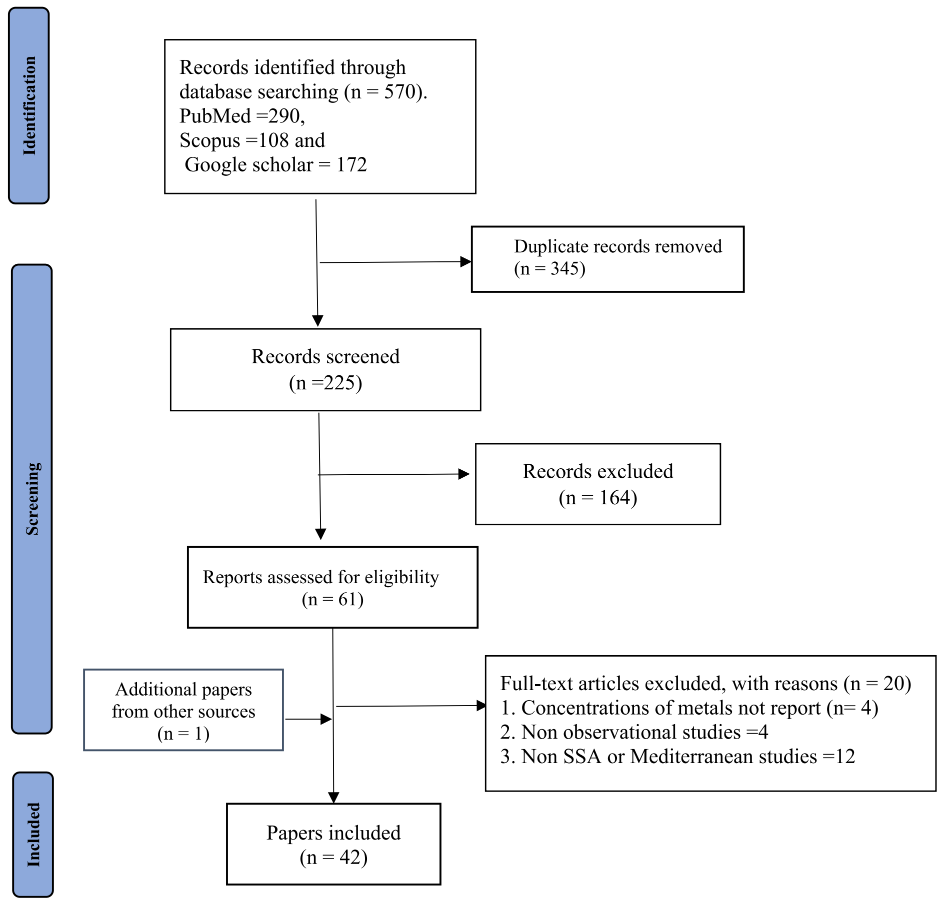

Fig. 1. A PRISMA diagram showing the article screening and selection process.

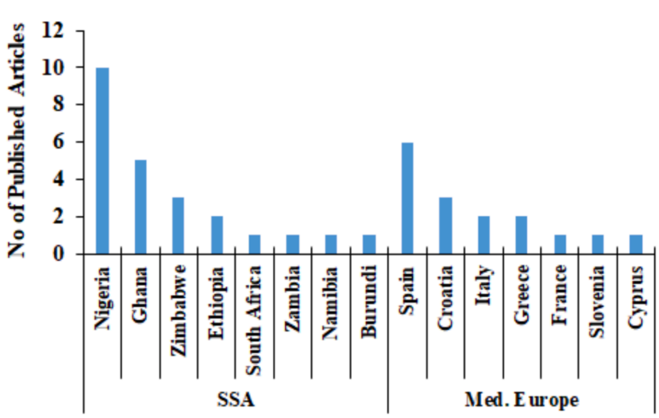

Fig. 2. Studies Conducted in Sub-Saharan Africa (SSA) and Mediterranean Europe (Med. Europe).

may contain environmental pollutants, such as phthalates, polychlorinated biphenyls (Pajewska-Szmyt et al., 2019; Picone and Paolillo, 2013), and metals (e.g., arsenic, lead, cadmium, and mercury), which can expose infants to harmful toxins, potentially causing health issues (Lehmann et al., 2018).

Environmental contaminants may accumulate in the body well before pregnancy and can be released during gestation and lactation, presenting risks to both the mother and the infant (Anadón et al., 2022). These contaminants can transfer from mothers to infants through breastfeeding and may have adverse effects on reproductive development in animals and potentially in humans (Krysiak-Baltyn et al., 2012; Bratlid, 2009). The transfer of contaminants like metals to breast milk varies based on their chemical forms and maternal blood levels, complicating the understanding of their adverse effects (Rebelo and Caldas, 2016; Vollset et al., 2019). Research has identified differences in metal concentrations between primiparous (first-time) and multiparous (those who have previously borne infants) mothers, with primiparous mothers typically exhibiting higher levels of certain metals in breast milk (Freire et al., 2022; Park et al., 2018). These variations may stem from cumulative exposure to metals and shifts in the body's ability to process and excrete metals during successive pregnancies.

The presence of elevated levels of methylmercury, lead, and manganese in breast milk, poses potential health risks to infants, including both carcinogenic and non-carcinogenic effects (Al-Saleh, 2021). Metal (loid)s like arsenic can be present in breast milk and adversely impact various systems, including the endocrine, respiratory, immune, and nervous systems (Candeias et al., 2021). Several studies have explored the contamination of breast milk with metals in Sub-Saharan Africa and Mediterranean Europe. In Sub-Saharan Africa, heavy metal contamination in breast milk presents a significant risk to infants (Motas et al., 2021; Ekeanyanwu et al., 2020; Bansa et al., 2017; Polychronaki et al., 2006). Similarly, women living in industrial areas of Spain, Mediterranean Europe, have higher levels of aluminium, zinc, arsenic, lead, mercury, and nickel in their breast milk compared to those in agricultural regions (Motas et al., 2021). These findings align with an earlier comparative analysis which highlighted substantial geographical differences in metal(loid) concentrations in breast milk, particularly between industrialised and developing regions (Parr et al., 1991).

Breast milk serves as an important matrix for biomonitoring, reflecting both maternal metal body burden and infant risk (Canale et al., 2021). Significant variations in trace elements such as copper, iron and zinc, across different populations, shaped by geographic location,

Table 1
Summary of studies on toxic metal levels in human breast milk in Sub-Saharan Africa.

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk examined	Sample size	Metal Concentrations (μg/L)	Determinants of metal exposure/ health risk to infants
Philip-Slaboh et al. (2023)	Nigeria	AAS, DMA for Hg	Mature milk	72	As:0.65 ± 0.36 Cd: 3.24 ± 1.87 Hg: 3.08 ± 1.74 Pb: 12.24 ± 5.13	Significant number of breast milk samples had high levels of Cd, Pb, As and Hg, indicating risk to the health of the neonate.
Olowoyo et al. (2021)	South Africa	ICP-MS	Up to one-month post-partum	64	As: 0.17 ± 0.30 Cd: 0.01 ± 0.01 Pb: 0.13 ± 0.14	Nature of employment, infant birth weight, passive smoking and maternal diet contributed to me levels in breast milk. Estimated daily intake of Cd from breast milk was negligible.
Toyomaki et al. (2021)	Zambia	NS	NS	407	Pb: 5.30 ± 7.0	Breast milk could be one of important sources of Pb exposure in these infants.
Asamoah-Antwi et al. (2020)	Ghana	HPLC-ICP-MS	Mature milk	48	Total Hg: 0.40 ± 0.35 Methyl Hg 0.18 ± 0.15	The hazard quotients showed that one-month-old infants had hazard quotient above the 0.2, indicating that there is a health concern for such infants.
Ekeanyanwu et al. (2020)	Nigeria	AAS	Mature milk	225	Cr: 19 ± 11[#] Cd: 29 ± 1.3[#] Pb: 38 ± 13[#]	Metal levels not significantly correlated with maternal diet
Bose-O'Reilly et al. (2020)	Zimbabwe	CV-AAS	Mature milk	 42 51 27	Hg: N.E: <0.50 (1.55)[a] ME: 1.10 (10.48)[a] HE: 1.2 (24.80)[a]	Breastfed infants were exposed to toxic levels of mercury via breast milk. The environment and gold mining are sources of Hg exposure.
Bansa et al. (2017)	Ghana	ICP-MS	Mature milk	114	As: 26.70 (22.01, 31.39)[b, c] Cd:1.23 (0.96, 1.5)[b, c] Hg:7.61 (5.14, 10.09) [b, c] Pb:13.83 (8.36,19.30)[b, c]	Significant number of babies in this region were exposed to Hg, As and Pb through breast milk and these may have health implication for the infants.
Klein et al. (2017)	Namibia	ICP-MS	Mature milk	4	As: 6.68 ± 2.46 Pb: 2.15 ± 0.24	Pb and As levels were higher in breast milk samples from Namibia compared with the other populations.
Edem et al. (2017)	Nigeria	AAS	Mature milk	92	Cd: 2.81 ± 0.67[#] Pb: 29.17 ± 5.19[#]	Cd levels higher than those reported in Europe and Asia.
Koka et al. (2011)	Ghana	AAS	Mature milk	48	Accra: Cd: 0.025 ± 0.01 Pb: 2.48 ± 1.10 Tema: Cd: 0.03 ± 0.13 Pb: 3.37 ± 1.13	There was a positive significant correlation between lead and cadmium levels in mothers' breast milk samples in both metropolis. Passive smoking is a determinant to higher breast milk metal levels.
Bentum et al. (2010)	Ghana	AAS	NS	20	As: 1.54 ± 1.94 Cd: 1.34 ± 2.91 Pb: 4.33 ± 9.02	–
Bose-O'Reilly et al. (2008)	Zimbabwe	AAS	NS	46 9 18 4 18 14 14	Hg: 1.87 (<1–149.6)[a] Cd 3.69 ± 2.03[d] Co: 0.64 ± 0.11 [d] Cr: 4.35 ± 1.78 [d] Hg: 2.15 ± 0.56 [d] Ni: 12.2 ± 3.6 [d] Pb: 4.9 ± 1.2	Hg concentrations in breast milk correlated well with the levels in urine, blood and hair. Gold mining was a source of Hg exposure in this population.
	Congo			20 15 69 11 69 59 69	As: 0.26 ± 0.08 [d] Cd: ND Co: 0.36 ± 0.04 [d] Cr: 1.07 ± 0.55 [d] Hg: 2.66 ± 0.66 [d] Ni: 4.9 ± 1.7 [d] Pb: 5.0 ± 0.8 [d]	
Balogun et al. (1994)	Nigeria	INAA-PIXE	Colostrum Mature milk	22	Al: 11.6 ± 4.7[c] 13.7 ± 3.8[c]	–
Parr et al. (1991)	Nigeria	Several techniques	Mature milk	6	As: 1.78 ± 0.02[d]	Not stated

(*continued on next page*)

Table 1 (*continued*)

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk examined	Sample size	Metal Concentrations (μg/L)	Determinants of metal exposure/ health risk on infants
				9	Cd 3.69 ± 2.03^{d}	
				18	Co: 0.64 ± 0.11^{d}	
				4	Cr: 4.35 ± 1.78^{d}	
				18	Hg: 2.15 ± 0.56^{d}	
				14	Ni: 12.2 ± 3.6^{d}	
				14	Pb: 4.9 ± 1.2	
	Congo			20	As: 0.26 ± 0.08^{d}	
				15	Cd: ND	
				69	Co: 0.36 ± 0.04^{d}	
				11	Cr: 1.07 ± 0.55^{d}	
				69	Hg: 2.66 ± 0.66^{d}	
				59	Ni: 4.9 ± 1.7^{d}	
				69	Pb: 5.0 ± 0.8^{d}	

[#] = unit of measurement converted from original unit; [a] = Median (Range); [b] = Geometric Mean (95 % CI); [c] = values reported as ng/g; [d] = values reported as median ± 1 SD; DMA HE = Heavily exposed; ME = Moderately exposed; NE = Non-exposed; NS = Not Stated.

diet, and environmental exposure has previously been identified (Parr et al., 1991). While environmental pollution has been addressed in various studies, a comprehensive comparative analysis of heavy metal and metalloid concentrations in breast milk between Sub-Saharan Africa and Mediterranean Europe remains scarce. This review aims to fill that gap by presenting a comparative analysis of metal(loid)s in breast milk from these two regions. It examines methodological variations, identifies key determinants, and highlights regional disparities, with the ultimate goal of informing strategies to protect infant health amidst environmental challenges.

