Food and Chemical Toxicology 180 (2023) 114037

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Assessing heavy metal levels in pediatric enteral nutrition formulas available in the Turkish market: Implications for consumer health

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ARTICLE INFO

Handling Editor: Dr. Bryan Delaney

Keywords:
Enteral nutrition formula
Health risk assessment
Heavy metal
Carcinogenic risk
Hazard quotient

ABSTRACT

In this study, we assessed the levels of lead (Pb), cadmium (Cd), mercury (Hg), and inorganic arsenic (iAs) in 27 pediatric enteral nutrition (EN) formulas from five international brands available in the Turkish market. Analysis was conducted using inductively coupled plasma mass spectrometry (ICP-MS). Non-carcinogenic and carcinogenic risk assessment was performed using hazard quotient (HQ), hazard index (HI), carcinogenic risk (CR), Toxicological contribution % of Provisional Tolerable Weekly Intake (PTWI) models. Our objective was to evaluate heavy metal exposure in EN formulas, specifically focusing on Cd, Pb, iAs, and Hg levels according to recommended amounts for different age groups based on their energy requirements. Average concentrations of iAs in polymeric (PC), oligomeric (OC), and monomeric (MC) EN formulas were as follows: PC: 2.13 ± 0.16 (<LOD-13.86) μg/kg, OC: 4.29 ± 0.10 (0.38–11.98) μg/kg, MC: 8.62 ± 0.19 (1.60–27.20) μg/kg. For Cd levels, average concentrations in PC, OC, and MC formulas were: PC: 0.57 ± 0.03 (<LOD-3.09) μg/kg, OC: 1.31 ± 0.07 (0.40–3.12) μg/kg, MC: 0.93 ± 0.07 (0.07–2.33) μg/kg. Similarly, average concentrations of Hg in PC, OC, and MC formulas were: PC: 0.13 ± 0.01 (<LOD-0.14) μg/kg, OC: 0.18 ± 0.01 (<LOD-0.18) μg/kg, MC: 0.20 ± 0.02 (<LOD-0.34) μg/kg. Lastly, average concentrations of Pb in PC, OC, and MC formulas were: PC: 2.32 ± 0.06 (1.52–2.96) μg/kg, OC: 0.97 ± 0.06 (0.37–2.26) μg/kg, MC: 2.58 ± 0.08 (1.95–3.28) μg/kg. The exposure levels of Cd, Pb, iAs, and Hg calculated in this study did not exceed the PTWI threshold values established by the European Food Safety Authority (EFSA). Average HQ values for each heavy metal exposure in males and females were below 1. However, P95 values for iAs exceeded 1.00 in all age groups. The HI value was greater than 1.00 in all age groups and genders. The presence of heavy metals in EN formulas may pose health risks, particularly for sensitive individuals.

1. Introduction

Pediatric malnutrition is defined by the Pediatric Malnutrition Definitions Working Group of the American Society for Parenteral and Enteral Nutrition as a condition characterized by cumulative deficiencies in energy, protein, or micronutrients that can affect growth, development, and other relevant outcomes due to an imbalance between nutritional requirements and intake (Mehta et al., 2013). The prevalence of pediatric malnutrition has been reported to range from 15% to 50% (Daskalou et al., 2016; Pichler et al., 2014; Rinninella et al., 2017). Ensuring proper nutrition in hospitalized children is essential for preventing the development of malnutrition and improving the effectiveness of medical treatment, reducing hospital stay duration, and lowering the risk of mortality (Agarwal et al., 2013; Ruiz et al., 2019). Enteral nutrition (EN) is the basic and important method of nutritional intervention in patients who cannot consume sufficient nutrients (Yi, 2018). The EN is the provision of nutritional requirements to the stomach or small intestine, orally or through a tube (nasogastric, nasoduodenal, gastrostomy or gastrojejunostomy) in patients who have a functional gastrointestinal tract but cannot consume enough nutrients. These products are ready-to-use formulations containing water, macronutrients (fats, carbohydrates and proteins) and micronutrients (vitamins and minerals) (Braegger et al., 2010). The carbohydrate components of EN formulas are mainly maltodextrin, corn syrup products and starch. Protein sources can be obtained from animal (casein from cow's milk, whey fractions, egg albumin, etc.) or plant-based (soybean) foods. The

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https://doi.org/10.1016/j.fct.2023.114037
Received 27 June 2023; Received in revised form 25 August 2023; Accepted 11 September 2023

fat content is derived from vegetable sources such as sunflower, corn, rapeseed, canola, olive, soybean, coconut, and date seed oils (Savino, 2018; Zadák and Kent-Smith, 2009). Similar to all foods, EN formulas have the potential to harbor physical, chemical, and microbiological hazards that can adversely affect human health due to factors such as raw material characteristics, production, and storage conditions. Therefore, they should be subject to control measures for food safety. The main components of EN formulas, which are foods of plant and animal origin and their by-products,can become contaminated with pollutants such as nitrites, nitrates, pesticides, and heavy metals through natural events or human activities (such as pesticide and fertilizer use in agriculture, industry, and vehicle exhaust). Heavy metal contamination, which can occur through bioaccumulation in the food chain, is a significant consumer health concern (Onakpa et al., 2018). Chronic exposures to heavy metals can lead to respiratory (Madrigal et al., 2018) and cardiovascular system (Chowdhury et al., 2018) damage, birth defects (Wang et al., 2022), lower intelligence scores (Heidari et al., 2022), skeletal damage (Nishijo et al., 2017), autism (Shiani et al., 2023), Alzheimer's Disease (Bakulski et al., 2020), Parkinson's Disease (Vellingiri et al., 2022), kidney damage (Moody et al., 2018), and even death (Engwa et al., 2019). Specialized nutritional formulas used to support the nutrition of vulnerable groups should be subject to food safety control. When reviewing the literature on EN and food safety, studies were found to mainly focus on microbial contamination (Ojo et al., 2020; Sinha et al., 2020), while studies investigating heavy metal contamination primarily concentrated on total parenteral nutrition solutions (Bohrer et al., 2005; Do Nascimento et al., 2011). However, there is a lack of research on determining the levels of heavy metals in EN formulas available in the market based on their structural characteristics, type, and energy properties. In this context, the objectives of this study are (1) to determine the levels of heavy metals (Hg, Pb, iAs, and Cd) in pediatric EN formulas available in the Turkish market and (2) to perform deterministic health risk assessment in vulnerable groups following the consumption of EN formulas containing heavy metals.

