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Association between bone trace metal accumulation and idiopathic aseptic osteonecrosis of the femoral head in a mining region of Katanga (DR Congo)

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Abstract

Background Aseptic osteonecrosis of the femoral head (ONFH) is a debilitating orthopedic disorder that predominantly affects young adults and has a multifactorial etiology. In mining-intensive regions such as Katanga (Democratic Republic of the Congo), chronic exposure to trace metal elements (TMEs) has raised concerns about potential environmental contributors to bone disease. This study aimed to investigate the association between bone TME accumulation and the occurrence of idiopathic ONFH in an environmentally exposed population.

Methods A case–control study was conducted between 2017 and 2025 at Medpark Clinic, Lubumbashi. Femoral head specimens were collected from 56 patients undergoing total hip arthroplasty, including 36 cases of idiopathic ONFH and 20 controls with primary osteoarthritis. Bone concentrations of eleven TMEs (Pb, Co, Cd, Cr, Zn, Cu, As, Mn, Mg, Ni, Al) were quantified using inductively coupled plasma–optical emission spectrometry (ICP–OES). Exposure was defined as a Z-score > 2 compared with a local reference population. Bivariate and multivariate logistic regression analyses were performed to assess associations.

Results Patients with ONFH were significantly younger than controls (mean age: 49.5 vs. 62.9 years; $p = 0.004$). Bone concentrations of lead and cobalt were markedly higher in ONFH cases. In multivariate analysis, elevated bone lead levels (adjusted OR = 23.75; 95% CI: 2.30–181.57) and age ≤ 50 years were independently associated with ONFH. No significant associations were found for other TMEs.

Conclusion This study provides the first direct evidence that chronic bone accumulation of lead and cobalt is strongly associated with idiopathic ONFH in a mining-exposed African population. These findings highlight the urgent need for environmental monitoring, targeted public health interventions, and early clinical surveillance in high-risk regions.

Keywords Aseptic osteonecrosis, Femoral head, Lead, Cobalt, Trace metal elements, ICP-OES, Environmental exposure, Mining pollution, Democratic republic of the congo

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Introduction

Aseptic osteonecrosis of the femoral head (ONFH) is a severe bone disorder characterized by the death of bone cells in the femoral epiphysis in the absence of infection or malignancy [1, 2]. It represents a major cause of hip disease in young adults, often progressing silently but rapidly toward subchondral collapse and irreversible joint destruction, thereby necessitating total hip arthroplasty (THA) [3, 4].

The pathogenesis of ONFH is multifactorial, involving vascular compromise, bone marrow ischemia, impaired bone cell viability, and metabolic disturbances [5]. Known risk factors include both traumatic etiologies, such as femoral neck fractures and hip dislocations, and non-traumatic causes such as prolonged corticosteroid therapy, chronic alcoholism, sickle cell disease, and lipid, endocrine, or coagulation abnormalities [6–9].

Recent studies have highlighted the role of genetic susceptibility, particularly polymorphisms of the estrogen receptor gene (ESR1) and apolipoprotein E (APOE), as well as other variants involved in lipid and coagulation pathways [10]. ESR1 variants may alter bone turnover and vascular homeostasis, increasing vulnerability to ischemic bone injury, while certain APOE genotypes impair lipid clearance and promote intraosseous fat embolism. Dyslipidemia and impaired triglyceride metabolism can further elevate intraosseous pressure and compromise femoral head perfusion [11, 12]. Disturbances in coagulation and fibrinolysis, such as increased plasminogen activator inhibitor-1 (PAI-1) activity and hypofibrinolysis, contribute to microvascular thrombosis and impaired bone blood flow [11, 13]. Emerging evidence also suggests that gut microbiota dysbiosis can modulate lipid metabolism and systemic inflammation, creating a prothrombotic environment that may accelerate ONFH in genetically predisposed individuals [13]. Despite these insights, approximately 30% of ONFH cases remain idiopathic [4].

In industrial and mining regions, chronic exposure to trace metal elements (TMEs), commonly referred to as heavy metals, poses a major public health challenge [14–17]. Elements such as lead, cadmium, arsenic, mercury, and chromium are frequently released into the environment through mining, smelting, and other industrial processes [18]. Owing to their persistence and bioaccumulative potential, these contaminants can build up in biological tissues, particularly bone [19–22].

This issue is of particular concern in the Greater Katanga region, especially the Katangan Copperbelt in southeastern Democratic Republic of the Congo (DRC), now administratively subdivided into Haut-Katanga, Lualaba, Haut-Lomami, and Tanganyika. Historically the country's main mining basin, this area hosts extensive deposits of copper, cobalt, zinc, uranium, and other strategic metals [23, 24]. In recent decades, the global energy transition has fueled a sharp rise in demand for critical "green metals" such as cobalt, copper, and lithium, driving intensive industrial and artisanal mining but often without adequate environmental oversight [25, 26]. As a result, local populations are chronically exposed to poorly regulated mining-related pollution, with potential skeletal and systemic toxicity.

Experimental and clinical evidence indicates that TMEs disrupt bone homeostasis. Lead impairs osteoblast differentiation, inhibits type I collagen synthesis, and promotes apoptosis [28–32]; cadmium interferes with calcium-phosphate metabolism and reduces bone mineral density [33]; while cobalt and chromium induce mitochondrial dysfunction, oxidative stress, and abnormal osteogenesis [34, 35]. These toxic effects raise concern in highly contaminated regions such as the Katangan Copperbelt (Fig. 1), where long-term, low-dose exposure may silently accumulate in bone and contribute to degenerative skeletal diseases, including idiopathic ONFH [36].

