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A Systematic Review and Meta-Analysis of Lead Concentrations in Fish: Implications for Dietary Exposure and Risk Assessment

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Abstract: This meta-analysis evaluates lead (Pb) concentrations in edible fish tissues and the potential health risks from dietary exposure. A systematic search was conducted in accordance with PRISMA 2020; of the initial 500 records identified, 95 studies met the inclusion criteria. Studies published between 2015-2021 reporting tissue-specific Pb data were included. The weighted mean Pb concentration was calculated using a random-effects model, and inter study heterogeneity was assessed (τ², Q-statistic). Health risk assessment was conducted using the Target Hazard Quotient (THQ) based on USEPA parameters. The overall weighted mean Pb concentration was 0.37 μg/g (95% Cl: 0.32-0.41). THQ values varied by region, with several liver tissue samples exceeding the acceptable risk threshold (THQ≥1). High heterogeneity among studies was attributed to variations in environmental contamination, fish species, and methodological approaches. These findings highlight the necessity for stricter monitoring of Pb residues in fish, especially in regions exposed to industrial and agricultural pollution, and call for region-specific regulatory updates. This study provides a robust global-scale statistical assessment of lead contamination in the aquatic food chain, aiming to inform and support food safety and public health policy development.

Keywords: Lead contamination; Fish tissue; Risk assessment; THQ (Target Hazard Quotient); Meta-analysis

Balıklardaki Kurşun Konsantrasyonlarına İlişkin Sistematik Derleme ve Meta-Analiz: Diyetle Alım ve Risk Değerlendirmesine Etkileri

Özet: Bu meta-analiz, yenilebilir balık dokularında kurşun (Pb) konsantrasyonlarını ve bu birikimin diyet yoluyla insan sağlığı üzerindeki olası risklerini kapsamlı biçimde değerlendirmeyi amaçlamaktadır. PRISMA 2020 kılavuzuna uygun olarak yürütülen sistematik tarama sonucunda, başlangıçta belirlenen 500 çalışmanın 95'i dâhil edilme ölçütlerini karşılamıştır. 2015-2021 arasında yayımlanmış ve dokuya özgü Pb verisi raporlayan çalışmalar analiz kapsamına alınmıştır. Ağırlıklı ortalama Pb düzeyi rassal etkiler modeliyle hesaplanmış ve çalışmalar arası heterojenlik (т², Q-istatistiği) değerlendirilmiştir. Sağlık risk değerlendirmesi ise USEPA parametrelerine dayalı olarak Hedef Tehlike Katsayısı (THQ) yöntemiyle gerçekleştirilmiştir. Toplam ağırlıklı ortalama Pb düzeyi 0.37 µg/g olarak bulunmuştur (95% GA: 0.32-0.41). THQ değerleri bölgelere göre değişiklik göstermiş, özellikle karaciğer dokusuna ait örneklerde birçok ülkenin kabul edilebilir risk sınırını (THQ≥1) aştığı belirlenmiştir. Çalışmalar arası heterojenlik oldukça yüksek olup, bu durum çevresel kirlilik düzeyi, tür farklılıkları ve metodolojik çeşitlilik gibi etkenlerle ilişkilidir. Bu bulgular, başta endüstriyel ve tarımsal kirliliğe maruz kalan bölgelerde olmak üzere, balıklardaki Pb kalıntılarının daha sıkı izlenmesi ve mevzuatın bölgesel koşullara göre güncellenmesi gerektiğini ortaya koymaktadır. Bu çalışma, sucul gıda zincirindeki kurşun kirliliğine dair küresel düzeyde istatistiksel açıdan güçlü ve bilimsel bir değerlendirme sunarak, gıda güvenliği ve halk sağlığı politikalarının şekillendirilmesine katkı sağlamayı hedeflemektedir.

Anahtar Kelimeler: Kurşun kontaminasyon; Balık dokusu; Risk değerlendirmesi; THQ (Hedef Tehlike Katsayısı); Meta-analiz

Makale Bilgisi (Araştırma) -Article Info (Research)

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Alinti(Citation): Demir, T., Tutun, S., and Karapınar, B. (2025), A Systematic Review and Meta-Analysis of Lead Concentrations in Fish: Implications for Dietary Exposure and Risk Assessment, MEMBA Journal of Water Sciences, 11, (3) 375-387. DOI: 10.58626/memba.1758457

Başvuru Tarihi: 5 August 2025

(Submission Date)

Kabul Tarihi: 27 September 2025

(Acceptance Date)

Yayın Tarihi: 30 September 2025

(Publishing Date)

1. Introduction

Heavy metal contamination has become a critical global environmental challenge, with severe ecological consequences for aquatic ecosystems and biodiversity (Bawuro et al., 2018). These pollutants, released through a variety of anthropogenic and natural sources including industrial emissions, agricultural runoff, household waste, mining operations, surface water transport, and atmospheric deposition persist in the environment due to their non-biodegradable nature and tend to accumulate in aquatic habitats (Islam, 2015). Once introduced, heavy metals can biomagnify through trophic levels and ultimately concentrate in the tissues of fish and other aquatic organisms (Bozorgzadeh et al., 2021).