2. Materials and methods

2.1. Materials

A total of 27 pediatric EN formula samples were included in the research sample, considering the expiration dates, energy content (Hypocaloric: 0.68 kcal/mL, Isocaloric: 1–1.2 kcal/mL, Hypercaloric: >1.2 kcal/mL), protein content (polymeric, oligomeric, monomeric), and structural properties (liquid:L, powder:P). The EN formula samples were purchased from 5 brands between October 2022 and January 2023, based on the types and characteristics specified on the packaging labels. All EN formulas were selected based on recent production dates and stored under refrigeration conditions until analysis. Table 1 displays some characteristics of the EN formulas.

2.2. Chemicals and reagents

All chemicals and reagents used in this study were of analytical grade. Nitric acid (HNO_3) with a purity of 65% (Suprapur®, Merck), hydrogen peroxide (H_2O_2) with a purity of 30% (Suprapur®, Merck), and ICP multielement standard solution VIII were sourced from Supelco (Merck KGaA, Darmstadt, Germany). The Inductively coupled plasma mass spectrometry (ICP-MS) tuning solution, internal solution, and standard mercury solution were procured from Agilent (Santa Clara, USA). Ultrapure water with a resistivity of 18.2 MΩ cm at 25 °C, obtained from the Direct-Q® 8 UV Remote Water Purification System (Merck KGaA, Germany), was used for the preparation of solutions.

Table 1
Heavy metal levels of EN formulas (μg/kg).

Types of EN	EN Formulas	iAs (μg/kg)	Cd (μg/kg)	Hg (μg/kg)	Pb (μg/kg)	Forms of EN
Polimeric (PC)	Type 1	3.61 ± 0.19	0.90 ± 0.01	<LOD	1.88 ± 0.11	Liquid
	Type 2	0.20 ± 0.06	0.23 ± 0.00	<LOD	2.92 ± 0.03	Liquid
	Type 3	0.23 ± 0.03	0.13 ± 0.01	<LOD	2.02 ± 0.05	Liquid
	Type 4	0.66 ± 0.06	<LOD	0.14 ± 0.00	1.32 ± 0.08	Liquid
	Type 5	0.63 ± 0.10	0.04 ± 0.00	<LOD	2.46 ± 0.15	Liquid
	Type 6	0.23 ± 0.22	0.19 ± 0.05	<LOD	2.59 ± 0.06	Liquid
	Type 7	<LOD	0.31 ± 0.04	<LOD	1.80 ± 0.02	Liquid
	Type 8	13.86 ± 0.08	0.24 ± 0.05	<LOD	1.52 ± 0.15	Liquid
	Type 9	1.28 ± 0.32	0.36 ± 0.06	0.12 ± 0.03	2.62 ± 0.08	Liquid
	Type 10	0.47 ± 0.07	0.43 ± 0.01	<LOD	2.96 ± 0.04	Liquid
	Type 11	0.62 ± 0.04	0.18 ± 0.03	<LOD	2.96 ± 0.01	Liquid
	Type 12	1.93 ± 0.07	0.40 ± 0.05	<LOD	2.93 ± 0.05	Liquid
	Type 13	0.90 ± 0.97	0.06 ± 0.01	0.14 ± 0.02	2.91 ± 0.00	Liquid
	Type 14	5.56 ± 0.04	0.24 ± 0.01	<LOD	2.51 ± 0.04	Liquid
	Type 15	0.26 ± 0.03	0.21 ± 0.01	<LOD	2.42 ± 0.06	Liquid
	Type 16	1.79 ± 0.05	3.09 ± 0.03	<LOD	1.74 ± 0.02	Liquid
	Type 17	1.77 ± 0.22	2.09 ± 0.01	0.12 ± 0.00	1.92 ± 0.06	Liquid
	Mean - SD (Min.-Max.)	**2.13 ± 0.16 (<LOD-13.86)**	**0.57 ± 0.03 (<LOD-3.09)**	**0.13 ± 0.01 (<LOD-0.14)**	**2.32 ± 0.06 (1.32–2.96)**	
Oligomeric (OC)	Type 1	11.98 ± 0.05	0.81 ± 0.06	<LOD	0.66 ± 0.05	Powder
	Type 2	3.24 ± 0.14	3.12 ± 0.04	0.18 ± 0.01	0.58 ± 0.07	Powder
	Type 3	1.55 ± 0.12	0.40 ± 0.01	<LOD	0.37 ± 0.08	Liquid
	Type 4	0.38 ± 0.10	0.90 ± 0.15	<LOD	2.26 ± 0.04	Liquid
	Mean –SD (Min.-Max.)	**4.29 ± 0.10 (0.38–11.98)**	**1.31 ± 0.07 (0.40–3.12)**	**0.18 ± 0.01 (<LOD-0.18)**	**0.97 ± 0.06 (0.37–2.26)**	
Monomeric (MC)	Type 1	3.27 ± 0.08	0.66 ± 0.03	<LOD	1.95 ± 0.03	Powder
	Type 2	27.20 ± 0.30	0.07 ± 0.10	<LOD	3.28 ± 0.10	Powder
	Type 3	1.60 ± 0.14	0.63 ± 0.02	0.14 ± 0.05	2.67 ± 0.04	Powder
	Type 4	2.44 ± 0.11	1.19 ± 0.18	0.34 ± 0.01	2.44 ± 0.15	Powder
	Type 5	11.60 ± 0.12	0.72 ± 0.07	<LOD	2.99 ± 0.10	Powder
	Type 6	5.58 ± 0.38	2.33 ± 0.04	0.13 ± 0.01	2.15 ± 0.04	Powder
	Mean –SD (Min.-Max.)	**8.62 ± 0.19 (1.60–27.20)**	**0.93 ± 0.07 (0.07–2.33)**	**0.20 ± 0.02 (<LOD-0.34)**	**2.58 ± 0.08 (1.95–3.28)**	

SD,Standard deviation.

2.3. ICP-MS analysis

2.3.1. Apparatus and instruments

The heavy metal analysis in this study was conducted using an ICP-MS instrument (Agilent 7800, Agilent Technologies, Japan). The instrument has advanced features including the High Matrix Input (HMI) system and the fourth generation Octopole Reaction System (ORS) collision/reaction cell (CRC) technology. Microwave digestion (Ethos Up, Milestone, Bergamo, Italy) was employed for efficient breakdown of the sample matrix, and an ultrasonic cleaner (Shenzhen, China) was used to further enhance sample cleanliness. Ultra-distilled water (Millipore Direct Q 8 UV) was used to ensure the purity of the analysis. Overall, the combination of the advanced ICP-MS instrument, optimized ORS technology, controlled sample introduction system, efficient sample preparation techniques, and ultra-pure water device ensures the accuracy of the heavy metal analysis in this study.