This study is crucial due to the vital role breast milk plays in providing infants with essential nutrients and bioactive components (Caba-Flores et al., 2022). It aims to compare metal(loid) concentrations in breast milk samples from Sub-Saharan Africa and Mediterranean Europe and to elucidate the potential health risks posed to infants. The comparison of these regions, with their differing environmental, industrial, and nutritional contexts, offers unique insights into the factors influencing lactational exposure to metal(loid)s and subsequent infant health outcomes. In Sub-Saharan Africa, diverse environmental conditions, including industrial, mining, and agricultural areas, contribute to variable exposure to heavy metals and metalloids through both environmental contamination and diet (Ekeanyanwu et al., 2020; Bansa et al., 2017). Limited waste management infrastructure and regulatory frameworks may also increase pollutant levels in the region. Understanding breast milk composition in this context is crucial due to high breastfeeding rates (Freire et al., 2022; Park et al., 2018). In contrast, Mediterranean Europe's established industries and urban centres, along with its varied diet, present distinct pollution sources and environmental challenges for breast milk composition (Yuanan et al., 2020; Vollset et al., 2019).

2. Materials and methods

Search Strategy: This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). PubMed, Scopus, and Google Scholar databases were searched from inception to December 2023, identifying studies that reported concentrations of metal(loid)s in breast milk of mothers in Sub-Saharan Africa and Mediterranean Europe. Boolean operators, wildcards, truncations, and MeSH terms were used and tailored to the specific databases. An example search string is: (''Breast milk'' OR ''human milk'' OR ''women milk'' OR breastfeeding OR ''breast feeding'' OR ''exclusive breastfeeding'' OR lactation OR ''lactating women'' OR ''lactat* womn'') AND (Metal OR metals OR metalloids OR ''heavy metals'' OR ''trace elements'' OR elements OR ''inorganic contaminants'' OR lead OR cadmium OR arsenic OR chromium OR iron OR copper OR mercury OR zinc OR nickel OR aluminium) AND (Newborn OR ''newborn baby'' OR neonate OR infant OR infan OR neonatal OR postnatal OR child*) AND ("sub-Saharan Africa'' OR ''name of each country in Sub-Saharan Africa" OR ''Mediterranean Europe'' OR name of each country in Mediterranean Europe''). Manual searches, grey literature, conference abstracts, proceedings, and study author contact were also undertaken.

Eligibility Criteria: Studies were included if they (i) reported metal (loid) concentrations in human breast milk, (ii) were conducted in Sub-Saharan Africa or Mediterranean Europe, (iii) involved healthy, disease-free women, and (iv) were original observational studies (cohort, case-control, or cross-sectional). Case reports, animal studies, and those assessing metal levels in non-breast milk biological samples were excluded. In studies comparing metal levels in breast milk of diseased and healthy mothers, only data from healthy mothers were used. Two independent reviewers screened titles and abstracts, resolving disagreements through discussion.

Data Extraction: Full-text screening was conducted by two authors based on the inclusion and exclusion criteria. Data extracted included authors, publication year, country, trace element assessment technique, breast milk stage, sample size, trace element concentrations, determinants of metal(loid) levels, and infant health risks (where available). Discrepancies were resolved through dialogue.

Quality Assessment: The included articles were evaluated using a 7-point scale. Studies were scored 0 or 1 based on the following criteria:

a) Study design description: A paper was scored as 1 if it employed a cross-sectional study design that was clearly and adequately described. This means the study focused on capturing data from a population at a specific point in time. Papers that did not utilize a cross-sectional design or failed to adequately describe their study design were scored as 0. Although cross-sectional studies are often used to determine prevalence, they are also applicable to descriptive analyses, such as examining the chemical composition of breast milk at a single time point, as long as the design is explicitly stated.

b) Random sampling strategy: A paper was scored 1 if it utilized a random sampling strategy or 0 if the sampling was not random.

c) Sample collection method: A paper was scored 1 if sample collection method was adequately described with measures to minimize trace element contamination or 0 if the sample method or its description were not adequate.

d) Population representativeness: A paper was scored 1 or 0 respectively, depending on if the included subjects were representative of the population or not.

e) Population health and exposure status: A paper was scored 1 if the included subjects were healthy and not occupationally exposed to metals and 0 if the subjects were not healthy or were occupationally exposed to metals.

f) Stage of breast milk reported: A paper was scored 1 or 0 depending

Table 2
Summary of studies on toxic metal levels in human breast milk in Mediterranean Europe.

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (μg/L)	Determinants of metal exposure/ health risk on infants
Freire et al. (2022)	Spain	ICP-MS	Mature milk	242 pooled breast milk from 83 donors	As: 1.66 (1.16 – 1.98)[a] Cd: <0.04 (<0.04—0.09)[a] Hg: 0.28 (0.15 – 0.53)[a] Pb: 0.22(< 0.10 – 1.14)[a]	Cd concentrations in milk were generally low and were not associated with food intake. Pb, As and Hg levels were associated with smoking habits, parity and intake of fatty fish and meat, respectively.
Motas et al. (2021)	Spain	ICP-MS	NS	50	Al: 34.3 ± 133.0 As: 0.9 ± 2.71 Cd: 0.4 ± 1.6 Hg: 5.6 ± 12.4 Ni: 25.3 ± 33.8 Pb: 5.2 ± 16.7	Breast milk of women living in the industrial/mining zone had the highest levels of Al, Ni, Hg, As and Pb. Cd levels in milk were lower in mothers with older children and higher in the milk of mothers of children with lower weight.
Mandiá et al. (2021)	Spain	ICP-MS	Preterm milk Colostrum Trans. milk Mature milk	100 70 70 70	As: 1.17 ± 0.60 0.93 ± 1.54 1.11 ± 0.171 1.37 ± 1.82 Cd: 0.45 ± 0.49 0.18 ± 0.07 0.16 ± 0.05 0.15 ± 0.20 Hg: 0.42 ± 0.31 0.34 ± 0.18 0.32 ± 0.12 0.31 ± 0.08 Ni: 1.89 ± 0.83 1.8 ± 0.00 2.18 ± 1.12 2.35 ± 2.69 Pb: 0.10 ± 0.01 0.51 ± 1.56 0.33 ± 0.38 0.30 ± 0.23	Cd and Hg concentrations were higher in preterm milk compared full-term milk samples. There were significant associations between As levels and residence in an urban area, and between Pb levels and both smoking and the consumption of well water.
Authors **(Year of publication)**	**Country**	**Element assessment technique**	**Stage of breast milk**	**Sample size**	**Metal Concentrations (μg/L)**	**Determinants of metal exposure/ health risk on infants**
Tratnik et al. (2019)	Slovenia	ICP-MS	Mature milk	470	As: 0.18 (0.17–0.19)[b] Cd: < LOD Hg: 0.14 (0.13–0.16)[b] Pb: 0.23 (0.21–0.25)[b]	Seafood and amalgam fillings were determinants for As and Hg, while Pb levels were determined by alcohol consumption, smoking, game meat consumption and type of water supply.
Kunter et al. (2017)	Cyprus	ICP-MS	NS	50	As: 0.73 ± 0.58 Cd: 0.45 ± 0.23 Hg: 0.00 ± 0.2 Pb: 1.19 ± 1.53	–
García-Esquinas et al. (2011)	Spain	AAS	Mature milk	100	Cd: 1.31 (1.15 – 1.48)[b] Hg: 0.53 (0.45 – 0.62)[b] Pb: 15.56 (12.9–18.72)[b]	Smoking and dietary habits are main factors linked to heavy metals levels in breast milk.
Miklavčič et al. (2013)	Italy	ICP-MS, Cold Vapour-AAS for Hg	Mature milk	605	As: 0.3 (0.04 – 12)[cd] Hg: 0.2 (<LOD – 28)[cd]	Differences in As and Hg exposure between countries were attributed to differences in amounts and species of fish and other food consumption.
	Slovenia			284	As: 0.4 (0.04 – 2.9)[cd] Hg: 0.2 (<LOD – 28)[cd]	
	Croatia			125	As: 0.2 (0.04 – 119)[cd] Hg:0.2 (<LOD – 24)[cd]	
	Greece			44	As: 0.8 (0.3 – 4.8)[cd] Hg: 0.6 (<LOD – 12)[cd]	

(continued on next page)

Table 2 (*continued*)

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk examined	Sample size	Metal Concentrations (μg/L)	Determinants of metal exposure/ health risk on infants
Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk examined	Sample size	Metal Concentrations (μg/L)	Determinants of metal exposure/ health risk on infants
Leotsinidis et al. (2005)	Greece	AAS	Colostrum	180	Cd: 0.190 ± 0.150 Pb: 0.48 ± 0.60	Estimated weekly intakes of Cd and Pb were found to be low in this population.
Turconi et al. (2004)	Italy	AAS	Colostrum	143	Cd: 1.00 (1.00—1.00)[a] Pb: 7.75 (4.20—14.30)[a]	Cd and Pb presence in human milk presented risk for some new-born children in this population.
Frković et al. (1997)	Croatia	AAS	Transitional milk	29	Cd: 2.54 ± 2.06 Pb: 7.3 ± 8.3	–
Mandić et al. (1995)	Croatia	AAS	Mixed	42	Al: 38 ± 38[#]	Mothers older than 25 years had more breastmilk Al concentrations than those under 25 years. Al content of breast milk tends to decline with increasing parity and lactation period.