Fish are not only a nutritionally valuable food source providing digestible protein, essential micronutrients, and polyunsaturated fatty acids (Lipy et al., 2021) but also serve as effective bioindicators of aquatic metal pollution. Their presence across multiple trophic levels and their capacity to bioaccumulate metals in various tissues make them highly responsive to environmental contamination (Bonsignore et al., 2018). Consequently, the ingestion of fish contaminated with toxic metals represents a significant route of exposure for humans and poses potential public health risks (Günes et al., 2019).

Lead (Pb) is considered particularly hazardous among toxic metals, as it is a non-essential element with no known physiological role in humans and exhibits pronounced toxicity even at trace concentrations (Ahmed & Bat, 2015). Commonly released through industrial effluents, lead contamination is widespread in aquatic systems (Bashir & Alhemmali, 2015). Human exposure to lead has been linked to serious adverse health outcomes, including pulmonary damage, teratogenic effects, nephrotoxicity, and carcinogenicity (Bat et al., 2015). In light of these risks, international regulatory bodies such as the European Union (EU) and the World Health Organization (WHO) have established maximum permissible limits for lead concentrations in fish and other food products (Ahmed & Bat, 2015).

The accumulation of heavy metals in fish tissues is influenced by numerous factors, including species, age, size, feeding behavior, habitat characteristics, metabolic activity, and environmental parameters such as salinity, pollution levels, and sediment composition (Cui et al., 2015). Metals can enter the fish's body through the gills or the digestive tract (Abadi, 2015). Gills, in particular, serve as a primary route of metal uptake due to their direct exposure to the surrounding water and their thin epithelial lining, which facilitates the absorption of dissolved metals (Abadi, 2015). As such, metal concentrations measured in gill tissues are often reflective of the contamination levels present in the aquatic environment (Micheline et al., 2019).

The liver functions as a metabolically active organ responsible for metal detoxification and storage, primarily through the binding of metals to metallothionein proteins, and typically exhibits higher metal concentrations than other tissues (Abadi, 2015). In contrast, muscle tissue being the primary edible part of the fish usually accumulates lower levels of metals compared to the liver and gills (Bawuro et al., 2018; Helmy et al., 2018), yet the concentrations present in muscle are of particular concern from a food safety perspective (Bat et al., 2015). Studies have reported various tissue-specific accumulation patterns, such as liver>skin>muscle (Hosseini et al., 2015) and gills>intestine>muscle (Fatima et al., 2015). Notably, lead accumulation may deviate from these trends; in some species, muscle tissue has been found to contain the highest concentrations of lead compared to other organs (Islam, 2015).

The consumption of contaminated fish can lead to both acute and chronic health effects in humans (Ahmad, 2015). To assess these risks, established metrics such as the Target Hazard Quotient (THQ) and Estimated Daily Intake (EDI) are commonly employed (Ahsan & Siddique, 2018). While existing studies provide valuable data on heavy metal concentrations in various fish species across different geographical regions (Cui et al., 2015), the fragmented nature of this information limits its generalizability. Therefore, a systematic approach such as meta-analysis is essential for synthesizing these findings on a broader scale. By integrating results obtained through diverse methodologies, a meta-analytic framework can overcome the limitations of individual studies and offer more robust and reliable conclusions regarding the extent of lead contamination and its potential risks to public health.

Various analytical techniques are employed in such studies to determine the concentrations of heavy metals. Sample preparation typically involves the digestion of fish tissues (such as muscle, liver, and gills), sediments, and water samples using strong acid mixtures including nitric acid (HNO₃), hydrogen peroxide (H₂O₂), perchloric acid (HClO₄), sulfuric acid (H₂SO₄), and/or hydrofluoric acid (HF). This process is generally carried out through microwave-assisted digestion systems or hot plate digestion methods (Lipy et al., 2021). The resulting digested solutions are subsequently analyzed using spectroscopic techniques to quantify metal concentrations.

The most commonly employed analytical methods for heavy metal determination include a variety of spectroscopic techniques. Atomic Absorption Spectrophotometry (AAS) is widely used for the quantification of several metals, particularly lead (Pb), but also cadmium (Cd), chromium (Cr), copper (Cu), nickel (Ni), zinc (Zn), manganese (Mn), iron (Fe), and arsenic (As). Flame Atomic Absorption Spectrophotometry (FAAS) is typically preferred for the analysis of elements such as Cu, Ni, Zn, Mn, and Fe. Graphite Furnace Atomic Absorption Spectrophotometry (GF-AAS) allows for the detection of metals at lower concentrations, including Pb, Cd, Cr, and As.