In southeastern DRC, the Katangan Copperbelt extends from Zambia's Copperbelt Province into the former Kolwezi District, over ~500 km in length and 60 km in width. It comprises two main metallogenic districts: NW (Kolwezi–Lubumbashi, ~300 × 50 km) and SE (Musoshi–Bwana Mkubwa, ~180 × 70 km) and hosts abundant copper-group metals (copper, cobalt, uranium, zinc, nickel, lead, cadmium, etc.).

Multiple environmental health investigations have documented markedly elevated concentrations of heavy metals in blood, urine, and hair samples from populations residing in mining-impacted regions, particularly among children living in close proximity to industrial sites [24, 39]– [40]. Yet, data specifically addressing the long-term skeletal consequences of chronic trace metal exposure remain extremely limited, and to date, no study from this region has directly assessed their relationship with aseptic osteonecrosis of the femoral head.

A recent investigation in the Katanga region reported that nearly one-third (29%) of ONFH cases were idiopathic, despite occurring in a mining-intensive environment with well-documented environmental contamination [41]. This observation strengthens the hypothesis that chronic exposure to trace metal elements could contribute to the pathogenesis of ONFH. Supporting evidence from animal and human studies indicates that bone serves as a long-term reservoir for metals such as lead, which can persist in the skeleton for decades [28, 42]. The toxic effects of TMEs on bone cells, including impaired intraosseous angiogenesis, heightened oxidative stress, and osteoblast dysfunction, mirror key mechanisms implicated in ONFH development [32, 35].

Beyond etiology, the management of ONFH has evolved substantially in recent years. Joint-preserving

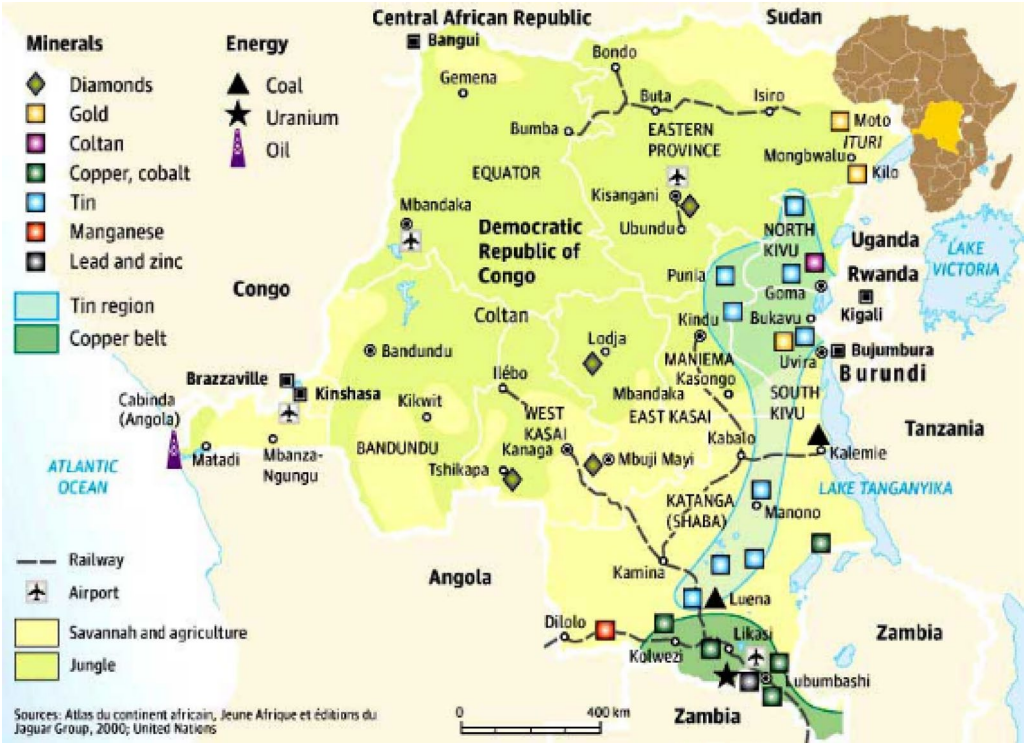

Fig. 1 Geographical context of the Katangan Copperbelt

strategies such as core decompression augmented with biologics (e.g., stem cells, bone grafts), cell-based therapies, and corrective osteotomies have demonstrated promising mid-term outcomes, while early total hip arthroplasty remains the standard for advanced disease [43–47]. Nevertheless, these interventions are often inaccessible in low-resource settings, where diagnosis is frequently delayed and specialized surgical options for joint preservation remain scarce.

A key strength of the present study lies in its direct quantification of bone TME concentrations using femoral head specimens obtained during THA and analyzed via inductively coupled plasma-optical emission spectrometry (ICP-OES). This approach provides a robust retrospective marker of chronic exposure, superior to blood or urine testing in populations with long-term, low-dose metal accumulation.

This study aims to fill a critical knowledge gap by investigating the association between bone TME burden and idiopathic ONFH in a Congolese mining population. The findings are intended to inform public health policy and clinical strategies for the early detection and prevention of metal-induced skeletal disease in high-risk communities.

Materials and methods

Design

This was a retrospective analytical case-control study aiming to compare bone trace metal concentrations between two groups of patients who underwent total hip arthroplasty: cases with radiologically confirmed idiopathic ONFH and controls with primary hip osteoarthritis (Fig. 2a, b,c).

Study setting

This study was conducted in the Katanga region, located in the southeastern part of the Democratic Republic of the Congo, an area historically renowned for its exceptional mineral wealth. Industrial mining began in 1906 with the establishment of the Union Minière du Haut-Katanga (UMHK), a Belgian company that played a central role in the extraction of copper, cobalt, zinc, and uranium. Lubumbashi, founded in 1910 as Élisabethville, quickly became the administrative and economic hub of mining activities, hosting corporate headquarters, metallurgical plants, and associated infrastructure.