[#] = unit of measurement converted from original unit; [a] = Median (interquartile range); [b] = Geometric Mean (95 % CI); [c] = values reported as ng/g; [d] = median (5th and 95th percentile); AAS = Atomic absorption spectrometry; ICP-MS = Inductively coupled plasma –mass spectrometry; DMA = Direct mercury analyzer; NS = Not Stated.

on if the stage of breast milk assessed was reported or not.

g) Trace element assessment technique: A paper was scored 1 or 0, if the method/technique used in trace element measurement was adequately reported.

Studies scoring 6–7 were ranked as high-quality, 4–5 as moderate, and ≤ 3 as low-quality. Quality assessments were independently conducted by two authors, resolving disagreements via discussion.

Data synthesis: Data on the concentrations of metal(loid)s in breast milk were summarized using tables. Studies were grouped by metal(loid)s and regions. Data were synthesized by estimating the weighted mean concentration of metal(loid)s reported in the studies in each region. Some studies did not report summary statistics as mean and standard deviations and so, were excluded from the analysis.

Weighted means were calculated using the following formula:

$$Mean_W = \frac{\sum (n_1{*}m_1) + (n_2{*}m_2) + \cdots\cdots. + (n_i{*}m_i)}{\sum (n_1 + n_2 + \cdots\cdots\cdots + n_i)}$$

Where:

- n_1 = sample size for study 1
- n_i = sample size for study i
- m_1 = mean for study 1
- m_i = mean for study i

Pooled standard deviation was calculated using the following formula:

$$S_{pooled} = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2 + \cdots\cdots\cdots. + (n_i - 1)S_i^2}{n_1 + n_2 + \cdots\cdots + n_i - i}}$$

Where:

- n_1 = sample size for study 1
- n_i = sample size for study i
- S_1 = standard deviation for study 1
- S_i = standard deviation for study i

The calculated effect size represents the weighted mean and pooled standard deviation of individual metal(loid)s concentrations in breast milk for the particular region. Differences in breast milk concentrations of individual metal(loid)s between the two regions were estimated using independent sample *t*-test. Data on the determinants of metal levels in breast milk samples from each region were synthesized using a narrative approach.

3. Results and discussion

General Study Characteristics: The search and selection process for this review is summarised in Fig. 1. A total of 570 studies were retrieved from the three databases: 290 from PubMed, 108 from Scopus, and 172 from Google Scholar. After removing irrelevant studies, reviews, and duplicates, 61 papers were considered for eligibility, with one additional study identified through manual searching on Google Scholar. During the screening process, 40 articles were excluded based on the inclusion and exclusion criteria (as outlined in Fig. 1), resulting in 42 studies being included in the final review.

Twenty-five (25) of these studies were conducted in Sub-Saharan Africa, with Nigeria contributing the highest number (10). The lowest number of studies, one each, came from South Africa, Zambia, Namibia, and Burundi (Fig. 2). In contrast, seventeen (17) of the 42 reviewed studies were conducted in Mediterranean Europe. Of these, six were from Spain, three from Croatia, two each from Italy and Greece, and one study each from France, Slovenia, and Cyprus (Fig. 2). One study included samples from four countries in Mediterranean Europe: Italy, Greece, Slovenia, and Croatia.

All the Sub-Saharan African (SSA) studies, except one (Philip-Slaboh et al., 2023), were cross-sectional in design, focusing on metal(loid) concentrations in breast milk. Cross-sectional studies assess metal(loid) concentrations in breast milk at a single point in time, thus providing a snapshot of exposure levels within the population and enabling a descriptive analysis of contaminants. The study by Philip-Slaboh et al. (2023), a case-control design, compared metal concentrations in the breast milk of diabetic and non-diabetic mothers in Nigeria. However, only data from the healthy controls were included in this review. All of the Mediterranean European studies were also cross-sectional and investigated metal(loid) concentrations in different stages of breast milk.

The descriptive statistics regarding the methods used to measure metal(loid) concentrations (supplementary file) showed that Atomic Absorption Spectrometry (AAS) accounted for 31 samples (37.8 %), Inductively Coupled Plasma Mass Spectrometry (ICP-MS) for 33 samples (40.2 %), Fluorometry for 3 samples (3.7 %), Instrumental Neutron Activation Analysis and Proton-Induced X-ray Emission (INAA-PIXE) for 6 samples (7.3 %), and Inductively Coupled Plasma-Atomic Emission Spectrometry (ICP-AES) for 5 samples (6.1 %). From this data, it is clear that ICP-MS (40.2 %) and AAS (37.8 %) were the most commonly used methods, collectively accounting for nearly 78 % of all samples. This may be attributed to their high sensitivity, accuracy, and ability to detect multiple elements simultaneously. Fluorometry, INAA-PIXE, and

Table 3
Summary of studies on essential trace elements levels in human breast milk in Sub-Saharan Africa.

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (µg/L)	Determinants of metal exposure/ health risk on infants
Hailu et al. (2023)	Ethiopia	ICP-MS	Mature milk	51 73	Se: East Amhara: 12.2 ± 3.9 West Amhara: 3.4 ± 1.56	Breastmilk Se levels were positively correlated with maternal Se status. Lower Se concentrations in breast milk samples from West than East Amhara.
Ezeama et al. 2023	Nigeria	AAS	Mature milk	124	Se: 6.57 ± 2.69	There were no statistically significant associations between breast milk Se concentration and time postpartum as well as maternal diet except for eggs.
Kalaotaji et al. (2021)	Nigeria	AAS	Colostrum/ trans. milk	59	Zn: Urban: 350 ± 200 Sub-urban: 140 ± 100	Area of residence had significant effect on Zn concentrations in breast milk.
Ekeanyanwu et al. (2020)	Nigeria	AAS	Mature milk	225	Cu: 35.0 ± 13.0[#] Fe: 49.0 ± 39.0[#] Zn: 9.0 ± 8.0[#]	Element levels not significantly correlated with maternal diet.
Awua et al. (2019)	Ghana	ICP-MS	Mature milk	114	Cu: 2.12 (0.41—131.96)[a] Se: 171.65 (109.28–95.88)[a] Zn: 11.91 (3.20 –26.08)[a]	Se, Cu and Zn levels were lower than those previously reported.
Klein et al. (2017)	Namibia	ICP-MS	Mature milk	4	Cu: 130.94 ± 63.49 Fe: 1530 ± 860[#] Mn: 11.6 ± 9.78 Zn: 1340 ± 1290[#]	Mn levels were higher while Cu levels were lower in breast milk samples from Namibia compared with other populations.
Edem et al. (2017)	Nigeria	AAS	Mature milk	92	Zn: 945.86 ± 116.05[#]	Breastmilk Zn levels correlated positively with Cd levels.
Authors **(Year of publication)**	**Country**	**Element assessment technique**	**Stage of breast milk**	**Sample size**	**Metal Concentrations (µg/L)[#]**	**Determinants of metal exposure/ health risk on infants**
Maru et al. (2013)	Ethiopia	AAS	Colostrum	27 18	Jimma Cu: 280 ± 140[#] Fe: 500 ± 8[#] Zn: 2300 ± 1200[#] Welkite Cu: 160 ± 8[#] Fe: 410 ± 170[#] Zn: 2490 ± 880[#]	Breast milk Zn levels were found to be influenced by dietary intake of the trace elements.
Bamgbose et al. (2012)	Nigeria	AAS	NS	86	Zn: 3760 ± 41[b]	Zn levels in breast milk decrease with progressive lactation.
Ejezie and Nwagha (2011)	Nigeria	AAS	Colostrum Trans. Milk Trans. Milk Trans. Milk Trans. Milk	10 14 19 22 15	Zn: Day 0 – 3: 712 ± 40.6[#] Day 4 – 6: 655.5 ± 37.4[#] Day 7 – 9: 613.2 ± 31.4[#] Day 10 – 12:587.6 ± 27[#] Day 13–15: 541.8 ± 34.4[#]	There was a progressive decline in breastmilk Zn concentrations as the lactation period increased.
Okolo et al. (2000)	Nigeria	ICP-OES	Mature milk	15	Cu: 170 (11 – 2040)[a] Fe:1510 (70 – 7330)[a] Mn: 30 (10 – 60) Zn: 1070 (67 – 4540)[#a]	Breast milk from the women contained adequate levels of Mn and Fe but low levels of Zn and Cu. However, infants sera contained adequate levels of these elements.
Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (µg/L)[#]	Determinants of metal exposure/ health risk on infants
Robberecht et al. (1995)	Burundi	AAS	Colostrum Trans. milk Mature milk	8 10 6	Cu: 590 ± 10[#] Se: 15.2 ± 2.3[#] Zn: 3760 ± 510[#] Cu: 550 ± 10[#] Se: 16.9 ± 1.8[#] Zn: 3080 ± 600[#] Cu: 80 ± 40[#] Se: 5.2 ± 0.1[#]	Trace element concentrations in breast milk decreased with increase in lactation age. Estimated daily intake of trace elements in infants showed that the RDA (as proposed by the National Research Council of the USA, 1989) was only met for Burundian infants < 1 month of age.

(continued on next page)

Table 3 (*continued*)

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (μg/L)[#]	Determinants of metal exposure/ health risk on infants
					Zn: 750 ± 20[#]	
Balogun et al. (1994)	Nigeria	INAA and PIXE	Colostrum	22	Cu: 6.6 ± 1.2[c] Fe: 11.1 ± 5.1[c] Mn: ND Zn: 38.6 ± 9.3[c]	Trace element concentrations were higher in colostrum than mature milk.
			Mature milk		Cu: 5.3 ± 2.3[c] Fe: 9.4 ± 4.8[c] Mn: ND Zn: 29.1 ± 5.8[c]	
Nyazema et al. (1989)	Zimbabwe	AAS	Colostrum Trans. Milk Mature milk	280	Zn: 8200 ± 1020[#] 4330 ± 130[#] 380 ± 3[#]	Zn levels decreased with progression in lactation period.

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (μg/L)[#]	Determinants of metal exposure/ health risk on infants
Parr et al. (1991)	Nigeria	Several techniques	Mature milk	18 18 18 9 18 18	Cu: 278 ± 25[d] Fe: 523 ± 56[d] Mn: 15.84 ± 4.10[d] Mo: 2.65 ± 0.68[d] Se: 24.2 ± 2.4[d] Zn: 1680 ± 220[d]	Not stated
	Congo			68 69 68 15 69 69	Cu: 201 ± 16[d] Fe: 556 ± 74[d] Mn: 11.21 ± 2.45[d] Mo: 1.39 ± 0.78[d] Se: 19.3 ± 1.1[d] Zn: 1920 ± 120[d]	
Mbofung et al. (1984)	Nigeria	AAS	Colostrum	96	Cu: 520 Fe: 550 Zn: 5830	Trace element concentrations in breast milk decreased with increase in lactation age and Zn levels showed the fastest rate of decrease.
			Mature milk	284	Cu: 290 Fe: 380 Zn: 3080	

[#] = unit of measurement converted from original unit; [a] = Median (range); [c] = values reported as ng/g; [d] = values reported as median ± 1 SD; AAS = Atomic absorption spectrometry; ICP-MS = Inductively coupled plasma –mass spectrometry; OES = Optical emission spectrometry; INAA = Instrumental neutron activation analysis; PIXE = Proton-induced X-ray emission.

