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Research Article

Evaluation of a Cement Dust Generation and Exposure Chamber for Rodents: Blood Heavy Metal Status, Haematological Variables and Gastrointestinal Motility in Rats

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ABSTRACT

Exposure to cement dust has been documented to cause various occupational and long-term health complications both in human and animal. However, investigations on the extent of toxicity associated with cement dust exposure have been limited by lack of suitable model for controlled laboratory exposures. In this study, a glass house animal exposure chamber was fabricated using a plexi-glass and a blowing fan of adjustable revolution. Model simulations were validated using experimental data showing the effects of cement dust exposure on haematological indices, trace element status and gastrointestinal motility in rats. Thirty male Wistar rats were randomly divided into three groups. The unexposed group (n = 10) served as control while the other groups were exposed for five hours daily to cement dust (200g) at a revolution of 2400-3000rpm. Blood collected was analysed for some haematological variables as well as plasma concentrations of cadmium, lead, silicon, aluminium, manganese, calcium, iron and magnesium. Organ weights were measured and histopathological features of the kidney, lungs stomach and liver were assessed to determine the degree of tissue damage. Intestinal motility was assessed *in vivo* using the Charcoal meal method while colonic motility was studied by measuring the distance travelled by beads inserted 2cm into the distal colon through the anal opening. Data were expressed as Mean ± SEM, analysed using one-way ANOVA and $p<0.05$ was significant. Blood analysis from exposed rats on days 14 and 28 showed significant increase in concentrations of Calcium, Silicon, Manganese, Iron, Lead, Cadmium, Aluminium and magnesium compared with unexposed animals. Significant reductions were observed in haematocrit values, red and white blood cell counts after cement dust exposure. Also, significant increases were observed in the neutrophil-lymphocyte ratio and erythrocyte sedimentation rate in exposed rats compared with control. There was a significant decrease in organ weights - stomach, lungs, kidney when compared with control. Rats exposed to cement dust had significantly decreased small intestinal motility but increased colonic transit time. Histopathological examination from exposed rats revealed peribronchiolar infiltration by lymphocytes in the lungs while gastric gland was severely infiltrated by inflammatory cells. The results from this study are comparable to data obtained from earlier reported on haematological and heavy metals in humans occupationally exposed to cement.

Keywords: *Cement dust, fabricated chamber, haematological indices and gastric motility*

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INTRODUCTION

Man's environment is constantly being polluted by remains of industrial activities which poses serious threat to human health. One of such activities in developing countries is increased construction of structures such as houses, roads, schools, factories, hospitals etc. for which usage of cement is inevitable. Cement is a powdery composition (limestone, laterites, clay and gypsum) used in making and holding blocks or bricks in-place during construction (Amodu and Egwuogu, 2014). The major components of cement are derived from toxic heavy metals such as nickel, cobalt, lead, chromium and Silica (Gbadebo and Bankole 2007; Baby *et al*., 2008; Ogunbileje *et al*, 2013). It also contains Thallium and many other impurities (Short and Petsonk, 1996). Many of these toxic compounds have been shown to cause damages at both cellular and organ levels in the lungs (Ade-Ademilua and Obalola, 2008); Akpan *et al*. 2011), blood (Goyer *et al*, 1973) gut (Olaleye *et al*, 2006, 2007; Adeleye and Olaleye, 2016; Adeleye *et al*, 2018) in addition to their roles in genetic

disorders and cancers. In most developed countries, dusts from cement factories is a major problem that both factory workers and nearby residents are faced with as it affects the quality of air they inhale. Apart from factory workers, cement dusts also pose environmental threat to the ecosystem with adverse impact on vegetation and aquatic life (Anda, 1986; Iqbal and Shafiq, 2000).

Several reports are available in literature which underscore the adverse effects of repeated and or prolonged exposure to cement dusts on the health status of most cement factory workers as well as those living around cement factories (Calistrusjudge *et al*., 2002; Fell *et al*., 2003; Lameed, 2008). Excessive exposure to cement dusts Cough and phlegm production, chest tightness, impairment of lung function, obstructive and restrictive lung disease, pleural thickening, fibrosis, emphysema, lung nodulation, pneumoconiosis and carcinoma of lung (Alakija *et al*., 1990; Meo, 2004; Baccarelli *et al*., 2014,). In the gastrointestinal tract, cement dust exposure is believed to cause mechanical trauma, mucosal inflammation, loss of tooth surface, periodontal disease, dental abrasion, dental caries, Stomach ache and cancer of stomach (Kolev and Shumkov, 1975; Struzak-Wysokinska and Bozyk, 1989; Jakobsson *et al*, 1990; Tuominen and Tuominen, 1992).

Most of the reports on the effects of cement dust exposure on body functions have been on human studies carried out on industry workers or on animals taken to production areas. In such studies, quantification of the extent of exposure are practically impossible. The implication of this is that information on mechanistic and detailed laboratory-based exposure models of cement dust exposure in animals are not available, leading to limitations in the knowledge of cement dust toxicity in the body. In this study, the efficacy of a fabricated cement dust exposure chamber was tested and validated by assessing and comparing the effects of cement dust exposure on hematological indices, trace metal status and intestinal motility in rats.

MATERIALS AND METHODS

The Exposure chamber: The fabricated plexiglass house animal exposure chamber consists of a square shaped box made up plastic glass with two compartments. One of the inner compartments houses the experimental animal during exposure (Plate 1) while the second inner smaller compartment contains two industrial fans which is been connected to electricity to blow the cement dust been deposited into the compartment to the other compartment that houses animal during the exposure at a revolution of 2400-3000rpm

The bigger compartment has a height of 60cm and a width of 59.9cm. The smaller inner chamber has a height of 19.6cm and a width of 26.1cm. The chamber also contains outlet opening (vent) which regulates the temperature of the chamber during exposure at every 30minutes interval to prevent suffocation of the experimental animal. It has a height of 9.9cm and a width of 10.6cm.

Animals: Fifteen male Wistar rats (100 – 110g were randomly divided into three groups viz: 1-unexposed group (control) while other groups 2 and 3 were exposed to cement dust for 14 and 28 days respectively. Animals were acclimatized for two weeks with free access to standard commercial rat chow and tap water *ad libitum* before commencement of studies. The animals were housed under standard conditions of temperature (23 ± 2ºC), humidity (55 ± 15%) and environmental 12hour light and dark cycle in the Animal house of Department of Physiology, University of Ibadan, Ibadan. They were kept in plastic cages with beddings which were adequately changed throughout the study period. They were exposed for five hours daily to cement dust (200g) at a revolution of 2400-3000rpm in the enclosed plexiglass exposure chamber between 8:00 am to 12 noon.

Plate 1
Fabricated enclosed cement dust chamber before exposure (plate 1a) and during exposure (plate 1b)

Exposure procedure: 200g of cement was weighed daily and kept in the inner compartment of the exposure chamber for circulation. A thick transparent hollow glass plate was placed inside the chamber filled with 50ml of distilled water in order to ascertain the level of cement dust that will be diffused in to the water during exposure so as to measure the effectiveness of the chamber and also to compare the concentration found in water and that in the blood throughout the period of fourteen days and twenty eight days of exposure. Afterwards, animals were placed in the outer compartment (as shown in plate 1b) and the fan switched on.

Hematological examination: Blood collection was through the retro-orbital sinus using heparinized capillary tubes and EDTA bottles on days 14 and 28. The blood parameters (PCV, HB, WBC and RBC) were determined according to the method described by Dacies and Lewis (1994).

Histological Analysis: On sacrificing the animals, the lungs and stomach were harvested, weighed and a small section were fixed in formalin before Histological evaluation was carried out on them.

Metal analysis in blood: After collecting 1 ml of blood into a test tube, 2 ml of Nitric acid (HNO_3) was added and left overnight after thorough mixing. The digested blood was placed in water bath and heated for 30 minutes at 98-100°C. After cooling, 12mL of distilled water was added to the digested blood and filtered. The filtrate was then analyzed for the major heavy metals found in cement viz: Calcium, Silicon, Manganese, Iron, Lead, Cadmium, Aluminum and magnesium using atomic absorption spectrophotometry (Awad *et al*, 2013).

Intestinal motility: In another experiment, intestinal transit was determined following the method described by Teke *et al*. (2007). Briefly, Healthy Wistar rats were grouped into 3 (n=5) and exposed to cement dust as described earlier. A control group was not exposed. All animals were fasted for 18 h prior to the administration of charcoal meal. The charcoal meal (1 mL) (10% charcoal and 5% acacia gum suspended in distilled water and made up to 100 mLs of solution) was administered by oral gavage to all the groups. The animals were sacrificed 30 minutes after charcoal meal was given by ketamine overdose (100 mg/kg) followed by cervical dislocation. The small intestine was removed carefully and lengths of intestine, as well as the leading end of the charcoal meal were measured. The percentage of distance covered by the charcoal was computed to calculate percentage inhibition.
% transit = (distance traveled by charcoal meal / total length of the intestine) x 100 .

Colonic motility: The effect of cement exposure on altered gastrointestinal motility was also studied in Wistar rats fasted for 24 hours prior to experiment. The animals were grouped into 3 and exposed to cement dust as described earlier. Beads of about 2mm were be inserted 2cm into the distal colon through the anal opening using the nasogastric tube (NG) which was well lubricated. The animals were then placed in different plastic cages lined with white tissue rolls and the time at which each animal expelled the beads was be noted. Colonic motility was be calculated by computing the time between bead placement and expulsion of the bead (Osiniki *et al*.,1999).

Ethical considerations; This study was conducted in accordance with the current Animal Care Regulations and standards approved by the Institute for Laboratory Animal Research (ILAR, 1996) and the experimental protocol approved by the Animal Care and Use Research Ethics Committee of the University of Ibadan. Ibadan, Nigeria

Statistical analysis: All values are expressed as Mean ± SEM of the animals used in each group. Independent T-test and one-way ANOVA were employed to compare differences among variables. Comparisons between groups were done using appropriate post hoc test and the statistical differences was taken to be significant at $p<0.05$.

RESULTS

Body and organ weight changes

The changes in body weight of the animals after 14- and 28-days exposure to cement dust are shown in Figure 1. Significant decreases in the body weight of exposed animals were apparent when compared with the unexposed (control) animals. Table 1 shows that the relative weights of the kidneys, stomach and lungs were significantly decreased in cement dust-exposed rats. Liver weight was not significantly affected.

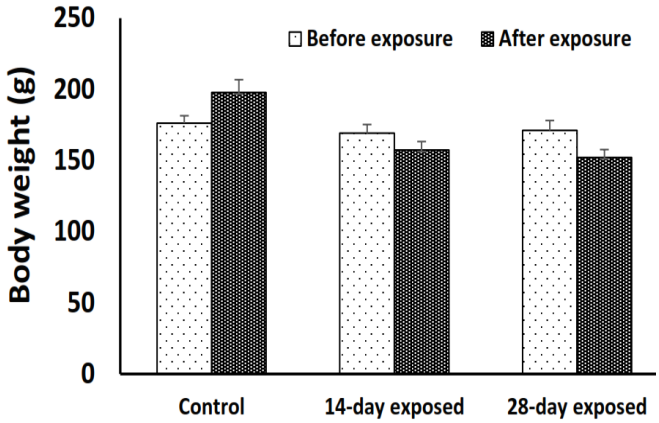

Figure 1:
Boy weight profile of rats before and after exposure to cement dust. Each vertical bar represents mean ± SEM of 10 rats per group.

Blood parameters:

The results of studies on the effects of cement dust exposure on blood variables are shown in Table 2. The values of red and white blood cell counts, platelets as well as Packed Cell Volume (PCV) and hemoglobin were significantly decreased in rats exposed to cement dust. The effects were marked more on the 28-day exposed animals.

Table 1:
Effect of cement dust exposure on body organ weight.

Groups	Organs			
	Lungs (g)	**Liver (g)**	**Kidney (g)**	**Stomach (g)**
Control	1.56 ±0.06	6.20 ± 0.17	1.28 ± 0.04	1.42 ± 0.10
14 days CDE	1.057 ± 0.06**	5.25 ± 0.25	1.11 ± 0.02*	1.14 ± 0.02*
28 days CDE	1.37 ± 0.09	6.80 ±0.39	1.07 ± 0.01*	0.96 ± 0.02**

Values are presented as Mean ± SEM, n=5. *Significant when compared to control (P<0.05). ** Highly Significant when compared to control (P<0.01)

Differential white blood cell counts revealed significant decreases in the lymphocyte and eosinophil counts in exposed rats while neutrophil and monocyte counts were significantly increased after 28 days of exposure. However, the decreases observed in lymphocyte, neutrophil and eosinophil counts on day 14 were not significant when compared with the control groups (Table 2).

As shown in Fig. 2, Erythrocyte Sedimentation Rate (ESR) was significantly increased after 14 and 28 days of exposure to cement dust. The figure also shows the relative increase in the Neutrophil-Lymphocyte ratio in the exposed rats when compared with the control.

