

# Maternal Morbidity Associated to Exposure to Trace Elements in Lubumbashi

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**Abstract:** *Background:* Pregnant women are exposed to toxic trace elements (TE) from mining plants. The aim of this study was to determine the incidence of morbid conditions among pregnant women and their relations to blood's concentration of TE and their exposure factors in Lubumbashi. *Methodology:* A prospective cohort study of 378 mothers and 378 newborns exposed to TE was conducted from November 30, 2018, to May 30, 2019. The groups were constituted whether the TE concentration was higher or lower than the reference value. (Determined by ICP- OES Optima 8300 at the laboratory of the OCC/Lubumbashi). Correlation between the morbid conditions in the two groups and with each exposure factors by calculating chi square and the relative risk were obtained. ( $p < 0.05$ ) *Results:* Among pregnant women 61.4% had malaria, 47.6% anemia, 21.2% hypertension, 11% IUGR newborns and 8.7% a premature birth. Geophagia increased two times the risk of anemia [RR: 2.127 (1.410-3.209)] and hypertension [RR: 1.958 (1.177-3.259)]. The proximity to mining plants increased three times the risk of anemia [RR: 2.887 (1.830-5.554)] and hypertension [RR: 3.126 (1.876-5.208)]. The use of well water for drinking and housework increased two times the risk of hypertension [RR: 2.308 (1.385-3.845)] and IUGR newborn [RR: 1.752 (1.232-2.490)]. Biomass used for cooking increased three times the risk of hypertension [RR: 3.204 (1.114-9.212)]. Women working in mining plants had two times the risk of malaria: [RR 1.725 (1.145-2.599)]. Women whose husband worked in mining plants had three times the risk of premature birth [RR: 3.204 (1.552-6.616)]. High lead concentration increased five times the risk of anemia [RR: 4.63 (2.933-7.310)]; height times the risk of hypertension [RR: 8.170 (4.657-14.333)]; three times the risk of a IUGR newborn [RR: 2.601 (2.078-3.256)]. The linear correlation between lead and maternal hemoglobin was negative ( $r -0.335$ ). High maternal concentration of cobalt, arsenic and cadmium increased two times the risk of hypertension. High maternal magnesium and high neonate cadmium concentrations increased two times the risk of premature births. High neonate lead, cobalt, zinc, and magnesium' concentrations increased two times the risk of maternal anemia. But high neonate selenium concentration reduced to 60% [RR: 0.59 (0.360-0.978)] this risk. Low neonate selenium concentration increased four times the risk of IUGR neonate [RR: 4.116 (2.004-8.452)]. *Conclusion:* High concentration of toxic TE and low concentration of some essential TE in the blood of pregnant women are associated to morbid conditions such as anemia, malaria, maternal hypertension, IUGR and prematurity.

**Keywords:** Trace Elements, Maternal Morbidity, Exposure Factors, Mining Plants, Lubumbashi

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## 1. Introduction

Women's health during pregnancy, childbirth, and the postpartum period is a big concern among health workers and health policies makers. One of the main indicators of a country's status in maternal health is the maternal mortality ratio. This ratio is only a small fraction of the burden of maternal morbidity. Maternal deaths are the tip of the iceberg and maternal morbidity the base; for every woman who dies of pregnancy-related causes, twenty or thirty others experience acute or chronic morbidity [1].

Maternal morbidity is defined as any health condition attributed to and/or aggravated by pregnancy and childbirth that has a negative impact on the woman's wellbeing and /or functioning [2]. However, the true burden of maternal morbidity is still not known, the causes are many and complex, they vary in duration and severity, they cover a broad range of diagnoses requiring a wide variety of treatments [3].

Maternal morbidity and mortality are estimated to be highest in low and middle-income countries, especially among the poorest women [4].

In the Democratic Republic of the Congo the maternal mortality ratio was estimated to 693 deaths per 100000 live births in 2015 then to 473 deaths per 100000 live births in 2017 being among of the highest in the world [5]. Several morbid conditions contribute to the maternal mortality, they have been observed through years, strategies to treat and prevent them implemented. But the maternal morbidity ratio is still high.

