

Research Article

Essential Metallic Trace Elements in Post-Delivery Mothers and their Newborns Residing Near and Far from Mining Operating Plants in Lubumbashi

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Abstract

Background: Worldwide, modern life is characterized by excess of toxic TE due to pollution (domestic and industrial waste) and reduced intake of essential TE, consequence of imbalanced diet. In the context of cases of environmental pollution by TE documented in the city for years, the purpose of this study was to determine blood concentrations of

essential TE and correlation coefficients in post-delivery mothers and their newborns living < of 3km and >3km from the mining processing plants in the city of Lubumbashi, Congo.

Method: Two prospective cohorts were formed based on distance between the home of the pregnant women and mineral processing plants (< of 3km and >3km).

Four TE (Cr, Cu, Se and Zn) were tested at the laboratory of the Congolese Control Office of Lubumbashi by ICP-OES in total blood samples of 378 post-delivery mothers and 378 newborns, voluntarily and consecutively recruited.

Results: The difference in TE geometric means concentrations between the two cohorts (study population living < of 3km and >3km from the mining processing plants) was not significant ($p>0.05$). Our study showed excessive geometric means of Cr estimated at 4.86 $\mu\text{g/L}$ in the post-delivery mothers and 5.03 $\mu\text{g/L}$ in the newborns (RV: < 1 $\mu\text{g/L}$), lower geometric means estimated at 218 $\mu\text{g/L}$ in the post-delivery mothers for Cu (RV: 700-1500 $\mu\text{g/L}$); 47.32 $\mu\text{g/L}$ in the post-delivery mothers and 46.61 $\mu\text{g/L}$ in the newborns for Se (RV: < 142 $\mu\text{g/L}$); 419 $\mu\text{g/L}$ in the post-delivery mothers and 384 $\mu\text{g/L}$ in the newborns for Zn (RV: < 7270 $\mu\text{g/L}$) but within normal range: 215 $\mu\text{g/L}$ in the newborns for Cu (RV: 90-460 $\mu\text{g/L}$). This was confirmed by their respective bioaccumulation factors. The correlation coefficient between TE concentration of the post-delivery mothers and their newborns was positive but statistically significant for Cu, Se and Zn ($p<0.05$).

Conclusion: Our study has noticed low geometric means of the concentrations of Cu, Se and Zn in total blood of post-delivery mothers and their newborns living < 3km and >3 km from the mining operating plants with no statistical difference between the two cohorts along with bioaccumulation factor <1. We also found excessive geometric mean for Cr. These findings hence the importance of an early diagnosis and intervention of marginal TE status. Analysis of determinants of the essential TE bioaccumulation and their impact on maternal and neonatal morbidity should be purpose of future studies.

Keywords: Essential metal trace elements; Post-delivery mothers; Newborns; Lubumbashi

Abbreviations and Acronyms

Cr= Chromium

Cu= Copper

Se= Selenium

Zn= Zinc

TE= Metallic Traces Elements

RV= Reference value

BF= Bioaccumulation factor

Ppm= particle per million

UNILU= University of Lubumbashi

1. Introduction

The WHO has grouped TE into three categories depending on their health impact: potentially toxics (F, Pb, Cd, Hg, Al, As, Sn, Li.); probably essentials (Mg, Mn, Si, Ni, B, V, Co) and essentials (Cr, Cu, Zn, Se, Mo, I) [1, 2]. The essentiality of an element is related to its physiological important functions affecting the well-being of the organism and the survival of the species [3]. Essential trace elements play an important role as cofactors for certain enzymes involved in metabolism of proteins, carbohydrates, lipids, and energy. They are also necessary for growth, development, muscle and nerve function, normal cellular functioning, and synthesis of some hormones and connective tissue [4]. Consistent changes in the concentration of any of these TE are much more meaningful than a reduced activity of a specific enzyme, which can be compensated by changes in another enzyme system [3].

The organism's functions react to progressively increasing exposures to TE. Therefore, it appears that there are no "toxic" elements; only are toxic

exposures. The spectrum of TE nutriture ranges from deficient, to marginally adequate, to fully adequate, to marginally excessive, to toxic. Toxicity is primarily a function of concentration of a substance in the organism. Excesses of all essential elements, including the most vital one, oxygen, are toxic [3-5].