Heavy metal levels in blood:
As shown in Fig. 3, the blood levels of lead and cadmium (3a), silicon, aluminum an manganese (3b) as well as calcium, iron an magnesium (3c) were all increased the end of the 28 day exposure period.

Table 2:
Effect of cement dust exposure on blood parameters

	Control	14 Days CDE	28 Days CDE
PCV (%)	40.40±0.67	39.80±1.16	33.80±1.72 *#
RBC (millions/mm^3)	6.53±0.18	6.88±0.19	5.72±0.23 *#
HB (g/dl)	13.56±0.27	13.68±0.34	11.14±0.58 *#
WBC (millions/mm^3)	8910±737.30	9050±1131	4770±94.34 *#
Platelet (x10^3/mm^3)	2.55±0.26	1.62±0.90*	1.66±0.89*
Lymphocyte	70.50±1.04	71.50±1.04	65.50±1.32 *#
Neutrophils	25.75±0.85	27.25±0.85	31.50±1.19 *#
Monocytes	1.25±0.25	2.25±0.25 *	2.75±0.25 *
Eosinophils	2.60±0.24	2.80±0.20	1.20±0.20 *#

Values are presented as Mean ± SEM, n=10
** Significant when compared to control (P<0.05).*
 # Significant when compared with 14 days CDE (P<0.05)
CDE stands for cement dust exposure

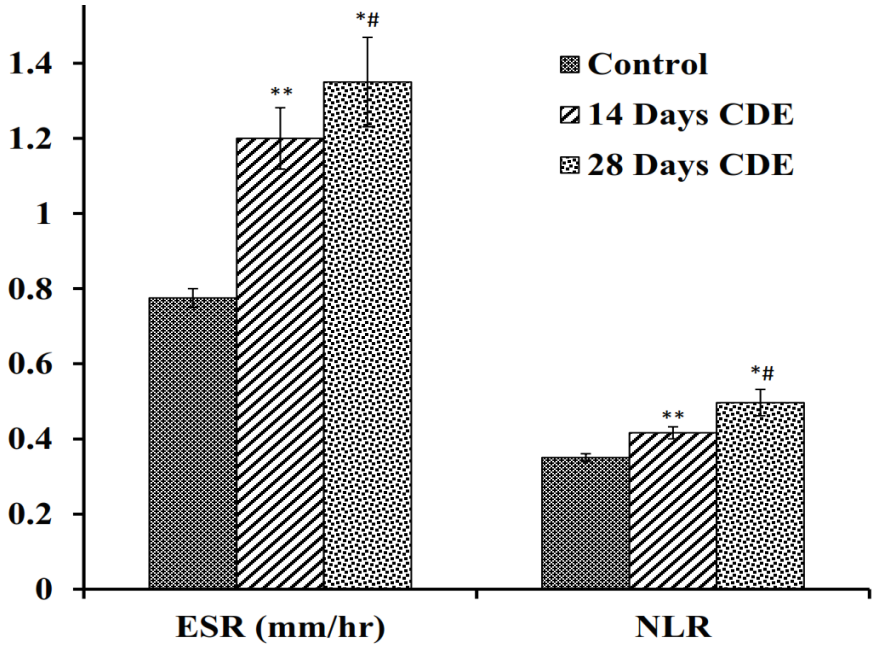

Figure 2:
Effect of cement dust exposure on erythrocyte sedimentation rate and neutrophil-lymphocyte ratio. Values are presented as Mean ± SEM, n=5
** Significant when compared to control (P<0.05). # Significant when compared with 14 days CDE (P<0.05) .*

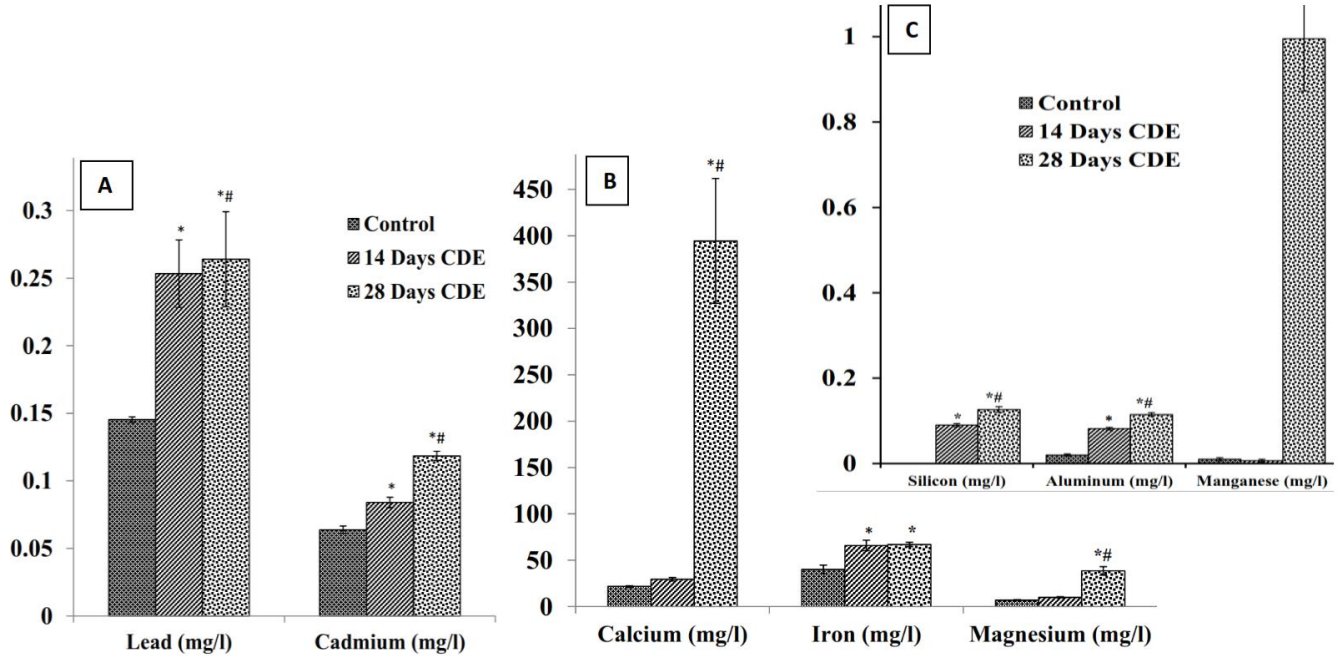

Figure 3.
Effect of cement dust exposure on Lead and Cadmium (A), Calcium, iron and magnesium (B) and Silicon, Aluminum and manganese levels. *Values are presented as Mean ± SEM. * and # Significant when compared to control and with 14 days CDE (P<0.05)*

Intestinal and colonic motility

Intestinal motility was significantly decreased 14 and 28 days after cement dust exposure compared with control group (Fig 4). Figure 5 shows the effect of cement dust on colonic transit time. Colonic transit time was significantly increased in all exposed animals

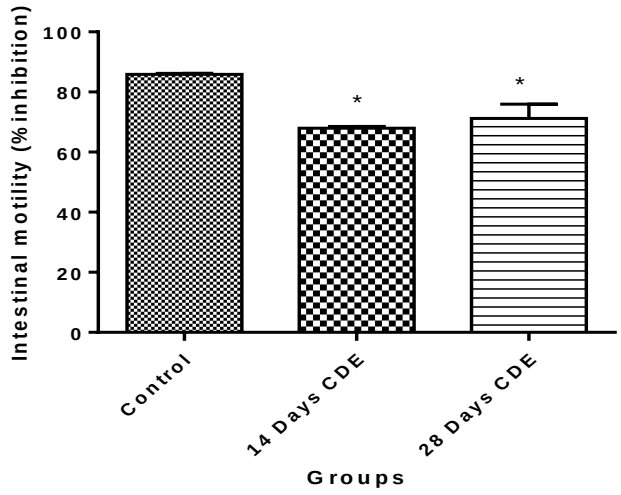

Figure 4:
Effect of cement dust on Intestinal motility
Values are presented as Mean ± SEM, n=10
* Significant when compared to control.

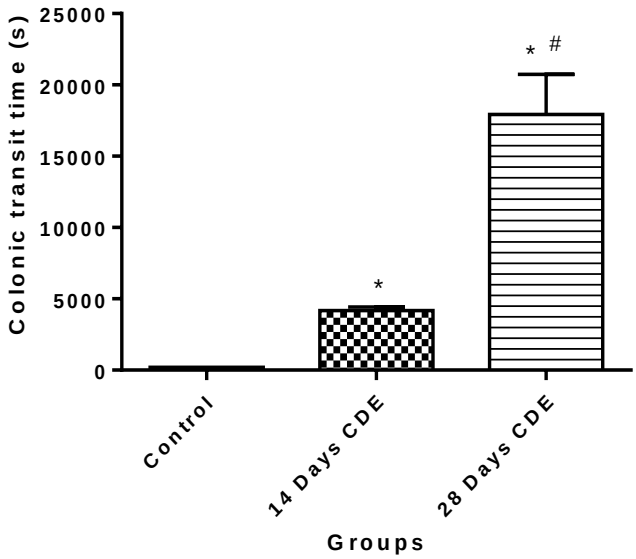

Figure 5:
Effect of cement dust on colonic transit time
Values are presented as Mean ± SEM, n=10
* Significant when compared to control.
# Significant when compared with 14 days CDE

Histology

The results of the histological examinations of the lung and stomach tissues of the exposed rats showed marked microscopic changes when compared the tissues of the control rats (Plates 2 and 3).

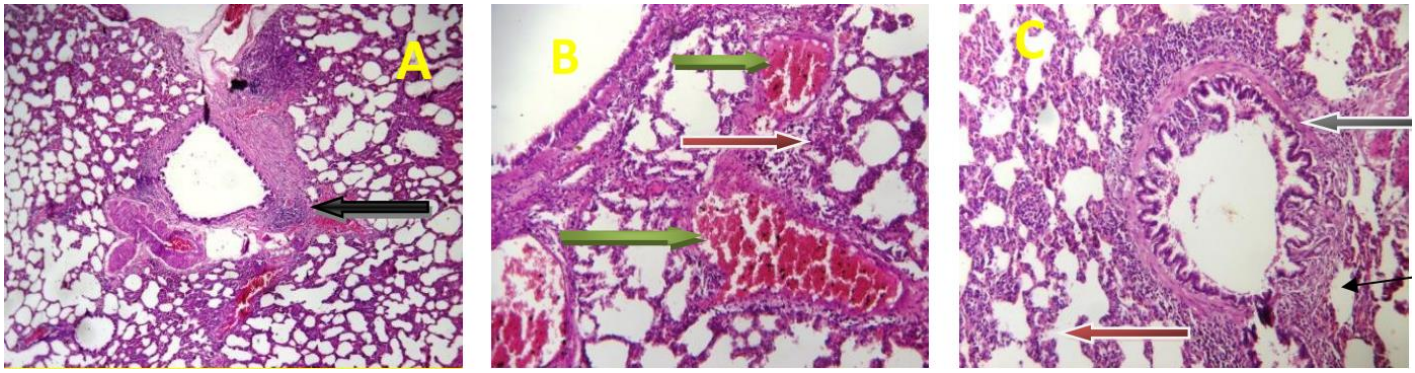

Plate 2:
Histology of The Lungs (H&E Stain MAG. X 100) showing A-Control: showing moderate peri-lymphocyte bronchiolar and vascular infiltration (black arrow), there is mild fat deposit at the perivascular region, no vascular congestion is noted. The intra alveolar spaces are not infiltrated and alveolar ducts appear normal, B-group 2, day 14: showing moderate lymphocyte follicle and severe peri-bronchial ar infiltration of lymphocytes (green arrow). There is moderate thickening of vascular wall and mild vascular congestion noted. The intra alveolar spaces and alveolar ducts (red arrow) are severely infiltrated. C-group 3, day 28: showing moderate fibrosis, severe peri bronchiolar infiltration of lymphocytes (black arrow). There is moderate thickening of vascular of vascular and mild vascular congestion noted. There is focal area of mild fat deposits. The intra alveolar spaces (slender arrow) and alveolar ducts (red arrow) are severely infiltrated (slender arrow)

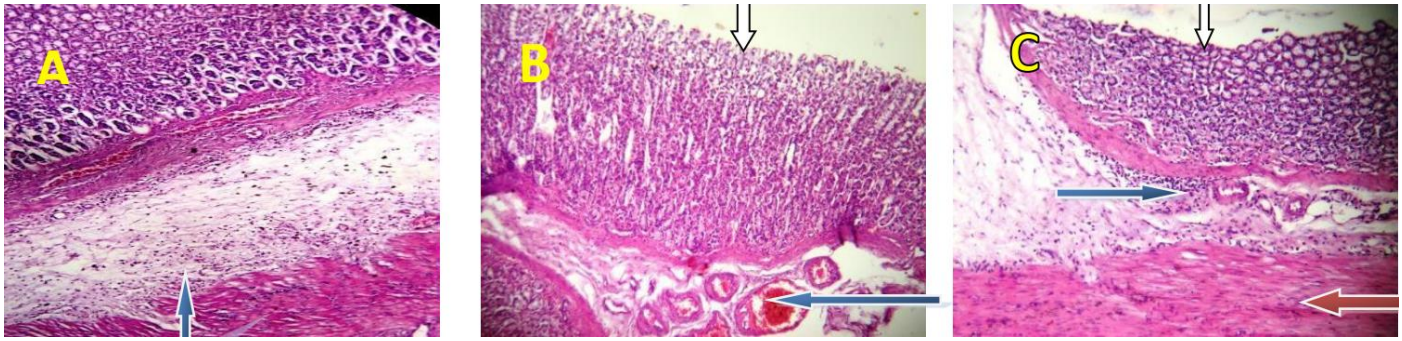

Plate 3:
Histology of the Stomach (H&E Stain MAG. X 100) showing Group 1 (A), Unexposed Control; moderate architecture, the mucosa layer shows scanty infiltration of the gastric gland and lamina propria. The submucosa layer shows mild infiltration of inflammatory cells (blue arrow). Group 2 (B), day 14 CDE: moderate architecture and poorly preserved mucosa epithelial cells layer (white arrow) which are severely eroded, there is moderate papillary infoldings, the mucosa layer shows no infiltration of the gastric glands and lamina propria. The submucosal layer appear mildly infiltrated by inflammatory cells and moderately vascularized with thickened vascular walls and mild congestion (blue arrow), the circular muscle layer (red arrow) appears normal. Group 3 (C), day 28 CDE: fair architecture, the mucosa epithelial cells layer is poorly preserved (white arrow), the mucosa layer shows moderate to severe infiltration of the gastric glands and lamina propria. The submucosal layer appears severely infiltrated by inflammatory cells (blue arrow) and also show moderate vascularization and mild fibrosis. The circular muscle layer (red arrow) appears normal

DISCUSSION

In this study, rats were exposed in the laboratory to cement dusts via a fabricated exposure chamber. The efficacy of the exposure chamber was tested by investigating the effect of the exposure on some indicators of toxicity.