2.3.2. Microwave digestion for heavy metal analysis

The heavy metal analysis of EN formulas was conducted using the microwave digestion method with the following procedure. This method is described in the "Baby food" section of the Microwave Digestion System application notes (HPR–FO–03) for the Microwave Digestion System. Firstly, accurately weighed samples of EN formulas, weighing exactly 0.5 g, were placed into Teflon sample vessels. The digestion process was initiated by adding 6 mL of HNO_3 and 2 mL of H_2O_2 to the sample vessels. To ensure the accuracy of the analysis, a blank digestion was performed using the same procedure to account for any potential contamination or interference during the digestion process.

2.3.3. ICP-MS conditions

Before starting the analysis, all glassware was washed with a 10% (v/v) HNO_3 solution, rinsed with high-purity water, and kept in a desiccator for drying. A 45-min helium gas purge was performed to ensure proper cleaning of all instrument components. Subsequently, the device was activated with specific parameters: the plasma gas flow rate was set to 15 L/min, the auxiliary gas, the carrier gas, and the make-up/dilution gas flow rate to 1 L/min, and the carrier gas pressure to 1450 Pa.

2.4. Quality control and quality assurance

In order to ensure the quality control and quality assurance of the heavy metal analysis, calibration curves were prepared for the elements iAs, Cd, and Pb at concentrations of 0, 10, 25, 50, 100, 250, and 500 μg/L, and for the element Hg at concentrations of 0, 2.5, 5, 7.5, and 10 μg/L, while preserving the numerical values. Furthermore, recovery analyses were conducted by adding the metals Cd, iAs, and Pb at concentrations of 8 μg/L, and Hg at a concentration of 2.5 μg/L, to both powdered and liquid forms of the EN formulas. The limits of quantification (LOQs) and limits of detection (LODs) was calculated in accordance with the guidelines established by the American Chemical Society (Workman et al., 2011).

2.5. Target population in simulated research

For the simulation, we assumed stable pediatric patients who exclusively rely on EN formulas for their nutritional needs. We considered energy requirements specific to different age groups, including 6-month-old infants, 2-year-old toddlers, 4-year-old preschoolers, 8-year-old children, and 13-year-old adolescents. The quantities of pediatric EN formulas to be consumed by the models were calculated based on the estimated energy requirements recommended by the Institute of Medicine (IOM) for each age group (2006). The individuals' physical activity level was considered as "sedentary" with an activity coefficient of 1.0. To calculate daily energy requirements, we used the 50th percentile values of body weight (kg) and height (m) corresponding to each individual's age (Neyzi et al., 2008).

2.6. Health risk assessment

Health risk assessment plays a crucial role in evaluating the potential health effects and risks related to prolonged exposure to toxic substances. In the context of EN formulas, the analysis of heavy metal concentrations allows for the estimation of daily intake of metals (EDI) and the calculation of the hazard quotient (HQ). The chronic EDI, which accounts for heavy metal exposure through the consumption of EN formulas, was determined using Eq. (1) as specified by the United States Environmental Protection Agency (US EPA, 2019)

$$\mathrm{EDI} = [(\mathrm{C} \times \mathrm{IR}) / (\mathrm{BW})] \tag{Eq. 1}$$

In the calculation of EDI for heavy metals in EN formula samples, factors such as the heavy metal concentration (C) in the samples, body weight (BW) of the individual, and the daily consumption rate (IR) of the EN formula are taken into consideration.

2.6.1. Non-carcinogenic risk assessment

2.6.1.1. Hazard quotient (HQ). The non-carcinogenic health risk assessment involves the calculation of the HQ, which is determined using Eq (2). (US EPA, 2019).

$$\mathrm{HQ} = \mathrm{EDI}/\mathrm{RfD} \tag{Eq. 2}$$

Here, RfD is the oral toxicity reference dose of heavy metals (mg/kg/day). RfD values for iAs (EFSA, 2009a), Cd (EFSA, 2009b), Pb (Su et al., 2020), and Hg (EFSA, 2012) are 3.0×10^{-4}, 1.0×10^{-3}, 4.0×10^{-3} and 3.0×10^{-4} mg/kg/day, respectively.

2.6.1.2. Hazard index (HI). The HI is a scientific method developed to evaluate the cumulative potential of non-carcinogenic effects resulting from exposure to multiple toxic substances. In the context of orally ingested EN formula, the HI values were determined using the calculation presented in Eq. (3) (US EPA, 2019).

$$\mathrm{HI} = \Sigma\mathrm{HQ} = + \mathrm{HQ}\ (\mathrm{Pb}) + \mathrm{HQ}\ (\mathrm{Cd}) + \mathrm{HQ}\ (\mathrm{Hg}) + \mathrm{HQ}\ (\mathrm{iAs}) \tag{Eq. 3}$$

The HQ and HI values greater than 1.0 signify the presence of potential human health risks resulting from exposure to toxicants. Conversely, HQ and HI values below 1 indicate a negligible concern for consumer health risks associated with oral exposure (US EPA, 2019).

2.6.2. The cancer risk (CR) for arsenic and lead

The CR assessment is of utmost importance in the estimation of potential dose and lifetime CR for individuals exposed to carcinogenic substances (Antoine et al., 2017). The CR index associated with the consumption of EN formula was determined using Eq. 4

$$\mathrm{CR} = [(\mathrm{C} \times \mathrm{IR} \times \mathrm{CSF}) / (\mathrm{BW})] \tag{Eq. 4}$$

In the provided equation, the concentration of heavy metals in the EN formulas is denoted as C and expressed in milligrams per kilogram (mg/kg). The daily intake of the EN formula, represented by IR, is measured in milliliters per day (mL/day). The CSF is a parameter used to assess the potential risk of developing cancer through oral exposure to specific substances. For Pb, the CSF value has been determined as 8.5×10^{-3} mg/kg BW/day by the Office of Environmental Health Hazard Assessment (OEHHA, 2023). Likewise, for iAs, the CSF value has been established as 1.5 mg/kg BW/day based on guidelines provided by the US EPA (2015).