The morbid conditions mostly reported among pregnant women in the Democratic Republic of the Congo are anemia, pre-eclampsia, urinary tract infections and malaria. In Lubumbashi, the prevalence of anemia among pregnant women varies from 42% to 80% depending on studies [6-8]; the prevalence of hypertension pathologies in the peripartum was estimated at 4,8% [9], anemia was associated to malaria in 40% of pregnant women and intestinal parasitism at 9% [7], the overall maternal HIV prevalence rate was 4,6% [10], the prevalence of malaria among pregnant women in Lubumbashi was between 25.14% and 42,83% [11].

Anemia is the most predominant morbid condition among pregnant women, worldwide it affects 32 million (28–36 million) pregnant women per year [12]. The causes are multifactorial: the immediate risk factors are mainly attributable to insufficient dietary intake and micronutrient deficiencies involving iron, copper, zinc, folic acid; common causes of nutritional anemia. Other immediate risk factors include physiological adaptations during pregnancy or breastfeeding, and infections such as malaria, hookworm, and HIV. Besides these immediate risk factors of anemia, there are ranges of known distal factors that operate at the household and community levels. These include education status, household sanitation and hygiene, source of drinking water and rural/urban residence [13].

Among these distal factors causing anemia should be included the concentration and exposure factors to toxic TE;

studies report the effect of toxic TE causing hypochromic microcytic anemia (Pb and Cd) [14]. Toxic effect of lead is related, among others, to metabolic interactions with essential TE (Fe, Zn and Cu). Lead stimulates urinary excretion of these elements interfering with their reabsorption in kidney as well as inhibits ceruloplasmin activity in plasma, ferrochelatase activity in reticulocytes and copper-zinc-dependent superoxide dismutase activity in tissues. Lead is particularly pernicious to iron metabolism: it is taken up by the iron absorption machinery, and secondarily blocks iron through competitive inhibition. Furthermore, it interferes with several important iron dependent metabolic steps such as heme biosynthesis [15, 16].

Iron, zinc, and copper deficiency increase lead toxicity through enhancement of lead absorption from intestinal tract as well as decrease of metalloenzymes activity; in these conditions greater degree of maternal anemia may result causing intrauterine growth retardation, poor motor and mental performance in children, several maternal deleterious outcomes and in the extreme, maternal and child death [16-20].

The role of toxic TE in the pathogeny of pre-eclampsia has been reported: blood lead (Pb) concentrations were significantly and substantially associated with preeclampsia, an increase in blood Pb of 1 µg/dL in pregnant women was associated with a 1.6% increase in likelihood of pre-eclampsia [21].

A study on pre-eclampsia in Kinshasa reported high urinary excretion of toxic TE among pre eclamptic and eclamptic compared to healthy pregnant (Al, Cr, Mn, Co, Ni, Cu, Zn, Cd, Sn, Sb, Ba, Pb and U) and low concentration of Se [22].

In Lubumbashi, pregnant women are exposed to toxic TE from mining plants. A study reports high concentration of Al, As, Cd and Pb in the total blood of post-delivery mothers with bio accumulation factors above 1 [23], in the same population essential TE such as Cr, Cu, Se and Zn in the total blood of the post-delivery mothers are found to be low with bioaccumulation factor under 1 [24]. For these women geophagia, immediate proximity to mining plants, use of well water for drinking or housework were among the predominant exposure factors associated to high concentration of toxic TE in the total blood [25].

Toxic TE are associated to several maternal morbid conditions depending on the element, its concentration, the exposure duration, and the individual characteristics. In our settings where high concentration of toxic TE in the total blood of post-delivery mothers have been reported [23], and high prevalence of anemia noted [6-8] what can be the relation between several morbid conditions, blood concentration of toxic TE and exposure factors to them.

The aim of this study was to determine: the incidence of morbid conditions; their relations to the exposure factors to toxic TE and to blood's concentration of toxic TE among pregnant women living in Lubumbashi.

Findings from this study will help implement preventive measures toward associated maternal morbidity in mining cities such as Lubumbashi.

## 2. Methodology

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

**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.

**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.

**Initial exposure factor (theoretical):** the proximity of the pregnant women's homes to mining operations within a perimeter of 3km [16].

**Factor of real exposure of pregnant women in our environment:** beyond the geographical proximity of the women's homes to the mining operations, the blood concentration of TE was the real factor of exposure of pregnant women and their newborns [25].