The body weights of the animals exposed to cement dust in this study were decreased when compared with the unexposed control rats. Decreased body weights have been attributed to several factors such as impaired gastrointestinal functions (Chokshi, 2007) probably resulting from increased toxic end products during inappropriate food conversion (Klaassen *et al*., 2001). It could also be as a result of impairment or disturbances in the metabolic breakdown between carbohydrate, protein and fats (Klaassen *et al*., 2001) which can be linked to altered food appetite (Ezeonwumelu *et al*., 2011). Changes in body weight have been reported by several workers as an indication of toxicity (Lamanna and Hart, 1968; Kwan Yuet Ping *et al*., 2013). Decreased in body weight may be used as an index of toxicity or deleterious effect of certain substances (Hilaly *et al.,* 2004) which is evident in this study.

The weights of the liver were not remarkably altered by cement dust exposure in this study. This is in line with the work of Mojiminiyi *et al., (*2008) that reported that the liver function parameters remained similar in exposed workers compared to unexposed workers. Results of this study indicate that kidney and lung weights decreased as a result of cement dust exposure.

The proper functioning of the body system or cells is dependent on adequate nourishment, a factor determined by the efficacy of blood cells. Blood cells function in oxygenation, removal of waste products from organs and ultimately conferring immunity to the body system (Barrett *et al*, 2010). Anaemia has been documented over time as an index of toxicity. In this study, the blood cells- erythrocytes, leucocytes and platelets were significantly diminished in rats exposed to cement dusts. The adverse effect of cement dust on

hematological variables in humans (Mojimoniyi *et al*., 2007; Mohammed and Sambo, 2008) and animals taken to cement manufacturing sites (Yahaya *et al*, 2011) have been well documented. However, while Mojiminiyi *et al*., (2008) and Erhabor *et al*., (2013) increases in the platelet counts in exposed humans, Jude *et al*., (2002) observed decreases in the platelet count in exposed subjects. This disparity thus suggests for more investigations.

Erythrocyte sedimentation rate has been used clinically to denote presence of tissue damage during stress conditions. It is also a common haematological test used to measure non-specific inflammation (Gabriel *et al*., 2004; Punzi *et al*., 2005). Erythrocyte sedimentation rate is also an indirect measurement of fibrinogen level which are observed as acute phase protein in disease state (Husain and Kim 2002). In this study, the Erythrocyte sedimentation rate was elevated after cement dust exposure. This is similar to the observations of Erhabor *et al.,* (2013). An elevated ESR means fragile and reduced levels of red blood cell production which was observed in this study and suggesting adverse effect cement dust exposure may exert on erythrocyte formation, structure and function.

Ratios of blood cells- neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), platelet-lymphocyte ratio (PLR), and mean platelet volume (MPV) have been projected as useful markers of disease conditions including cancers and systemic inflammation response (Liu *et al.,* 2011, Seretis *et al*, 2013; Lee *et al*, 2018). In this study, neutrophil counts remarkably increased in animals exposed to cement dust, similar to the report of Okonkwo *et al*., (2015) and Yahaya *et al.,* (2011). Also, Neutrophil/Lymphocyte ratio significantly increased in rats exposed to cement dust.

Similar to reports in humans occupationally exposed to cement and in studies involving animals taken to sites of cement production, our study shows significantly elevated levels in blood concentration of Cadmium, Calcium, Magnesium, Silicon, Manganese, Lead, Aluminum and Iron after 14 and 28 days of cement dust exposure. This finding is a confirmation of the previous where elevated levels of these heavy metals were detected in blood and lungs of exposed humans and animals (Abdul-Wahab, 2006; Gbadebo and Bankole, 2007; Akinola *et al*. 2008; Ade-Ademilua and Obalola, 2008; Akpan *et al*., 2011; El-Absay *et al*., 2011).

The decrease in the two types of intestinal motility tests (small intestinal transit and colonic motility) from this study did not present mechanistic evidence to trace the pathways of reported findings. However, the reduced motility is an indication of stasis in the gut. This slow dynamism of the gut movement in the presence of ingested heavy metals might be a signal suggestive of danger to the gut's health. The report by Manjula *et al* (2013) where factory workers exposed to cement dust presented with series of gastrointestinal problems ranging from diarrhea as well as constipation might suggest modulatory roles that the cement dust can play when exposed to the gut.

Chromium which is a component of cement was recently reported to possess decreased intestinal and colonic motility properties in rat models exposed to trivalent chromium (Odukanmi *et al*, 2017). This further buttress the reported role of delayed in motility adduced to cement dust exposure in this current study. Certain gastrointestinal cancers were also linked to exposure to cement in some factory workers (Jakobsson *et al*, 1990) and even though this could occur through series of pathways, delayed motility is certainly a strong precursor in development of gastrointestinal cancers. More importantly if the heavy metals have potentials of generating reactive oxygen species (Bishak *et al*, 2015).

The observed findings in this study which were very similar to animals taken to cement factory environment further confirms for the first time that this model mimicks pollutions as though in the cement factory. It also buttresses the fact that cement dust exposure can be performed experimentally using this exposure chamber model. Pathological observations of the lungs and kidney, adverse observations of the haematological variables of exposed rats as well as elevated heavy metal levels found in blood of cement exposed animals confirms that cement dust is pathogenic to rats as also observed in humans. This study is therefore in concordance with most of the research works conducted previously regarding the toxicity effects of cement dust exposure to animals and humans

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Evaluation of Contamination and Ecological Risk of Heavy Metals Associated with Cement Production in Ewekoro, Southwest Nigeria

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Background. Exposure to heavy metals emanating from cement production and other anthropogenic activities can pose ecological risks.
Objectives. A detailed investigation was carried out to assess the contamination and ecological risk of heavy metals associated with dust released during cement production.
Methods. Sixty samples, including 30 soils and 30 plants, were collected around Lafarge Cement Production Company. Control samples of soil and plants were collected in areas where human activities are limited. Samples were dried, sieved (for soil; 65 µm), packaged and analyzed using inductively coupled plasma mass spectrometry at Acme Laboratory in Canada.
Results. The average concentration of heavy metals in soils of the area are: copper (Cu): 41.63 mg/kg; lead (Pb): 35.43 mg/kg; zinc (Zn): 213.64 mg/kg; chromium (Cr): 35.60 mg/kg; cobalt (Co): 3.84 mg/kg and nickel (Ni): 5.13 mg/kg. Concentrations of Cr in soils were above the recommended standards, while other metals were below recommended limits. The average concentrations of heavy metals in plants were: Cu: 26.32 mg/kg; Pb: 15.46 mg/kg; Zn: 213.94 mg/kg; Cr: 30.62 mg/kg; Co: 0.45 mg/kg and Ni: 3.77 mg/kg. Levels of heavy metals in plants were all above international limits. Geo-accumulation of metals in soils ranged between -0.15 and 6.32, while the contamination factor ranged between 0.53 and 119.59. Ecological risk index of heavy metals in soils ranged between 49.71 and 749.
Discussion. All metals in soils of the study area except for Cr were below the allowable limits, while the levels of metals in plants were above the permissible limits. Levels of heavy metals reported in this study were higher than those from similar cement production areas. Soils around the Ewekoro cement production area were low to extremely contaminated by toxic metals. Cement production, processing, transportation in conjunction with the abandoned railway track in the area greatly contribute to the high degree of contamination observed in the area. Metal transfers from soil to plant are a common phenomenon. The metals pose low to considerable ecological risk.
Conclusions. Anthropogenic sources, especially cement processing activities, release heavy metals which leads to progressive pollution of the environment and poses high ecological risk.
Competing Interests. The authors declare no competing financial interests
Keywords. cement production, contaminated, ecological, heavy metals mobilized, soil.
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Introduction

Emission of toxic metals from industries is a source of environmental degradation, and can affect human heath.[1-10] Cement production emits dust particles of various sizes, volatile substances and dangerous metals, harming the environment.[11,12] Cement dust reduces crop yield (through stomata clogging), gaseous exchange, rate of transpiration and inhibits intercellular processes, and also affects surrounding ecosystems.[13-17] The main materials used in the production of cement are limestone, shells, and chalk or marl combined with shale, clay, slate, blast furnace slag, silica sand, and iron ore.[18] Metals and compounds, such as lead, zinc, and sulfuric acid, originate from cement manufacturing plants.[19]

In developing countries, like Nigeria, soil quality plays a crucial role in food production, as metals emitted from industries can bioaccumulate in plants from soil.[20-23] Ingestion of these plants can lead to health problems and eventually mortality.[20-26] Cement dust has a high percentage of calcium silicate which is harmful to human health when ingested.[27,28] The alkaline compound has the ability to transform to C-S-H bond when it reacts with

oxygen in the soil, this consequently makes the presence of calcium silicate a major problem when ingested or even with dermal contact.[29]

Cement dust also contains hexavalent chromium, a compound that is highly toxic in nature, and has major health impacts when bioaccumulation occurs up the food chain.[35-37]

Little or no study has been carried out to assess the extent of contamination of heavy metals in soils and plants or evaluate the health and ecological risks associated with cement production in the study area.[38-40] The research was therefore carried out to assess the impact of heavy metals found in cement dust on the soils and plants within and around Ewekoro Portland cement factory and also evaluates the health impacts.

Methods

Ewekoro is located within latitude N 6°53'00"-N 6°55'00" and longitude E 3°12'00"-E 3°13'00" in southwestern Nigeria *(Figure 1)*. Ewekoro is found along the Sango-Ifo-Abeokuta Expressway of Ogun State, bordering Papalanto in the west and Abeokuta in the east. The town is 54 km from Lagos and 24 km from Abeokuta. Ewekoro is easily accessible and drained mainly by the River Ewekoro, which is seasonal in nature and has many tributaries.[41] The topography of Ewekoro is an immeasurable low land. The area experiences high levels of humidity and shrubbery is primarily located on tree plantations. The climate is significantly marked by two alternating wet and dry seasons. The average temperature in the area is 27.1°C with the highest and lowest temperatures recorded in March and August, respectively. The mean annual rainfall in the area is 1305 mm with the highest rainfall observed in June and the lowest rainfall in

Abbreviations

CD	Contamination degree	*Igeo*	Geo-accumulation index
CF	Contamination factor	*PLI*	Pollution load index
ER	Ecological risk	*RI*	Risk index
ERI	Ecological risk index		