Following Congo's independence in 1960, UMHK was nationalized in 1967 and transformed into Gécamines (Générale des Carrières et des Mines), the state-owned mining company that dominated the sector for decades. The economic downturn and structural reforms of the 1990s led to the progressive liberalization of the mining industry, allowing the emergence of private and artisanal

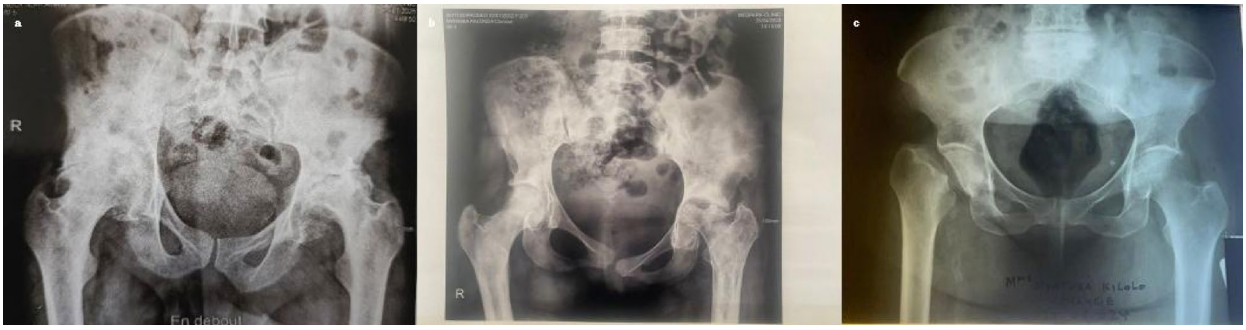

Fig. 2 radiographs of ONTF (a), osteoarthritis (b) and Neck femoral fracture (c)

operators. Today, the Haut-Katanga and Lualaba provinces remain among the world's leading producers of cobalt, with significant economic and environmental stakes linked to the global demand for renewable energy and electric batteries.

The study was conducted at Medpark Clinic in Lubumbashi, Haut-Katanga province, between February 2017 and March 2025. The site was selected based on three key criteria:

- *Geographical relevance*: Its proximity to active mining zones makes it ideal for studying orthopedic conditions potentially related to environmental exposures, such as ONFH.
- *Technical capacity*: The clinic offers modern surgical facilities capable of performing advanced orthopedic procedures, including total hip arthroplasties.
- *Academic partnership*: Medpark Clinic maintains a strong affiliation with the University of Lubumbashi, contributing to clinical research and the training of healthcare professionals, and serving as a regional reference center for musculoskeletal disorders.

All trace metal analyses were performed using ICP-OES at the certified laboratory of the Congolese Office of Control (OCC), specialized in trace metal quantification in biological matrices.

Population

Patients aged ≥ 18 years who underwent hip arthroplasty were eligible. Cases were defined as individuals diagnosed with idiopathic ONFH and having available femoral head specimens. Controls were patients undergoing hip replacement for primary osteoarthritis or femoral neck fracture, with no clinical or radiological signs of bone necrosis.

All included patients had resided for ≥ 5 years in the Katanga mining region and provided informed written consent. Exclusion criteria included sickle cell disease, neoplastic bone lesions, joint infections, rare systemic disorders (e.g., systemic lupus), or residence outside Katanga or less than 5 years in the region. Specimens that were degraded, contaminated, or unsuitable for ICP-OES analysis were also excluded.

Variables and definitions

The primary outcome variable was the presence or absence of ONFH, with patients classified as cases if ONFH was present and as controls if absent. The independent variables consisted of bone concentrations of eleven trace metals: lead (Pb), cadmium (Cd), cobalt (Co), arsenic (As), chromium (Cr), zinc (Zn), copper (Cu), manganese (Mn), magnesium (Mg), nickel (Ni), and aluminum (Al).

Exposure definition (Z-score method)

Bone trace metal concentrations were analyzed using the Z-score method in reference to a control population. The Z-score formula was:

$$z = \frac{X - \mu}{\sigma}$$

where:

- X is the individual bone concentration,
- μ is the mean concentration in the reference group.
- σ is the standard deviation in the reference group.

Reference group

The reference population consisted of 13 patients who underwent surgery for knee osteoarthritis and had no known necrotic pathology. Bone samples were collected from the knee (during total knee arthroplasty), and the concentrations of 11 TMEs were measured using the same procedure as for the case and control groups. The means and standard deviations of each measured TME in this group served as the basis for the calculation of Z-scores and are presented in the table below (see Table 1).

Table 1 Bone trace metal Concentrations - reference group

ETM	PARAMETRES							
	N	Xmin	Q1	Median	Mean	SD	Q3	Xmax
Pb	13	−0,92	−0,48	0,001	**−0,11**	**0,43**	0,16	0,68
Cd	13	−0,27	−0,01	−0,004	**−0,001**	**0,02**	−0,001	0,07
Zn	13	0,005	34,91	53,05	**45,35**	**19,34**	56,86	75,76
Cu	13	−0,73	0,27	1,48	**2,09**	**2,10**	3,69	6,54
As	13	0,001	0,50	0,71	**0,87**	**0,57**	1,10	2,19
Cr	13	0,002	1,52	7,07	**8,78**	**8,03**	14,68	26,77
Co	13	0,001	0,19	0,28	**0,35**	**0,24**	0,47	0,95
Mn	13	0,001	0,54	1,007	**1,004**	**0,54**	1,41	1,93
Mg	13	0,11	813,6	1058	**1012,91**	**468,70**	1212,5	1769
Al	13	−23,5	1,21	16,37	**11,85**	**15,29**	23,76	32,64
Ni	13	0,001	0,62	1,91	**2,52**	**2,16**	4,21	7,29