**The exposed:** The exposed pregnant are those whose home was within the perimeter of 3km around an industrial exploitation of minerals according to the theoretical approach to do this the google-map software allowed us to identify the neighborhoods of residence of the pregnant included within the 3km perimeter of the mining operations. However, in practice it is the excessive blood concentrations of TE that constitute the real exposure [25].

**The unexposed:** Pregnant women whose blood concentrations of TE are normal.

Subjects were grouped in accordance with TE concentration in total blood. The groups were constituted whether the TE concentration was higher or lower than the TE reference value [23].

**Data collection:** Data collection sheets with a semi-closed questionnaire were used. Trained investigators collected information on history, physical and morbid information during pregnancy and at delivery 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 10°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. Data concerning exposure conditions, TE concentration in total blood samples, and morbid conditions were collected.

**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 TE (Al, As, Co, Cu, Mn, Se, Zn, Cr, Mg, Cd and Pb) were measured.

*Definition of morbid conditions observed among pregnant women.*

1. Anemia was defined according to WHO classification as a hemoglobin level below 11 g% for the pregnant women. Hemoglobin was determined by hemocue 301 after a peripheral blood puncture.
2. Maternal hypertension was retained if the pregnant women had a blood pressure above or equal to 140/90 mmHg. The systolic and diastolic blood pressure was measured in accordance with recommendations by the American Heart Association using a digital sphygmomanometer (Omron, Japan). A replicate measurement was taken for each participant and the mean value recorded as the blood pressure.
3. Malaria was confirmed if laboratory test (immunological or cytological) had proven the presence of plasmodium in the blood of the pregnant women.
4. IUGR defined the birth weight under the 5<sup>th</sup> percentile in our population a birthweight under 2500 gr.
5. Prematurity was defined as the delivery of a fetus aged under 37 weeks of gestation calculated from the last menstrual date or a sonography done in the first trimester.
6. Stillbirths was the death of a fetus in maternal womb after 22 weeks of gestation.
7. Birth defects was any visible malformation seen at the delivery.
8. Neonatal deaths was defined as the death of the newborn within 28 days of living.

**Statistical Analysis:** Our data were encoded using the EPI info 7 software, SPSS 23 allowed us to set the two groups according to TE concentration (higher or lower than the reference value) first then the presence or not of exposure factors in relation with the morbid conditions. This allowed us to calculate the chi square and relative risk for each exposure factor and each high TE concentration in total blood samples. We have correlated the two groups of each TE concentrations (higher or lower than the reference value) to the morbid conditions observed in pregnant women and the presence or not of each exposure factors to the above-mentioned morbid conditions by calculating a chi square. If the Chi square value was statistically significant, we calculated the relative risk for each high TE concentration to be

associated to each morbid condition observed; the same was done for each exposure factors. Only significant results are reported in this study.

Exposure assessments onset: In settings like ours it is difficult to precisely identify the onset of the exposure to TE because of multiple sources of environmental pollution and human exposure. Numerous confounding factors exist and should be considered when identifying exposure conditions [25]. It is also unethical to expose pregnant women to known health hazard and longitudinally follow them till the onset of morbid conditions.

Based on a previous study in the same city; the proximity to mining plants were not statistically associated to the concentration of TE [23]. We assumed that the concentration of TE found in post-delivery mothers and their newborns was a reflect of chronic exposure starting early in pregnancy or

even before. The concentration of TE in post-delivery mothers and their newborns is the result from absorption, metabolization and excretion processes of TE occurring in the pregnant woman and can be used as a tool for assessment of chronic exposure to TE [25]. Therefore, in our methodological approach, high maternal or neonatal concentration of TE has been considered as significant exposure factor which could be related to morbidity found during pregnancy.

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.

### 3. Results

*Table 1. Incidence of morbid conditions observed among pregnant women.*

Morbid conditions	N	%	Comments
Maternal anemia	180/378	47.6	Mean 10.94 $\pm$ 1.5g% Min 6 g%- Max 16.3g%
Maternal hypertension	80/378	21.2	
Prematurity	33/377	8.7	
Maternal malaria	232/378	61.4	
IUGR	43/377	11	
Neonatal deaths	19/354	53.67 per 1000	
Maternal deaths	-	-	
Stillbirths	2/376	0.5	
Birth defects	4/378	0.01	Multiple malformations (1), omphalocele (1); syndactyly (2)

In the above table the predominant morbid conditions among pregnant women were maternal malaria (61.4%), followed by maternal anemia (47.6%) and maternal hypertension (21.2%).