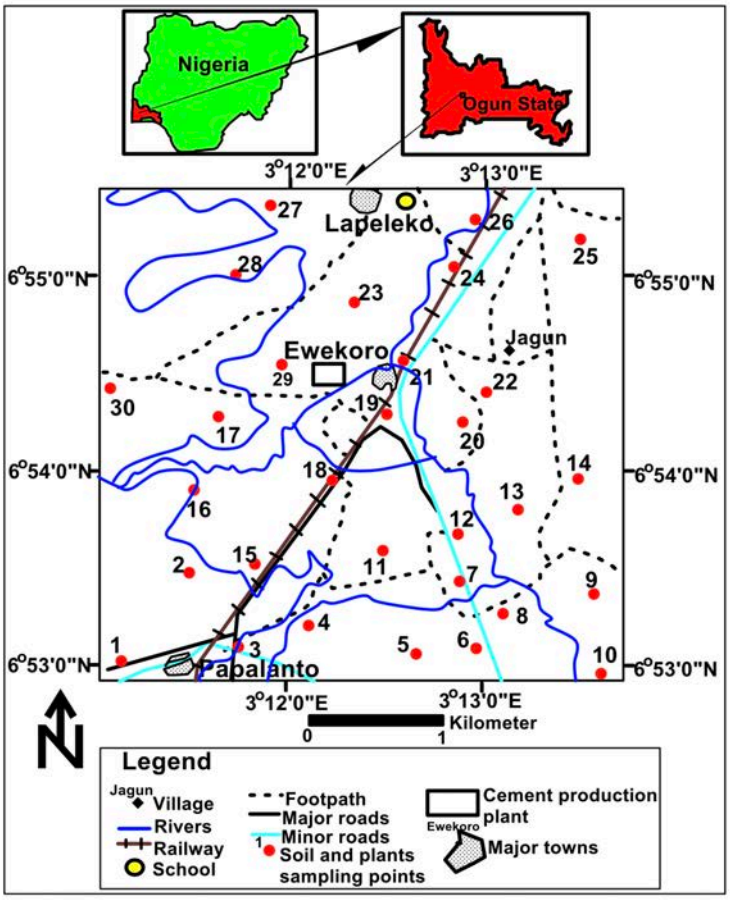

Figure 1 — Map of Study Area

January.[42] According to the United States Department of Agriculture classification scheme, the soils of the area are ferric, quartz and highly weathered clay minerals.[43,44] Human activities in the area include mining, quarrying, farming and cement production, and has a population of 55,156.[45,46] The area is found within the Dahomey basin, which is one of the major sedimentary basins in Nigeria. Ewekoro is a type locality for limestone deposits in the country and soil type reflects the presence of clay minerals.[47,48]

Sampling

Thirty (30) topsoil samples weighing 1 kg each were collected at a depth of 20 cm in March 2015 using a hand auger. After each sample was collected, all instruments used for sample collection were washed using distilled water and dried before use at the next sampling point.[49] This method was repeated for of all of the collected samples. Three control samples were collected in areas with no observed anthropogenic activities. Likewise, 30 healthy plant samples, commonly consumed by locals were collected from four species of plants: *Celosia argentea* (soko), *Corchorus olitorius* (ewedu), *Colocasiaesculenta* (cocoyam), *Musa* sp.(banana) and *Saccharum officinarum* (sugar cane). The foliage was picked into a container and tagged.[50,51] Two (2) control samples of soils and plants were also collected in areas with no observed anthropogenic activities.

Chemical analysis

In the laboratory, all the soil and plant samples were dried at room temperature. The sods were pulverized and sieved using an impact electric sieve shaker. After sieving, clay-sized (63 µm) sediments were collected and packed into small zip-lock bags. The grains were divided into roots, stems, and leaves and pulverized to fineness (<0.002 mm) using a china clay mortar and pestle. Soil and plant samples were then digested before analysis.

One (1) gram of soil was weighed from each pulverized sample and dissolved with 15 ml nitric acid, 20.0 ml perchloric acid and 15.0 ml hydrofluoric acid, and heated for three hours and thereafter measured into a 100 ml flask with distilled water.[51] Plant samples were thoroughly washed in deionized water because they are more prone to battering of sediments, heated at 105°C for 5 minutes, cooled at 70°C for 48-72 hours to a stable mass, then turned into a powdery form in a 100 µm blender so they could be easily dissolved.[52-54] A homogenized measured mass of 0.25 g was put in a 100-ml dry Pyrex digestion tube and digested with 5 ml of concentrated nitric acid was measured with it for the metals analysis. Digested samples were diluted with ultrapure water using a 1:50 dilution factor. Digestates were sent for analysis at Acme Laboratory Canada. Metals analyzed in the samples included copper (Cu), lead (Pb), zinc (Zn), chromium (Cr), cobalt (Co) and nickel (Ni). Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS) software program version 21. It was used to calculate mean, minimum, maximum, standard deviation and bivariate correlation.

Contamination and risk assessment

The equations described below were used to evaluate the contamination, ecological and health risks of heavy metals in samples. Heavy metal contamination in soils was calculated using the geo-accumulation index (Igeo), contamination factor (CF), contamination degree (CD) and pollution load index (PLI).

Geo-accumulation index

The Igeo was used to assess contamination of a specific metal in soils by evaluating metal enrichment above baseline or background values. Geo-accumulation index was calculated according to Equation 1.[55]

Equation 1

$$I_{geo} = log_2 \, x \, C_n / (1.5 \times B_n)$$

where, C_n is the metal concentration in the sample; B_n is the concentration of metal in the background sample, and the constant 1.5 is introduced to minimize the effect of possible variations in the background values which may be attributed to lithologic variations in the samples. The following interpretation for the Igeo was given by Loska*et al.*: Igeo<0 = practically unpolluted, 0<Igeo<1 = unpolluted to moderated polluted, 1<Igeo<2 = moderately polluted, 2<Igeo<3 = moderately to strongly polluted, 3<Igeo<4=strongly polluted, 4<Igeo<5= strongly to extremely polluted and Igeo>5 = extremely polluted.[56]

Contamination factor

The assessment of soil contamination was also carried out using the CF in Equation 2. The CF is the single element index, and all four classes are recognized.[57]

Equation 2

$$CF = \frac{\text{Metal concentration in soils}}{\text{Concentration of element in background soils}}$$

The CF can be classified as follows: CF<1: low contamination; 1<CF<3: moderate contamination; 3<CF<6: considerable contamination; CF≥6: very high contamination.

Contamination degree

The sum of contamination factors for all examined elements represents the CF of the environment.[58] The CD is aimed at providing a measure of the degree of overall contamination in surface layers in a particular sampling site. The formula for calculating the CD is shown in Equation 3.

Equation 3

$$C_d = \Sigma_{i=1}^{n} C_f^i$$

where, C_d is the contamination degree and C_f is the contamination factor. A CD<6 indicates a low degree of contamination, while 6<CD<12 implies a moderate degree of contamination. In addition, 12<CD<24 indicates a considerable degree of contamination, while CD> 24 reflects a high degree of contamination.

Pollution load index

The PLI is defined as the ratio of element concentration in the study to the background content of the abundance of chemical elements in the continental crust and is used to assess environment quality.[59,60] The PLI for the soil samples was determined by the equation below, as proposed by Tomilson *et al.* and used by Anjos *et al.*[58,59]

Equation 4

$$PLI = (CF_1 \times CF_2 \times CF_3 \times \ldots \times CF_n)^{1/n}$$

According to Chen *et al.*, the PLI of each metal is classified as either low (PI≤1), middle (1<PI≤3) or high (PI>3).[60]

Contamination load index

Equation 5 was used to determine the rate of contamination of specific metals in the grain/plant.

Equation 5

$$CLI = {}^{C_{crop}}/_{MPC}$$

Where, CLI is the contamination load index; C_{crop} is the concentration of metal in a plant; MPC is the maximum permitted concentration of metals in crops, and a contamination load index >1 indicates contamination of grains by metals.[61]

Bioaccumulation factor

Bioaccumulation factor is defined as the ratio of metal concentration in plant to that in the soil.[62] It is expressed using Equation 6.

Equation 6

$$BAF = {}^{C_p}/_{C_{so}}$$

Where, BAF is the bioaccumulation factor, and C_p and C_{so} are the metal concentration in aerial parts of the plant (mg/kg) and in soil (mg/kg), respectively. When the bioaccumulation factor>1 there is mobility of metal from soil to plant.

Ecological risk assessment for metals in soils

Ecological risks of metals were evaluated using the ecological risk index (ERI) *(Equation 7)* as presented by Mamut *et al.*[63]

Equation 7

$$ERI = T_R^i \times C_f^i$$

Where, ERI is the potential ecological risk of a single element; T_R is the toxic-response factor; and C_F is the pollution of a single element factor, which is also the contamination factor. The toxic-response factors for some metals used in the study were Zn = 1, Cr = 2, Cu = 5, Pb = 5, cadmium (Cd) = 30, Ni = 5. The results from Equation 7 help to produce the risk index (RI), which is the summation of the ecological risk assessment (*Equation 8*).[64]

Equation 8

$$RI = \Sigma_{i=1}^{m} \times E_R^i$$

When the ecological risk (ER) is <40 and RI<150, this implies low ecological risk, while 40≤ER<80 and 150≤RI<300 indicate moderate ecological risk. A 80≤ER<160 and 300≤RI≤600 indicates considerable ecological risk, while 160≤ER<320 implies high ecological risk. An ER≥320 and RI>600 indicate very high ecological risk.

Results

The average concentrations of heavy metals in soils in the study area are presented in Table 1. The mean soil concentrations of the metals were Cu: 41.63 mg/kg; Pb: 35.43 mg/kg; Zn: 213.64 mg/kg; Cr: 35.60 mg/kg; Co: 3.84 mg/kg and Ni: 5.13 mg/kg *(Table 1)*. The results revealed a decreasing order of Zn>Cu>Cr>Pb>Ni>Co *(Table 1)* for the metals concentrations. Sample 21 had the highest concentration of Co, while sample 30 has the least concentration (*Figure 2*). For Ni, sample 20 had the highest concentration, while sample 30 had the lowest (*Figure 2*). The concentration of Zn was highest in sample 4 and lowest in sample 1 *(Figure 3)*. The concentration of Cr was highest in sample 27 and lowest in sample 1 *(Figure 3)*. The highest concentration of Cu was found in sample 27, while the lowest was found in sample 1 *(Figure 4)*. The highest concentration of Pb was found around sample 23, while the least values were found in sample 1 *(Figure 4)*. The study further showed that the concentrations of Cr in soils in the study area were above

Metal	Media	Mean (mg/kg)	Standard Deviation (mg/kg)	Minimum (mg/kg)	Maximum (mg/kg)	Significance value	Background value (mg/kg)	USEPA (2002)[65] (mg/kg)	FAO (2001)[61] (mg/kg)	Ashaka Cement (Wufem *et al.*,)[66] (mg/kg)	Objana (Odoh *et al.*,)[67] (mg/kg)
Cu	Soil	41.63	20.01	15.25	72.18	ρ = 0.01	5.29	270		0.30	0.083
	Plants	26.52	52.81	2.59	305.6	ρ = 0.01			0.60		
Pb	Soil	35.43	27.92	8.00	132.45	ρ = 0.01	11.26	200		-	0.046
	Plants	15.46	28.51	0.66	109	ρ = 0.01			0.20		
Zn	Soil	213.64	231.71	14.00	877	ρ = 0.01	26.37	1100		9.80	0.262
	Plants	135.87	444.58	14.90	252	ρ = 0.01			0.60		
Cr	Soil	35.60	24.86	8.00	102.15	ρ = 0.01	5.91	11			
	Plants	30.62	63.62	1.20	343	ρ = 0.01			1.30		
Co	Soil	3.84	1.63	0.05	6.28	ρ = 0.01	0.08	-		27.37	0.026
	Plants	0.45	0.9	0.02	4.54	ρ = 0.01			-		
Ni	Soil	5.13	4.35	1.00	26.31	ρ = 0.01	0.22	72		2.56	0.035
	Plants	3.77	7.22	0.06	29.10	ρ = 0.01			0.11		

Abbreviations: USEPA, United States Environmental Protection Agency; FAO, Food and Agricultural Organization.

Table 1 — Average Concentration of Heavy Metals in Soils and Plants of the Study Area

the United States Environmental Protection Agency (USEPA) standards, while the concentrations of Zn, Cu, Pb, Ni and Co were below this standard.[65] The average concentrations of the metals in soils were greater than those in the control samples (*Table 1*).

Metal concentrations in plants

The decreasing order of metals in plants in the present study area are Zn>Cr>Cu>Pb>Ni>Co (*Table 1*). Zinc had a mean value of 135.87 mg/kg, a minimum value of 14.90 mg/kg and a maximum value of 252.00 mg/kg; with a significance of ρ = 0.01. Chromium had a mean value of 30.62 mg/kg, a minimum value of 1.20 mg/kg and a maximum of 343.00 mg/kg, with a significant value of ρ = 0.01. Copper had a mean value of 26.52 mg/kg, with a minimum value of 2.59 mg/kg and maximum value of 305.60 mg/kg. The concentrations of Zn, Cr, Cu, Pb, Ni and Co in plants are above CODEX recommended limits.[61]

Contamination assessment of soils and plants

Results of the contamination assessment of heavy metals in soils in the study area are presented in Table 2. Copper had minimum and maximum Igeo values of 0.94 and 3.19, respectively, with an average of 2.23, while Pb had minimum and maximum Igeo values of -1.08 and 2.97, respectively, with a mean value of 0.69. Zinc showed a mean Igeo value of 1.84, while the average value of Igeo for Cr was 1.70. The minimum Igeo value for Co was -1.26, with a maximum value of 5.71 and a mean of 4.66, while the minimum Igeo value for Ni was 1.57 with a maximum Igeo value of 6.32. In addition, the results showed that the CF for Cu in soils of the area showed a minimum and maximum of 2.88 and 13.64, respectively, while for Pb the CF ranged between 0.71 and 11.76.The average CF value for Zn was 9.05 and 6.03 for Cr. For Co, the CF ranged between 0.63 and 78.58, and for Ni the minimum CF was 4.45 and the maximum was 119.59. The minimum CD for heavy metals in soils in the study area was 11.90, while the maximum was 105.82. In plants in the area, the mean contamination load index for Cu, Pb, Zn, Cr and Ni was 44.20, 77.30, 226.45, 23.55 and 34.27, respectively (*Table 3*).