A Z-score > 2 was considered indicative of high exposure for a given metal

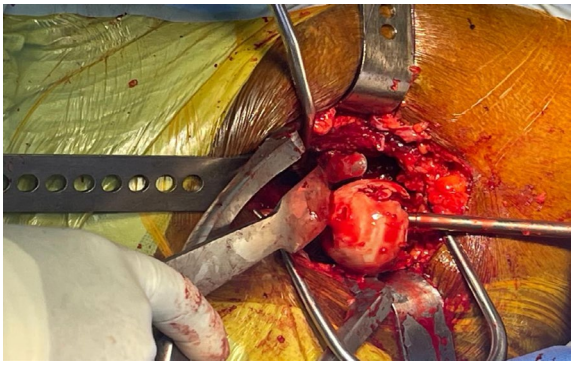

Fig. 3 Femoral head excision

Sample collection and analysis procedures

Femoral head specimens were collected during total hip arthroplasty procedures (Fig. 3). Immediately after extraction, each sample was handled under strict aseptic conditions to preserve its analytical integrity for trace metal analysis. The femoral heads were placed in sterile, additive-free polypropylene tubes to prevent any external contamination. Subsequently, the samples were stored at − 20 °C and maintained under continuous cold-chain conditions until their secure transfer to the analytical laboratory.

Laboratory pre-treatment

Bone fragments were first oven-dried at 105 °C using a Binder oven for approximately four hours until a

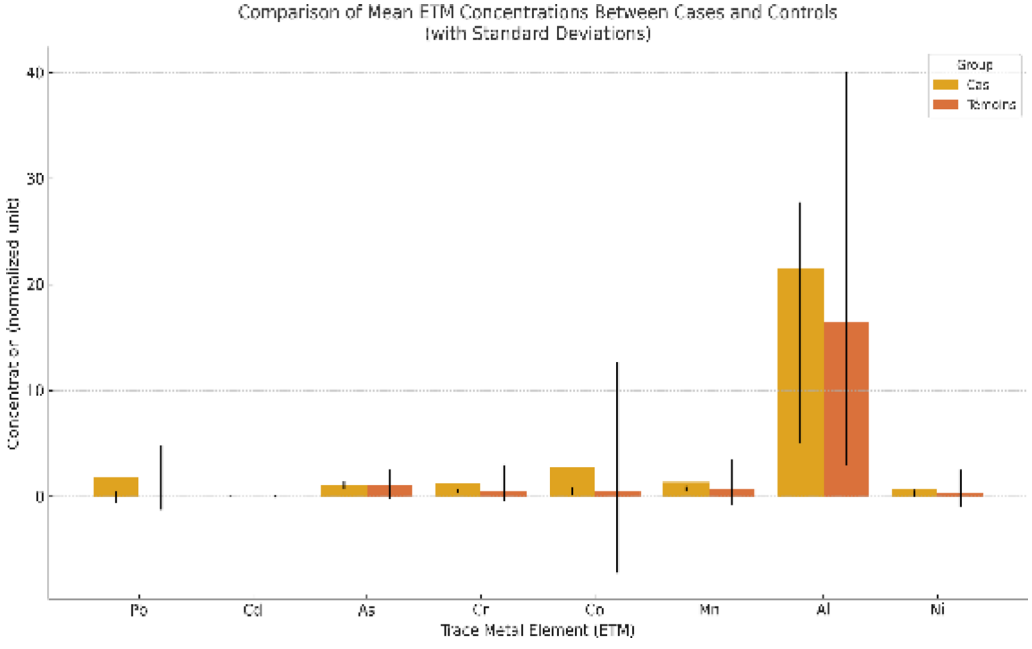

Fig. 4 Comparison of mean cases /controls

constant weight was achieved, ensuring complete moisture removal. The dried samples were then finely ground into a homogeneous powder. Exactly 0.3500 g of this bone powder was weighed using a Mettler Toledo analytical balance. Each sample underwent acid digestion using a 3:1 mixture of 37% hydrochloric acid (HCl) and 65% ultrapure nitric acid (HNO_3), with controlled heating until complete mineralization of the organic matrix was achieved. After cooling, the digest was diluted with ultrapure distilled water to a final volume of 40 mL and filtered through Whatman filter paper to eliminate lipid residues and solid particles. The resulting solution was analyzed using ICP-OES, a method known for its high sensitivity and accuracy in detecting ultra-trace levels of metals in biological tissues.

Trace metal quantification

Trace element concentrations were measured at the certified laboratory of the Congolese Control Office using a Perkin Elmer Optima 8300 ICP-OES system.

Analytical procedures

The analytical procedures included a rigorous calibration process performed using certified standard solutions provided by the National Institute of Standards and Technology (NIST) [48], covering the expected concentration ranges. Quality control measures incorporated reagent blanks and certified standard reference materials (SRMs) of osseous origin to ensure analytical accuracy, reproducibility, and traceability of the results. The trace metals analyzed in each sample were Pb, Cd, Co, As, Cr, Zn, Cu, Mn, Mg, Ni, and Al.