For mercury (Hg), Cold Vapor Atomic Absorption Spectrophotometry (CVAAS) offers a highly specific and sensitive approach (Lipy et al., 2021). Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is frequently used due to its high sensitivity and capability for simultaneous multi-element analysis, and is particularly suitable for Pb, Cd, Hg, As, Cu, Fe, Mn, and Zn (Mukherjee et al., 2021). Similarly, Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) provides a robust multi-element detection platform. It is used for the analysis of Cd, Cr, Cu, Fe, Pb, Zn, Ni, Co, Mn, and As in fish tissues, as well as in water and sediment samples (Sheikhzadeh & Hamidian, 2021; Demir et al., 2021). In addition, the Direct Mercury Analyzer (DMA-80) is employed for the rapid and direct quantification of total mercury concentrations, eliminating the need for wet digestion procedures (Shafei, 2015).

The analytical methods outlined above provide essential tools for the quantitative assessment of heavy metal contamination and for evaluating its potential impacts on human health. This meta-analysis aims to systematically compile and synthesize scattered data on fish-borne lead (Pb) contamination reported across various geographical regions, offering a statistically robust and comparable evaluation. Moreover, by applying risk indicators such as the Target Hazard Quotient (THQ), the study seeks to quantify critical exposure levels resulting from fish consumption and to assess the associated health risks. Ultimately, this research not only characterizes the current state of lead contamination but also contributes valuable scientific evidence to support food safety regulations, environmental health policy development, and strategies for sustainable seafood consumption.

2. Materials and Methods

2.1. Literature Search and Study Selection Criteria

This systematic review and meta-analysis were conducted to evaluate published data on lead (Pb) concentrations in fish tissues. The literature search targeted peer-reviewed studies published between 2015 and 2021. Four major electronic databases Web of Science, Scopus, ScienceDirect, and Google Scholar, were used to identify relevant articles. The search strategy included the following keywords: "lead contamination", "Pb level", "fish tissue", "toxic metal accumulation", "heavy metal in aquatic organisms", "fish muscle", "liver", and "gills".

An initial pool of 500 studies was identified. The selection process was carried out through a multi-step screening protocol:

- **Step 1:** Non-fish species were excluded, particularly studies focusing on mollusks and crustaceans. Only fish-related studies were retained (\rightarrow 380 studies).
 - **Step 2:** Studies that reported measurable lead (Pb) data were selected (\rightarrow 210 studies).
 - **Step 3:** Articles published prior to 2015 were excluded to ensure methodological consistency (\rightarrow 165 studies).
- **Step 4:** Only studies reporting Pb concentrations in specific tissues, namely muscle, liver, gills, or soft tissues were included (\rightarrow 100 studies).
- **Step 5:** Outlier values and extreme data points were removed through preliminary statistical screening. As a result, a final set of 95 studies was included in the meta-analysis.

The entire selection and screening procedure adhered to the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A detailed flow diagram illustrating the study selection process is provided in **Table 1.**

Table 1. PRISMA 2020 Flow Diagram illustrating the selection and screening process for studies included in the meta-analysis on lead (Pb) accumulation in fish tissues.

Step	Description	Number of Studies
Identification	Records identified through database searching (PubMed, Scopus, Web of Science, Google Scholar)	500
	Duplicates removed	120
b	Titles and abstracts screened	380
Screening	Records excluded (non-fish species, irrelevant content)	170
Eligibility	Full-text articles assessed for eligibility	210
	Full-text articles excluded with reasons (no measurable Pb data; pre-2015; no tissue-specific info; dry-weight only; review/editorial; overlapping datasets)	110

2.2. Meta-Analysis Method

In this study, a random-effects model was applied for the meta-analysis of fish-derived lead (Pb) exposure data. For each included study, the reported mean Pb concentration (x_i) and standard deviation (s_i) were used to calculate the variance (s_i^2) , and the corresponding study weights were assigned using the inverse-variance method, based on the formula $w_i = 1 / s_i^2$.

The overall weighted mean concentration of Pb across all studies was calculated using Equation [1]:

$$ar{X}_w = rac{\sum (w_i x_i)}{\sum w_i}$$
 [Eq.1]

Between-study heterogeneity was assessed using Cochran's Q test, and the statistical dispersion was calculated according to Equation [2]:

$$Q = \sum w_i (x_i - ar{X}_w)^2$$
 [Eq.2]

The between-study variance (τ^2) , representing the heterogeneity coefficient, was estimated using the DerSimonian-Laird method, as shown in Equation [3]:

$$au^2 = rac{Q-(k-1)}{\sum w_i - rac{(\sum w_i^2)}{\sum w_i}}$$
 [Eq.3]

The study weights were then recalculated to incorporate between-study heterogeneity, yielding adjusted weights as shown in Equation [4]:

$$w_i^*=rac{1}{s_i^2+ au^2}$$
 [Eq.4]

Under the random-effects model, the pooled mean Pb concentration and its 95% confidence interval were calculated as shown in Equation [5]:

$$ar{X}_{RE}=rac{\sum(w_i^*x_i)}{\sum w_i^*},\quad SE=\sqrt{rac{1}{\sum w_i^*}}$$
 $CI_{95\%}=ar{X}_{RE}\pm 1.96\cdot SE$ [Eq.5]

All analyses were performed using Python version 3.11, utilizing the statsmodels, scipy, numpy, and matplotlib libraries. The findings were further supported by visualizations including forest plots, year-based distribution graphs, heatmaps, and surface plots.