ICP-AES were used less frequently, potentially due to their lower sensitivity or specificity compared to ICP-MS and AAS. The preference for ICP-MS and AAS suggests these methods are considered reliable for detecting trace metals in breast milk. ICP-MS is particularly well-suited for measuring low concentrations and a wide range of elements, while AAS, although slightly less sensitive than ICP-MS, remains a robust method for detecting specific metals. The limited use of other methods may be due to their comparative limitations in sensitivity, specificity, cost, or the complexity of instruments such as INAA-PIXE and ICP-AES.

The stages of breast milk analysed included preterm (5 samples, 6.1 %), colostrum (24 samples, 29.3 %), transitional milk (12 samples, 14.6 %), mature milk (35 samples, 41.5 %), mixed (2 samples, 2.4 %), and not stated (5 samples, 6.1 %). Mature milk (41.5 %) and colostrum (29.3 %) constituted the majority of the samples, indicating a significant focus on these stages. The analysis of mature milk may be due to its prevalence and longer duration in an infant's diet, whereas colostrum is critical for its high concentration of nutrients and immunological components (Koka et al., 2011; Mandiá et al., 2021). Transitional milk (14.6 %) and preterm milk (6.1 %) were less represented, likely due to their shorter production periods and the specific conditions under which they are produced. The presence of mixed samples (2.4 %) and unspecified stages (6.1 %) may reflect variations in sample collection and reporting.

Quality of included studies: Based on the quality assessment criteria outlined earlier, the rankings of the included studies are presented in Table 5 and Table 6. Among the 26 studies conducted in Sub-Saharan Africa (SSA), 14 were rated as high quality (6–7 points), seven studies were rated as moderate quality (4–5 points), while five studies (Olowoyo et al., 2021; Toyomaki et al., 2021; Bamgbose et al., 2012; Bentum et al., 2010; Okolo et al., 2000) were categorised as low quality (1–3 points).

In contrast, for the 17 studies conducted in Mediterranean Europe, five studies (Motas et al., 2021; Tratnik et al., 2019; García-Esquinas et al., 2011; Turconi et al., 2004; Navarro-Blasco and Alvarez-Galindo, 2004) were rated as high quality, and 12 studies were assessed as moderate quality. Notably, no study from this region was ranked as low quality.

Metal(loid)s concentrations in breast milk samples from Sub-Saharan Africa (SSA) and Mediterranean Europe

Aluminium (Al): Aluminium concentrations were reported in breast milk from Sub-Saharan Africa (SSA) and Mediterranean Europe. One study reported Al levels in colostrum and mature breast milk of women in SSA (Balogun et al., 1994), while two studies reported Al levels in breast milk samples from Mediterranean Europe (Motas et al., 2021; Mandić et al., 1995).

Weighted mean concentrations of Al in the studies is given in Table 7. The weighted mean concentrations were 12.65 ± 4.27 μg/L for SSA and 35.99 ± 101.43 μg/L for Mediterranean Europe, with no statistically significant difference between the two regions. The normal range for

Table 4
Summary of studies on essential trace elements levels in human breast milk in Mediterranean Europe.

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (μg/L)[#]	Determinants of metal exposure/ health risk on infants
Nouzha et al. (2023)	France	ICP-MS and ICP-OES for Fe	Mature milk	232	Se: 9.4 (5.5–18.9)[#a] Zn: 2867 (477–6993)[#a] Cu: 383.4 (108.9–842.7)[#a] Fe: 263.7 (69.8–641.9)[#a] Co: 0.72 (0.31–1.52)[#a] I: 36.7 (8.9–127.8)[#a]	Significant decrease of milk trace element composition through lactation progress and an important influence of birth term on copper.
Mandiá et al. (2021)	Spain	ICP-MS	Preterm milk Colostrum Trans. milk Mature milk	100 70 70 70	Se: 4.97 ± 3.77 10.82 ± 3.41 9.91 ± 1.95 8.87 ± 2.44 Zn: 558.95 ± 716 1005.21 ± 1019 1041.41 ± 911 1237.76 ± 949 Cu: 265.33 ± 71 339.34 ± 185 269.15 ± 135 250.11 ± 163 Fe: 138.43 ± 83 187.70 ± 90 185.28 ± 78 176.51 ± 94 Mn: 1.99 ± 0.93 2.60 ± 3.50 1.74 ± 0.75 1.68 ± 1.00 Co: 0.052 ± 0.01 0.057 ± 0.02 0.052 ± 0.06 0.044 ± 0.02 Cr: 3.61 ± 0.99 3.5 ± 0.00 3.5 ± 0.00 3.22 ± 1.04	Preterm infants were at increased risk of nutritional deficiencies. Se levels were associated with low birth weight.
Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (μg/L)[#]	Determinants of metal exposure/ health risk on infants
Motas et al. (2021)	Spain	ICP-MS	Mature milk	50	Se: 44.5 ± 49.5 Zn: 1402.6 ± 1742.7 Cu: 368.5 ± 301.0 Fe: 679.1 ± 1387.3 Mn: 10.7 ± 63.6 Cr: 16.1 ± 63.6	Breast milk of women in industrial and mining areas had highest levels of Zn, while the highest concentrations of Mn, Cr, Fe, were observed in the milk of women living in the agricultural zone. Zn levels also reduced with increase in lactation period.
Tratnik et al. (2019)	Slovenia	ICP-MS	Mature milk	470	Se: 12.6 (12.3–13.0)[b] Zn: 1935 (1842–2032)[b] Cu: 355 (346–365)[b]	Essential trace element levels were largely determined by certain dietary sources.
Miklavčič et al. (2013)	Italy Slovenia Croatia Greece	ICP-MS, Cold Vapour-AAS,	Mature milk	602 287 123 39	Se: 18 (4.6 – 87)[cd] 17 (1.7 – 69)[cd] 18 (8.4 – 49)[cd] 21 (<LOD – 168)[cd]	There was a significant relationship between the frequencies of fish consumption and Se exposure
Leotsinidis et al. (2005)	Greece	AAS	Colostrum	180	Zn; 4905 ± 1725 Cu: 381 ± 132 Fe: 544 ± 348 Mn: 4.79 ± 3.23	Dietary factors were linked to essential element concentrations in human milk.
Navarro-Blasco and Alvarez-Galindo (2004)	Spain	ICP-AES	Mature milk	31	Se: 16.3 ± 4.7	Se levels result from non-dietary factors linked to the geochemical characteristics of the region

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Table 4 (*continued*)

Authors (Year of publication)	Country	Element assessment technique	Stage of breast milk	Sample size	Metal Concentrations (µg/L)[#]	Determinants of metal exposure/ health risk on infants
Bocca et al. (2000)	Italy	ICP-AES	NS	60	Zn: 2720 ± 70 Cu: 370 ± 30 Fe: 650 ± 40; Mn: 30 ± 2	–
Authors (Year of publication)	**Country**	**Element assessment technique**	**Stage of breast milk**	**Sample size**	**Metal Concentrations (µg/L)[#]**	**Determinants of metal exposure/ health risk on infants**
Torres et al. (1999)	Spain	AAS	Colostrum: Transitional: Mature milk 1 Mature milk 2	22 12 15 6	Se: Colostrum: 11.4 ± 3.7[#] Transitional: 10.7 ± 4.6[#] Mature milk (1mo): 8.4 ± 3.4[#] Mature milk (2mo): 5.3 ± 1.9[#]	–
Mandić et al. (1997)	Croatia	AAS	Mixed	42 41	Zn: 6190 ± 3728[#] Cu:510 ± 190[#]	Zn concentrations decreased with increase in lactation period.
Bratakos and Ioannou (1991)	Greece	Fluorimetry	Colostrum Trans. Milk Mature milk	11	Se: 41 ± 16[#] 23 ± 6[#] 17 ± 3[#]	Se concentrations decreased with lactation time, reaching a plateau, at 17 µg/L after 20 days. Babies fed with breast milk alone received approximately 5–11 µg Se/day up to 6 months of age.

[#] = unit of measurement converted to µg/L from original unit; [a] = mean (5th and 95th percentile); [b] = Geometric Mean (95 % CI); [c] = values reported as ng/g; [d] = median (5th and 95th percentile); AAS = Atomic absorption spectrometry; ICP-MS = Inductively coupled plasma –mass spectrometry; AES = Atomic emission spectrometry;

aluminium in breast milk has not been established.

Arsenic (As): Arsenic levels ranged from 0.17 ± 0.30 µg/L in South African women (Olowoyo et al., 2021) to 26.70 µg/L in Ghanaian women (Bansa et al., 2017). In Mediterranean Europe, the highest mean level (1.66 µg/L) was found in Spanish women (Freire et al., 2022).

The weighted mean As concentrations (Table 7) were 0.72 ± 0.82 µg/L for SSA and 1.07 ± 1.41 µg/L for Mediterranean Europe, with SSA showing significantly lower levels ($p < 0.003$).

Cadmium: Nine (9) studies from SSA measured Cd concentrations in breast milk (Table 1). Among these, the highest mean Cd level (mean ± SD: 29 ± 1.3 µg/L) was reported in mature milk of women from Nigeria (Ekeanyanwu et al., 2020), while the lowest (0.013 ± 0.01 µg/L) was reported for women from South Africa (Olowoyo et al., 2021). The reported mean Cd levels exceeded < 1.0 µg/L in six of the studies (Philip-Slaboh et al., 2023; Ekeanyanwu et al., 2020; Bansa et al., 2017; Edem et al., 2017; Bentum et al., 2010; Parr et al., 1991). Nine (9) studies from Mediterranean Europe measured Cd concentrations in breast milk (Table 2). The highest mean Cd concentration (2.54 ± 2.06 µg/L) was observed in Croatian women (Frković et al., 1997). Cd levels were below the limit of detection (LOD) in two of the European studies (Freire et al., 2022; Tratnik et al., 2019). Two of the nine studies (García-Esquinas et al., 2011, Frković et al., 1997) reported mean Cd levels above 1.0 µg/L.

The weighted mean Cd concentrations (Table 7) were 12.38 ± 1.21 µg/L for SSA, much higher than 0.22 ± 0.51 µg/L in Mediterranean Europe. The mean difference of 12.16 µg/L is statistically significant ($p < 0.0001$).

Chromium: Two studies have reported chromium (Cr) levels in the breast milk of women in SSA (Ekeanyanwu et al., 2020; Parr et al., 1991). The Cr levels reported were 19 ± 11 µg/L (Ekeanyanwu et al., 2020) and 4.35 ± 1.78 µg/L (Parr et al., 1991).