Table 2 Sociodemographic characteristics

Variable	Case ($n=36$)	Controls ($n=20$)	p-value
Age (years)	49,53 ± 15,71 (21–73)	62,90 ± 12,37 (26–78)	0,004
< 50	20 (55,6%)	2 (10%)	
≥ 50	16 (44,4%)	18 (90%)	
Sex			0,733
F	11 (30,6%)	7 (35%)	
M	25 (69,4%)	13 (65%)	
Provenance			0,359
Lubumbashi	17 (47,2%)	12 (60%)	
Outside Lubumbashi	19 (52,8%)	8 (40%)	
Worker (Mine)			0,882
Yes	12 (33,3%)	5 (31,3%)	
No	24 (66,7%)	11 (68,7%)	
Duration of residence (Years)			0,64
≥ 5	12(33,3%)	7(35%)	
5–9	10(27,7%)	4(20%)	
10–14	5(13,8%)	3(15%)	
≥ 15	7(19,4%)	6(30%)	

Data analysis

Data were entered in Microsoft Excel 2013 and processed using SPSS version 25 and Epi Info version 7.1.0.6.

Statistical approach

The statistical approach included both univariate and bivariate analyses. For quantitative variables with a symmetric distribution, the mean and standard deviation were calculated, whereas for asymmetric distributions, the median and interquartile range were used. Qualitative variables were summarized using absolute frequencies and percentages. Bivariate analysis was performed to assess associations between the dependent variable (presence of ONFH) and categorical independent variables, using the Chi-square test when expected frequencies were ≥ 5, or Fisher's exact test otherwise. An association was considered statistically significant when the p-value was less than 0.05 and the 95% confidence interval (CI) for the odds ratio (OR) did not include 1. For continuous variables, the normality of distributions was assessed using the Shapiro–Wilk test. Depending on the results, either the Student's t-test (for normally distributed variables, $p > 0.05$) or the non-parametric Mann–Whitney U test (for non-normal distributions, $p < 0.05$) was applied.

Results

Study population

A total of 56 patients were included in the analysis: 36 cases diagnosed with idiopathic ONFH and 20 controls who underwent hip arthroplasty for primary osteoarthritis.

Age and demographic characteristics

The mean age was significantly lower in ONFH cases compared to controls (49.5 ± 15.7 vs. 62.9 ± 12.4 years, $p = 0.004$). Patients under the age of 50 accounted for 55.6% of ONFH cases versus only 10% of controls ($p = 0.001$). There were no statistically significant differences between groups with respect to sex ($p = 0.733$), place of residence (Lubumbashi vs. outside, $p = 0.359$), or declared occupational exposure to mining activities ($p = 0.882$) (Table 2).

Bone trace metal concentrations

Bone samples from all participants were analyzed for 11 TMEs (Table 3). Overall, metal concentrations displayed considerable inter-individual variability. Lead and cobalt showed particularly high dispersion, with extreme values reaching 14.15 µg/g for Pb and 60.81 µg/g for Co. Most variables were non-normally distributed, as indicated by Shapiro–Wilk tests, supporting the use of non-parametric statistical methods.

Table 3 Bone trace metal Concentrations - ONFH / Controls groups

ETM	Reduction statistics								Distribution Nomality	
	n	Xmin	Q1	Median	Mean	SD	Q3	Xmax	statistic test	*P*-value
Pb	56	**−1,013**	−0,20	**0,38**	1,08	2,61	1,42	**14,15**	Shapiro-w	0,000
Cd	56	**−0,482**	−0,05	**−0,008**	−0,001	0,13	0,009	**0,79**	Shapiro-w	0,000
Zn	56	**33,15**	38,16	**51,9**	895,78	5640,87	61,99	**42,050**	Shapiro-w	0,000
Cu	56	**−0,387**	0,07	**0,97**	6,87	29,17	2,19	**202,5**	Shapiro-w	0,000
As	56	**0,061**	0,68	**0,98**	1,08	1,13	1,28	**8,88**	Shapiro-w	0,000
Cr	56	**0,321**	0,51	**0,77**	1,02	1,41	1,03	**10,51**	Shapiro-w	0,000
Co	56	**0,158**	0,37	**0,60**	1,93	8,07	1,02	**60,81**	Shapiro-w	0,000
Mn	56	**0,307**	0,54	**0,79**	1,09	1,81	1,10	**14,02**	Shapiro-w	0,000
Mg	56	**609,2**	970,67	**1111**	1357,30	1740,13	1299,75	**14,012**	Shapiro-w	0,000
Al	56	−18,08	8,35	19,49	**19,69**	**16,39**	27,64	72,13	Shapiro-w	0,128
Ni	56	**−0,007**	0,15	**0,25**	0,56	1,41	0,39	**9,20**	Shapiro-w	0,000

Table 4 Bone trace metal Concentrations - ONFH group

ETM	Reduction statistics								Distribution Nomality	
	n	Xmin	Q1	Median	Mean	SD	Q3	Xmax	statistic Test	*P*-value
Pb	36	**−0,42**	−0,15	**0,80**	1,75	3,04	2,17	**14,15**	Shapiro-wi	0,000
Cd	36	**−0,48**	−0,03	**−0,005**	0,002	0,16	0,02	**1,274**	Shapiro-wi	0,000
Zn	36	**33,15**	45,21	**57,31**	198,47	850,82	63,00	**5160**	Shapiro-wi	0,000
Cu	36	**−0,13**	0,87	**1,88**	10,57	36,02	3,74	**202,5**	Shapiro-wi	0,000
As	36	**0,06**	0,63	**0,93**	1,10	1,39	1,17	**8,88**	Shapiro-wi	0,000
Cr	36	**0,42**	0,71	**0,93**	1,30	1,70	1,13	**10,51**	Shapiro-wi	0,000
Co	36	**0,15**	0,51	**0,74**	2,71	10,02	1,21	**60,81**	Shapiro-wi	0,000
Mn	36	**0,30**	0,64	**4,96**	1,32	2,22	1,20	**14,02**	Shapiro-wi	0,000
Mg	36	**609,2**	948,75	**1159,5**	1498,89	2164,93	1348	**14,012**	Shapiro-wi	0,000
Al	36	−18,08	8,35	20,82	**21,51**	**18,50**	31,57	72,13	Shapiro-wi	0,297
Ni	36	**0,03**	0,18	**0,30**	0,74	1,72	0,45	**9,20**	Shapiro-wi	0,000

Concentrations in ONFH cases

In ONFH cases, mean concentrations of several TMEs were markedly elevated. Notably:

- Lead: mean = 1.75 µg/g, maximum = 14.15.
- Cobalt: mean = 2.72 µg/g, maximum = 60.81.
- Copper: mean = 10.57 µg/g, maximum = 202.5.