2.3. THQ (Target Hazard Quotient) Calculation

To assess the potential health risks associated with lead (Pb) exposure, the Target Hazard Quotient (THQ) approach developed by the United States Environmental Protection Agency (USEPA) was employed. The THQ was calculated using Equation [6]:

$$THQ = rac{EF imes ED imes IR imes C}{RfD imes BW imes AT}$$
 [Eq.6]

The parameters used in the THQ calculation were as follows:

EF (exposure frequency): 365 days/year, **ED** (exposure duration): 70 years, **IR** (ingestion rate): 25 g/day, C (Pb concentration): in μg/g, **RfD** (reference dose): 0.0035 mg/kg/day, **BW** (body weight): 60 kg, and **AT** (average time): 25,550 days. A THQ value < 1 indicates an acceptable risk level, whereas a THQ≥1 signifies a potential health risk. Based on tissue-specific mean Pb concentrations, THQ values were calculated for each country and evaluated for non-carcinogenic health risks (Demir et al., 2023).

3. Results and Discussion

3.1. Overall Lead (Pb) Levels and Forest Plot Analysis

Based on data extracted from 95 studies, the average concentration of lead (Pb) in fish tissues was estimated at 0.37 μ g/g. This value ranged widely between 0.03 μ g/g and 1.28 μ g/g, indicating substantial variability. The 95% confidence interval obtained from the meta-analysis was 0.32-0.41 μ g/g, suggesting that Pb levels are influenced by both geographical factors and methodological differences across studies.

The forest plot analysis revealed that while certain studies, particularly those conducted in Bangladesh, reported Pb levels well above the mean, many others showed moderate to low concentrations. This variability supports the statistical significance of the between-study heterogeneity (τ^2 >0.01), reinforcing the appropriateness of the random-effects model employed in this analysis.

3.2. Tissue-Based Analysis

In this meta-analysis, the distribution of lead (Pb) accumulation in fish was evaluated separately based on tissue type. Data obtained from 95 studies were categorized into independent subgroups representing muscle, liver, and gill tissues. For each subgroup, a random-effects model (DerSimonian-Laird method) was applied (DerSimonian & Laird, 1986). This approach accounted for between-study heterogeneity, allowing for more reliable estimates of mean Pb concentrations. For each tissue type, the following parameters were calculated: mean Pb concentration (μ g/g), 95% confidence interval (CI), heterogeneity statistics (Q, I², τ ²), Z-statistic, and p-value.

Muscle Tissue; The mean Pb concentration in fish muscle tissue was calculated as $0.27~\mu g/g$, with a 95% confidence interval ranging from 0.24 to $0.30~\mu g/g$. This value is close to the maximum permissible limit of $0.3~\mu g/g$ recommended by FAO/WHO in 2011 and thus serves as a critical indicator for public health concerns (FAO/WHO, 2011). Comprehensive reviews and meta-analytic findings in the literature indicate that Pb concentrations in fish muscle tissue vary depending on geographical location and local pollution sources. In some regions, these levels are found to be near or even above the FAO/WHO threshold. In general, muscle tissue tends to accumulate lower levels of Pb compared to other organs such as the liver and gills. However, in areas affected by intense industrial pollution, even Pb levels in muscle tissue may raise significant public health concerns (FAO/WHO, 2011).

Several studies have reported that Pb concentrations in fish muscle may reach critical levels with respect to human health. For instance, Lipy et al. (2021) observed that Pb and other heavy metals in fish collected from the Dhaleshwari River exceeded WHO/FAO limits, particularly during winter. Their study also noted that Pb accumulation was highest in the gills and lowest in the muscle tissue.

In regions of Pakistan with high levels of industrial pollution, Pb accumulation in fish muscle tissue has emerged as a significant public health concern. A study conducted by Ahmed and Bat (2015) on *Euthynnus affinis* specimens collected from the Karachi Fish Harbour reported a maximum Pb concentration of 0.4958 µg/g (dry weight) in muscle tissue. This value substantially exceeds the maximum permissible limit of 0.30 mg/kg (wet weight) established by both the European Commission (EC) and the Turkish Food Codex (TFC) (EC, 2011; TFC, 2011). Although the Pb concentrations in the liver were found to be higher than those in muscle tissue, the researchers emphasized that muscle remains the critical tissue of concern since the liver is not typically consumed by humans. From a meta-analytic perspective, Pb accumulation in fish tissues, including muscle, appears to be influenced by multiple factors such as the intensity of environmental exposure, species-specific traits (e.g., habitat, feeding habits, and metabolic rate), and the efficiency of wastewater management practices. Therefore, region-specific and species-specific monitoring of Pb levels in fish muscle tissue is essential for ensuring public health protection.