Lead (Pb): Breast milk Pb levels were measured in ten (10) studies each from SSA (Table 1) and Mediterranean Europe (Table 2). Mean Pb levels in breast milk reported in studies from SSA ranged from 0.13 ± 0.14 µg/L for women in South Africa (Olowoyo et al., 2021) to 38 ± 13 µg/L for women in Nigeria (Ekeanyanwu et al., 2020). In five studies (Philip-Slaboh et al., 2023; Toyomaki et al., 2021; Ekeanyanwu et al 2020; Bansa et al., 2017; Edem et al., 2017), the reported breast milk mean Pb levels were above the 5 µg/L. Mean Pb levels in breast milk reported in studies from Mediterranean Europe ranged from 0.22 ± 0.14 µg/L (Freire et al., 2022) to 15.56 µg/L in earlier sample of Spanish women (García-Esquinas et al., 2011). Four of the reported breast milk mean Pb levels exceeded 5 µg/L (Motas et al., 2021; García-Esquinas et al., 2011; Turconi et al., 2004; Frković et al., 1997).

Weighted mean concentrations of Pb in Sub-Saharan Africa and Mediterranean Europe are given in Table 7. Breast milk samples from SSA had higher mean Pb levels (mean ± SD:14.96 ± 8.10 µg/L) than those of Mediterranean Europe (1.16 ± 4.00 µg/L; $p < 0.0001$).

Mercury (Hg): In SSA, Hg levels ranged from 0.17 ± 0.30 µg/L to 7.61 µg/L in Ghanaian women (Asamoah-Antwi et al., 2020; Bansa et al., 2017). One study from Mediterranean Europe reported Hg levels exceeding this range (Motas et al., 2021). The weighted mean Hg concentrations (Table 7) was lower (2.01 ± 1.37 µg/L) for SSA than Mediterranean Europe (0.95 ± 4.32 µg/L; $p = 0.008$).

Nickel (Ni): Two Mediterranean European studies reported nickel levels in breast milk (Motas et al., 2021; Mandiá, et al., 2021). For one of the studies (Motas et al., 2021), high levels (25.3 ± 33.8 µg/L) was reported in breast milk. One study reported Ni levels in breast milk of women in Nigeria and Congo (Zaire) (Parr et al., 1991).

Essential trace elements in breast milk samples from Sub-Saharan Africa and Mediterranean Europe

Copper (Cu): The reported mean breast milk Cu levels in SSA studies varied from 2.12 µg/L for Ghanaian women (Awua et al., 2019) to 290 µg/L, for women in Nigeria (Mbofung et al., 1984). In contrast, mean breast milk Cu levels of women in Mediterranean Europe were considerably higher ranging from 250.11 ± 163 µg/L (Mandiá et al., 2021) for Spanish women to 510 ± 190 µg/L (Mandić et al., 1997) for Croatian women.

Weighted mean breast milk concentrations of Cu in the two regions are given in Tables 7. The breast milk mean concentration of Cu in Mediterranean Europe (338.14 ± 153.97 µg/L) was significantly higher ($p < 0.0001$) than those of SSA (99.12 ± 44.27 µg/L).

Iron (Fe): Reported mean breast milk Fe levels in SSA studies ranged from 9.4 µg/L for Nigerian women (Balogun et al., 1994) to 1530 ± 860

Table 5
Summary of Quality assessment for studies from Sub-Saharan Africa.

Study	Appropriateness of Study Design	Appropriateness of Sampling Strategy	Appropriateness of sample collection method	Representativeness of the Study Population	Appropriateness of the sampled population	Description of Stage of breast milk	Trace element assessment technique	Total score
Philip-Slaboh et al. (2023)	1	1	1	1	1	1	1	7
Hailu et al. (2023)	1	1	1	1	0	1	1	6
Ezeama et al. 2023	1	1	0	1	1	1	1	6
Olowoyo et al. (2021)	1	0	1	0	0	0	1	3
Toyomaki et al. (2021)	1	0	1	1	0	0	0	3
Kalaotaji et al. (2021)	1	1	0	1	1	1	1	6
Ekeanyanwu et al. (2020)	1	1	0	1	1	1	1	6
Asamoah-Antwi et al. (2020)	1	1	1	1	0	1	1	6
Bose-O'Reilly et al. (2020)	1	1	0	1	1	1	1	6
Awua et al. (2019)	1	1	0	1	1	1	1	6
Bansa et al. (2017)	1	1	0	1	1	1	1	6
Klein et al. (2017)	1	0	0	0	1	1	1	4
Edem et al. (2017)	1	0	0	0	1	1	1	4
Maru et al. (2013)	0	0	1	0	1	1	1	4
Bamgbose et al. (2012)	1	0	0	1	0	0	1	3
Ejezie and Nwagha (2011)	1	1	0	1	1	1	1	6
Koka et al. (2011)	1	0	1	0	1	1	1	5
Bentum et al. (2010)	1	0	1	0	0	0	1	3
Bose-O'Reilly et al. (2008)	1	1	1	0	0	0	1	4
Okolo et al. (2000)	1	0	0	0	0	1	1	3
Robberecht et al. (1995)	1	0	1	0	1	1	1	5
Balogun et al. (1994)	1	0	1	0	0	1	1	4
Parr et al., 1991	1	1	1	0	1	1	1	6
Nyazema et al. (1989)	1	1	0	1	1	1	1	6
Mbofung et al. (1984)	1	1	0	1	1	1	1	6

μg/L for women in Namibian women (Klein et al., 2017). In Mediterranean Europe mean breast milk Fe levels ranged from 176.51 ± 94 μg/L (Mandiá et al., 2021) to 679.1 ± 1387.30 μg/L (Motas et al., 2021) for Spanish women. Weighted mean concentrations of Fe in Sub-Saharan Africa and Mediterranean Europe are given in Table 7. Breast milk samples from SSA had lower mean Fe levels (Mean: 138.78 ± 106.33 μg/L) than those of Mediterranean Europe (371.97 ± 446.74 μg/L). The mean difference was statistically significant ($p < 0.0001$).

Manganese (Mn): Mean breast milk Mn levels in European studies varied from 1.68 ± 1.00 μg/L for Spanish women (Mandiá et al., 2021) to 30 ± 2 μg/L for Italian women (Bocca et al., 2000). Mn levels were reported in three SSA studies (Okolo et al., 2000; Klein et al., 2017; Balogun et al., (1994). While Balogun et al., (1994) reported Mn levels below detection limits, the reported mean Mn levels were 11.6 ± 9.78 μg/L in Namibia (Klein et al., 2017) and 30 (10–60) μg/L in Nigeria (Okolo et al., 2000).

Selenium (Se): Four (4) studies from SSA measured Se concentrations in breast milk (Table 3). There is substantial variation in mean Se levels in mature breast milk reported from studies in this population, ranging from 3.4 ± 1.56 μg/L for women living in West Amhara city of Ethiopia (Hailu et al., 2023) to 171.65 μg/L for Ghanaian women (Awua et al., 2019). Eight (8) studies from Mediterranean Europe assessed Se concentrations in breast milk (Table 4). Among these studies, the highest mean Se level (44.5 ± 49.5 μg/L) was reported in mature milk samples of Spanish women (Motas et al., 2021), and the lowest (5.3 ± 1.9 μg/L) was reported for another sample of Spanish women (Torres et al., 1999). Miklavčič et al., (2013) measured breast milk Se concentration in women from 4 countries in Mediterranean Europe. Their reports showed that daily intake of Se for infants fed breast milk alone met the recommended daily allowance of Se for infants consuming approximately 0.8

Table 6
Summary of Quality assessment for studies from Mediterranean Europe.

Study	Appropriateness of study design	Appropriateness of sampling Strategy	Appropriateness of sample collection Method	Representativeness of the study population	Appropriateness of the sampled population	Description of stage of breast milk	Trace element assessment technique	Total score
Nouzha et al. (2023)	0	0	1	1	1	1	1	5
Freire et al. (2022)	0	0	0	1	1	1	1	4
Motas et al. (2021)	1	1	1	1	1	1	1	7
Mandiá et al. (2021)	1	0	0	1	1	1	1	5
Tratnik et al. (2019)	1	1	1	1	1	1	1	7
Kunter et al. (2017)	1	1	1	0	1	0	1	5
García-Esquinas et al. (2011)	1	1	1	1	1	1	1	7
Miklavčič et al. (2013)	1	0	1	1	0	1	1	5
Leotsinidis et al. (2005)	1	0	1	1	0	1	1	5
Turconi et al. (2004)	1	1	1	1	1	1	1	7
Navarro-Blasco and Alvarez-Galindo (2004)	1	0	1	1	1	1	1	6
Bocca et al. (2000)	1	0	1	1	1	0	1	5
Torres et al. (1999)	0	0	0	1	1	1	1	4
Mandić et al. (1997)	1	0	1	1	0	0	1	4
Frković et al. (1997)	1	0	1	0	1	1	1	5
Mandić et al. (1995)	1	0	1	1	0	0	1	4
Bratakos and Ioannou (1991)	1	1	1	0	1	1	0	5

Table 7
Weighted mean concentrations of metal(loid)s in breast milk samples from Sub-Saharan Africa and Mediterranean Europe.

Metal (loid)s	Sub-Saharan Africa		Mediterranean Europe		Mean difference (95 % CI)	P-value
	Total Number of Breast Milk Samples	Weighted mean ± S.D	Total Number of Breast Milk Samples	Weighted mean ± S.D		
Toxic elements						
Al	44	12.65 ± 4.27 μg/L	92	35.99 ± 101.43 μg/L	−23.34 (−53.65 to 6.97)	0.13
As	160	0.72 ± 0.82 μg/L	410	1.07 ± 1.41 μg/L	−0.35 (−0.58 to −0.12)	0.003
Cd	569	12.38 ± 1.21 μg/L	1089	0.22 ± 0.51 μg/L	12.16 (12.08 to 12.24)	<0.0001
Hg	120	2.01 ± 1.37 μg/L	410	0.95 ± 4.32 μg/L	1.06 (0.27 to 1.85)	0.008
Ni	–	–	360	5.27 ± 12.63 μg/L		
Pb	980	14.96 ± 8.10 μg/L	1074	1.16 ± 4.00 μg/L	13.80 (13.25 to 14.35)	<0.0001
Essential elements						
Cr			360	5.23 ± 23.64 μg/L		
Cu	298	99.12 ± 44.27 μg/L	641	338.14 ± 153.97 μg/L	−239.02 (−256.88 to −221.16)	<0.0001
Fe	274	138.78 ± 106.33 μg/L	600	371.97 ± 446.74 μg/L	−233.19 (−286.91 to −179.47)	<0.0001
Mn			600	6.36 ± 18.43 μg/L		
Se	272	7.38 ± 2.67 μg/L	446	13.09 ± 16.89 μg/L	−5.7 (−7.74 to −3.68)	<0.0001
Zn	1514	2828.78 ± 470.73 μg/L	642	2588.80 ± 1534.75 μg/L	239.98 (154.34 to 325.62)	<0.0001

Al = Aluminium; As = Arsenic; Cd = Cadmium; Cr = Chromium; Cu = Copper; Fe = Iron; Hg = Mercury; Mn = Manganese; Ni = Nickel; Pb = Lead; Se = Selenium; Zn = Zinc.