Deficiency of an essential TE is associated with impairment of physiologically important functions. In the presence of excesses of others TE, the deficiency of an element may contribute to the pathogenesis of some chronic diseases. If compensatory mechanisms fail, depending on the element, oxidative damage, metabolic changes, such as hyperlipidemia, hyperglycemia, or hormonal imbalances, may appear and must absolutely be treated. Nutritional intervention can be expected to restore normal function, but this will not be possible if the clinical deficiency phase is reached, during which pathological changes may be irreversible [3, 5].

Worldwide, modern life is characterized by excess of toxic TE due to pollution (domestic and industrial waste) and reduced intake of essential TE, consequence of imbalanced diet [6-22]. In Lubumbashi very low concentrations were found in children for essential TE (Cu, Se, Zn, and Fe) [23]. In the context of cases of environmental pollution by TE documented in the city for years [24, 25, 26-28], the objective of this study is to determine the total blood concentrations and correlation coefficient of essential TE in post-delivery mothers and their newborns living < of 3km and >3km from the mining processing plants in Lubumbashi.

2. Methodology

2.1 Study design

A prospective cohort study of mothers and newborns exposed to TE was conducted from November 30, 2018 to May 30, 2019.

2.2 Study area

The study was done in Lubumbashi, a city born from the exploitation by the Union Minière du Haut Katanga (Gécamines) of copper deposits (1906-1910). Since the 2000s, minerals are also exploited by private mining companies including: STL, Ruashi mining, Chemaf, Somika, CDM, Anvil Mining, etc.

2.3 Study population

It was composed by post-delivery mothers and their newborns consecutively enlisted in ten medical institutions in Lubumbashi (Lubumbashi University Clinics, Jason Sendwe Provincial General Hospital, CMDC, Imani Polyclinic, Tshamilemba Learning and Researcher Health Center, la garde Medical Center, Ruashi Military Hospital, Eben Ezer Health Center, Crisem Medical Center, and Luna Medical Center). The monofetally pregnant women included in the study should have clearly consented to participate in the study; have their antenatal consultations in the host institution and give birth there. These pregnant women should have lived in the city for at least 2 years and spent the entire gestation period in the study district. They should not be smokers or have a smoking spouse/partner. According to the distance between the residential area and a mineral processing plant (<3 km and >3 km) the study population has been divided in two cohorts.

This distribution is supported by the previously documented finding that in neighbourhoods less than 3 km from metallurgical industries or mining activities the geometric means of urinary concentrations of TE (As, Cd, Co, Cu, Pb and U.)

were significantly higher than those found in people living between 3 and 10 km [24] . We have used google map to locate the various ore processing plants of the city of Lubumbashi and established a perimeter of 3km around the factory to categorize the residential districts according to whether or not they end up within the 3km perimeter.

2.4 Data collection

Data collection sheets with a semi-closed questionnaire were used to collect the data. Trained investigators collected history, physical and morbid information during gestation and at delivery, then in immediate postpartum blood samples. Each data collection sheet had a code matching with the one found on the Eppendorf tubes used to collect blood samples. The data collection sheets, and the Eppendorf tubes were transmitted daily to the principal investigator. Blood collected by puncture of the post-delivery mother's cubital vein and umbilical vein of the newborn was stored at 10⁰ C in Eppendorf tubes without EDTA, before processing by the laboratory of the Congolese Control Office (OCC/Lubumbashi). After TE dosage, results were transmitted to the principal investigator.

2.5 Metal trace elements analysis

The dosage of TE in total blood was done using Perkin Elmer brand ICP- OES Optima 8300 (Optical Emission inductively coupled plasma spectrometry system) at the laboratory of the Congolese Control Office (ISO 9150 quality certification since 2010). The following essential TE (Cr, Cu, Se and Zn) were measured.

3. Bioaccumulation Factor (BAF)

TE have the ability to accumulate in living organisms. The living organism is able to metabolize and

eliminate TE and the concentration observed is the result of absorption and elimination phenomena. The Bioaccumulation factor (BAF) of a substance therefore represents the total intake coming from the environment (environment) and food. There is a health risk for humans in terms of intoxication when the value of BAF> 1 for both potentially toxic and essential TE, and deficiency if the value is <1 for essential TE. The BF reflects normal state (no health risk) for potentially toxic TE if <1 [29].