The mean hemoglobin concentration was 10.94  $\pm$  1.5 g% with a minimum of 6 g% and a maximum of 16.3%.

*Table 2. Relation between exposure factors to TE and maternal morbidity.*

Exposure factors to TE	Maternal morbidity	p	RR	Comments
Geophagia	Maternal anemia	0.000	2.127 (1.410-3.209)	
	Maternal hypertension	0.012	1.958 (1.177-3.259)	
Proximity to mining plants	Maternal anemia	0.000	2.887 (1.830-5.554)	
	Maternal hypertension	0.000	3.126 (1.876-5.208)	
Use of well water for drinking	Maternal hypertension	0.001	2.308 (1.385-3.845)	
	IUGR	0.008	1.752 (1.232-2.490)	
Use of well water for housework	Maternal hypertension	0.001	2.353 (1.421-3.897)	
	IUGR	0.000	2.010 (1.622-2.490)	
Biomass	Maternal hypertension	0.002	3.204 (1.114-9.212)	
Women working in mining plants	Maternal malaria	0.011	1.725 (1.145-2.599)	
Husband working in mining plants	Prematurity	0.002	3.204 (1.552-6.616)	

Geophagia increased two times the risk of maternal anemia and maternal hypertension.

The proximity to mining plants increased almost three times the risk of maternal anemia and three times the risk of maternal hypertension.

The use of well water for drinking and housework increased two times the risk of maternal hypertension and

delivering a IUGR newborn.

The use of biomass for cooking increased three times the risk of maternal hypertension.

Women working in mining plants increased two times the risk of maternal malaria.

Women whose husband worked in mining plants had three times the risk of premature birth.

**Table 3.** Relation between the total blood trace elements concentration and maternal morbidity.

T E concentration	Maternal morbidity	p	RR	Comments
High maternal lead concentration	Maternal anemia	0.000	4.63 (2.933-7.310)	Linear correlation (p=0.000) Pearson: -0.335 Kendall's tau: -0.222 Spearman's rho: -0.308
	Maternal hypertension	0.000	8.170 (4.657-14.333)	
	IUGR	0.000	2.601 (2.078-3.256)	
	Maternal anemia	0.026	1.909 (1.093-3.334)	
High neonatal lead concentration	Maternal hypertension	0.041	1.760 (1.041-2.976)	
High maternal cobalt concentration	Maternal anemia	0.029	1.586 (1.053-2.390)	
High neonatal cobalt concentration	Maternal hypertension	0.011	2.118 (1.179-3.803)	
High maternal arsenic concentration	IUGR	0.010	1.305 (1.118-1.524)	
High maternal cadmium concentration	Maternal hypertension	0.058	1.663 (1.009-2.743)	
	Maternal malaria	0.000	1.329 (1.085-1.628)	
High neonatal cadmium concentration	Prematurity	0.058	2.034 (0.999-4.172)	
High maternal chromium concentration	Maternal malaria	0.009	1.282 (1.074-1.530)	
High maternal magnesium concentration	Prematurity	0.044	2.184 (1.058-4.509)	
High maternal selenium concentration	Maternal malaria	0.000	1.449 (1.181-1.777)	
High neonatal selenium concentration	Maternal malaria	0.034	1.277 (1.025-1.590)	
Low neonatal selenium concentration	Maternal hypertension	0.043	0.59 (0.360-0.978)	
	IUGR	0.000	4.116 (2.004-8.452)	
High neonatal zinc concentration	Maternal anemia	0.037	1.668 (1.033-2.693)	
High neonatal magnesium concentration	Maternal anemia	0.035	1.287 (1.017-1.629)	

High lead concentration in the total blood of mothers increased five times the risk of maternal anemia; height times the risk of maternal hypertension; three times the risk of the delivering a IUGR newborn. The linear correlation between the maternal blood lead concentration and the maternal hemoglobin concentration was negative ( $r$  -0.335).