2.6.3. Toxicological contribution of Provisional Tolerable Weekly Intake (PTWI)

The toxicological contribution level % of PTWI for target heavy metals, as calculated in this study, was determined using Equation (5) based on the guidelines provided by the JECFA (2002).

$$\text{PTWI \%} = [(\text{Mean, P95 EDI} \times 7) / \text{PTWI})] \times 100 \qquad \text{(Eq. 5)}$$

The established Provisional Tolerable Weekly Intake (PTWI) values for iAs, Pb, Cd, and Hg are as follows: iAs - 15 μg/kg/day (EFSA, 2009a), Pb - 25 μg/kg/day (EFSA, 2010), Cd - 2.5 μg/kg/day (EFSA, 2009b), and Hg - 4.0 μg/kg/day (EFSA, 2012).

2.7. *Statistical analysis*

The statistical analysis was conducted using the SPSS Statistics 20 software package (IBM, Armonk, New York), providing a solid foundation for data evaluation. To examine the statistical significance between group means for all data, ANOVA (Analysis of Variance) was employed. For mean values exhibiting a significant difference, Duncan's multiple range tests ($P < 0.05$) were conducted for comparisons.

2.8. *Ethical standards disclosure*

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Prior to the commencement of the study, necessary approvals were obtained from the Ethics Committee of Afyonkarahisar Health Sciences University Medical Faculty (Approval number: 2022/339; Date: June 3, 2022).

3. Results

3.1. *Analytical performance*

The employed method exhibited strong linearity and sensitivity, as indicated by R^2 surpassing 0.995 for all target heavy metals. Detailed information on the method verification parameters can be found in Table 2. The method's LOD and LOQ values fell within the ranges of 0.003–0.11 ng/mL and 0.01–0.36 ng/mL, respectively. The spiking concentrations were 8 ng/mL for Cd, iAs, and Pb, and 2.5 ng/mL for Hg. The recovery values of the four heavy metals in both forms ranged from 93.73% to 95.99%, with corresponding RSDs ranging from 2.02% to 4.92%. These findings further support the suitability and accuracy of the method for quantifying heavy metal content in EN formulas.

3.2. *Heavy metal levels of EN formulas*

This study presents the mean concentrations of heavy metals in a total of 27 EN formulas, as shown in Table 1. The average levels of iAs in polymeric (PC), oligomeric (OC), and monomeric (MC) EN formulas were determined as 2.13 ± 0.16 (<LOD-13.86), 4.29 ± 0.10 (0.38–11.98), and 8.62 ± 0.19 (1.60–27.20) μg/kg, respectively. The mean Cd levels in PC, OC and MC EN formulas were 0.57 ± 0.03 (<LOD-3.09), 1.31 ± 0.07 (0.40–3.12), and 0.93 ± 0.07 (0.07–2.33) μg/kg, respectively. Similarly, the mean content of Hg in PC, OC and MC EN formulas were 0.13 ± 0.01 (<LOD-0.14), 0.18 ± 0.01 (<LOD-0.18), and 0.20 ± 0.02 (<LOD-0.34) μg/kg, respectively. Lastly, the average concentrations of Pb in PC, OC and MC EN formulas were 2.32 ± 0.06 (1.52–2.96), 0.97 ± 0.06 (0.37–2.26), and 2.58 ± 0.08 (1.95–3.28) μg/kg, respectively. Among the different types of EN formulas, Type 8 exhibited the highest average concentration of iAs (13.86 μg/kg) for PC formulas, Type 1 (11.98 μg/kg) for OC formulas, and Type 2 (27.20 μg/kg) for MC formulas. Regarding Cd levels, the highest averages were observed in Type 16 (3.09 μg/kg) for PC formulas, Type 2 (3.12 μg/kg) for OC formulas, and Type 6 (2.33 μg/kg) for MC formulas. Type 4 and Type 13 showed the highest average levels of Hg (0.14 μg/kg) for PC formulas, Type 2 (0.18 μg/kg) for OC formulas, and Type 4 (0.34 μg/kg) for MC formulas. Lastly, Type 10 and Type 11 displayed the highest mean levels of Pb (2.96 μg/kg) for PC formulas, Type 4 (2.26 μg/kg) for OC formulas, and Type 2 (3.28 μg/kg) for MC formulas. Statistically significant differences were detected in the mean levels of iAs, Cd, and Pb across the various types of EN formulas ($p < 0.05$). However, no significant differences were observed in the mean Hg levels among the different formula types ($p > 0.05$). Based on the total heavy metal levels, the order of EN formulas was as follows: MC (12.33 μg/kg) > OC (6.75 μg/kg) > PC (5.15 μg/kg).

3.3. *Health risk assessment*

3.3.1. *Non-carcinogenic risk assessment*

3.3.1.1. Hazard index (HI) and Hazard quotient (HQ). This study assessed the non-carcinogenic health risks associated with the consumption of EN formulas in terms of heavy metal exposure, using HQ and HI calculations. The results of exposure for EN formula consumption can be found in Table 3. The average HQ values for iAs in female children aged 6 months, 4 years, 8 years, and 13 years were determined as 0.450, 0.391, 0.287, and 0.190, respectively. Similarly, for males in the same age groups, the average HQ values for iAs were calculated as 0.453, 0.407, 0.306, and 0.226, respectively. These values indicate that the non-carcinogenic health risk associated with iAs from consuming different EN formulas in this study is relatively low, as they are below the USEPA's recommended threshold value of 1.00. However, it should be noted that in all age groups, the upper value of the P95 exceeds the threshold value, suggesting a potential higher risk for individuals at the upper end of the exposure range. For Pb, the mean HQ values for female children aged 6 months, 4 years, 8 years, and 13 years were found to be 0.020, 0.030, 0.022, and 0.015, respectively. Similarly, for males in the same age groups, the mean HQ values for Pb were calculated as 0.020, 0.031, 0.023, and 0.017, respectively. For Cd, the mean HQ values for female children aged 6 months, 4 years, 8 years, and 13 years were determined as 0.022, 0.030, 0.022, and 0.015, respectively. Likewise, for males in the corresponding age groups, the mean HQ values for cadmium were calculated as 0.022, 0.032, 0.024, and 0.018, respectively. Regarding exposure to Hg, the average HQ values for females aged 6 months, 4 years, 8 years, and 13 years were determined as 0.005, 0.006, 0.004, and 0.003, respectively. Similarly, for males in the same age groups, the average HQ values for Hg were calculated as 0.003, 0.006, 0.005, and 0.003, respectively. Overall, the average HQ values for all analyzed heavy metals suggest a low non-carcinogenic health risk associated with their exposure through the consumption of EN formulas. However, it is crucial to consider the upper value of the P95 for iAs, as it exceeds the threshold across all age groups, indicating a potential higher risk for individuals at the upper end of the exposure range. The P95 HI value exceeding 1.00 in all age groups and both gender is noteworthy and indicates a potential health risk. According to the US EPA (2019), HI values greater than 1.0 indicate a potential health risk. Based on these findings, it should be emphasized that all age groups analyzed in this

Table 2
Method verification parameters.