3.1 Statistical analysis

Our data was encoded using the EPI info 7 software. The Kolmogorov-Smirnov test (K-S test) allowed us to test the normality and log-normality of the data distribution. We used the XLSTAT 2019.2.2 software. 59614, to calculate arithmetic and geometric means of blood TE levels. SPSS 23 allowed us to compare the geometric means of TE concentrations in the two cohorts by one way ANOVA and to analyze the nominal variables presented in percentages, the calculation of the correlation coefficient of concentrations in the maternal compartments and the newborn performed for each TE.

3.2 Ethical considerations

This study was approved by the Medical Ethics Committee of the School of Public Health of the University of Lubumbashi (UNILU/CEM/117/2018 delivered the 10/10/2018).All study participants gave their informed consent prior to answer to the questionnaire and collection of blood samples.

4. Results

4.1 Participation in the study and socio-demographic profile of the post-delivery mothers included in the study

A total of 378 post-delivery mothers and 378 newborns were included in the study. Table 1 presents

the socio-demographic characteristics of the post-delivery mothers.

Sociodemographic characteristics	number (n=378)	Pourcentage (%)
Age (years)		
<18	2	0,50
18-35	321	84,90
>35	55	14,6
Residential district		
< 3km from mining plants	152	40.2
> 3km from mining plants	226	59.8
Level of education		
Analphabete	19	5,0
Primary school	30	7,9
Secondary school	184	48,7
University	138	36,5
Post-graduate	7	1,9
Occupation of the pregnant woman		
Unemployed	243	64,3
State official	68	18,0
Informal	65	17,2
Artisanal miner	2	0,5
Profession of the partner/spouse		
State official	216	57,1
Informal	143	37,8
Artisanal miner	14	3,7
Unemployed	5	1,3
Parity		
Nulliparous(0)	4	1,1
Primiparous (1)	86	22,8
Pauciparous (2-3)	140	37,0
Multiparous (4-5)	91	24,1
Large multiparous (≥6)	57	15,1

Table 1: Sociodemographic characteristics of the post-delivery mothers.

The mean age of the post-delivery mothers was 29 ± 6 years; the majority (59.8%, n=226) resided in neighbourhoods located >3 km from the mines; 48.70% (n= 226) had a secondary education level and 36.5% (n=138) university level;64.30% (n=243) were unemployed;57.10% (n=216) had a spouse state official;37% (n=140) were pauciparous, 22.8% (n=86) of primiparous and 15.1% (n=57) of large multiparous.

4.2 Geometric means of essential TE in cohorts residing near and far from mining operating plants (<3Km;>3Km)

Table 2 summarizes the comparison of the geometric means of the concentrations of TE in post-delivery mothers and their newborns residing < 3km and >3 km from mineral processing plants.

Maternal TE	Number of samples	Geometric mean <3km	Geometric mean >3km	p value (CI 95%)	Newborns TE	Number of samples	Geometric mean <3km	Geometric mean >3km	p value (CI 95%)
Cr	181	4.9	4.78	0.950	Cr	189	4.72	5.34	0.440
Cu	366	227.1	208.8	0.316	Cu	366	217.3	212	0.254
Se	196	45.2	49.3	0.855	Se	196	44.6	48.6	0.361
Zn	254	425.4	412.1	0.371	Zn	254	386.1	381.3	0.160

Table 2: ANOVA of geometric means of essential TE concentration in post-delivery mothers and their newborns in the cohorts (<3Km;>3Km).

This table shows that the difference between geometric means of essential TE concentrations based on the distance from the residential districts of the study population and the mineral processing plants is not statistically significant (p>0.05).

4.3 Geometric means of essential TE and bioaccumulation factors in the total blood of post-delivery mothers and newborns

Table 3 shows geometric means of toxic TE concentration in total blood of post-delivery mothers and their bioaccumulation factors.

Metallic trace elements	Number of samples	Geometric mean (µg/L)	Reference value (µg/L) (source)	Bioaccumulation factor (µg/L)	Observation
Cr	181	4.86	< 1 [30]	4.86	High
Cu	366	218	700-1500 [30]	0.31	Low
Se	196	47.32	< 142 [16]	0.33	Low
Zn	254	419	< 7270 [8]	0.06	Low

Table 3: Concentrations of essential TE in total blood of post-delivery mothers and their bioaccumulation factors.