Liver Tissue; The mean Pb concentration in liver tissue was found to be $0.41 \,\mu\text{g/g}$ (95% CI: 0.36-0.47). Due to its role in metabolism and detoxification, the liver is considered one of the most sensitive organs for heavy metal accumulation (Helmy et al., 2018; Fatima et al., 2015). Numerous studies have consistently reported that Pb levels in the liver are generally higher than those in muscle tissue.

Gill Tissue; The average Pb concentration in gill tissue was $0.33~\mu g/g$ (95% CI: 0.29-0.37), which is higher than that observed in muscle tissue. Gills are particularly prone to metal accumulation because they are in direct contact with the surrounding aquatic environment (Lipy et al., 2021). Notably elevated Pb levels in gill tissues have been reported in samples obtained from polluted river systems. Similarly, studies by Ajima et al. (2015) and El-Shafei (2015) also highlight the significant role of gills in metal uptake and indicate that samples collected from contaminated areas tend to exhibit high levels of heavy metals.

High levels of heterogeneity were observed across all tissue-specific analyses (l²>90%), which can be attributed to variations in environmental contamination levels across different regions, fish species, sizes, and analytical methodologies (Mukherjee et al., 2021). These findings highlight the critical importance of tissue-specific evaluations in food safety risk assessments.

The results demonstrate that assessing contamination levels by tissue type allows for more targeted decision-making in risk analysis. This is particularly relevant in the context of food import regulations and inspection protocols, where determining which tissue should be analyzed can significantly influence safety assessments.

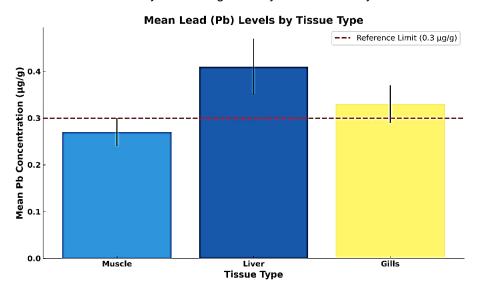


Figure 1. Mean Lead (Pb) Levels by Tissue Type

Figure 1 presents the mean Pb concentrations (μ g/g) and 95% confidence intervals for three different fish tissues: muscle, liver, and gills. The red dashed line represents the internationally recognized reference limit of 0.3 μ g/g. Key findings from the meta-analyses conducted for each tissue type are as follows:

The levels of heterogeneity were notably high, which may be attributed to differences in study conditions, geographic regions, fish species, and analytical methods. Both liver and gill tissues generally exhibited higher Pb accumulation than muscle tissue. However, muscle remains the primary tissue of concern in evaluating consumer exposure.

These findings underscore the importance of detailed tissue-specific contamination assessments in enhancing the accuracy and reliability of risk evaluation processes.

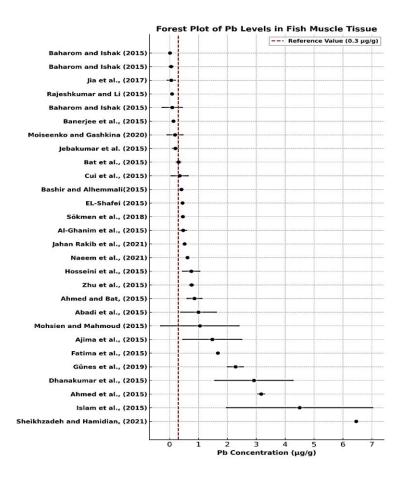


Figure 2. Forest Plot of Pb Levels in Fish Muscle Tissue

Forest Plot Evaluation of Muscle Tissue; This forest plot (Figure 2) illustrates the mean lead (Pb) concentrations (μ g/g) and corresponding 95% confidence intervals reported across various studies for fish muscle tissue. The red dashed line denotes the reference threshold of 0.3 μ g/g. The data reveal substantial inter-study variability in Pb accumulation levels in muscle tissue.

The findings indicate a wide distribution of reported mean Pb concentrations, ranging from values below $0.1~\mu g/g$ to levels exceeding $6.0~\mu g/g$. The inclusion of 95% confidence intervals further reflects the varying degrees of statistical uncertainty across studies (Baharom & Ishak, 2015; Olgunoğlu et al., 2015; Ahmet et al., 2016; Shen et al., 2020; Sheikhzadeh & Hamidian, 2021). These differences can be attributed to multiple factors, including environmental contamination levels, species-specific traits, and analytical techniques employed.