Analytes	Spiking level (ng/mL)	Linear range		Recovery (%)		RSD (%)		Quantification	
		(ng/mL)	R2	Powder	Liquid	Powder	Liquid	LOD (ng/mL)	LOQ (ng/mL)
iAs	8	0–500	0.999	93.77	93.99	4.09	4.92	0.076	0.251
Pb	8	0–500	0.999	95.53	95.99	4.69	4.79	0.003	0.010
Cd	8	0–500	0.999	95.30	93.97	2.02	4.42	0.026	0.086
Hg	2.5	2.5–10	0.996	93.90	93.73	4.78	4.40	0.110	0.363

Table 3
Hazard quotient (HQ) and Hazard index (HI).

Gender Age	HQ								Total HQ	
	iAs		Pb		Cd		Hg		HI	
Female	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean**	**P95**
6 Months	0.450 ± 0.466	0.630–1.510	0.020 ± 0.020	0.003–0.06	0.022 ± 0.021	0.021–0.074	0.005 ± 0.007	0.007–0.010	0.497	(0.661–1.650)
4 Age	0.391 ± 0.640	0.120–2.750	0.030 ± 0.012	0.010–0.050	0.030 ± 0.037	0.010–0.050	0.006 ± 0.010	0.007–0.010	0.457	(0.147–2.860)
8 Age	0.287 ± 0.470	0.123–2.020	0.022 ± 0.009	0.007–0.039	0.022 ± 0.027	0.008–0.027	0.004 ± 0.007	0.003–0.007	0.335	(0.164–2.174)
13 Age	0.190 ± 0.310	0.123–1.340	0.015 ± 0.006	0.005–0.026	0.015 ± 0.018	0.017–0.072	0.003 ± 0.005	0.003–0.010	0.223	(0.148–1.448)
Male	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean±SD**	**P95**	**Mean**	**P95**
6 Months	0.453 ± 0.470	0.637–1.520	0.020 ± 0.018	0.003–0.061	0.022 ± 0.021	0.021–0.075	0.003 ± 0.006	0.007–0.010	0.498	(1.612–1.612)
4 Age	0.407 ± 0.665	0.123–2.860	0.031 ± 0.012	0.010–0.055	0.032 ± 0.038	0.037–0.155	0.006 ± 0.01	0.007–0.020	0.476	(0.222–3.040)
8 Age	0.306 ± 0.501	0.123–2.153	0.023 ± 0.009	0.008–0.042	0.024 ± 0.029	0.028–0.116	0.005 ± 0.008	0.003–0.007	0.358	(0.116–2.341)
13 Age	0.226 ± 0.370	0.123–1.593	0.017 ± 0.007	0.006–0.030	0.018 ± 0.021	0.021–0.085	0.003 ± 0.006	0.003–0.010	0.264	(0.153–1.694)

SD, Standard deviation.

Table 4
Heavy metal exposure from consumption of EN formulas (μg/kg BW/day) and toxicological contribution % of PTWI.

Gender/Age	Heavy metal exposure from EN formula (μg/kg BW/day)			
iAs Exposure				
Female	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.135 ± 0.140 (0.017–0.454)	0.189–0.454	0.019–0.071	8.82 %–21.19%
4 Age	0.117 ± 0.192 (0.016–0.826)	0.037–0.826	0.037–0.072	1.73%–38.55%
8 Age	0.086 ± 0.141 (0.012–0.607)	0.037–0.607	0.027–0.072	1.73%–28.33%
13 Age	0.057 ± 0.093 (0.011–0.401)	0.037–0.401	0.018–0.115	1.73%–18.71%
Male	**Mean±SD (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.360 ± 0.141 (0.017–0.456)	0.192–0.456	0.019–0.072	8.96%–21.28%
4 Age	0.122 ± 0.199 (0.017–0.858)	0.037–0.858	0.039–0.072	1.73%–40.04%
8 Age	0.092 ± 0.155 (0.010–0.646)	0.037–0.646	0.029–0.072	1.73%–31.15%
13 Age	0.068 ± 0.111 (0.010–0.478)	0.037–0.478	0.022–0.072	1.73%–22.31%
Pb Exposure				
Female	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.081 ± 0.075 (0.009–0.242)	0.010–0.242	0.009–0.167	0.28%–6.78%
4 Age	0.115 ± 0.050 (0.026–0.211)	0.040–0.211	0.026–0.119	1.12%–5.91%
8 Age	0.085 ± 0.036 (0.024–0.155)	0.013–0.155	0.019–0.087	0.36%–4.34%
13 Age	0.057 ± 0.023 (0.013–0.103)	0.019–0.103	0.013–0.058	0.53%–2.88%
Male	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.085 ± 0.076 (0.010–0.245)	0.011–0.245	0.010–0.169	0.31%–6.86%
4 Age	0.033 ± 0.038 (0.002–0.155)	0.037–0.155	0.015–0.030	1.036%–4.34%
8 Age	0.091 ± 0.038 (0.021–0.166)	0.031–0.166	0.021–0.093	0.87%–4.65%
13 Age	0.067 ± 0.028 (0.015–0.122)	0.023–0.122	0.015–0.069	0.64%–3.42%
Cd Exposure				
Female	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.023 ± 0.015 (0.001–0.074)	0.021–0.074	0.011–0.019	5.88%–20.72%
4 Age	0.031 ± 0.036 (0.002–0.148)	0.036–0.148	0.014–0.029	10.08%–41.44%
8 Age	0.022 ± 0.027 (0.001–0.108)	0.027–0.108	0.011–0.021	7.56%–30.24%
13 Age	0.015 ± 0.017 (0.001–0.072)	0.017–0.072	0.007–0.014	4.76%–20.16%
Male	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.023 ± 0.020 (0.001–0.075)	0.021–0.075	0.011–0.019	5.88%–21.00%
4 Age	0.032 ± 0.038 (0.002–0.155)	0.037–0.155	0.015–0.030	10.36%–43.4%
8 Age	0.025 ± 0.028 (0.001–0.116)	0.028–0.116	0.011–0.022	7.84%–32.48%
13 Age	0.018 ± 0.021 (0.001–0.085)	0.021–0.085	0.008–0.017	5.88%–23.80%
Hg Exposure				
Female	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.004 ± 0.002 (0.002–0.006)	0.003–0.006	0.002–0.003	0.53%–1.05%
4 Age	0.002 ± 0.003 (0.002–0.010)	0.007–0.010	0.002–0.006	1.23%–1.75%
8 Age	0.001 ± 0.002 (0.001–0.007)	0.005–0.007	0.001–0.004	0.88%–1.23%
13 Age	0.001 ± 0.001 (0.001–0.005)	0.003–0.005	0.001–0.003	0.53%- 0.88%-
Male	**Mean (Min.-Max.)**	**P95**	**P50**	**% of PTWI (Min.-Max.)**
6 Months	0.004 ± 0.014 (0.002–0.006)	0.003–0.006	0.002–0.003	0.53%–1.05%
4 Age	0.002 ± 0.003 (0.002–0.010)	0.007–0.010	0.002–0.006	1.23%–1.75%
8 Age	0.001 ± 0.002 (0.001–0.008)	0.004–0.008	0.001–0.002	0.70%–1.40%
13 Age	0.001 ± 0.002 (0.001–0.006)	0.004–0.006	0.001–0.003	0.70%–1.05%