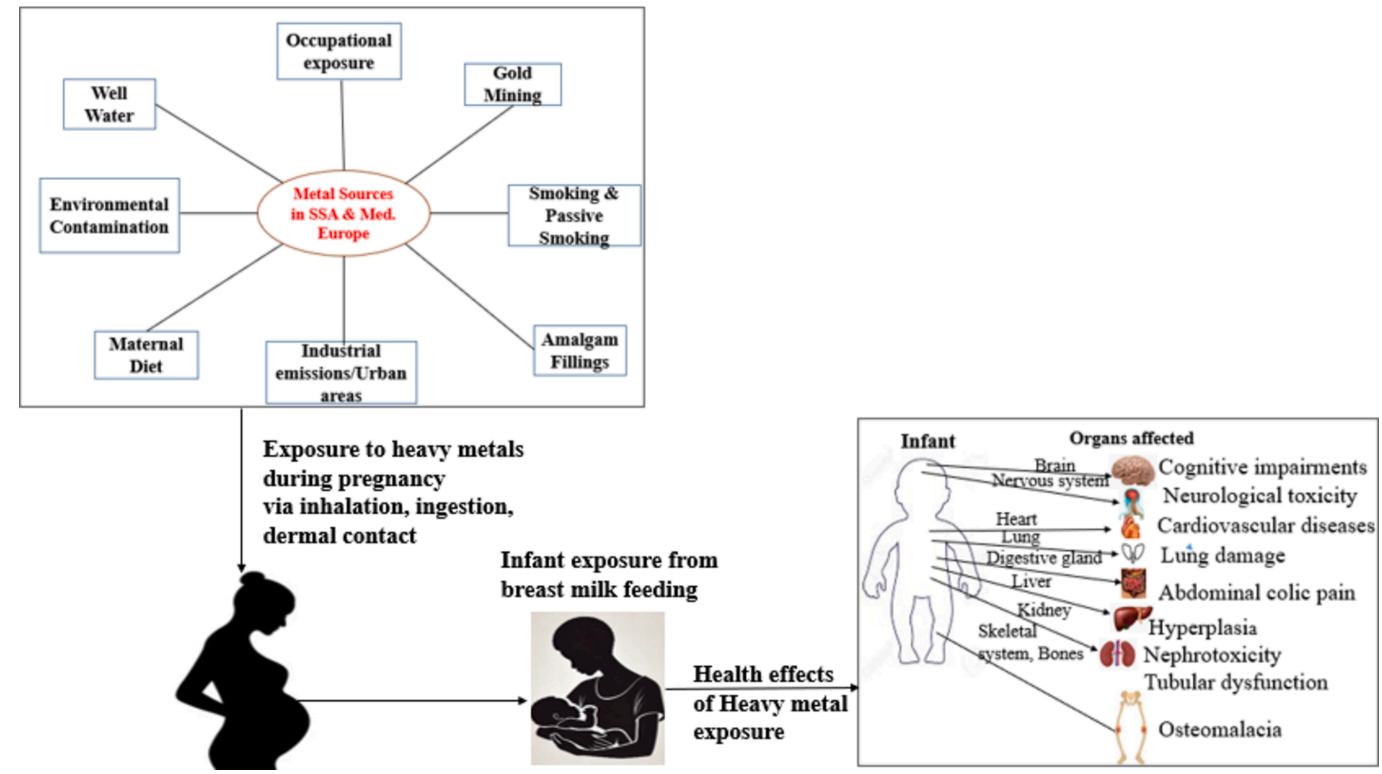

Fig. 3. Metal exposure pathways and health effects on infants through breastfeeding.

L/day.

Weighted mean concentrations of Se in Sub-Saharan Africa and Mediterranean Europe are given in Table 7. Breast milk samples from SSA had lower mean Se levels (Mean ± SD: 7.38 ± 2.67 μg/L) than those of Mediterranean Europe (13.09 ± 16.89 μg/L). The mean difference was statistically significant ($p < 0.0001$).

Zinc (Zn): Breast milk Zn levels were measured in thirteen (13) studies from SSA (Table 3). Reported mean breast milk Zn levels in these studies varied from 9.0 ± 8.0 μg/L for women in South-Eastern Nigeria (Ekeanyanwu et al., 2020) to 3760 ± 41 μg/L for women in Abeokuta, South-Western, Nigeria (Bamgbose et al., 2012). On the other hand, breast milk mean Zn levels reported in studies from Mediterranean Europe (Table 4) ranged from 1237 μg/L for Spanish women (Mandiá et al., 2021) to 6190 μg/L in earlier study of Croatian women (Mandić et al., 1997).

Weighted mean concentrations of Zn in Sub-Saharan Africa and Mediterranean Europe are given in Table 7. Breast milk samples from SSA had higher mean Zn levels (Mean ± SD: 2828.78 ± 470.73 μg/L) than those of Mediterranean Europe (2588.80 ± 1534.75; $p < 0.0001$ μg/L).

Lactational exposure to metal(loid)s in infants from Sub-Saharan Africa and Mediterranean Europe poses significant health risks, reflecting regional variations in environmental pollution and dietary practices. Elevated levels of Cd, Pb, and Hg in breast milk, often linked to industrial and mining activities have been associated with developmental impairments, cognitive deficits, and increased susceptibility to infections in infants (Freire et al., 2022; Mandiá et al., 2021; Bose-O'Reilly et al., 2020). In SSA, such heavy metal exposure is particularly concerning due to higher environmental contamination from industrial and mining activities (Table 3).

Conversely, while Mediterranean Europe generally exhibit lower toxic metal levels due to adherence to diets rich in plant-based foods and fish, concerns remain regarding As and Se exposure. Arsenic exposure in both regions can affect neurological development, while selenium imbalances may impact immune function (Miklavčič et al., 2013; Motas et al., 2021) (Fig. 3).

Determinants of metal(loid) levels in breast milk of women in Sub-Saharan Africa and Mediterranean Europe

A total of twenty-four studies have investigated the determinants of metal(loid) levels in breast milk among women in Sub-Saharan Africa and Mediterranean Europe. These studies highlight the impact of both dietary and non-dietary factors on metal(loid) concentrations. Table 8 provides information regarding intrinsic and extrinsic Factors (dietary and non-dietary) influencing metal(loid) levels in breast milk in SSA and Mediterranean Europe.

3.1. Intrinsic factors

One of the key intrinsic factors is the stage of lactation. Multiple studies have reported that the levels of certain metals in breast milk fluctuate as lactation progresses. For instance, Zn levels have been observed to decrease over time, as documented in various studies from different regions (Nouzha et al., 2023; Motas et al., 2021; Ejezie and Nwagha, 2011; Bamgbose et al., 2012; Mandić et al., 1997; Robberecht et al., 1995; Balogun et al., 1994; Nyazema et al., 1989). Similarly, Cd levels have shown a decline during the later stages of lactation (Mandiá et al., 2021; Motas et al., 2021).

Parity, another intrinsic factor, has also been associated with variations in metal concentrations. Studies have found that women with multiple births tend to exhibit higher levels of certain metals, such as As, a trend that is especially pronounced in those living in industrial and mining areas (Freire et al., 2022; Mandiá et al., 2021).

3.2. Extrinsic factors

3.2.1. Dietary factors

Dietary habits play a significant role in determining metal(loid) levels in breast milk. Several studies identified maternal diet as a key determinant for the levels of Cd (García-Esquinas et al., 2011), As (Miklavčič et al., 2013; Tratnik et al., 2019), and Hg (García-Esquinas

Table 8
The key intrinsic and extrinsic (dietary and non-dietary) factors influencing metal(loid) levels in breast milk across SSA and Mediterranean Europe.

Region	Factors	Key Determinants	Cd	As	Hg	Se	Zn	References
Sub-Saharan Africa	**Intrinsic Factors**	Influence of lactation stage	Reduction as lactation progressed	–	–	–	Reduction as lactation progressed	Ejezie and Nwagha, 2011; Bamgbose et al. 2012; Nyazema et al. 1989
	Extrinsic Factors	**Dietary Factors**	No association in Ghanaian women	–	–	No correlation in Nigerian studies	No correlation in Nigerian studies	Koka et al., 2011; Ezeama et al., 2023; Ekeanyanwu et al., 2020
		Maternal diet influencing levels, alcohol consumption, use of well water, game meat	–	–	–	–	Influence of diet on Se and Zn levels	Hailu et al., 2023; Maru et al. 2013
	Non-Dietary Factors	Smoking	Increased by passive smoking	Higher levels in industrial/ mining zones	Living in gold mining areas	–	Higher concentrations in urban areas	Olowoyo et al. 2021; Koka et al., 2021
		Living in urban, industrial/mining zones	–		Higher levels in industrial/ mining zones	–	Higher concentrations in urban areas	Kalaotaji et al., 2021; Bose-O'Reilly et al., 2020
		Nature of employment, infant birth weight					Co levels correlated positively with infant birth weight	Olowoyo et al. 2021
Mediterranean Europe	**Intrinsic Factors**	Influence of lactation stage	–	–	–	Se decreases with lactation time	Decrease in Zn, Al as lactation increased	Bratakos and Ioannou, 1991 Tratnik et al., 2019; Mandić et al. 1995, 1997
	Extrinsic Factors	**Dietary Factors** Seafood and food consumption	Found association (Spain)	Found association	Found association	Influence of diet on Se levels	Found association (Spain)	García-Esquinas et al., 2011; Miklavčič et al., 2013; Tratnik et al., 2019; Mandiá et al., 2021
			No association	No association	No association		No association for Zn and Fe levels	Freire et al., 2022
	Non-Dietary Factors	Smoking, alcohol, dental amalgam, living in mining zones	Elevated by smoking	Higher in industrial/ mining zones	Use of dental amalgam, living in mining zones	–	–	Freire et al., 2022; Mandiá et al., 2021; Tratnik et al., 2019; Motas et al., 2021; García-Esquinas et al., 2011
		Geochemical characteristics				Se level linked to the geochemical area		Navarro-Blasco and Alvarez-Galindo, 2004

et al., 2011; Miklavčič et al., 2013). However, some studies found no association between diet and Cd levels in Spanish (Freire et al., 2022) and Ghanaian women (Koka et al., 2011). Additionally, the influence of diet on Se and Zn levels in breast milk was observed in several regions (Motas et al., 2021; Tratnik et al., 2019), though no such correlation was found in Nigerian studies (Ezeama et al., 2023; Ekeanyanwu et al., 2020). Maternal diet also influenced Cu levels in one study (Maru et al., 2013) but did not affect Zn and Fe levels. Other dietary factors contributing to higher Pb levels include the consumption of game meat (Tratnik et al., 2019), alcohol consumption (Tratnik et al., 2019), and the use of well water (Mandiá et al., 2021; Tratnik et al., 2019).