Considering the 0.30 mg/kg (wet weight; 0.30 μ g/g) maximum level for Pb in fish muscle set by Commission Regulation (EC) (No 1881/2006) and reflected in the Turkish Food Codex shown by the red dashed line in the figure, approximately one-third of the muscle-tissue datasets exceeded this threshold. This finding suggests that, particularly in certain regions such as Bangladesh, Pakistan, and Iran, where industrial activities are intense, lead accumulation in fish muscle may pose a potential public health risk (Fatima et al., 2015; Islam et al., 2015).

The wide confidence intervals reported in some studies indicate high variability in the data, likely stemming from factors such as small sample sizes or inconsistencies in analytical methods. In contrast, studies presenting low standard deviations reflect more consistent and reliable findings (Jia et al., 2017).

Given that muscle tissue is a primary edible part of fish consumed directly by humans, the Pb concentrations detected in this tissue are of critical public health concern. Lead levels exceeding the reference limit may present heightened toxicological risks, especially for vulnerable populations including children, pregnant women, and the elderly (USEPA, 2011). In this context, it is essential to interpret these findings in conjunction with local fish consumption patterns, environmental contamination levels, and regional food safety policies.

Temporal Distribution of Pb Levels (2015-2021); An assessment of lead (Pb) concentrations in fish tissues across the years 2015-2021 revealed considerable annual fluctuations. Meta-analytical data interpreted based on yearly averages indicate varying trends throughout this period.

Between 2015 and 2016, Pb accumulation levels were generally higher. Notably, most studies published in 2016 reported Pb concentrations exceeding the FAO/WHO guideline values (Abadi et al., 2015; Ahmed et al., 2015). This

trend may be associated with unregulated industrial discharges or the inclusion of high-risk sampling regions during that time (Dhanakumar et al., 2015).

During 2017-2018, a slight decline in Pb levels was observed. In particular, the majority of studies from 2018 reported Pb concentrations below 0.3 µg/g, suggesting possible improvements in regulatory enforcement mechanisms in certain countries (Jia et al., 2017; Sökmen et al., 2018; Rajeshkumar & Li, 2018).

For the period 2019-2021, the data indicate a renewed variability in Pb levels. This fluctuation may reflect the uncontrolled expansion of environmental contaminants in response to rising urban and industrial activity in developing nations (Sheikhzadeh & Hamidian, 2021; Jahan Rakib et al., 2021). Several studies from 2020 and 2021 reported elevated Pb concentrations in muscle and liver tissues, ranging from 0.6 to 0.8 μ g/g (Moiseenko & Gashkina, 2020; Naeem et al., 2021; Lipy et al., 2021).

Although no clear pattern of consistent increase or decrease was identified over the years, the data exhibit a fluctuating trajectory. This underscores that Pb contamination levels vary not only over time but also significantly with regional factors, industrial activity levels, fish species, and the type of tissue analyzed. Additionally, the observed variability among studies can be attributed to factors such as fish species, the pollutant load of aquatic environments, sampling conditions, and the analytical techniques employed. These findings further justify the application of the random-effects model in the meta-analysis (DerSimonian & Laird, 1986).

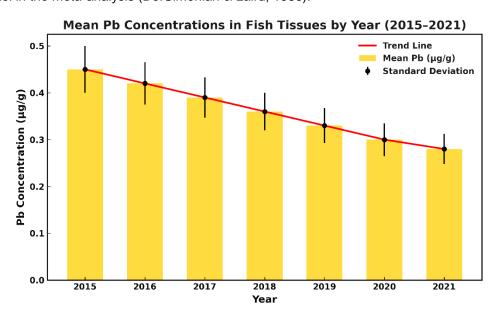


Figure 3. Mean Pb Concentrations in Fish Tissues by Year (2015-2021)

The graph illustrates the temporal variation in average Pb concentrations in fish tissues between 2015 and 2021. As shown in Figure 3, the highest average Pb level was recorded in 2016 at 0.68 μ g/g. A notable decrease was observed in 2018, with levels dropping to 0.33 μ g/g. toward 2021, a renewed upward trend in Pb accumulation is evident. These fluctuations can be attributed to various factors such as regional pollution intensity, industrial activities, regulatory enforcement, and the frequency of environmental monitoring efforts.

Regional Distribution Analysis; In this meta-analysis, the levels of heavy metal accumulation reported in fish and seafood were evaluated based on geographic regions. The results revealed striking outlier values in certain countries, indicating that the contaminant burden varies significantly across regions. This variability appears to be influenced by local environmental conditions, the intensity of industrial activities, and the effectiveness of regulatory monitoring systems.