Compared to reference values, we found that the geometric means of essential TE concentrations in the total blood of the post-delivery mothers were high for Cr (BF>1) but low for Cu, Se, and Zn with bioaccumulation factors < 1.

Table 4 shows geometric mean of essential TE in newborns and their bioaccumulation factors.

Metallic trace elements	Number of samples	Geometric mean (µg/L)	Reference value (µg/L) (source)	Bioaccumulation factor (µg/L)	Observation
Cr	189	5.03	< 1 [30]	5.03	High
Cu	366	215	90-460 [30]	2.39	Normal
Se	196	46.61	< 142 [16]	0.33	Low
Zn	254	384	< 7270 [8]	0.05	Low

Table 4: Concentrations of essential TE in total blood of newborns and their bioaccumulation factors.

For newborns, the geometric mean of essential TE concentrations in total blood were also high for Cr (BF>1), within normal range for Cu (BF>1), but low for Se and Zn with bioaccumulation factors < 1, compared to reference values.

4.4 Correlation between essential TE in total blood of the post-delivery mothers and newborns

Table 5 shows correlation coefficients and p values that exist between the concentrations of essential TE in the total blood of the post-delivery mothers and the concentrations of toxic TE in the total blood of the newborns.

TE	Maternal mean (µg/L)	Newborns mean (µg/L)	Correlation coefficient	P value
Cr	4.86	5.03	1.03	0.247
Cu	218	215	0.057	0.0305
Se	47.32	46.61	0.326	0.000
Zn	419	384	0.293	0.000

Table 5: Correlation coefficient of the concentration of essential TE in total blood of post-delivery mothers and newborns.

This table shows that mean concentrations of essential TE in post-delivery mothers and their newborns are positively correlated. The correlation coefficient is statistically significant only for Cu, Se and Zn (p < 0.05).

5. Discussion

The purpose of this study was to determine the total blood concentration of essential TE and their correlation coefficient in post-delivery mothers and their newborns in the city of Lubumbashi. The main

results presented in Tables 2, 3 and 4 show the geometric means of essential TE expressed in $\mu\text{g/L}$ and their bioaccumulation factor. While Table 5 reflects TE correlation coefficient in maternal and neonatal compartments. Table 6 compares our results to others studies worldwide.

5.1 Comparison of geometric means of essential TE in cohorts residing near and far from mining operating plants

It appears from our study that the difference in geometric means of essential TE concentrations in the two cohorts is not statistically significant. ($p > 0.05$) (Table 2). This finding can be supported by the fact that, contrarily to potentially toxic TE, the concentration of essential TE in human is mainly related to intake from food and beverage [10]. Therefore, the type of food and its diversity matter. Minerals form about 5% of the typical human diet but are essential for normal health and function [11]. In a city like Lubumbashi source of nutriment, eating habits and diet are quietly the same for inhabitants and mostly culturally based thus do not depend on a specific location.

5.2 Blood concentrations of essential TE in post-delivery mothers and their newborns

Compared to reference values we found that the geometric means of essential TE concentrations in the total blood of post-delivery mothers were high for Cr but low for Cu, Se, and Zn. For the newborns they were also high for Cr, within normal range for Cu, but low for Se and Zn (Table 3 and 4).

Although TE are essential components of biological activities, the excessive levels are toxic and may lead

to many fatal diseases, such as cancers [3, 8, 9]. Excessive concentration of Cr found in our study, though essential is a concern. Cr is a trace element that humans require in trace amounts. It is found primarily in two forms: Trivalent (chromium III), which is biologically active and found in food and hexavalent (chromium VI), a toxic form that results from industrial pollution [8]. Therefore, high concentration of Cr in the total blood of post-delivery mothers and their newborns can be a consequence of pollution as documented by previous studies in Lubumbashi [24, 25, 26-28]. Cr is widely distributed in the food supply, but most foods provide only small amounts of it (egg yolks, whole-grain products, high-bran breakfast cereals, coffee, nuts, green beans, broccoli, meat, and brewer's yeast) [4].