Manganese and zinc also presented high median values, suggesting possible metabolic or environmental imbalances. Aluminum was the only metal to follow a normal distribution ($p = 0.297$), while the others exhibited significant deviations from normality (Table 4).

Concentrations in controls

In contrast, the control group showed substantially lower median levels of Pb and Co. The distribution of most TMEs, including Pb, Cd, Mn, Mg, and Al, approximated normality. A few outlier values were observed for Zn and Cu, likely reflecting isolated environmental or dietary exposures (Table 5).

Association between lead exposure and ONFH

Elevated bone lead levels (defined as Z-score > 2) were observed in 55.6% of ONFH cases, compared to just 5.0% of controls ($p = 0.0002$). The calculated odds ratio (OR) for ONFH in patients with high lead levels was 23.75 (95% CI: 2.86–197.01), with a chi-square statistic of 14.02 (Table 6).

Association between Cobalt exposure and ONFH

Similarly, elevated bone cobalt levels were present in 41.7% of ONFH cases versus 5.0% of controls ($p < 0.05$). Exposure to high cobalt levels was associated with a 13.57-fold increased risk of ONFH (95% CI: 1.63–112.76) (Table 7).

Association with other trace metals

In bivariate analyses, no statistically significant associations were found between ONFH and elevated bone concentrations of Cd, Cr, As, Ni, Mn, Zn, Cu, Al. Only cobalt and lead remained significantly associated with the disease (Tables 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17; Fig. 4).

Table 5 Bone trace metal Concentrations - Control group

ETM	Reduction statistics								Distribution Nomality	
	n	Xmin	Q1	Médian	Mean	SD	Q3	Xmax	Statistic Test	*P*-value
Pb	20	−1,01	−0,55	−0,17	−0,11	0,55	0,27	1,42	Shapiro-wi	0,169
Cd	20	−0,43	−0,02	−0,01	−0,009	0,02	0,003	0,05	Shapiro-wi	0,170
Zn	20	37,18	44,75	49,0	2150,95	9391,26	56,29	42,050	Shapiro-wi	0,000
Cu	20	−0,38	−0,24	0,03	0,23	0,55	0,68	1,62	Shapiro-wi	0,048
As	20	0,26	0,74	1,2	1,04	0,40	1,37	1,47	Shapiro-wi	0,009
Cr	20	0,32	0,39	0,44	0,52	0,18	0,60	1,10	Shapiro-wi	0,004
Co	20	0,18	0,31	0,43	0,52	0,37	0,60	1,92	Shapiro-wi	0,000
Mn	20	0,32	0,45	0,67	0,68	0,25	0,88	1,12	Shapiro-w	0,300
Mg	20	885,9	975,87	1067,5	1102,45	159,0	1253,5	1386	Shapiro-w	0,113
Al	20	−6,17	9,31	19,04	16,43	11,36	24,59	33,07	Shapiro-w	0,114
Ni	20	-0,007	0,01	0,17	0,24	0,36	0,25	1,73	Shapiro-w	0,000

Table 6 Association between lead and ONFH

Pb Exposure	Cases (*n*)	%	Controls (*n*)	%	Total (*n*)	%	Chi-square	*p*-value	OR [95% CI]
Yes	20	55.6	1	5.0	21	35.7	14.02	0.0002	23.75 [2.86–197.01]
No	16	44.4	19	95.0	35	62.5			1 (reference)
Total	36	100	20	100	56	100			

Table 7 Association between Cobalt and ONFH

Co Exposure	Cases	%	Controls	%	Total	%	Chi-square	*p*-value	OR [95% CI]
Yes	15	41.7	1	5.0	16	28.6	8.47	0.004	13.57 [1.63–112.76]
No	21	58.3	19	95.0	40	71.4			1 (reference)
Total	36	100	20	100	56	100			

Table 8 Association between cadmium and ONFH

Cd Exposure	Cases	%	Controls	%	Total	%	Statistical Test	*p*-value	OR [95% CI]
Yes	5	13.9	1	5.0	6	10.7	Fisher's Exact Test	0.405	3.06 [0.33–28.26]
No	31	86.1	19	95.0	50	89.3			1 (reference)
Total	36	100	20	100	56	100			

Comment: The proportion of individuals with elevated cadmium concentrations was higher among cases (13.9%) than controls (5.0%), but the difference was not statistically significant ($p > 0.05$)

Table 9 Association between chromium and ONFH

Cr Exposure	Cases	%	Controls	%	Total	%
Yes	0	0.0	0	0.0	0	0.0
No	36	100	20	100	56	100
Total	36	100	20	100	56	100

No elevated chromium exposure was observed in either cases or controls

Table 10 Association between arsenic and ONFH

As Exposure	Cases	%	Controls	%	Total	%	Statistical Test	*p*-value	OR [95% CI]
Yes	1	2.8	0	0.0	1	1.8	Fisher's Exact Test	1.000	–
No	35	97.2	20	100	55	98.2			1 (reference)
Total	36	100	20	100	56	100			