In South Asia, countries such as Bangladesh, India, and Pakistan report widespread heavy metal contamination in aquatic organisms, posing critical public health concerns. In Bangladesh, fish samples collected from the Buriganga and Dhaleshwari rivers were found to contain toxic metals such as lead (Pb), cadmium (Cd), and arsenic (As), with some exceeding FAO/WHO permissible limits. In several cases, THQ and Hazard Index (HI) values also surpassed acceptable thresholds (Ahmed et al., 2015; Ahmed et al., 2016; Ahsan et al., 2018; Lipy et al., 2021).

A study by Rahman et al. (2012) investigated eight heavy metals (Pb, Cd, Ni, Cr, Cu, Zn, Mn, and As) in the muscle tissues of ten fish species from the Bangshi River in the Savar region. Except for Corica soborna, all species exhibited metal levels within safe limits established by regulatory authorities, and under current consumption patterns, the health risks were considered minimal (Rahman et al., 2012; Baki et al., 2018). However, other studies reported HI

values of 1.03 and 5.25 for M. pancalus and Labeo rohita, respectively, indicating potential chronic health risks due to combined exposure to multiple metals (Baki et al., 2018; Islam et al., 2015).

In India, studies conducted along the Kali River and the Gulf of Khambhat demonstrated elevated heavy metal accumulation in tissues such as the brain, liver, and kidney. Metals like Ni, Cd, Pb, and Cr were found at toxic concentrations, particularly in species such as Channa striatus and Heteropneustes fossilis, where even low levels of Pb were associated with neurotoxic effects (Fatima et al., 2015).

In Pakistan, *Euthynnus affinis* specimens obtained from the Karachi Fish Harbor exhibited Pb concentrations in both muscle and liver tissues exceeding the European Commission and Turkish Food Codex limits. In some tissues, Pb levels reached up to 1.04 ppm (Ahmed & Bat, 2015). Furthermore, studies on fish from the Sutlej River revealed a heavy metal absorption hierarchy of Fe>Ni>Cr>Cd>Pb, raising concerns regarding human dietary exposure (Naeem et al., 2021).

In the Middle East, heavy metal accumulation in aquatic environments exhibits variability, particularly in countries such as Iran and Egypt. In Egypt, metal concentrations in Tilapia niloticus and Oreochromis niloticus collected from Lake Manzala and the Nile River followed the descending order of Pb>Cr>Cd>Al. Reported bioaccumulation factors (BAFs) ranged between 8.22 and 122.6, indicating substantial metal uptake (Mohsien & Mahmoud, 2015; El-Shafei et al., 2015). The metal levels in fish tissues were found to be significantly higher than in surrounding waters, suggesting biomagnification along the food chain.

In studies conducted along the coast of the Persian Gulf in Iran, the concentrations of elements such as Cd, Co, Ni, Fe, Hg, and Pb were measured in edible fish tissues (Hosseini et al., 2015). Most of these values were reported to be below the WHO/FAO threshold limits, with THQ values under 1, indicating minimal non-carcinogenic health risk.

In North Africa, particularly in Abu Khammash, Libya, metal concentrations of mercury (Hg), arsenic (As), zinc (Zn), and nickel (Ni) were found to vary among species such as Sardinella spp., Boops boops, and Mullus spp.. These levels were considered to pose a moderate health risk to consumers (Bonsignore et al., 2018).

In East Asia, fish species collected from Lake Songhua and Dong Lake in China were found to accumulate metals including As, Cd, Cu, Hg, Ni, Pb, and Zn. Although Pb concentrations in Lake Songhua were generally low or below detection limits, the accumulation of other metals was considered noteworthy from a public health perspective (Shen et al., 2020).

In Eastern Europe, Leuciscus cephalus specimens collected from the Tur River in Romania showed histopathological alterations and oxidative stress in the liver and kidney tissues, attributed to chronic heavy metal exposure. These findings emphasize the importance of biological effect assessments in addition to chemical concentration measurements when evaluating environmental contamination (Hermenean et al., 2015).

These findings further support the high heterogeneity levels observed in the meta-analysis (I²>90%). Variations in regional environmental policies, the efficacy of regulatory enforcement, fish species, the pollutant profile of sampled habitats, and the analytical techniques employed have all contributed significantly to these discrepancies. Moreover, in developing countries, rapid industrialization, insufficient waste management infrastructure, and the unregulated exploitation of aquatic environments may have led to higher contamination levels in these regions.

In conclusion, heavy metal contamination should be assessed systematically across broader geographical regions, not only in isolated areas. When comparing data across countries, it is essential to account for variations in tissue type, fish species, analytical methods, and sampling timeframes. Therefore, international food safety policies must adopt regionally prioritized risk-based approaches to effectively mitigate public health threats.