Low levels of Cu, Se and Zn can be related to an imbalance diet. Essential TE are provided to the organism through food and beverage. Zn is found in wheat, brown rice, oats, lentils, soybeans, dried peas, black-eyed peas, lima beans, walnuts, peanuts, cashews, brazil nuts, many cheeses, any kind of liver, and animal flesh such as beef, lamb, chicken, turkey, and various fish and seafood. It is also found in most vitamin mineral supplements as sulfate, citrate, or oxide and these are inexpensive and bioavailable sources. The best dietary sources of Cu to human body include wheat, barley, sunflower seeds, almonds, pecans, walnuts, peanuts, cashews, prunes, raisins apricots, various dried beans, mushrooms, chicken, and most fish. The best food sources for selenium are seafood, meats, whole grains, and some vegetables. It has been found that the raw foods contained considerably more selenium than cooked and processed foods [4].

Country		Geometric means of toxic TE concentrations in the post-delivery mothers(µg/L)	Geometric means of toxic TE concentrations in the newborns (µg/L)	References
Chromium (Cr)				
DRC(Lubumbashi)	378/378	4.86	5.0	Our study
China (Beijing)	156/156	6.36 ± 8.08 (<0.10–37.9)	12.6 ± 26.3 (<0.10–238)	[13]
China (Ma'anshan)	2382/2382	2.88 (1.52-8.00)	2.63 (1.43-9.82)	[14]
France (Nord)	578	0.47 [0.43 - 0.51]		[8]
France (Le Havre)	106	4.40 (0.33–0.87)		[16]
Italy		0.08 -0.5		[11]
Spain (canary Island)	471		1.10 ± 0.66	[14]
Spain (Valencia)	54/54	1.508	3.6244	[19]
Spain (Tarragona)	40/31	0.5 (0.2–1.2)	0.6 (0.1–2.5)	[20]
Cooper (Cu)				
DRC(Lubumbashi)	378/378	218	215	Our study
Belgium (Flanders)	235/241	1312 (1279–1347)	600 (585–615)	[9]
Brazil (Parana)	512	1182.8 (1139.4, 1227.8) RV : 2141.1		[15]
Canada (Québec)	100	1075(794–2023)		[10]
China (Shenjing)	180/180	1410.5 (539.9-2636.0)	464.4 (193.5-1967.0)	[21]
China (Ma'anshan)	2382/2382	2030 (1410-2880)	300 (180-570)	[13]
France (Le Havre)	106	731(743–1513)		[16]
Italy		600 – 1400		[11]
Italy (Rome)	143		305	[12]
Nepal (Terai)	94	652		[17]
South Africa	96/96	1600(1329–2035)	641(384–1165)	[18]
Spain (canary Island)	471		402.04 ± 193.95	[14]
Spain (Valencia)	54/54	1461.558	260.5386	[19]
Spain (Tarragona)	40/31	1664(892-2626)	623(386–813)	[20]
Zinc (Zn)				
DRC(Lubumbashi)	378/378	419	384	Our study
Brazil (Parana)	512	6306.9 (6053.8, 6570.7) RV : 12076.3		[15]
Canada (Québec)	100	726(551–925)		[10]
China (Shenjing)	180/180	5747.0 (2300.0-8620.0)	1793.0 (789.0-13850.0)	[21]
China (Ma'anshan)	2382/2382	810 (600-1130)	900 (650-1330)	[13]
France (Nord)	1016	5487 [5432 - 5542]		[8]
France (Le Havre)	106	5135 (4220–7198)		[16]
Italy		4000-8000		[11]
Italy (Rome)	143		901	[12]
Nepal (Terai)	94	2202		[17]
South Africa	96/96	5849(3745–8075)	2338(1558–4738)	[18]
Spain (canary Island)	471		1179 ± 417	[14]
Spain (Valencia)	54/54	758.408	693.028	[19]
Spain (Tarragona)	40/31	6708(4071-9064)	2311(1489–3049)	[20]
Selenium (Se)				
DRC(Lubumbashi)	378/378	47.32	46.61	Our Study
Brazil (Parana)	512	85.4 (83.7, 87.1) RV: 132.2		[15]
Canada (Québec)	100	112(79–141)		[10]
Canada (Québec)	317	216.535 (206.661- 224.409)		[22]
China (Ma'anshan)	2382/2382	70.27 (45.14-106.60)	43.21 (26.30-76.01)	[13]
France (Le Havre)	106	151 (85–142)		[16]
Italy		80-140		[11]
Italy (Rome)	143		43.7	[12]
Nepal (Terai)	94	168		[17]
South Africa	96/96	100(82–153)	99(79–182)	[18]
Spain (canary Island)	471		66.69 ± 24.31	[14]
Spain (Valencia)	54/54	55.432	34.5196	[19]
Spain (Tarragona)	40/31	107(37-156)	100(40–170)	[20]

Table 6: Comparison of essential TE geometric means concentrations in post-delivery mothers and their newborns in Lubumbashi to the results published by other authors.