Exposure to elevated arsenic levels was observed in 2.8% of cases versus none in controls; the difference was not statistically significant ($p > 0.05$)

Table 11 Association between nickel and ONFH

Ni Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	1	2.8	0	0.0	1	1.8		1.000	–
No	35	97.2	20	100	55	98.2			1 (reference)
Total	36	100	20	100	56	100			

No significant association observed between nickel exposure and ONFH

Table 12 Association between manganese and ONFH

Mn Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	3	8.3	0	0.0	3	5.4		0.545	–
No	33	91.7	20	100	53	94.6			1 (reference)
Total	36	100	20	100	56	100			

The difference in manganese exposure between cases and controls was not statistically significant ($p > 0.05$)

Table 13 Association between zinc and ONFH

Zn Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	2	5.6	2	10.0	4	7.1		0.611	0.53 [0.07–4.07]
No	34	94.4	18	90.0	52	92.9			1 (reference)
Total	36	100	20	100	56	100			

No significant difference in zinc exposure was observed between groups ($p > 0.05$)

Table 14 Association between copper and ONFH

Cu Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	5	13.9	0	0.0	5	8.9		0.148	–
No	31	86.1	20	100	51	91.1			1 (reference)
Total	36	100	20	100	56	100			

Higher copper exposure was observed in 13.9% of cases versus none in controls, without statistical significance ($p > 0.05$)

Table 15 Association between magnesium and ONFH

Mg Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	1	2.8	0	0.0	1	1.8		1.000	–
No	35	97.2	20	100	55	98.2			1 (reference)
Total	36	100	20	100	56	100			

Magnesium exposure was observed in one case only; difference not statistically significant ($p > 0.05$)

Table 16 Association between aluminum and ONFH

Al Exposure	Cases	%	Controls	%	Total	%	Fisher	*p*-value	OR [95% CI]
Yes	4	11.1	0	0.0	4	7.1		0.285	–
No	32	88.9	20	100	52	92.9			1 (reference)
Total	36	100	20	100	56	100			

Aluminum exposure was higher among cases (11.1%) but did not reach statistical significance ($p > 0.05$)

Table 17 Summary association between other metals and ONFH

Metal	Estimeted OR	IC 95%	significant Association
Pb	23,75	2,86–197,01	✓ Yes
Co	13,57	1,63–112,76	✓ Yes
Cd	3,06	0,33–28,26	✖ No
Cr	1		✖ No
Cu	~ 10	0,5–200	✖ No
Al	~ 7	0,4–150	✖ No
Zn	0,53	0,07–4,07	✖ No (protective tendency)
Mn	1	0,06–17,00	✖ No
Ni	1	0,01–150	✖ No
Mg	1	0,01–150	✖ No
As	1	0,01–150	✖ No

Discussion

Aseptic osteonecrosis of the femoral head is a complex and multifactorial disorder characterized by ischemic disruption of the subchondral bone, ultimately leading to necrosis, collapse, and secondary degenerative joint disease [1, 2]. Recent molecular studies have highlighted the role of genetic susceptibility, including ESR1 and APOE polymorphisms, as well as dysregulation of lipid metabolism and coagulopathy, which may predispose individuals to idiopathic forms [10–13]. In the southeastern provinces of DRC, widespread environmental contamination from unregulated mining activities raises the possibility that chronic exposure to heavy metals contributes to ONFH pathogenesis [33, 36].

Sociodemographic profile

Our findings confirm that ONFH disproportionately affects younger adults, with a significantly lower mean age among cases (49.5 years) compared to controls (62.9 years), consistent with previous reports [1, 49]. No significant association was found with sex, geographic origin, or declared mining activity, despite more than half of ONFH patients residing outside Lubumbashi. This pattern may reflect diffuse environmental exposure

independent of occupational mining, aligning with earlier studies documenting elevated heavy metal levels among non-miners living near industrial sites [40].

Environmental epidemiology and skeletal disorders

Global epidemiological evidence supports a link between chronic trace metal exposure and bone pathology. In Japan, the historical Itai-Itai disease investigation revealed severe cadmium-induced osteomalacia among chronically exposed women [50]. In China, elevated fracture rates and diffuse bone pain were reported in communities exposed to lead-polluted environments [51]. In South Africa, a higher prevalence of joint disorders was documented in workers exposed to chromium and cobalt in mining industries [52]. Despite this growing body of evidence, few studies have directly quantified metal levels in bone tissue, and even fewer have explored their role in ONFH pathogenesis, particularly in African populations. Our study contributes to closing this critical knowledge gap.

Bone metal accumulation profiles

We observed elevated bone concentrations of lead and cobalt in ONFH cases, both significantly associated with disease presence after multivariate adjustment. High bone lead levels were linked to a 23-fold increased risk of ONFH (adjusted OR = 23.75; 95% CI: 2.30-181.57), while cobalt exposure showed an adjusted OR of 13.57 (95% CI: 1.63-112.76). Lead is a well-recognized skeletal toxicant: it accumulates in bone, inhibits osteoblast proliferation and differentiation, disrupts angiogenesis, promotes osteoclast activity, and suppresses collagen synthesis [22, 30]– [31]. In rodent models, chronic lead exposure produces structural bone changes and necrotic lesions mimicking ONFH [53]. Cobalt, although classically associated with metallosis from metal-on-metal prostheses, also induces oxidative stress, mitochondrial dysfunction, and apoptosis in osteogenic cells [54–56]. Our detection of elevated cobalt in native bone (without implants) suggests chronic environmental accumulation, potentially via contaminated food or groundwater in cobalt-rich mining zones [33, 34]. Beyond bulk levels, the nanoparticulate fraction of cobalt has gained attention for its toxicokinetic and biological impact, an important avenue for future research.