Bivariate correlation

The results of the significant values (> 0.01) *(Table 3)* revealed that all metals in plants and soils originated from the same source, with the exception of Zn, which showed a varied value in soils and plants, suggesting different sources for the two media. This was confirmed in the results of the bivariate

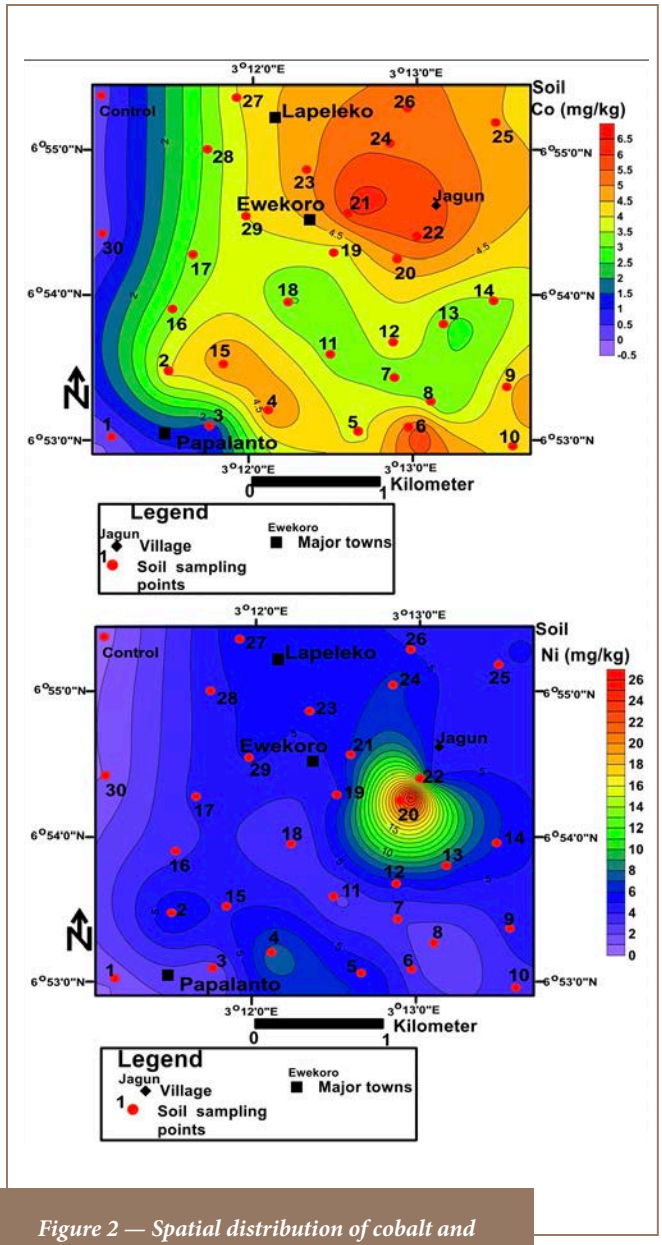

Figure 2 — Spatial distribution of cobalt and nickel in topsoil in the study area

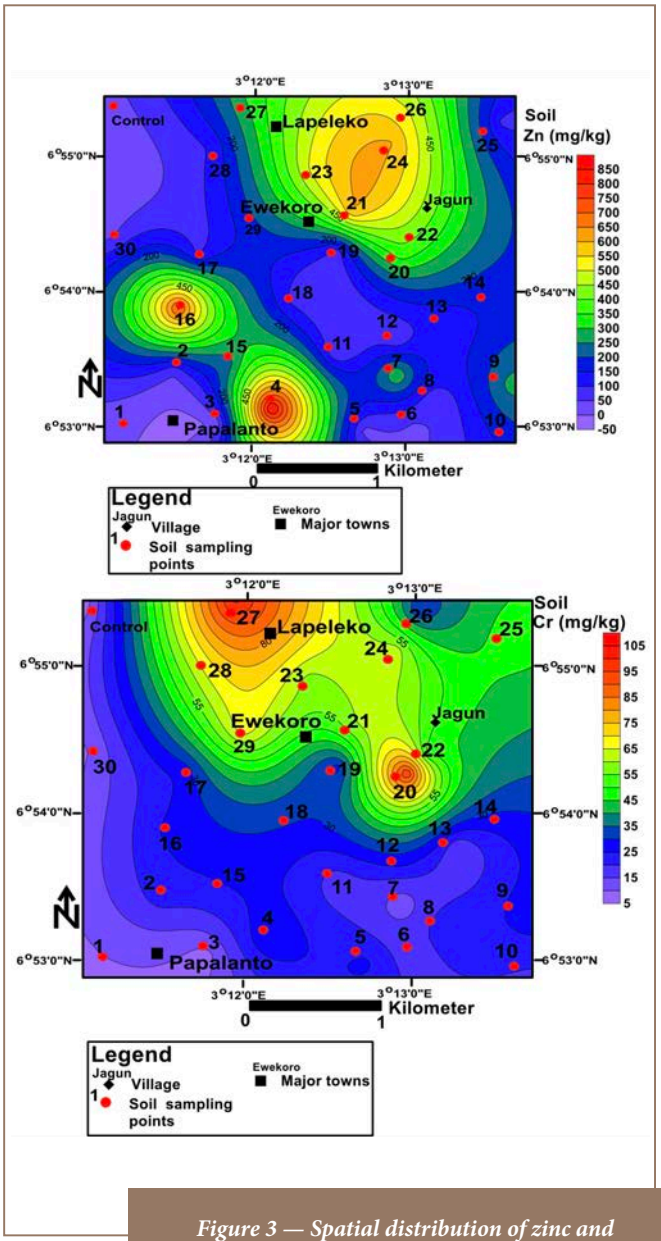

Figure 3 — Spatial distribution of zinc and chromium in topsoil in the study area

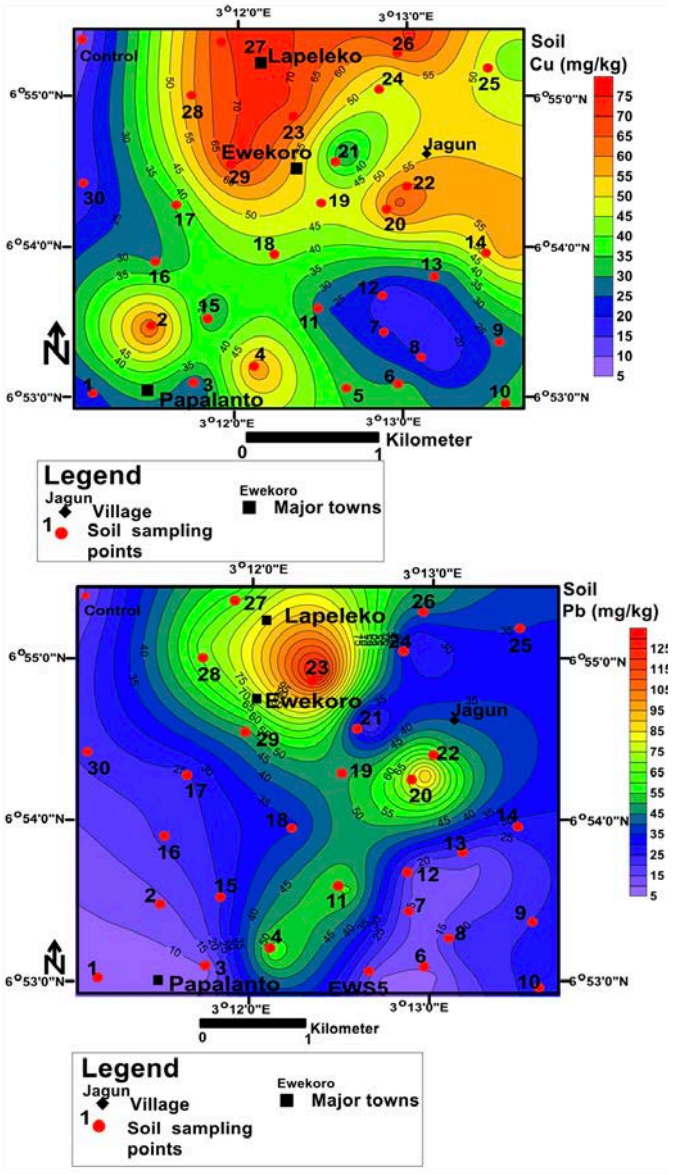

Figure 4 — Spatial distribution of copper and lead in topsoil in the study area

correlation *(Table 4)* that revealed the following significant correlations: Pb-Cu (r=0.680); Cu-Cr (r=0.699); Co-Cu (r=0.553); Pb-Cr (r=0.638); Co-Zn (r=0.529); Co-Cr (r=0.509) and Co-Ni (r=0.624) in soil and (Cu: r=0.682; Pb: r=0.606; Zn: r=0.923; Cr: r=0.973 and Ni: r=0.924) in plants, implying that the sources of these metals in plants in the study area originate predominantly from uptake from soils.

Bioaccumulation assessment of heavy metals in plants

The outcomes of the bioaccumulation assessment of heavy metals in plants in the study area are shown in Table 3. The minimum and maximum bioaccumulation factor for Cu was 0.04 and 1.84, respectively, and ranged between 0.01 and 5.09 for Pb. The average bioaccumulation factor for Zn, Cr, Co and Ni was 1.39, 0.86, 0.43 and 0.78, respectively.

Ecological risk

Results of the ecological risk assessment of heavy metals in soils in the study area are presented in Figure 5. The minimum ERI for Cu was 14.41, while the maximum was 68.22. For Pb, the minimum and maximum ERI was 3.55 and 58.81, respectively. For Zn, the ERI ranged between 0.53 and 33.26, with an average of 9.05, while the minimum and the maximum ERI for Cr was 2.71 and 34.57, respectively. Nickel had a minimum and maximum ERI of 22.27 and 597.95, respectively. The overall ERI for all the metals ranged between 49.71 and 749, with an average of 350.26

Discussion

Except for Cr in soils of Ewekoro, concentrations of heavy metals were below the recommended limits set by the USEPA.[65] However, they were above their corresponding measured

Metals	Igeo			CF/CD*/PLI**		
	Minimum	Maximum	Average	Minimum	Maximum	Average
Cu	0.94	3.19	2.23	2.88	13.64	7.87
Pb	-1.08	2.97	0.69	0.71	11.76	3.15
Zn	-1.49	4.47	1.84	0.53	33.26	9.05
Cr	-0.15	3.53	1.70	1.35	17.28	6.03
Co	-1.26	5.71	4.66	0.63	78.58	47.99
Ni	1.57	6.32	3.68	4.45	119.59	23.33
				11.90*	105.82*	97.42*
				1.37**	23.76**	9.73**

Table 2 — Geo-Accumulation Index, Contamination Factor, Contamination Degree and Pollution Load Index of Heavy Metals in Soils

Metals	Bioaccumulation factor			Contamination load index
	Minimum	Maximum	Average	Average
Cu	0.04	1.84	0.57	44.20
Pb	0.01	5.09	0.54	77.30
Zn	0.03	6.93	1.39	226.45
Cr	0.02	5.11	0.86	23.55
Co	0.01	7.40	0.43	-
Ni	0.05	3.87	0.78	34.27

Table 3 — Bioaccumulation Factor and Contamination Load Index of Heavy Metals in Plants

concentrations in the background soils *(Table 1)*. Relating the above results with similar studies done in Ashaka and Obajana cement production areas in Nigeria, the concentrations of Cu, Pb, Zn and Ni in soils of the study area were above those reported in the two areas.[55-58] However, concentrations of Co in soils were lower than those reported in Ashakasoils, and higher than those in Obajana soils. In addition, concentrations of potentially toxic metals in plants in this area were above the recommended limits.[60] The spatial distribution of Co and Ni in soil *(Figure 2)* revealed that Jagun had higher concentrations of Co than other parts of the study area. In addition, Zn was highly concentrated in the northeast and southwest of the study area *(Figure 3)*. Concentrations of Cr were high in the northwest around Ewekoro, Lapeleko and Jagun *(Figure 3)*. Copper was well distributed in soils across the study area, but was highly concentrated around Ewekoro, Lapeleko, Jagun and Papalanto (*Figure 4*). Concentrations of Pb were high in soils around Ewekoro and Lapeleko *(Figure 4)*. The study revealed that aerial deposition of metal-laden soils might have contributed significantly to their concentration in the area. A study by Afolabi *et al.* showed that more than 70% of the inhabitants of the area live in houses about 2 km from the cement processing factory.[45] This indicates that toxic metals in soils of the area are highly concentrated in