High blood concentration of lead, cobalt, zinc, and magnesium in the neonate increased two times the risk of maternal anemia.

High maternal blood concentration of cobalt, arsenic and cadmium was associated to two times the risk of maternal hypertension.

But high neonatal selenium concentration reduced this risk up to 60%.

Low neonatal selenium concentration was associated to four times the risk of IUGR neonate.

High maternal concentration of cadmium, chromium, selenium, and high neonate selenium concentration were slightly associated to the risk of maternal malaria.

High maternal magnesium concentration and high neonatal cadmium concentration were associated to two times the risk of premature births.

## 4. Discussion

The impact of climate change on the future of the planet, diseases associated to environmental pollution are emerging subjects among scientists nowadays. The increasing awareness of the role of environmental conditions on the health of the livings (human; animals and vegetables) is a consequence of many dramatic conditions reported in settings heavily polluted.

The quality of the air, the water, the soil, the foods are factors associated to quality of life and wellbeing of humans. They are considered as criterion for sustainable development.

The development of industry and manufacture especially where drastic controls are not assessed, generate waste products that pollute the environment. Humans living in such conditions are in contact with toxic components leading to morbid conditions.

Pregnant women and children in these conditions are vulnerable and highly exposed. Therefore, they can develop several morbid conditions, many of them related to the exposure.

In Lubumbashi, a city where several types of mines are increasing in number, and where many cases of environmental pollution have been reported, we conducted a study on maternal morbidity related to the exposure to TE issued from mining operating plants.

We aimed to evaluate the weight and impact of TE exposure on maternal morbidity, nevertheless we also assume that the results presented in this study are not supported by molecular basis; bias due to the study design and methodological approach along with confounding factors may have influenced our findings, but our results show for the first time in Lubumbashi the picture and the magnitude of the health risk associated to the exposure to toxic TE among pregnant women and their newborns. These findings can be applied in similar settings.

We discuss here the different morbid conditions found to have statistical relation to exposure factors and high concentration TE in the total blood of the studied population.

### 4.1. Maternal Anemia

In our study 47.6% of pregnant women had anemia, this prevalence is in accordance with the worldwide and Lubumbashi 's prevalence of anemia [6, 8, 12] being the most predominant morbid conditions among pregnant women with several negative outcomes for the pregnant women herself and the fetus.

This important proportion of anemia in this vulnerable population is in relation with many factors. In settings like ours, nutritional and infectious factors play important role in the pathogeny of anemia, but we should also consider environmental factors among them the exposure to TE.

The demand for nutrients increases during pregnancy causing pregnant women with micronutrient deficiencies to develop a craving for soils (geophagia) to supplement their dietary micronutrient intake, especially for calcium, zinc, and iron [26, 27].

The ingested soils may contain essential TE such as calcium, iron, zinc, magnesium, potassium, copper, and manganese but their bioavailability and their nutritional significance cannot be guaranteed. These soils may also contain toxic TE such as lead, cadmium, arsenic etc. which when introduced into the body, can be detrimental and reduce bioavailability of potassium, iron, and zinc, which could lead to micronutrient deficiencies [28, 29, 32, 33].

In another hand, exposure to microorganisms in the soil confers some immunity to the mother and the fetus (production of immunoglobulin A antibodies). Immunoglobulin A prevents attachment of bacteria and some virus on mucosal services directly therefore protecting the infant from infections [34].

The soils cation exchange capacity can help adsorb plant toxins (tannins, glycoalkaloids, and phytotoxins), detoxifying them and making them less harmful. Depending on the type of soil ingested different properties can result; fuller's earth, diatomaceous earth, kaolin-pectin, and termite earth can bind microbes, offering protection to the individual; smectite clays bind with mucus in the intestinal mucosa making its linings less permeable to toxins and pathogens, thus protecting body organs especially during times of rapid cell division, notably pregnancy and childhood [33, 35].

In our study geophagia, proximity to mining plants, high maternal concentration of lead, cobalt and high neonatal concentration of lead, cobalt, zinc, and magnesium increased seriously the risk of anemia among the exposed pregnant women. We also noticed a negative Pearson linear correlation between lead concentration and maternal hemoglobin ( $-0.335$ ). In a previous study in the same city, geophagia and proximity to mining plants were associated to high concentration of toxic trace elements in the total blood of pregnant women and neonate [25]. Therefore, in settings like our toxic TE contribute to the pathogeny of anemia along with nutritional and infectious factors (61.4% of pregnant women had malaria).