Relevance of bone as a biomarker

Bone serves as a long-term reservoir for heavy metals, especially lead, which may remain sequestered for decades and can be mobilized during bone turnover, inflammation, or trauma [42, 57]. Compared to serum or urine, bone sampling provides a more robust indicator of chronic exposure, representing a key methodological strength of this study. To explore cumulative exposure, we stratified patients by duration of residence in the Copperbelt (5–9, 10–14, and ≥ 15 years). Although the chi-square test for trend was not statistically significant ($\chi^2 = 0.89$; $p = 0.64$), case distribution suggested progressive accumulation with longer residence. Interestingly, the higher proportion of cases in shorter-duration groups may reflect periods of intensified mining activity driven by global demand, potentially increasing local contamination. While speculative, this observation underscores the need for longitudinal environmental monitoring and larger multicenter cohorts to refine exposure–response thresholds.

Analytical methodology: strengths of ICP-OES

Inductively coupled plasma–optical emission spectrometry remains the gold standard for ultra-trace detection of metals in biological samples, offering high precision and simultaneous multi-element analysis [22, 58]. Our protocol employed certified reference standards and blanks to ensure accuracy and reproducibility, contrasting with earlier studies that relied on less reliable biomarkers such as blood or hair.

Strengths and limitations

Key strengths include the direct quantification of bone metal burden, the use of a local reference population for Z-score standardization, and multivariate adjustment for major confounders such as age and known risk factors. Limitations include a modest sample size ($n = 56$), which may reduce power for detecting less frequent exposures; the absence of environmental measurements (soil, water, air); and potential unmeasured confounders such as diet, micronutrient status, and genetic predisposition [10, 11].

Implications and perspectives

Our findings demonstrate that lead and cobalt bioaccumulation in bone is independently associated with ONFH in a mining-exposed population. This provides novel evidence in environmental orthopedics and highlights the musculoskeletal risks of chronic heavy metal exposure. It calls for: large-scale, prospective cohort studies in highly exposed populations, environmental surveillance integrating skeletal biomarkers, public health interventions including soil remediation and community education, and stricter regulation of mining and metallurgical emissions.

From a clinical standpoint, ONFH management is increasingly stage-adapted and hip-preserving whenever feasible. Core decompression remains the cornerstone for early disease and achieves better outcomes when combined with biologic augmentation (bone marrow stem cells, growth factors) [43, 44]. Cell-based and scaffold-assisted techniques show promising mid-term results in precollapse stages [45]. Corrective osteotomies

may still benefit selected young patients with localized lesions [46]. In advanced collapse, modern THA with durable bearings offers excellent function and long-term survivorship even in relatively young adults [47]. However, such advanced therapies remain largely inaccessible in low-resource settings, where delayed diagnosis and limited surgical capacity hinder timely intervention.

Conclusion

This study provides the first direct evidence that chronic bone accumulation of lead and cobalt is strongly associated with idiopathic aseptic osteonecrosis of the femoral head in a population chronically exposed to mining-related pollution in the Democratic Republic of the Congo. By using femoral head bone tissue obtained during total hip arthroplasty and analyzing trace metal concentrations with ICP-OES, we were able to capture a retrospective and integrative marker of long-term exposure, which is more reliable than transient biomarkers such as blood or urine.

Our findings suggest that lead and cobalt may contribute to the pathogenesis of ONFH through mechanisms including osteoblast dysfunction, impaired angiogenesis, oxidative stress, and mitochondrial damage, thereby promoting bone ischemia and structural collapse. These data add an important environmental dimension to the current understanding of ONFH, which has previously focused primarily on genetic predisposition, metabolic dysregulation, and corticosteroid or alcohol exposure.

From a clinical perspective, these results highlight the need to consider chronic environmental metal exposure in the diagnostic evaluation of patients presenting with idiopathic ONFH, particularly in mining-intensive regions. They also call for integrated public health strategies, including environmental monitoring, regulation of mining activities, and community education to reduce exposure. In parallel, improving early detection and facilitating access to hip-preserving interventions could help delay or prevent the need for total hip arthroplasty in affected populations.

Future studies with larger cohorts, longitudinal designs, and direct environmental measurements are needed to confirm these findings, define exposure thresholds, and explore gene–environment interactions that may modulate susceptibility to ONFH.

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Author contributions

Author ContributionsCédrick Sangwa Milindi: Conceptualization, methodology, data collection, surgical procedures, formal analysis, writing original draft.Celestion: Laboratory analysis of trace metal concentrations, data curation.Michel, Willy : Statistical analysis, data validation, critical review of the methodology. Adelin, Luc : Supervision, project administration, manuscript review and editing.All authors read and approved the final version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent of participate

This research followed international bioethical principles, including respect for autonomy, justice, non-maleficence, and beneficence. Ethical approval was obtained from the Medical Ethics Committee of the University of Lubumbashi (Ref: UNILU/CEM/131/2022, dated 15/06/2022). All participants (both ONFH cases and controls) signed informed consent forms after being fully informed about the study's objectives, procedures, risks, and potential benefits. Bone samples were obtained exclusively from residual tissue collected during routine therapeutic surgery (hip arthroplasty), with no additional invasive procedures. While participants received no direct therapeutic benefit, the study aims to improve future ONFH management by identifying underrecognized environmental risk factors. All data were handled with strict confidentiality and scientific integrity.

Competing interests

The authors declare no competing interests.

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