	Cu_{Plant}	Pb_{Plant}	Zn_{Plant}	Cr_{Plant}	Co_{Plant}	Ni_{Plant}	Cu_{Soil}	Pb_{Soil}	Zn_{Soil}	Cr_{Soil}	Co_{Soil}	Ni_{Soil}
Cu_{Plant}	1											
Pb_{Plant}	0.670**	1										
Zn_{Plant}	0.966**	0.663**	1									
Cr_{Plant}	0.930**	0.723**	0.895**	1								
Co_{Plant}	0.872**	0.737**	0.855**	0.877**	1							
Ni_{Plant}	0.926**	0.783**	0.911**	0.981**	0.933**	1						
Cu_{Soil}	0.682	0.752	0.862	0.746	0.927	0.817	1					
Pb_{Soil}	0.666	0.606	0.546	0.522	0.995	0.517	0.680**	1				
Zn_{Soil}	0.610	0.240	0.923	0.516	0.951	0.863	0.390**	0.375*	1			
Cr_{Soil}	0.951	0.226	0.867	0.973	0.849	0.851	0.699**	0.638**	0.379*	1		
Co_{Soil}	0.969	0.247	0.829	0.873	0.376	0.631	0.553**	0.363*	0.529**	0.509**	1	
Ni_{Soil}	0.931	0.765	0.976	0.976	0.941	0.924	0.473**	0.470**	0.313	0.624**	0.438*	1

*Correlation significant at 0.01 level
** Correlation significant at 0.05 level

Table 4 — Bivariate Correlation of Heavy Metals in Soils and Plants

areas where people live. In addition, concentrations of heavy metals in plants of the area were above the recommended limits set by CODEX.[61]

In the study area, the Igeo revealed that soils are unpolluted to strongly polluted by Cu Pb and Cr (the classification has been clearly defined in Equation 1), while they are unpolluted to extremely polluted by Zn and Co *(Table 2)*. In addition, soils are moderately to extremely polluted by Ni (Loska *et al*).[56] However, the results of the CF showed that the soils in the area ranged from lowly to very highly contaminated by Pb, Zn and Co, while Cu and Cr present moderate to very high contamination (the classification is defined in Equation 2). Nickel showed considerable to very high contamination in soils of this area. The CD showed that heavy metals in soils of the area pose a moderate to high degree of contamination *(Table 2)*. This was affirmed by the PLI which also revealed a moderate

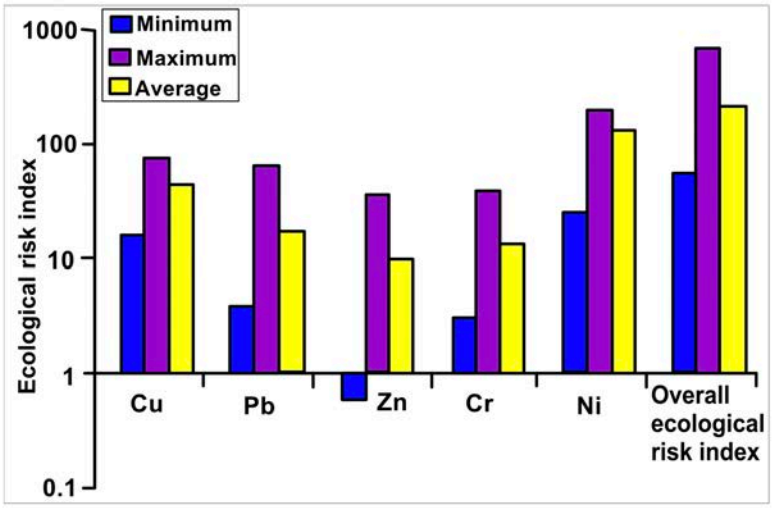

Figure 5 — Ecological risk index of heavy metals in soils in the study area

to high degree of pollution *(Table 2)*. This showed that cement production, processing, and transportation coupled with the abandoned railway track in the area might have significantly contributed to the high degree of contamination recorded in the area. According to Afolabi *et al.*, land and aerial pollution contributed 6.40% and 80.81% of the total pollution in the study area.[45] Oral ingestion, dermal contact and inhalation of contaminated soils and dusts might have contributed significantly to the spread of diseases in the area as reported by Afolabi *et al.*[45] In addition, the contamination load index revealed that plants in this area are highly contaminated by heavy metals. Consumption of contaminated vegetables and plants may also contribute to health issues in the study area.

The present study further revealed the presence of metals transfer from soil to plants across most of the study area *(Table 3)*. Bivariate correlation *(Table 4)* revealed that Cu, Pb, Zn, Cr and Ni were mobilized from soils to plants, while Co was not. Although metals in plants might have originated from soils in the area, aerial deposition of contaminated dusts is another possible means of contamination, entering plants through their stomata.

Correlation analysis of metals in soils showed that the potentially toxic elements in soils of the area might have originated from common mixed anthropogenic and point sources. Major possible sources of metals in soils of the area are cement production, processing, processing, rail and vehicular transportation. It was observed that Cu, Pb, Zn and Cr in soils of the study area posed low to considerable ecological risk (*Figure 5*), while Ni posed considerable to very high ecological risk (the classification is defined in Equation 8).

Conclusions

The present study was carried out to assess the extent of heavy metals contamination and their potential ecological risk in soils and plants of Ewekoro, southwest Nigeria. Concentrations of heavy metals in soils and plants in the area were above those in background samples and cement production areas across the country. Soils and plants in the area are contaminated by heavy metals which possibly originate from anthropogenic activities, especially from cement production and processing as well as rail and vehicular transportation. In addition, crops in the area are strong bioaccumulators of these heavy metals, although aerial deposition of contaminated dust is also a potential source of metals. Furthermore, the ecological risk potential of heavy metals in soils of the area ranged from low to considerably high. Further studies should be conducted on the extent of heavy metal bioaccumulation in this area and the potential health risk to local residents. Stricter rules should be introduced to regulate cement production activities to lower the emission rate of cement dust polluted with metals into the environment.

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ORIGINAL PAPER

Bioaccumulation of Toxic Metals in Children Exposed to Urban Pollution and to Cement Plant Emissions

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Abstract

Cement plants located in urban areas can increase health risk. Although children are particularly vulnerable, biomonitoring studies are lacking. Toenail concentration of 24 metals was measured in 366 children (6–10 years), who live and attend school in a city hosting a cement plant. Living addresses and schools were geocoded and attributed to exposed or control areas, according to modeled ground concentrations of PM_{10} generated by the cement plant. Air levels of PM_{10} and NO_2 were monitored. PM_{10} levels were higher in the exposed, than in the control area. The highest mean PM_{10} concentration was recorded close to the cement plant. Conversely, the highest NO_2 concentration was in the control area, where vehicular traffic and home heating were the prevalent sources of pollutants. Exposed children had higher concentrations of Nickel (Ni), Cadmium (Cd), Mercury (Hg), and Arsenic (As) than controls. These concentrations correlated each other, indicating a common source. Toenail Barium (Ba) concentration was higher in the control- than in the exposed area. The location of the attended school was a predictor of Cd, Hg, Ni, Ba concentrations, after adjusting for confounders. In conclusion, children living and attending school in an urban area exposed to cement plant emissions show a chronic bioaccumulation of toxic metals, and a significant exposure to PM_{10} pollution. Cement plants located in populous urban areas seem therefore harmful, and primary prevention policies to protect children health are needed.

Keywords Heavy metals · Cement plants · PM_{10} · Nitrogen dioxide · Biomonitoring · Children health

Introduction

Cement plants are frequently located in urban areas at high population density. However, the production of cement generates emission of particulate matter (Leone et al., 2016; Mohebbi and Baroutian 2007), gaseous pollutants (i.e., nitrogen oxides, sulfur oxides, carbon oxides (Lei et al., 2011)), heavy metals (Chen et al., 2010; Chen, 2020; Gupta et al., 2012; Liu et al., 2019; Wu, 2021), and persistent organic pollutants (i.e., polychlorinated dibenzo-p-dioxins and dibenzofurans, polychlorinated biphenyls Richards and Agranovski 2017; Zou et al., 2018)). Thus, the presence of cement plants has been linked with altered air quality in working areas (Noto et al., 2015) and in urban areas (Leone et al., 2016). Furthermore, previous studies indicate an increased risk of adverse health outcomes in exposed adults (Bertoldi et al., 2012; Eom et al., 2017; Raffetti et al., 2019) and children (Bertoldi et al., 2012; Garcia-Perez et al., 2017; Marcon, 2014).

Although fly ashes from industrial combustion in cement kilns are released into atmosphere after appropriate purification, this procedure does not seem to adequately avoid the unintentional contamination of environmental matrices and, as a consequence, human exposure to toxic chemicals.

In particular, previous evidence points to cement production as a relevant contributor for the atmospheric emissions of several heavy metals as mercury (Chen et al., 2020; Wu et al., 2021), copper, arsenic, nickel, cadmium (Chen et al., 2010; Gupta et al., 2012; Liu et al., 2019), and chromium (Hwang et al., 2018; Isikli et al., 2003). Some of these metals have been identified as biomarkers of exposure deriving from cement production (Raffetti et al., 2019).

Heavy metals produced by human industrial activities can generate negative effects to human health and to the environment, because of their persistence, toxicity, biological accumulation, and molecular interactions (Rehman et al., 2018; Wu et al., 2016). In children, in particular,

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health risks include altered growth and development (Shah, 2020), obesity (Fan et al., 2017; Shao et al., 2017), neurologic (Alemany, 2017; Pujol, 2016; Rehmani et al., 2017), cognitive (Lucchini, 2019), respiratory disorders (Madrigal et al., 2018; Zheng et al., 2013), and cancer (Xu 2019; Zhang, 2019a; Zumel-Marne et al., 2019). In adults, long-term exposure t-o heavy metals has been mainly linked with impaired cognitive function and cognitive decline (Bakulski et al., 2020), osteopenia or osteoporosis (Jalili et al., 2020), altered glucose metabolism, insulin resistance and metabolic syndrome (Cortes et al., 2021; Guo et al., 2019; Moon 2014; Wen et al., 2020; Yang et al., 2020), obesity (Wang et al., 2018b), hypertension (Wu, 2018), cardiovascular risk (Domingo-Relloso, 2019; Wang et al., 2019), decrease renal function (Tsai et al., 2017), and cancer (Duan, 2020; IARC 2012).

In proximity of cement plants, heavy metals have been detected in environmental air (suspended particulate matter) (Ali-Khodja et al., 2008), in soil (Bermudez et al., 2010; Lv, 2018; Wang et al., 2018a; Yatkin and Bayram 2010) and, in humans (adult age), in biological samples as blood, urine and hair (Afridi, 2011; Dong et al., 2015; Hwang et al., 2018; Isikli et al., 2006).

Although the paediatric age appears particularly vulnerable to emissions generated by cement plants (Bertoldi et al., 2012; Garcia-Perez et al., 2017; Marcon et al., 2014), scarce information exists on body accumulation of several metals in children living close to these industrial facilities.

An increased health risk can also be present when children living in the surrounding of a cement plant are exposed to air concentration of particulate matter not exceeding the exposure limit (Marcon et al., 2014). Particulate matter vehiculates toxic metals, and children exposed to metal pollution early and chronically can accumulate negative health effects (Carrizales, 2006; Claus Henn, 2017,2016; Haynes, 2015; Torres-Agustin, 2013) mainly due to oxidative damage (Pizzino, 2017; Zheng et al., 2013), and to a more significant lung deposition of fine particles, as compared with adults (Sanchez-Soberon et al., 2015).

In this complex scenario, the pathways linking the environmental concentration of pollutants, the bioaccumulation of toxic elements, and the possible development of health effects in the short- and in the long-term, cannot be comprehensively depicted by separate analyses on environmental or biological monitoring. Thus, the combined evaluation of human biomonitoring techniques and environmental monitoring appears as a key tool for an adequate assessment of the body burden of toxic chemicals, and to explore the individual risk linked with an unhealthy environment. This approach adequately evaluates the combined results of different modalities of metals intake (i.e., inhalation, ingestion, dermal absorption) (Joas, 2012; Llobet et al., 2003).

Human nail clips, in particular, represent a valuable sample to assess metal exposure of various origin (Esteban and Castano 2009). The procedure is validated and noninvasive for the assessment of metal concentration, and has been used extensively used in pediatric age (Carneiro et al., 2011a; da Silveira Fleck et al., 2017; Menezes-Filho, 2018; Rodrigues 2018; Slotnick et al., 2005). Thus, the assessment of metal concentration in human nails represents a suitable indicator of long-term exposures (Hunter 1990; Slotnick and Nriagu 2006) to pollutants of anthropogenic origin (Hopps 1977; Hunter et al., 1990; Slotnick and Nriagu 2006; Sukumar 2006; Yaemsiri et al., 2010).