3.2.2. Non-dietary factors

Non-dietary factors also significantly influence metal(loid) concentrations in breast milk. Maternal smoking has consistently been linked to elevated levels of Pb and Cd (Freire et al., 2022; Mandiá et al., 2021; García-Esquinas et al., 2011; Koka et al., 2011). The use of dental amalgam was associated with increased Hg levels (Tratnik et al., 2019), while residing in gold mining areas contributed to elevated Hg exposure (Bose-O'Reilly et al., 2020). Urban living was also found to be a determinant of higher Zn concentrations among Nigerian women (Kalaotaji et al., 2021).

3.3. Limitations and sources of heterogeneity observed in this study

This review has some limitations that may affect the interpretation of the results. Differences in study design, sample collection, and analytical techniques contribute to heterogeneity. Environmental factors, such as mining activities and agricultural practices, also vary between studies and regions, leading to inconsistent results. Additional factors not covered in this review include the timing of breast milk sampling, the mother's nutritional status, and the potential effects of medication, hormonal contraceptives, and seasonal variations (Parr et al., 1991). These may have influenced the metal (loid) concentrations reported. The interpretation of breast milk trace element levels in these two populations and the associated health risks on infants in this population is currently limited due to apparent lack of established reference /action ranges for these elements in human breast milk. Establishment of appropriate reference/ action ranges for trace elements as well as other contaminants in breast milk is crucial for biomonitoring of exposure to these environmental pollutants and related risks to human health. This review's scope was also limited by the data sources used, as only three databases were searched, and only studies published in English were included. This could have excluded relevant studies in other languages or databases. Moreover, many studies had small sample sizes, potentially skewing the results. Despite these constraints, this review provides a comprehensive summary of metal(loid) levels in breast milk from SSA and Mediterranean Europe and identifies key determinants affecting these concentrations.

4. Conclusion

The analysis revealed significant regional differences in metal(loid)s (Cd, Pb, As, Hg, Al, Ni, Se, Zn, Fe, Cu, Mn) concentrations in breast milk samples between SSA and Mediterranean Europe. Elevated levels of Cd, Pb, and Hg in SSA raise concerns about potential health risks to infants (Table 1). In contrast, Se, Zn, and Fe were more abundant in breast milk from Mediterranean Europe (Table 4). The lower levels of Se and Fe in SSA breast milk could negatively impact infant health, as these elements are crucial for brain development, immune function, and antioxidant defence. Key contributors to elevated metal(loid) levels include maternal smoking, specific dietary habits (e.g., consumption of game meat), alcohol use, and reliance on well water. Living near industrial or mining areas further exacerbated exposure risk. To mitigate metal(loid)s exposure in breast milk, policies should be implemented to reduce environmental contamination. Moreover, promoting maternal behavioural changes and proper nutrition for essential trace elements could help minimise toxic metal exposure and safeguard infant health in both regions.

Author Contributions

Amarachi Paschaline Onyena, Onyinyechi Bede-Ojimadu, Taagbara Jolly Abaate, Dokuboba Amachree and Opeyemi M. Folorunso wrote the draft manuscript; Chiara Frazzoli and Beatrice Bocca reviewed and critiqued the manuscript. Orish E. Orisakwe conceptualized and drafted the manuscript.

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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Data availability

No data was used for the research described in the article.

References

Al-Saleh, I., 2021. Health risk assessment of trace metals through breast milk consumption in Saudi Arabia. *Biol. Trace Elem. Res.* 199 (12), 4535–4545.

Anadón, A., Martínez-Larrañaga, M.R., Ares, I., Martínez, M.A., 2022. Drugs and chemical contaminants in human breast milk. In: *Reproductive and Developmental Toxicology*. Academic Press, pp. 1019–1052.

Asamoah-Antwi, D., Kumi, S.A., Fianko, J.R., 2020. Assessment of levels of mercury in human breast milk in Obuasi municipality, Ghana. *Environ. Earth Sci. Res. J.* 7 (3), 95–102.

Awua, K.A., Boatin, R., Adom, T., Brown-Appiah, E.C., Diaba, A.M., Datohe, D., Bansa, D. K., 2019. Double burden of malnutrition: toxic metals in breast milk may limit the amounts of micronutrients available to infants through breast milk. *Food Nutr. Sci.* 10, 298–314.

Balogun, F.A., Akanle, O.A., Spyrou, N.M., Owa, J.A., 1994. A comparative study of elemental composition of human breast milk and infant milk substitutes. *Biol. Trace Elem. Res.* 43–45, 471–479. https://doi.org/10.1007/BF02917349.

Bamgbose, O., Opeolu, B.O., Bamgbose, J.T., 2012. Levels of zinc in breast milk of selected women in Abeokuta township Ogun State Nigeria. *Trace Elem. Electrolytes* 29 (3), 149–153.

Bansa, D.K., Awua, A.K., Boatin, R., Adom, T., Brown-Appiah, E.C., Amewosina, K.K., Diaba, A., Datoghe, D., Okwabi, W., 2017. Cross-sectional assessment of infants' exposure to toxic metals through breast milk in a prospective cohort study of mining communities in Ghana. *BMC Public Health* 17 (1), 505. https://doi.org/10.1186/s12889-017-4403-8.

Bentum, J.K., Sackitey, O.J., Tuffuor, J.K., Essumang, D.K., Koranteng-Addo, E.J., Owusu-Ansah, E., 2010. Lead, Cadmium and Arsenic in breast milk of lactating mothers in Odumanse-Atua community in Manya Krobo district of eastern region of Ghana. *J. Chem. Pharm. Res.* 2 (5), 16–20.

Bocca, B., Alimonti, A., Coni, E., Di Pasquale, M., Giglio, L., Piccioli Bocca, A., Caroli, S., 2000. Determination of the total content and binding pattern of elements in human milk by high performance liquid chromatography-inductively coupled plasma atomic emission spectrometry. *Talanta* 53 (2), 295–303. https://doi.org/10.1016/s0039-9140(00)00473-2.

Bose-O'Reilly, S., Lettmeier, B., Roider, G., Siebert, U., Drasch, G., 2008. Mercury in breast milk - a health hazard for infants in gold mining areas? *Int. J. Hyg. Environ. Health* 211 (5–6), 615–623. https://doi.org/10.1016/j.ijheh.2007.09.015.

Bose-O'Reilly, S., Lettmeier, B., Shoko, D., Roider, G., Drasch, G., Siebert, U., 2020. Infants and mothers levels of mercury in breast milk, urine and hair, data from an artisanal and small-scale gold mining area in Kadoma / Zimbabwe. *Environ. Res.* 184, 109266. https://doi.org/10.1016/j.envres.2020.109266.

Bratakos, M.S., Ioannou, P.V., 1991. Selenium in human milk and dietary selenium intake by Greeks. *Sci. Total Environ.* 105, 101–107. https://doi.org/10.1016/0048-9697(91)90332-9.

Bratlid, D., 2009. Environmental toxins in breast milk. *Tidsskrift for Den Norske Laegeforening: Tidsskrift for Praktisk Medicin, Ny Raekke* 129 (24), 2606–2609.

Caba-Flores, M.D., Ramos-Ligonio, A., Camacho-Morales, A., Martínez-Valenzuela, C., Viveros-Contreras, R., Caba, M., 2022. Breast milk and the importance of chrononutrition. *Front. Nutr.* 9, 867507.

Canale, S., Blute, N., Xia, T., Thomas, M., Gee, M., Chang, C.H., 2021. Arsenic, cadmium, lead, and mercury in lactation foods and prenatal vitamins: potentially avoidable exposure for breastfeeding mothers and infants. *Breastfeed. Med.* 16 (7), 558–563.

Candeias, C., Ávila, P.F., Ferreira da Silva, E., Rocha, F., 2021. Metal (Loids) bioaccessibility in road dust from the surrounding villages of an active mine. *Atmosphere* 12 (6), 685.

Dessì, A., Briana, D., Corbu, S., Gavrili, S., Cesare Marincola, F., Georgantzi, S., Pintus, R., Fanos, V., Malamitsi-Puchner, A., 2018. Metabolomics of breast milk: the importance of phenotypes. *Metabolites* 8 (4), 79.

Edem, V.F., Akintunde, K., Adelaja, Y.A., Nwozo, S.O., Charles-Davies, M., 2017. Zinc, lead, and cadmium levels in serum and milk of lactating women in Ibadan, Nigeria. *Toxicol. Ind. Health* 33 (1), 28–35. https://doi.org/10.1177/0748233716661073.

Ejezie, F., Nwagha, U., 2011. Zinc concentration during pregnancy and lactation in Enugu, South-East Nigeria. *Ann. Med. Health Sci. Res.* 1 (1), 69–76.

Ekeanyanwu, C.L., Alisi, C.S., Ekeanyanwu, R.C., 2020. Levels of aflatoxin m1 and selected heavy metals (Pb, Cd, Cr, Cu, Zn, Fe, As, and Hg) in the breast milk of mothers in South Eastern Nigeria. *Food Control* 112 (2020), 107150.

Ezeama, N.N., Okunna, N., Afonne, O.J. 2023. Dietary intake and status of selenium in breast milk and serum of lactating mothers in Awka, South East Nigeria. *Nutrition and Health,* 2601060231195083. Advance online publication. https://doi.org/10.1177/02601060231195083.

Freire, C., Iribarne-Durán, L.M., Gil, F., Olmedo, P., Serrano-Lopez, L., Peña-Caballero, M., Hurtado, J.A., Alvarado-González, N.E., Fernández, M.F., Peinado, F. M., Artacho-Cordón, F., Olea, N., 2022. Concentrations and determinants of lead, mercury, cadmium, and arsenic in pooled donor breast milk in Spain. *Int. J. Hygiene Environ. Health* 240, 113914. https://doi.org/10.3390/ijerph18179289.

Frković, A., Kras, M., Alebić-Juretić, A., 1997. Lead and cadmium content in human milk from the Northern Adriatic area of Croatia. *Bull. Environ. Contaminat. Toxicol.* 58 (1), 16–21. https://doi.org/10.1007/s001289900294.

García-Esquinas, E., Pérez-Gómez, B., Fernández, M.A., Pérez-Meixeira, A.M., Gil, E., de Paz, C., Iriso, A., Sanz, J.C., Astray, J., Cisneros, M., de Santos, A., 2011. Mercury, lead and cadmium in human milk in relation to diet, lifestyle habits and sociodemographic variables in Madrid (Spain). *Chemosphere* 85 (2), 268–276.

Hailu, K., Joy, E.J.M., Ferguson, E.L., Bailey, E.H., Wilson, L., Davis, K., Broadley, M.R., Gashu, D., 2023. Dietary selenium intake among Ethiopian children in areas known for selenium spatial variability. *Front. Nutr.* 10, 1250002. https://doi.org/10.3389/fnut.2023.1250002.

Kalaotaji, G.B., Jonathan, N., Emeji, R., Amadi, C.F., Nwisah, L., 2021. Zinc composition in breast milk of lactating mothers in urban and sub-urban areas in rivers state. *Asian J. Res. Nurs. Health* 4 (4), 165–169.