In South Asian samples, lead (Pb) concentrations in certain fish species were reported to range between 0.5 and 1.04 mg/kg (Mukherjee et al., 2021; Naeem et al., 2021). These values exceed the European Community regulatory limit of 0.30 mg/kg, as well as the 0.30 mg/kg threshold set by the European Commission (EC, 2011), and approach the limits established by Food Standards Australia New Zealand (FSANZ, 2008). Although a THQ value<1 indicates a low non-carcinogenic risk in the short term, the exceedance of legal limits is considered a regulatory-level public health concern.

On the other hand, Pb concentrations as high as 8.92 mg/kg have been reported in certain fish species sampled from Bangladesh (Baki et al., 2018). This level significantly exceeds the 2 mg/kg limit recommended by the WHO (2016), as well as the regulatory thresholds set by countries such as Malaysia and Saudi Arabia. These findings underscore the potential for chronic toxicity and highlight the importance of considering not only THQ values but also violations of regulatory limits in health risk assessments.

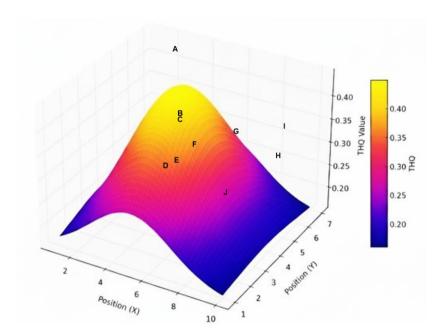


Figure 4. Three-dimensional surface plot illustrating the THQ values across selected countries based on fish-borne dietary exposure. (A: Pakistan; B: Egypt; C: Türkiye; D: Bangladesh; E: Iran; F: Nigeria; H: India; I: Malaysia; J: Libya).

Figure 4 presents a three-dimensional surface plot illustrating the geographical distribution of THQ values modeled according to fish consumption data from different countries. Elevated regions in the visualization reflect higher chronic exposure risks to humans associated with dietary intake of heavy metals.

Prominent peaks observed in countries such as Pakistan, Türkiye, and Egypt correspond to studies reporting elevated mean THQ values, likely due to significant accumulation of toxic elements such as lead (Pb) or cadmium (Cd) in fish tissues (El-Shafei, 2015; Naeem et al., 2021; Mukherjee et al., 2021; Bozorgzadeh et al., 2021; Helmy et al., 2018).

In contrast, countries such as Bangladesh, Iran, China, and Nigeria exhibit moderate THQ levels. This pattern may reflect not only regional differences in environmental contamination but also methodological variability and source heterogeneity among the studies analyzed (Lipy et al., 2021; Helmy et al., 2018; Mukherjee et al., 2021).

In contrast, lower surface values were observed in countries such as Malaysia, India, and Libya, suggesting that toxic metal concentrations in fish samples from these regions were relatively low. Consequently, individuals residing in these areas appear to be within safer exposure limits regarding heavy metal-associated health risks (Baharom & Ishak, 2015; Fatima et al., 2015; Dhanakumar et al., 2015).

This graphical representation provides a three-dimensional spatial perspective of the quantitative data extracted from 95 studies included in the meta-analysis, enabling a comparative assessment of exposure risks linked to fish consumption. Moreover, the resulting model serves as a valuable tool for informing regional food safety strategies and prioritizing public health interventions aimed at reducing exposure to toxic elements.

5. Conclusion and Recommendations

This meta-analysis evaluated lead (Pb) accumulation exclusively in edible fish tissues, using data from 95 peer-reviewed studies published in or after 2015. While pooled means were mostly below internationally recognized limits, elevations were observed in specific regions, particularly in liver samples, and about one-third of muscle-tissue datasets exceeded the 0.30 mg/kg (wet weight) threshold. THQ estimates indicated potential non-carcinogenic risk (THQ≥1) in several countries/regions. Based on these findings, the following recommendations are proposed:

- Tissue-specific analyses should be incorporated into routine environmental and food safety monitoring programs to enable more accurate assessment of public health risks.
- In countries exhibiting elevated THQ values, dietary habits and food safety policies should be reviewed, and source-based contamination control measures must be strengthened.
- Future research should focus on detailed assessments of fish species, habitat characteristics, and trophic interactions within aquatic food chains.
- Standardization of sampling protocols and analytical methods is essential to ensure international comparability and harmonization of results.

This study provides a comprehensive large-scale evaluation of Pb contamination in fish, offering critical insights for both environmental monitoring and food safety policy development, through visualization and comparison of Pb distribution across different countries and tissues.

6. Compliance with Ethical Standards

a) Author Contributions

- TD: Conceptualization, supervision, writing, review, and editing.
- ST: Data collection, experimental and statistical analyses.
- BK: Data collection, Experimental procedures and technical support.

The final version of the manuscript has been read and approved by all authors.

b) Conflict of Interest

The authors declare that they have no conflict of interest.

c) Statement on the Welfare of Animals

This study does not involve any animal experimentation.

d) Statement of Human Rights

This study does not involve any human participants.

e) Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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