Methods

Study Design

We measured toenail concentration of a wide panel of metals (see below) in children living and attending public elementary schools in the city of Barletta (Apulia region, Southern Italy, 93,275 residents in the year 2020), an urban area hosting a large cement plant with a production capacity of about one-million-ton cement/year, powered with fossil fuels and waste-derived fuel. According to the European Pollutant Release and Transfer Register (E-PRTR, https://prtr.eea.europa.eu/#/home), the main activity of this facility is the production of cement clinker and clinker grinding. An additional activity is the incineration of non-hazardous waste included in the EU directive 2000/76/EC.

A public campaign in five elementary schools (from November 2019 to January 2020) served to explain the aims of the study to teachers, parents and children. At the end of the campaign, a total of 366 children (188 females, age range 6–10 years) were enrolled on a voluntary basis, after both parents signed the informed consent. Children also agreed to participate as volunteers and expressed consent. The enrolled subjects were the 8.5% of children aged 6–10 years living in the city of Barletta in the year 2020 (4,289 children). Inclusion criteria were living at the same address in the last 6 months before enrollment, and the absence of known diseases.

In the explored area, ground concentrations of particulate matter with a diameter of ≤ 10 µm (PM_{10}) emitted by the cement plant had been previously modeled by a 3-D Lagrangian Particle Model (SPRAY) (Rotatori and Pirrone 2012). This model is particularly fit to assess the environmental impact of industrial facilities located in complex geographical areas, where land/sea breeze and topography generate complex circulation patterns. The model allows an accurate assessment of the atmospheric dispersion of pollutants in non-homogenous and non-stationary conditions, also considering a reliable reconstruction of complex wind and

turbulence fields (Gariazzo et al., 2004). The pollutant concentration used as input was the maximal PM_{10} stack emission limit allowed for the cement plant (20 mg/Nm^3) (Rotatori and Pirrone 2012). Results, expressed by a colorimetric map, represent the average yearly ground concentration of PM_{10} following atmospheric transport. According to the pollutant dispersion model, the urban area with the minimal estimated ground concentrations of PM_{10} (i.e., below 0.5 µg/m^3) was considered as the control area. Conversely, the exposed urban area was that with the estimated ground concentration of PM_{10} in the range 0.5–40 µg/m^3 (Fig. 1). The address of the five explored schools and the home address of each enrolled children were geocoded and attributed to exposed or control area. According to the E-PRTR, the only industrial facility releasing air pollutants in the exposed area is the cement plant. Other relevant sources of air pollutants in both the exposed and the control area are vehicular traffic and home heating.

According to geocoding, 174 children attended two schools in the exposed area, and 192 attended the remaining three schools in the control area (Fig. 1). Not all children lived in the same area of the attended school. Thus, in order to evaluate the role of the individual exposure during the whole day, children were also divided according to home address, and the following three subgroups were considered: children living and attending schools in the control area (group A, $n = 189$, the less exposed subgroup); children living or attending schools in the exposed area (group B, $n = 110$, children only exposed at school or at home); children living and attending schools in the exposed area (group C, $n = 67$, the most exposed subgroup).

The study was approved by the local ethics committee (inter-provincial ethics committee, ASL FG/ASL BAT authorization n. 108/CE/2019).

Nail Collection, Sample Preparation, and Analysis

Toenail sample collection was conducted in all schools in a unique day (February 26, 2020). Parents were asked not to cut children's nails in the month before sample collection (from January 25 to February 26, 2020). Toenails were selected for sampling as preferential to fingernails due to the minor risk of external contamination (Barbosa et al., 2005). The procedure for toenail collection, sample preparation, and analysis is a well standardized technique (Sanches and Saiki 2011), and used extensively (Butler, 2018; Carneiro et al., 2011b; Chanpiwat et al., 2015; Coelho, 2014; da Silveira Fleck et al., 2017; Di Ciaula et al., 2020; Gault, 2008; Grashow et al., 2014; Oyoo-Okoth et al., 2010; Slotnick et al., 2005; Wickre et al., 2004; Wilhelm et al., 1994).

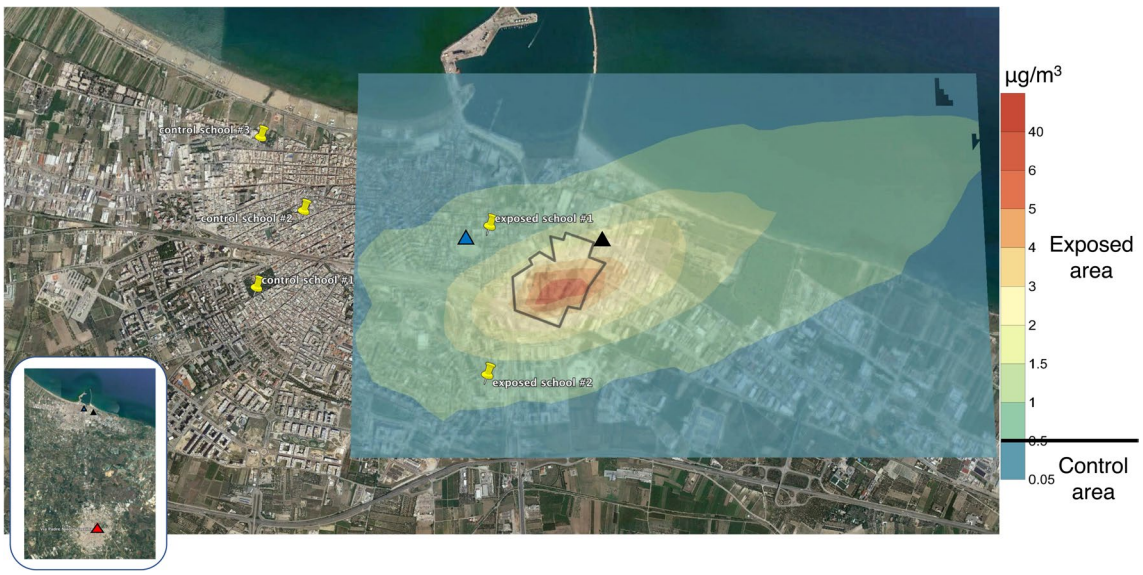

Fig. 1 Map of the explored city (Barletta, southern Italy, Apulia region), with a colorimetric modeling of the average yearly ground concentrations of PM_{10} emitted by the cement plant, following atmospheric transport. The site of the cement plant is delimited by a black line. The ground concentrations of PM_{10} generated by the cement plant have been estimated by a 3-D Lagrangian model (Rotatori and Pirrone 2012). According to the dispersion model, the urban area with the minimal estimated ground concentrations of PM_{10} (i.e., below 0.5 µg/m^3) has been considered as the control area. The exposed urban area was that with estimated ground concentration of PM_{10} in the range between 0.5 and 40 µg/m^3. The five yellow marks indicate the location of the explored schools (i.e., two exposed, three control schools). The black triangle indicates the location of the air monitoring station positioned in the high exposure area. The blue triangle indicates the location of the air monitoring station positioned in the intermediate exposure area. In the inlet, the red triangle indicates the monitoring station used for control exposure (see methods section). Map elaborated from Google Earth Pro and pollutant dispersion model (Rotatori and Pirrone 2012)

Toenails were clipped using ceramic blade to avoid possible contamination. Samples were stored in a 10 mL polypropylene tube for subsequent analysis, and scissors were cleaned with a light-acid solution.

Before assessing metal concentrations, samples were immersed in a 70% ethanol solution without stirring or sonication for a period of 10 min, to reduce the risk of microbiological contamination. Exogenous impurities were removed by a multistep washing procedure with acetone and Milli-Q purified water, and the cleaned samples were kept at room temperature for a period from 24 to 48 h for drying. The dry samples were weighed, and the concentration of 24 elements was subsequently calculated, using inductively coupled plasma mass spectrometry (ICP-MS): Antimony (Sb), Arsenic (As), Barium (Ba), Beryllium (Be), Boron (B), Cadmium (Cd), Chromium (Cr), Cobalt (Co), Manganese (Mn), Mercury (Hg), Molybdenum (Mo), Nickel (Ni), Lead (Pb), Copper (Cu), Selenium (Se), Silver (Ag), Thallium (Tl), Tellurium (Te), Thorium (Th), Titanium (Ti), Tungsten (W), Uranium (U), Vanadium (V) and Zinc (Zn). Given the mass variation of the nail samples, specific methodological Limits of Detection (LOD) were adopted for each sample. The analytical procedure was performed using a standardized technique, according to the EPA 6020A 2007 method. https://19january2017snapshot.epa.gov/sites/production/files/2015-07/documents/epa-6020a.pdf

Assessment of Air Pollutants

The average daily air concentrations of PM_{10} and nitrogen dioxide (NO_2) were assessed during the four months preceding toenail sampling (from November 1, 2019 to February 26, 2020), and during the whole year 2019 by three air monitoring stations positioned and regularly managed by the Regional Environmental Agency (ARPA Puglia). Periodic quality control and validation of recorded data are performed by ARPA Puglia according to technical criteria depicted by national and international directives (D. Lgs. 155/2010, EU Directive 2008/50/CE). The concentrations of PM_{10} and NO_2 are available, for each monitoring station, as average daily values expressed in $\mu g/m^3$. The full database of recorded data is publicly available (http://old.arpa.puglia.it/web/guest/meta-aria).

As shown in Fig. 1, the first monitoring station is positioned at about 0.5 km from the cement plant, in an area with an average yearly ground concentration of PM_{10} above 2 $\mu g/m^3$, as estimated by the dispersion model (Rotatori and Pirrone 2012). This was defined as high exposure area. The second monitoring station is positioned at about 0.7 km from the cement plant, in an area (defined as intermediate exposure) with an average yearly ground concentration of PM_{10} in the range 0.5–1 $\mu g/m^3$, as estimated by the dispersion model (Rotatori and Pirrone 2012). The third monitoring station (control exposure) is located at 9 km from the cement plant, in a nearby urban area (city of Andria, 98,414 residents in the year 2020), with characteristics similar to the city of Barletta but with urban pollution primarily generated by vehicular traffic and home heating. In this control area there are no industrial plants with stack emissions recorded in the E-PRTR.

Assessment of Potential Confounders

Further environmental conditions or personal behaviors possibly influencing the concentration of metals in toenails were explored by a specific questionnaire administered at enrollment. Considered as confounders were domestic heating using biomass, orthodontic treatments, regular outdoor sports, regular exposure to passive smoke, consumption of locally grown vegetables. The questionnaire was administered to parents for self-compilation.

Statistical Analysis

Frequencies of categorical variables, means, standard errors, medians and range of continuous variables were calculated. The χ^2 test (proportions), the Mann–Whitney U test (unpaired data) or the Kruskal–Wallis Multiple-Comparison Z Value test (inter-group differences) were employed to evaluate differences. Correlations were tested using the Spearman's rank correlation coefficient. Tobit regression models were employed to examine the associations between the toenail concentration of metals, the location of the attended schools, and the role of potential confounders. Tobit regression was used to accommodate the left-censored nature of values, due to the presence of samples with metal concentration below the limit of detection (Lubin, 2004). Metal concentrations were log-transformed to meet the normal assumption (Tobin 1958). P values < 0.05 were considered statistically significant. Analyses were performed using R software version 3.5.1 (R Project for Statistical Computing, available from https://www.r-project.org/).

Results

As shown in Table 1, in the four months preceding toenail sampling, the average daily (24 h) air concentration of PM_{10} was significantly higher in the two exposed areas, than in the control area. As expected, the highest PM_{10} air concentration was recorded in the high exposure area (i.e., closest to cement plant). The annual mean PM_{10} concentration was above 20 $\mu g/m^3$, the limit set by the World Health Organization (World Health Organization 2006), in the control and in the two exposed areas, and the highest value was recorded in the high exposure area.

Table 1 Average concentration of air pollutants in the exposed and in the control area

	Control area	Intermediate exposure area	**High exposure area**
PM_{10} (μg/m^3)	20.8 ± 0.9	23.3 ± 0.9*	27.8 ± 1.0*°
Mean of daily (24 h) concentrations in the 4 months before toenail sampling	21.8 ± 0.6	22.0 ± 0.6	25.5 ± 0.6*°
Annual mean (year 2019)			
NO_2(μg/m^3)	77.2 ± 2.7	59.0 ± 2.2*	50.8 ± 1.9*°
Mean of daily (24 h) concentrations in the 4 months before toenail sampling	62.0 ± 1.6	43.0 ± 1.5*	59.5 ± 1.6*°
Annual mean (year 2019)			

PM_{10} particulate matter with a diameter of ≤ 10 μm; *NO_2* nitrogen dioxide. Data are expressed as mean ± SEM of daily (24 h) concentrations of air pollutants measured during the 4 months before toenail sampling (November 1st to February 27, 2020), and during the whole year 2019 (annual mean). Differences were tested by Kruskal–Wallis Multiple-Comparison *Z* Value Test

*$P = 0.000001$ vs control area; $P = 0.000001$ vs intermediate exposure area

The two exposed schools were located in the intermediate exposure area (Fig. 1). In this site, the average daily PM_{10} concentration measured in the four months before toenail sampling was lower than in the high exposure area, but was still significantly higher than in the control area.