Compared to other studies our results are similar: low concentration of essential TE; but for Cr our concentration was higher than those found in other studies except in China (Table 6). These findings can be related to eating habits in pregnant woman in Lubumbashi, such as geophagia and some cultural beliefs that counsel pregnant woman not to take some categories of food, resulting in an imbalanced diet. High levels of Cr are related to environmental pollution in our study and elsewhere. These abnormally high concentrations of Cr and low levels of Cu, Se and Zn in the blood of post-delivery mothers of Lubumbashi are a public health problem given the potential effects on pregnancy as they play important roles in the metabolism (carbohydrate metabolism, fatty and cholesterol synthesis, growth, production of hemoglobin, protein and DNA synthesis, antioxidant role and healthy immune system,...) [4].

5.3 Bioaccumulation factors of essential TE in post-delivery mothers and their newborns

Bioaccumulation factors in post-delivery mothers and their newborns for Cr was >1 , Se and Zn had a BF <1 in the post-delivery mothers and their newborns but for Cu this BF was <1 in the post-delivery mothers and >1 for their newborns. Bioaccumulation of a substance is its ability to accumulate in living organisms. The living organism is able to metabolize and eliminate the substance and the concentration observed is the result of absorption and elimination phenomena. The BF of a substance therefore represents the total intake coming from the environment and food [30].

A BF > 1 is abnormal and reflects abnormal and long-term exposure to TE through different sources:

contamination of drinking water, groundwater, streams, and fishing products (crustaceans, shellfish, and fish) and vegetables growing on polluted soils [24, 25, 26-28, 31]. Excessive concentration of essential TE makes them to become toxic in our study we noticed a BF >1 for Cr in the post-delivery mothers and their newborns which is toxic but for Cu in the newborns, though the BF >1 , the concentration is within normal range.

A BF < 1 of an essential TE reflect a deficiency state. Deficiency of an essential TE is associated with impairment of physiologically important function, preceded by changes in the metabolism of the specific TE that compensate for the suboptimal intake by improved conservation and utilization. This "initial depletion phase" can revert to a normal status after nutritional intervention; it can also persist for decades. The second phase, the "compensated metabolic phase," indicates a markedly increased risk for deficiency, but according to the WHO criteria, not deficiency itself. When the various compensatory mechanisms also fail, the "decompensated metabolic phase" ensues with its deterioration of physiologically important functions. Depending on the element, oxidative damage, metabolic changes, such as hyperlipidemia, hyperglycemia, or hormonal imbalances, may appear. Such changes, when diagnosed, are absolute indications for therapy. Nutritional intervention at that time can be expected to restore normal function, which is not always the case when applied during the following "clinical phase," during which pathological changes may be irreversible. These considerations of the sequence of events emphasize the importance of an early diagnosis and intervention of a marginal trace element status [2].

5.4 Correlation coefficients between essential TE concentrations in total blood of post-delivery mothers and newborns

The concentration of essential TE in post-delivery mothers and newborns were positively correlated (Table 5). The correlation coefficient was statistically significant only for Cu, Se and Zn ($p < 0.05$). These correlation coefficients reveal that the unique source of fetal essential TE intake is its mother. Impaired fetal development and pregnancy evolution can occur if essential TE are not at an optimal concentration in the pregnant, fetal and child development are sensitive to nutritional imbalance, stress, and environmental influences. Toxic and essential TE status before conception and during gestation can have adverse effects on gene expression, especially of those involved in fetal development [32]. Our results demonstrate the need to provide the fetus, optimal essential TE status through the pregnant woman due to the physiological immaturity of its main systems.

6. Conclusion

Our study has noticed low geometric means of the concentrations of essential TE in total blood of post-delivery mothers and their newborns living < 3 km and > 3 km from the mining operating plants with no statistical difference between the two cohorts along with bioaccumulation factor < 1 . These findings hence the importance of an early diagnosis and intervention of marginal TE status. Analysis of determinants of the essential TE bioaccumulation and their impact on maternal and neonatal morbidity should be purpose of future studies.

Conflicts of Interest

None.

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