study may pose a risk in terms of non-carcinogenic health risks associated with the consumption of EN formulas. However, it is important to acknowledge the limited existing literature specifically addressing the non-carcinogenic health risks related to the consumption of EN formulas. Therefore, further research and investigations are warranted to gain a better understanding of the potential health risks associated with the consumption of these formulas and to establish more comprehensive guidelines and recommendations.

3.3.2. *Intake levels and toxicological contribution % of PTWI*

The heavy metal exposure levels of different age groups calculated in the study are given in Table 4. The mean exposure levels of iAs in females and males consuming EN formula were determined for different age groups. The mean ± SD values of iAs in females aged 6 months, 4 years, 8 years, and 13 years were found to be 0.135 ± 0.140 μg/kg BW/day, 0.117 ± 0.192 μg/kg BW/day, 0.086 ± 0.141 μg/kg BW/day, and 0.057 ± 0.093 μg/kg Bw/day, respectively. Similarly, the mean ± SD values of iAs in males aged 6 months, 4 years, 8 years, and 13 years were calculated as 0.360 ± 0.141 μg/kg BW/day, 0.122 ± 0.199 μg/kg BW/day, 0.092 ± 0.155 μg/kg BW/day, and 0.068 ± 0.111 μg/kg BW/day, respectively. The toxicological contribution of iAs calculated for all age groups consuming EN formula were from 1.73 to 38.55% in females and from 1.73 to 40.04% in males. The iAs exposure levels (mean, P50, and P95) observed in this study, which were derived from the consumption of various EN formulas, were found to be below the PTWI value of 15 μg/kg BW/day recommended by the EFSA (2009a). The mean ± SD values of Pb exposure in females aged 6 months, 4 years, 8 years, and 13 years were found to be 0.081 ± 0.075 μg/kg BW/day, 0.115 ± 0.050 μg/kg BW/day, 0.085 ± 0.036 μg/kg BW/day, and 0.057 ± 0.023 μg/kg BW/day, respectively. Similarly, the mean ± SD values of Pb exposure in males aged 6 months, 4 years, 8 years, and 13 years were calculated as 0.085 ± 0.076 μg/kg BW/day, 0.033 ± 0.038 μg/kg BW/day, 0.091 ± 0.038 μg/kg BW/day, and 0.067 ± 0.028 μg/kg BW/day, respectively. The toxicological contribution of Pb calculated for all age groups consuming EN formula were from 0.28 to 6.78% in females and from 0.31 to 6.86% in males. The Pb exposure levels (mean, P50, and P95) observed in this study, which were derived from the consumption of various EN formulas, were found to be below the PTWI value of 25 μg/kg BW/day recommended by the EFSA (2010). The mean ± SD values of Cd exposure in females aged 6 months, 4 years, 8 years, and 13 years were found to be 0.023 ± 0.015 μg/kg BW/day, 0.031 ± 0.036 μg/kg BW/day, 0.022 ± 0.027 μg/kg BW/day, and 0.015 ± 0.017 μg/kg BW/day, respectively. Similarly, the mean ± SD values of Cd exposure in males aged 6 months, 4 years, 8 years, and 13 years were calculated as 0.023 ± 0.020 μg/kg BW/day, 0.032 ± 0.038 μg/kg BW/day, 0.025 ± 0.028 μg/kg BW/day, and 0.018 ± 0.021 μg/kg BW/day, respectively. The toxicological contribution of Cd calculated for all age groups consuming EN formula were from 4.76 to 41.44% in females and from 5.88 to 43.4% in males. The Cd exposure levels (mean, P50, and P95) resulting from the consumption of various EN formulas were found to be below the PTWI value of 2.5 μg/kg BW/day recommended by the EFSA (2009b). The mean ± SD values of Hg exposure in females aged 6 months, 4 years, 8 years, and 13 years were determined as 0.004 ± 0.002 μg/kg BW/day, 0.002 ± 0.003 μg/kg BW/day, 0.001 ± 0.002 μg/kg BW/day, and 0.001 ± 0.001 μg/kg BW/day, respectively. Similarly, for males in the same age groups, the mean ± SD values of Hg exposure were calculated as 0.004 ± 0.014 μg/kg BW/day, 0.002 ± 0.003 μg/kg BW/day, 0.001 ± 0.002 μg/kg BW/day, and 0.001 ± 0.002 μg/kg BW/day, respectively. The toxicological contribution of Hg for all age groups consuming EN formulas ranged from 0.53% to 1.75% in females and males. The Hg exposure levels (mean, P50, and P95) resulting from the consumption of various EN formulas were found to be below the PTWI value of 4.0 μg/kg BW/day recommended by the EFSA (2012). In the case of individuals who consume EN formulas, it is typically observed that the age groups of 6 months and 4 years tend to have the highest levels of heavy metal exposure, irrespective of gender. Conversely, the 13-year age group usually demonstrates the lowest levels of heavy metal exposure among both males and females.