Despite the potential nutritional and immunological value, geophagia can induce adverse reactions: electrolyte imbalances and toxicity (ingestion of excess concentrations of useful minerals along with dangerously high amounts of toxic and nontoxic materials causing electrolyte imbalances and toxicity: Pb, Cd, Hg, As, Al, dioxins, and radionuclide isotopes). During the pregnancy, the risks from chemical exposures are greatest for the fetus.

Generally, there are about 8 mechanisms through which geophagia could lead to anemia: zinc and lead present in the

soil can compete for Ion uptake; Aluminum and Mercury interferes with production of red blood cells; charged ions in the geophagic material attract and bind nutrient reducing bioavailability; though geophagic materials can damage intestinal linings and thus inhibit absorption of Ion; raising pH in gastro intestinal tract inhibits oxidation of Ferric Ion to Ferrous Ion which is really absorbable; Alkaline pH favors proliferation of microbes and geohelminths resulting to competition for ingestion of foods; Chewing hard substances may destroy teeth making it difficult for mother to feed well; severe blood loss following hookworm infestation [34].

Our findings hence the impact of the exposure of pregnant women to TE in relation to anemia: geophagia and the proximity to mining plants are factors that may induce high concentration of TE such as lead, cobalt, zinc, magnesium. Zinc and lead are the most pernicious to hemoglobin by competing with Ion uptake [34]. In line with our findings for prevention of anemia in pregnant women living in settings like ours, clinicians and policy makers should consider apart from classical causes the role of factors exposing pregnant women to high toxic TE concentrations. It is also important to determine the type of soils ingested by pregnant women and its content in TE and microorganisms.

#### 4.2. Maternal Hypertension

Among pregnant women 21.2% had hypertension, this prevalence is more than two to four times higher compared to the prevalence of maternal hypertension in Kinshasa and in a previous study in Lubumbashi [9, 22]. This high prevalence of pre-eclampsia hence the role contributing factors to its pathogeny among them toxic TE, especially in settings where industrial waste is not properly managed.

In our study, the risk of maternal hypertension was increased by factors such as geophagia, proximity to mining plants, the use of well water for drinking or housework and the use of biomass for cooking. High concentration of maternal lead, cobalt, arsenic, and cadmium were also associated to an increased risk of maternal hypertension, but high neonate concentration of selenium seemed to be protective.

More importantly exposure to lead during pregnancy has been associated with the development of pregnancy-induced hypertension in the literature [30, 31]. In our study we support this statement regarding lead exposure. Almost all exposure factors favored lead exposure in our settings, but causation cannot be inferred from these data alone [24]. Maternal hypertension is caused by multiple factors, including genetic and environmental factors, and lead is only one of many such environmental factors. Lead exposure is known to affect neurocognitive development in children and increase the risk of cardiovascular disease in adults [36, 37].

The mechanisms by which lead increases blood pressure have not been fully elucidated. Besides oxidative stress, lead has been postulated to reduce bioactive nitrogen monoxide (NO) and downregulate soluble guanylate cyclase in vascular tissues. It causes a reduction in cyclic GMP production and attenuation of NO activity, leading to vascular remodeling

and inhibition in vasorelaxation. Lead also competes with calcium transport in the human body via ion channels. This mechanism contributes to changes in cytosolic calcium ion level, which regulate vascular tone [38, 39]. Lead is also increase angiotensin-converting enzyme activity as well and thus increase blood pressure [40]. Bones serve as the major reservoir for lead in the body; from bones lead passes into the bloodstream during pregnancy, and the fetus is therefore exposed to it during its development [41].

There is no threshold below which exposure to lead would not have harmful effects. In Lubumbashi, the mean concentration of lead was high in both post-delivery mothers and newborns which is a serious health concern [25].

On another hand we noticed the protective role of high concentration of selenium found in the neonates, knowing that a positive correlation was found between mothers and newborns TE concentration [26], we can support that this high neonate selenium level reflect mother's concentration as well.