Klein, L.D., Breakey, A.A., Scelza, B., Valeggia, C., Jasienska, G., Hinde, K., 2017. Concentrations of trace elements in human milk: comparisons among women in Argentina, Namibia, Poland, and the United States. *PLoS One* 12 (8), e0183367. https://doi.org/10.1371/journal.pone.0183367.

Koka, J.K., Koranteng-Addo, J.E., Bentum, J.K., Koka, D.M., Kamoah, G., 2011. Analysis of lead and cadmium in human milk in the greater Accra region of Ghana. *Pelagia Research Library Der Chemica Sinica* 2 (2), 240–246.

Krysiak-Baltyn, K., Toppari, J., Skakkebaek, N.E., Jensen, T.S., Virtanen, H.E., Schramm, K.W., Shen, H., Vartiainen, T., Kiviranta, H., Taboureau, O., Audouze, K., 2012. Association between chemical pattern in breast milk and congenital cryptorchidism: modelling of complex human exposures. *Int. J. Androl.* 35 (3), 294–302.

Kunter, İ., Hürer, N., Gülcan, H.O., Öztürk, B., Doğan, İ., Şahin, G., 2017. Assessment of Aflatoxin M1 and Heavy metal levels in mothers breast milk in Famagusta, Cyprus. *Biol. Trace Element Res.* 175 (1), 42–49. https://doi.org/10.1007/s12011-016-0750-z.

Lee, W.A., Ra, J.S., 2021. Olfactory stimulation of preterm infants with breast milk. *Clin. Nurs. Res.* 30 (8), 1183–1192.

Lehmann, G.M., LaKind, J.S., Davis, M.H., Hines, E.P., Marchitti, S.A., Alcala, C., Lorber, M., 2018. Environmental chemicals in breast milk and formula: exposure and risk assessment implications. *Environ. Health Perspect.* 126 (9), 096001.

Leotsinidis, M., Alexopoulos, A., Kostopoulou-Farri, E., 2005. Toxic and essential trace elements in human milk from Greek lactating women: association with dietary habits and other factors. *Chemosphere* 61 (2), 238–247. https://doi.org/10.1016/j.chemosphere.2005.01.084.

Mandiá, N., Bermejo-Barrera, P., Herbello, P., López-Suárez, O., Fraga, J.M., Fernández-Pérez, C., Couce, M.L., 2021. Human milk concentrations of minerals, essential and toxic trace elements and association with selective medical, social, demographic and environmental factors. *Nutrients* 13 (6), 1885. https://doi.org/10.3390/nu13061885.

Mandić, M.L., Grgić, J., Grgić, Z., Seruga, M., Hasenay, D., 1995. Aluminum levels in human milk. *Sci. Total Environ.* 170 (3), 165–170. https://doi.org/10.1016/0048-9697(95)04702-4.

Mandić, Z., Mandić, M.L., Grgić, J., Grgić, Z., Klapec, T., Primorac, L., Hasenay, D., 1997. Copper and zinc content in human milk in Croatia. *Eur. J. Epidemiol.* 13 (2), 185–188. https://doi.org/10.1023/a:1007337303724.

Maru, M., Birhanu, T., Tessema, D.A., 2013. Calcium, magnesium, iron, zinc and copper, compositions of human milk from populations with cereal and 'enset' based diets. *Ethiop. J. Health Sci.* 23 (2), 90–97.

Mbofung, C.M., Atinmo, T., Omololu, A., 1984. Mineral content of colostrum and mature milk of lactating Nigerian women as influenced by stage of lactation. *Nutr. Rep. Int.* 30 (5), 1137–1146.

Miklavčič, A., Casetta, A., Tratnik, J.S., Mazej, D., Krsnik, M., Mariuz, M., Sofianou, K., Špirić, Z., Barbone, F., Horvat, M., 2013. Mercury, arsenic and selenium exposure levels in relation to fish consumption in the Mediterranean area. *Environ. Res.* 120, 7–17. https://doi.org/10.1016/j.envres.2012.08.010.

Motas, M., Jiménez, S., Oliva, J., Cámara, M.Á., Pérez-Cárceles, M.D., 2021. Heavy metals and trace elements in human breast milk from industrial/mining and agricultural zones of southeastern Spain. *Int. J. Environ. Res. Public Health* 18 (17), 9289.

Navarro-Blasco, I., Alvarez-Galindo, J.I., 2004. Selenium content of Spanish infant formulae and human milk: influence of protein matrix, interactions with other trace elements and estimation of dietary intake by infants. *J. Trace Elem. Med Biol.* 17 (4), 277–289. https://doi.org/10.1016/S0946-672X(04)80030-0.

Nouzha, D.O., Louise, G., Claudia, S.B., Héloïse, F.M., Laurence, L., Joël, P., Virginie, R., 2023. Trace elements status in human breast milk of mothers from Île-de-France region. *J. Trace Elem. Med Biol.*, 127317 https://doi.org/10.1016/j.jtemb.2023.127317.

Nuzzi, G., Trambusti, I., Di Cicco, M.E., Peroni, D.G., 2021. Breast milk: more than just nutrition! *Minerva Pediatrics* 73 (2), 111–114.

Nyazema, N.Z., Mahomva, O., Andifasi, W., 1989. The levels of zinc in breast milk of urban African women in Zimbabwe. *Afr. J. Med. Med. Sci.* 18 (2), 159–162.

Okolo, S.N., Onwuanaku, C., Okonji, M., VanderJagt, D.J., Millson, M., Churchwell, C., Glew, R.H., 2000. Concentration of eight trace minerals in milk and sera of mother-infant pairs in northern Nigeria. *J. Trop. Pediatr.* 46 (3), 160–162. https://doi.org/10.1093/tropej/46.3.160.

Olowoyo, J.O., Macheka, L.R., Mametja, P.M., 2021. Health risk assessments of selected trace elements and factors associated with their levels in human breast milk from Pretoria, South Africa. *Int. J. Environ. Res. Public Health* 18 (18), 9754.

Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ (Clinical Research Ed.)* 372, n71. https://doi.org/10.1136/bmj.n71.

Pajewska-Szmyt, M., Sinkiewicz-Darol, E., Gadzała-Kopciuch, R., 2019. The impact of environmental pollution on the quality of mother's milk. *Environ. Sci. Pollut. Res.* 26, 7405–7427.

Park, Y., Lee, A., Choi, K., Kim, H.J., Lee, J.J., Choi, G., Kim, S., Kim, S.Y., Cho, G.J., Suh, E., Kim, S.K., 2018. Exposure to lead and mercury through breastfeeding during the first month of life: a CHECK cohort study. *Sci. Total Environ.* 612, 876–883.

Parr, R.M., DeMaeyer, E.M., Iyengar, V.G., Byrne, A.R., Kirkbright, G.F., Schöch, G., Niinistö, L., Pineda, O., Vis, H.L., Hofvander, Y., Omololu, A., 1991. Minor and trace elements in human milk from Guatemala, Hungary, Nigeria, Philippines, Sweden, and Zaire: results from a WHO/IAEA joint project. *Biol. Trace Elem. Res.* 29, 51–75.

Philip-Slaboh, T.P., Eleke, C., Ezejiofor, A.N., 2023. Comparison of toxic heavy metals in the breast milk of diabetic and non-diabetic postpartum mothers in Yenagoa, Nigeria. *PLoS One* 18 (4), e0264658. https://doi.org/10.1371/journal.pone.0264658.

Picone, S., Paolillo, P., 2013. Chemical contaminants in breast milk. *Early Hum. Dev.* 89, S117–S118.

Polychronaki, N., Turner, C.P., Mykkänen, H., Gong, Y., Amra, H., Abdel-Wahhab, M., El-Nezami, H., 2006. Determinants of aflatoxin M1 in breast milk in a selected group of Egyptian mothers. *Food Addit. Contam.* 23 (7), 700–708.

Rebelo, F.M., Caldas, E.D., 2016. Arsenic, lead, mercury and cadmium: toxicity, levels in breast milk and the risks for breastfed infants. *Environ. Res.* 151, 671–688.

Robberecht, H., Benemariya, H., Deelstra, H., 1995. Daily dietary intake of copper, zinc, and selenium of exclusively breast-fed infants of middle-class women in Burundi, Africa. *Biol. Trace Element Res.* 49 (2–3), 151–159. https://doi.org/10.1007/BF02788964.

Shoji, H., Shimizu, T., 2019. Effect of human breast milk on biological metabolism in infants. *Pediatr. Int.* 61 (1), 6–15.

Torres, M.A., Verdoy, J., Alegría, A., Barberá, R., Farré, R., Lagarda, M.J., 1999. Selenium contents of human milk and infant formulas in Spain. *Sci. Total Environ.* 228 (2–3), 185–192. https://doi.org/10.1016/s0048-9697(99)00044-3.

Toyomaki, H., Yabe, J., Nakayama, S.M.M., Yohannes, Y.B., Muzandu, K., Mufune, T., Nakata, H., Ikenaka, Y., Kuritani, T., Nakagawa, M., Choongo, K., Ishizuka, M., 2021. Lead concentrations and isotope ratios in blood, breastmilk and feces: contribution of both lactation and soil/dust exposure to infants in a lead mining area, Kabwe, Zambia. *Environ. Pollut.* 286, 117456. https://doi.org/10.1016/j.envpol.2021.117456.

Tratnik, S.J., Falnoga, I., Mazej, D., Kocman, D., Fajon, V., Jagodic, M., Stajnko, A., Trdin, A., Šlejkovec, Z., Jeran, Z., Osredkar, J., Sešek-Briški, A., Krsnik, M., Kobal, A. B., Kononenko, L., Horvat, M., 2019. Results of the first national human biomonitoring in Slovenia: trace elements in men and lactating women, predictors of exposure and reference values. *Int. J. Hyg. Environ. Health* 222 (3), 563–582. https://doi.org/10.1016/j.ijheh.2019.02.008.

Turconi, G., Guarcello, M., Livieri, C., Comizzoli, S., Maccarini, L., Castellazzi, A.M., Pietri, A., Piva, G., Roggi, C., 2004. Evaluation of xenobiotics in human milk and ingestion by the newborn–an epidemiological survey in Lombardy (Northern Italy). *Eur. J. Nutr.* 43 (4), 191–197. https://doi.org/10.1007/s00394-004-0458-2.

Vollset, M., Iszatt, N., Enger, Ø., Gjengedal, E.L.F., Eggesbø, M., 2019. Concentration of mercury, cadmium, and lead in breast milk from Norwegian mothers: association with dietary habits, amalgam and other factors. *Sci. Total Environ.* 677, 466–473.

World Health Organization, 2024. Breastfeading. https://www.who.int/health-topics/breastfeeding#tab=tab_1. Accessed 27th September, 2024.

Yuanan, H., He, K., Sun, Z., Chen, G., Cheng, H., 2020. Quantitative source apportionment of heavy metal(loid)s in the agricultural soils of an industrializing region and associated model uncertainty. *J. Hazard. Mater.* 391, 122244.