3.3.3. *Cancer risk (CR) assessment*

The CR system is a risk assessment and classification system developed by the US EPA (2012) to evaluate the potential CR associated with exposure to specific substances. This system utilizes CR values to determine the level of CR and categorize it into different grades. In the CR system, Grade A indicates a high CR, with CR values exceeding 1×10^{-4}. This implies a significant probability of developing cancer as a result of exposure to the substance. Grade B represents an acceptable CR, with CR values ranging from 1×10^{-6} to 1×10^{-5}. Within this range, the risk of developing cancer is considered lower but still measurable. Grade C signifies a negligible CR, with CR values below 1×10^{-6}. In this category, the estimated risk of developing cancer from exposure to the substance is considered very low and practically insignificant. The CR system provides a valuable framework for assessing and classifying potential CR associated with various substances, aiding in decision-making processes regarding regulatory measures, and ensuring public health and safety (Isci, 2023). The CR assessments for iAs and Pb were conducted among all age and gender groups using CSF values provided by authorities. The results of the CR assessment for different age groups of EN formula consumers are summarized in Table 5. The calculated CR factors for iAs in all groups ranged from 9.63E-05 to 1.29E-03, while the CR factors for Pb ranged from 8.98E-05 to 2.08E-03. The average CR values, based on the exposure to iAs and Pb resulting from the consumption of EN formulas in all age groups of both genders, indicated Grade A CR, which represents a high-risk classification. Consequently, it is crucial to limit the use and exposure to EN formulas containing iAs and Pb, and these results should be considered in the formulation of health policies and the implementation of preventive measures.

4. Discussion

4.1. *Comparison with heavy metal levels from the literature*

4.1.1. *Lead*

The Pb levels in different types of EN formulas (mean:1.957 μg/kg, range: 0.37–3.28 μg/kg) were found to be consistent with the reported ranges for Brazil (de Castro et al., 2010) (0.124–3.32 μg/kg), Sweden (Ljung et al., 2011) (0.82–1.50 μg/L), and Canada (Dabeka et al., 2011) (0.14–2.46 μg/kg). However, the Pb content observed in this study is significantly lower compared to Spain (Moreno-Rojas et al., 2002)

Table 5

Estimation of CR values of heavy metal exposure due to EN consumption.

Gender/ Age	iAs		Pb	
Female	**Mean (Min.-Max.)**	**P95**	**Mean (Min.-Max.)**	**P95**
6 Months	2.00E-04 (6.40E-5-6.81E-04)	6.81E-04	6.88E-04 (8.87E-5-2.05E-03	2.05E-03
4 Age	1.85E-04 (9.60E-5-1.29E-03)	1.29E-03	1.02E-03 (9.84E-4-1.80E-03)	1.80E-03
8 Age	1.84E-04 (9.60E-5-1.29E-03)	1.29E-03	7.45E-03 (8.81E-4-1.32E-03)	1.32E-03
13 Age	1.89E-04 (9.60E-5-1.29E-03)	1.29E-03	4.77E-04 (8.73E-4-7.64E-04)	7.64E-04
Male	**Mean (Min.-Max.)**	**P95**	**Mean (Min.-Max.)**	**P95**
6 Months	2.02E-04 (8.03E-5-6.83E-04)	6.83E-04	6.95E-04 (8.98E-5-2.08E-03)	2.08E-03
4 Age	1.85E-04 (9.60E-5-1.29E-03)	1.29E-03	1.06E-03 (8.35E-4-1.87E-03)	1.87E-03
8 Age	1.84E-04 (9.60E-5-1.29E-03)	1.29E-03	7.95E-04 (8.57E-4-1.41E-03)	1.41E-03
13 Age	1.90E-04 (9.63E-5-1.29E-03)	1.29E-03	5.69E-04 (8.83E-4-1.04E-03)	1.04E-03

(25.7–45.5 μg/kg), Spain (Navarro-Blasco and Alvarez-Galindo, 2005) (1.19–58.5 μg/L), Egypt (Salah et al., 2013) (450–1850 μg/kg), Pakistan (Kazi et al., 2009) (28.7–119 μg/kg) and (Lutfullah et al., 2014) (10.0–30.0 μg/kg), Turkey (Sipahi et al., 2015) (0.55–24.9 μg/kg), Poland (Mania et al., 2015) (2.4–56 μg/kg), Ethiopia (Eticha et al., 2018) (16.0–103 μg/kg), Tanzania (Sager et al., 2018) (1.0–7.0 μg/kg) in milk powder, and Lebanon (Elaridi et al., 2021) (31.0–1040 μg/kg). The results of this study demonstrate that the Pb content in EN formulas in Turkey is significantly lower compared to studies conducted on similar materials with comparable nutrient composition in the literature.

4.1.2. *Cadmium*

The present study reveals that the average level of Cd in EN formulas (mean: 0.936 μg/kg; range: <LOD–3.12 μg/kg) exceeds the levels reported in the UK (Ikem et al., 2002) (0.3 μg/L). These findings are consistent with previous investigations conducted in Canada (Dabeka et al., 2011) (0.23 μg/kg for milk-based formula, 1.18 μg/kg for soy-based formula) and Poland (Mania et al., 2015) (1.2 μg/kg for milk-based formula, 3.4 μg/kg for soy-based formula), confirming similar trends in Cd concentration. However, it is worth noting that the Cd content observed in our study is significantly lower compared to the ranges reported in Pakistan (Kazi et al., 2009) (7.86 μg/kg for milk-based formula, 11.7 μg/kg for soy-based formula), Brazil (de Castro et al., 2010) (median 10.3 μg/kg), Egypt (Salah et al., 2013) (mean: 322 μg/kg, range: 100–1450 μg/kg), Pakistan (Lutfullah et al., 2014) (mean: 355 μg/kg, range: 90–1180 μg/kg), Turkey (Sipahi et al., 2015) (4.72 μg/kg), and Lebanon (Elaridi et al., 2021) (mean: 255 μg/kg, range: 38.0–476 μg/kg). This disparity in Cd levels between EN formulas and infant formulas is significant, with EN formulas consistently exhibiting substantially lower levels. Hence, continuous monitoring and evaluation of Cd levels in EN formulas are crucial to ensure the safety and well-being of consumers.