Selenium is a key component of glutathione peroxidase (GPx), an enzyme that prevents the oxidation of lipids and atherosclerotic plaque formation. GPx also prevents indirectly the aggregation of platelets, thereby inhibiting blood clot formation. A direct relationship exists between Se and GPx activity when Se concentrations are low, but GPx activity plateaus off at high Se levels [42]. Therefore, higher GPx activity is thought to be protective against hypertension. The relationship between Se and hypertension is non-linear.

In populations with low Se intake, higher Se may be protective against hypertension; while in those with high Se intake, higher Se may be associated with hypertension risk. Therefore, it is possible that the amount of Se for maintaining normal blood pressure in normal subjects may be different from the amount required in hypertensive ones who may already have a damaged antioxidant defense system affecting the way Se and other antioxidants are metabolized and stored [43, 45].

The protective role of selenium in hypertension is supported by its antioxidant property but in women many other antioxidant substances such as vitamin E, estrogen, which reduces the number of superoxide anions and results in less endothelial dysfunction in females should be considered [43, 44].

We noticed an association in our study between maternal hypertension and high concentration of Cobalt though essential. In biological systems, cobalt (II) complexes produce oxygen radicals which cause severe deleterious effects on the cardiovascular, hematological, neurological, endocrine, and reproductive systems. Further, Cobalt has erythropoietic action which is attributable to its ability to mimic the pathological response to hypoxia in mammals. Consequently, cobalt salts are used for the treatment of certain types of anemia and as a blood doping agent in humans and racehorses. The hypoxic response induced by  $\text{CoCl}_2$  is reportedly associated with increase production of reactive oxygen species (ROS) leading to cellular damage and apoptosis in biological systems.  $\text{CoCl}_2$  functions as an oxidative stress inducing agent because Co (II)

reacts directly with  $\text{H}_2\text{O}_2$  in a Fenton-type reaction to produce ROS which in excess can affect cell survival through process that irreversibly alters the DNA. However, the generated ROS could be reduced by intracellular antioxidant enzymes such as GPx and CAT as well as some nonenzymatic antioxidant molecules like glutathione and vitamin E, respectively.  $\text{CoCl}_2$  precipitated significant reductions in the activities of the enzymatic antioxidants (GPx, GST, and CAT) and nonenzymatic intracellular antioxidant (GSH) together with increase in the level of the markers of oxidative stress (MDA,  $\text{H}_2\text{O}_2$ , AOPP, and sulphhydryl thiol content) in a dose-dependent manner. These observations suggest a potent induction of oxidative stress. The observed elevated MDA contents led to enhanced lipid peroxidation products, and this might be due to the production of superoxide anion, peroxy, and hydroxyl radicals. The increased peroxidation of membrane lipids is one principal consequence of oxidative damage produced by cobalt [45, 46]. Our findings support the fact that TE though essential but in high concentration acts as toxic having detrimental effects on health of humans [26].

Experimental studies previously published support the findings in our study where high concentration of arsenic were associated to an increased risk of maternal hypertension. These studies have indicated that arsenic exposure may be involved in the development of hypertension through the promotion of inflammation, oxidative stress, and endothelial dysfunction therefore explaining hypertension found in pregnant women with high blood concentration of arsenic [47].

Cadmium may induce maternal hypertension as seen in our study through vascular effects. A hypothesized mechanism of action is the inhibition of endothelial nitric oxide synthase protein in blood vessels, which suppresses acetylcholine induced vascular relaxation [48].

### 4.3. Maternal Malaria

We noticed that 61.4% of pregnant women had malaria, this prevalence is higher than that found in the same city in 2017 [11]. Pregnant women are particularly vulnerable to malaria, and their fetuses are at risk. In pregnancy malaria is associated with anemia, stillbirth, low birth weight, maternal and fetal death. Environmental factors (areas of low or high transmission), parasite species (*vivax*, *malariae*, *falciparum*, *vale*), and maternal factors (gravity, age, nutrition, immunity status) influence the severity of malaria in pregnancy [49].