4.1.3. *Arsenic*

In this study, the observed concentrations of iAs (mean: 5.01 μg/kg; range: <LOD–27.20 μg/kg) exceeded the reported ranges of iAs levels (0.17–1.58 μg/L) in Sweden (Ljung et al., 2011), Finland (0.09–0.28 mg/kg in rice-based baby foods) (Rintala et al., 2014), UK (0.11 mg/kg) (Meharg et al., 2008), Poland (2.9–12.3 μg/kg) (Mania et al., 2015), and USA (2.2–12.6 μg/kg) (Carignan et al., 2015; Jackson et al., 2012). Conversely, a study conducted in the USA demonstrated that non-dairy formulas had significantly higher levels of arsenic compared to milk-based formulas (Jackson et al., 2012). The elevated iAs content in non-dairy products is thought to be associated with the increased presence of rice-based ingredients (Rintala et al., 2014). These findings highlight the importance of continuous monitoring and regulatory measures to ensure the safety of EN formulas and to mitigate the risk of iAs exposure in vulnerable populations.

4.1.4. *Mercury*

The potential neurotoxicity of organic forms, especially methylmercury, remains a significant concern regarding Hg toxicity in populations exposed to low levels of this metal through their diet (De Roma et al., 2017). Organic Hg compounds have the capacity to cross the placental barrier, leading to various neurological disturbances in the developing fetus, such as impaired cognitive function and observable brain damage (Park and Zheng, 2012). Levels of Hg were detected in EN formulas within the range of <LOD to 0.34 μg/kg. Several studies have reported different levels of Hg in infant formula and follow-on formula. These include <0.0000–0.0013 mg/kg in Turkey (Başaran, 2022), 0.03 mg/kg (Martínez et al., 2019), and 0.0005 mg/kg (Martins et al., 2013) in Portugal, 0.0007 mg/kg in Poland (Mania et al., 2015), 0.01 mg/kg in Nigeria (Igweze et al., 2020), and 0.0000–0.0005 mg/kg in France (Guérin et al., 2017). Generally, the findings indicate that Hg levels in commonly consumed food items are typically low (WHO, 2021). However, the presence of organic Hg forms in EN formulas raises concerns about potential neurotoxic effects, particularly in young children. To ensure the safety of these formulas and minimize Hg exposure in vulnerable populations, further research and continuous monitoring efforts are necessary.

4.2. *Comparison with heavy metal exposure estimations from the literature*

The primary objective of the present study was to evaluate the extent of heavy metal exposure resulting from the consumption of EN. However, limited comparative assessments have been identified in the referenced studies and existing literature regarding the specific dietary exposure to heavy metals in EN formula. In contrast to our findings, Elaridi et al. (2021) reported significantly higher results, demonstrating a wide range of Average Weekly Intake (AWI) values for Pb, Cd, and iAs exposure derived from infant formula consumption in the United States. The AWI values ranged from 27.3 μg/kg BW/week to 74.2 μg/kg BW/week for Pb, 18.8 μg/kg BW/week to 51.0 μg/kg BW/week for Cd, and 6.47 μg/kg BW/week to 17.7 μg/kg BW/week for iAs. Furthermore, De Roma et al. (2017) estimated the dietary intake of Hg to range between 0.03 μg/kg BW/day and 0.12 μg/kg BW/day, while Pb intake ranged from 0.14 μg/kg BW/day to 0.58 μg/kg BW/day. Additionally, Mania et al. (2015) identified varying levels of heavy metal exposure in infants' diets, with iAs exposure ranging from 0.22 μg/kg BW/day for 3-month-old infants to 2.4 μg/kg BW/day for 1-year-olds. Hg exposure ranged from 0.01 μg/kg BW/day for 3-month-old infants to 0.08 μg/kg BW/day for 12-month-olds, and Pb exposure ranged from 0.17 μg/kg BW/day for infants to 1.05 μg/kg BW/day for 1-year-olds. Cd exposure ranged from 0.06 μg/kg BW/day to 0.77 μg/kg BW/day. The HQ and HI calculations are commonly employed methods for assessing non-carcinogenic risks. According to our research findings, HQ values below 1 were determined for all heavy metals except for iAs. In line with our study, de Almeida et al. (2022) reported HQ values below 1 (HQ < 1) for Hg, Cd, and Pb in Brazilian EN formulas. However, they observed that the HQ calculated for iAs exceeded 1 (HQ > 1). Similarly, Castro Gonzalez et al. (2017) reported HQ values ranging from 0.024 to 0.034 for Pb, 0.041 to 0.046 for Cd, and 2.93 to 3.05 for iAs in Mexico. Su et al. (2020) determined HQ values of 0.027–0.103 for iAs, 0.0015 to 0.0046 for Pb, and 0.0025 to 0.0090 for Cd in China. Başaran (2022) calculated HQ values of 0.01–0.04 for Cd, 0.02 to 0.14 for Pb, 0.00 to 1.60 for iAs, and 0.00 to 0.00 for Hg in Turkey. These collective findings underscore the need for advanced research and comprehensive studies to evaluate the potential risks associated with heavy metal exposure from EN formulas. Such investigations are of paramount importance in establishing effective guidelines and regulations to safeguard the safety and well-being of individuals consuming these products.

5. Conclusion

The primary objective of this study is to comprehensively evaluate the levels of Hg, Pb, Cd, and iAs in commercially available pediatric EN formulas within the region of Turkey. This research aims to contribute to the limited existing literature on the contamination of EN formulas with toxic metals, particularly within the context of Turkey. The findings demonstrate that the concentrations of Hg, Pb, and Cd in the tested EN formula samples are comparatively lower than similar products, while the levels of iAs are higher. The presence of toxic metals in EN formulas raises significant concerns, particularly considering the vulnerability of individuals who rely on these formulas as their primary source of nutrition, especially those with compromised immune systems. Even at relatively low concentrations, potential health risks associated with the ingestion of toxic metals can have adverse effects on these individuals, posing a potential threat to their overall well-being and development. Furthermore, the existing data gap regarding the presence of chemical pollutants in EN formulas necessitates further research and comprehensive studies to provide a more comprehensive understanding of the potential risks associated with the consumption of these formulas.

Funding

This research received support from the Scientific Research Projects Commission at Afyonkarahisar Health Sciences University under grant number: 22.GENEL.045.

CRediT authorship contribution statement

Gursel Isci: Supervision, Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Betul Orucoglu:** Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Merve Ekici:** Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, All authors have read and agreed to the published version of 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.

Data availability

Data will be made available on request.

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