In our study maternal malaria was associated to women working in mining plants and the slightly high concentration of maternal cadmium, Chromium, and Selenium. However, we cannot link them directly, but we can hypothesize on effects of TE on the maternal immunity. TE are needed for many metabolic and physiological processes in the human. Zinc and Copper are the essential TE that play a crucial role in the immune system. These TE act as cofactors for antioxidant enzymes involved in the destruction of toxic free radicals produced in the body. The serum levels of antioxidants vary in many diseases including malaria. These

alterations are part of defense strategies of organism and are induced by different cytokines. The immune function is deftly synchronized by zinc since both increased and decreased zinc levels result in a disturbed immune function. Zn is important in numerous critical biochemical processes; it is a cofactor in about 200 metalloenzymes including Cu/Zn-superoxide dismutase, a critical cytoplasmic antioxidant enzyme. One of the main clinical manifestations associated with Zn deficiency is increased susceptibility to infectious diseases [50].

Zinc has regulatory effect on inflammatory responses via Nuclear Factor Kappa B (NF- $\kappa$ B) signaling pathway to control oxidative stress and inflammatory cytokines. During the acute phase response of human body to infection, IL-6 stimulate the zinc transporter (ZIP14) which is settled in cell membrane and ease to zinc entering cells. zinc is placed within zinosome or organelles and decrease serum zinc levels. Therefore, maintenance of serum zinc uptake is necessary in pregnant women with infection [52, 53].

Cu could be a potential inducer of LDL oxidation. On one hand, Cu can involve in preventing oxidative injury. In addition, caeruloplasmin, a multifunctional protein which contains most of the Cu in blood, is thought to possess antioxidant functions, which could be beneficial in resisting disease. Cu is also essential for maintaining the strength of the skin and blood vessels. It plays a role in production of hemoglobin, myelin, and melanin [50].

In healthy pregnancy a significant increase in serum Cu levels is observed with the second trimester but the decrease trend in TE status during pregnancy might be depended on the physiological changes which include volume expansion, hormonal changes, and increased TE requirement with different trimesters. Micronutrient requirements might be changed with trimesters due to the role of micronutrients during pregnancy such as the formation of new cells and tissues, enzyme activity, signal transduction and transcription pathways, and combating oxidative stress [16].

In a previous study in the same population, we have noticed lower mean concentration of essential TE (Zn and Cu) which can explain our actual finding of high prevalence to malaria due to high susceptibility to infectious diseases therefore to malaria [26, 50]. To prevent infectious diseases among pregnant women, a normal intake of essential TE and a maintenance of their normal serum level should be assessed during prenatal care.

Though essential, TE can be detrimental to maternal and neonatal health if in excess and therefore act as toxic [24]. In this study high maternal and neonatal concentration of magnesium and selenium and high neonatal concentration of zinc were associated to morbid conditions. With cautious supplementation should be implemented.

#### **4.4. IUGR (Intra Uterine Growth Restriction) and Prematurity**

In our study 11% of newborns had IUGR and 8.7% of pregnant had a premature birth.

IUGR and premature delivery are multifactorial conditions

which depend on environmental, genetics, maternal and fetal factors. In our study IUGR was associated to use of well water for drinking or housework and the high concentration of maternal lead, arsenic, and low neonate concentration of Selenium, where prematurity was associated to the women whose husband worked in the mining plants, the high concentration of maternal magnesium, and high neonate concentration of cadmium. TE are closely associated with fetal growth and development during pregnancy. Deficiency can lead to adverse pregnancy outcomes. Lack of essential TE during pregnancy is detrimental to maternal and fetal health. In literature serum zinc and iron levels in patients who either had a miscarriage or a preterm delivery were significantly lower, serum copper, zinc, calcium, and iron were significantly lower in patients with intrauterine growth restriction (IUGR) [51].

Imbalance between toxic and essential TE is detrimental to the pregnant women and their fetuses: toxic TE influence the bioavailability of essential ones as seen in the same population and lead to adverse pregnancy outcomes observed such as IUGR and prematurity [24, 25].

## **5. Conclusion**

Anemia, malaria, hypertension, IUGR and prematurity are associated to high concentration of toxic TE and to low concentration of essential TE. Prevention of the exposure to toxic TE and supplementation with required amount of essential TE will help reduce associated maternal morbidity. More studies are needed to deeply understand the detrimental effects of environmental pollution on the health of pregnant women and their newborns in settings like ours.

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