The opposite trend was evident for NO_2. In fact, in the four months preceding toenail sampling, the highest air concentration of NO_2 was recorded in the control area, and the lowest in the high exposure area. This trend was also confirmed when the annual mean concentration of NO_2 was considered (Table 1). Although NO_2 is also emitted from cement industries, and not only from vehicular traffic and domestic heating, these findings might indicate a different prevalent origin of these two pollutants.

The analysis of toenail metal concentration found that Be, Te, Tl and Th levels were lower than LOD in all samples (Table 2; Fig. 2). The rate of samples with toenail metal concentrations above the LOD was comparable in children attending schools in the exposed or in the control area in all cases, except for Ni (37% exposed vs 55% control schools), Cd (19% exposed *vs* 11% control schools), Ba (94% exposed vs 99% control schools), and Hg (59% exposed *vs* 48% control schools) (Fig. **2**).

Table 2 shows the average concentration of each metal, as measured in children attending schools in the exposed or in the control area. Children attending schools in the exposed area had significantly higher concentrations of Ni, Cd, Hg, as compared with the control area. The opposite was evident in the case of Ba, since the toenail concentration of this metal was higher in children from the control, than in those from the exposed area.

Children with the highest individual toenail concentration of Ni (109.2 μg/g), Cd (4.2 μg/g) and Hg (1.56 μg/g) attended school in the exposed area. Conversely, the

Table 2 Absolute toenail metals concentration in children attending school in the exposed or control area

Metal	Exposed schools ($n = 174$)	Control school ($n = 192$)	*P*
Be	0	0	–
B	0.11 ± 0.11	0.1 ± 0.1	NS
Ti	0.15 ± 0.6	0.7 ± 0.3	NS
V	0.008 ± 0.004	0.047 ± 0.01	NS
Cr	0.28 ± 0.09	0.7 ± 0.2	NS
Mn	0.57 ± 0.13	1.5 ± 0.7	NS
Co	0.18 ± 0.1	0.19 ± 0.2	NS
Ni	0.97 ± 0.7	0.7 ± 0.1	0.0003
Cu	4.3 ± 0.5	4.5 ± 0.8	NS
Zn	76.5 ± 1.8	78.6 ± 3.8	NS
As	0.12 ± 0.07	0.05 ± 0.01	NS
Se	0	0.007 ± 0.003	NS
Mo	0.01 ± 0.01	0.04 ± 0.03	NS
Ag	0.02 ± 0.005	0.02 ± 0.009	NS
Cd	0.08 ± 0.03	0.01 ± 0.004	0.01
Sb	0.12 ± 0.03	0.16 ± 0.02	NS
Te	0	0	–
Ba	4.1 ± 0.5	7.8 ± 1.7	0.004
W	0.006 ± 0.006	0.027 ± 0.03	NS
Hg	0.15 ± 0.02	0.09 ± 0.02	0.001
Tl	0	0	–
Pb	0.36 ± 0.7	0.67 ± 0.2	NS
Th	0	0	–
U	0.008 ± 0.005	0.005 ± 0.001	NS

Data are expressed in μg/g. Values are reported as mean ± SEM. Differences were tested by Mann–Whitney *U* test

NS not significant

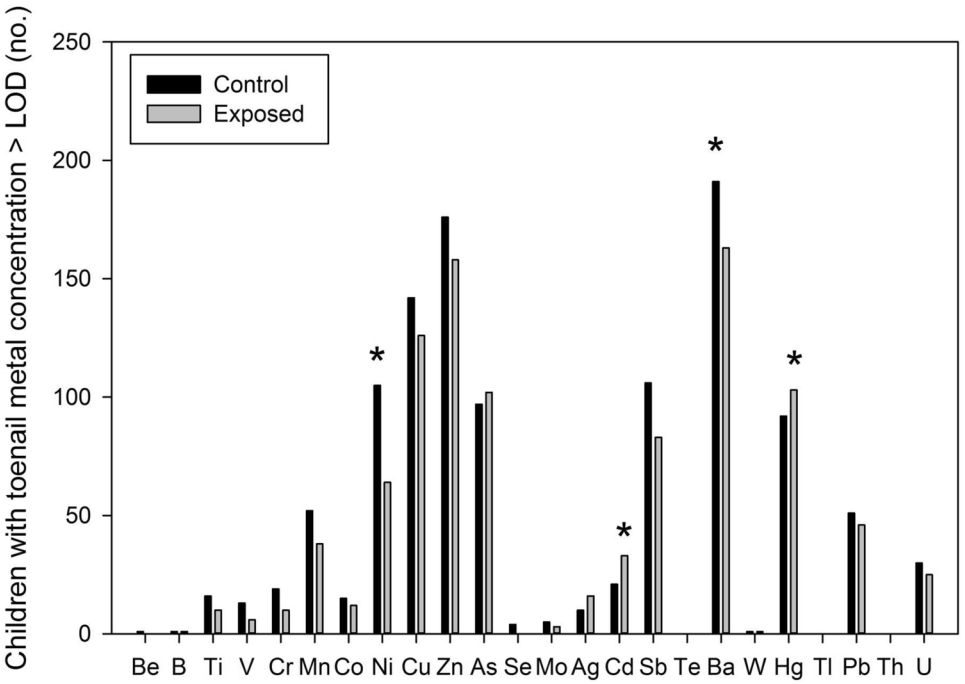

Fig. 2 Absolute number of toenail samples with metal concentration above the limit of detection (LOD) for each of the explored metals. Samples were from children attending school in the exposed or in the control area. Asterisks indicate $P < 0.01$ ($\chi 2$ test)

Table 3 Absolute toenail metals concentration in children selected according to the location of both attended school and home address

	Group A	Group B	Group C
n	189	110	67
Ni	0.7 ± 0.18 0.28 (0–22.9)	0.3 ± 0.07* 0 (0–4.5)	2.0 ± 1.7* 0 (0–109.2)
Cd	0.015 ± 0.004 0 (0–0.58)	0.06 ± 0.02* 0 (0–1.2)	0.1 ± 0.07 0 (0–4.2)
Ba	7.9 ± 1.7 3.2 (0–198.6)	4.6 ± 0.7 2.99 (0.58–61.7)	3.3 ± 0.3* 2.5 (0.26–14.8)
Hg	0.09 ± 0.01 0 (0–1.03)	0.14 ± 0.02* 0.07 (0–1.56)	0.16 ± 0.03* 0.08 (0–1.28)
As	0.04 ± 0.005 0.009 (0–0.55)	0.06 ± 0.02 0.036 (0–2.01)	0.25 ± 0.18* 0.05 (0–12.0)

Group A: children living and attending school in the control area; Group B: children living or attending school in the exposed area; Group C children living and attending school in the exposed area. Data are expressed in μg/g, and as means ± SEM, median (range)

*$0.002 < P < 0.03$ vs Group A (Kruskal–Wallis Multiple-Comparison *Z* Value test)

highest toenail concentration of Ba (198.6 μg/g) was recorded in a child attending school in the control area.

When both home and school address of enrolled children were considered, toenail concentration of metals in the group A, B and C were comparable in all cases (data not shown), except for Ni, Cd, Ba, Hg and As (Table 3). Children who either lived and attended schools in the exposed area had significantly higher toenail concentrations of Ni, Hg and As, than those living and attending schools in the control area. A similar trend was evident for Cd, and the opposite was shown in the case of Ba (Table 3).

According to results from the Tobit regression models (Table 4), the location of the attended school was a significant predictor of Cd, Hg, Ni and Ba concentrations, after adjusting for confounders. No significant effect on toenail metal concentrations derived from the analysis of covariates.

Considering the whole group of enrolled children, the Spearman's correlation matrix showed that toenail Cd concentration was correlated with Ni, Hg and As levels. Positive correlations were also shown between Ba, Ni, andAs concentrations (Table 5).

Discussion

The present study explored for the first time the chronic body accumulation of a wide panel of metals of anthropogenic origin in a cohort of children living and attending school in a populated urban area hosting a cement production plant.

In urban areas with pollution generated by multiple sources (i.e., natural sources, industrial facilities, vehicular traffic, domestic heating), monitoring air pollutants as unique technique of exposure assessment can underestimate the real individual exposure. Undervaluation can mainly derive from the multiple ways of intake of toxic chemicals (inhalation, oral ingestion, skin absorption), from the limited number of the air pollutants regularly monitored, from the effects of long-term exposure (i.e., accumulation of pollutants), and from the variable ground concentration of industrial pollutants generated by facilities located in urban areas

Table 4 Results of Tobit regression models on toenail metal concentrations in children attending control and exposed schools, and the effect of covariates

	Cd	Hg	Ni	Ba
Control vs. exposed	0.07* (− 0.12 to -0.018)	− 0.03** (− 0.05 to (− 0.02)	0.1* (0.03 to 0.18)	0.08** (0.03 to 0.13)
Domestic heating with biomass	−0.6 (−251.6 to 251.8)	0.08 (−0.09 to 0.3)	0.16 (−0.46 to 0.8)	0.008 (0.45 to 0.5)
Orthodontic treatments	0.0007 (−0.09 to 0.09)	0.007 (−0.03 to 0.04)	− 0.03 (0.04 to 0.5)	−0.04 (−0.14 to 0.05)
Outdoor sports	0.0004 (−0.06 to 0.06)	0.01 (−0.2 to 0.3)	−0.08 (−0.18 to 0.1)	−0.05 (−0.11 to 0.01)
Passive smoke	−0.8 (−250.1 to 251.8)	−0.08 (−0.008 to 0.04)	0.03 (−0.57 to 0.6)	−0.18 (−0.6 to 0.3)
Consumption of locally grown vegetables	− 3.3 (−0.1 to 0.05)	0.08 (−0.08 to 0.04)	0.5 (−0.1 to 1.1)	− 0.05 (−0.5 to 0.4)
Constant	− 1.67 (−1.8 to − 1.5)	−2.31 (−2.4 to −2.2)	−1.03 (−1.1 to −0.9)	−1.25 (−1.3 to − 1.18)

Only significant results (metal concentration) are presented. Metal concentrations were log-transformed to meet the normal assumption. Results (β coefficients and 95% confidence intervals) have been adjusted for covariates and consider the left-censored data present in metals distribution

*$P < 0.05$; **$P < 0.01$

Table 5 Spearman's correlation matrix considering the toenail concentrations of Ni, Cd, Ba, Hg, and as in the whole cohort of enrolled children

	Ni	Cd	Ba	Hg	As
Ni	–				
	–				
Cd	0.17				
	0.001	**–**			
Ba	0.21	0.089	–		
	0.0001	*ns*	–		
Hg	0.069	0.11	−0.03	–	
	ns	*0.03*	*ns*	–	
As	0.25	0.14	0.15	0.007	–
	0.000003	*0.008*	*0.005*	*ns*	–

Data are Spearman correlation coefficients (rho, normal text) and *P* values (in italic). Significant *P* values are marked in bold

with complex topography, inconstant wind directions and turbulence fields. Results from the present study point to the integration of environmental monitoring (i.e., the burden of specific pollutants in the environment) and biomonitoring techniques (i.e., the body burden of toxic chemicals) as a reliable method to assess the individual effects of environmental exposures, and the related health risk.

Distinct Patterns of Bioaccumulation in the Exposed and Control Area

The present study shows at least two patterns of metal bioaccumulation, according to the location of the attended school and the home address of children in the exposed or in the control area. Children either attending school and living in the area of maximal ground-level concentration of pollutants produced by the cement plant were the most exposed group. These subjects showed a higher accumulation of Ni, Cd, Hg and As, when compared to those living and attending schools in the control area. These metals correlated each other, indicating the possibility of a common source of emission.

On the other hand, children either attending school and living in the control area (i.e., the subgroup less exposed to plant emissions) showed a prevalent bioaccumulation of Ba. The concentration of this metal positively correlated with that of Ni, and previous evidence indicates that both Ba (Birmili et al., 2006; Figueiredo et al., 2007; Godri Pollitt et al., 2016) and Ni (Canteras et al., 2019) are markers of metal accumulation mainly deriving from vehicular traffic. These data confirm that vehicular traffic and home heating can be considered important sources of metal bioaccumulation in urban areas, besides industrial emissions. This hypothesis is in line with data deriving, in the present study, from the environmental monitoring of air pollutants. In this case, higher levels of NO_2 were present in the control, than in the exposed area. Of note, as Ba and Ni accumulation, also NO_2 air concentration is a well-known environmental marker of traffic density in an urban context (da Silveira Fleck et al., 2017).

Conversely, the increased body accumulation of Ni, Cd, Hg and As in the exposed area seems to be mainly related to the industrial emissions produced by the cement plant.

Cement Production as a Source of Pollution of Specific Metals

Raw material and fuels commonly employed for clinker/cement production (mainly fossil fuels as pet-coke and coal, but also waste-derived fuels), contain large amounts of heavy metals (in particular Hg, Co, Cd, Ni and Tl) (Gendebien et al. 2003; Genon and Brizio 2008; Zemba et al., 2011), and the emission of pollutants from cement kilns strongly depends on the primary fuel used (Zemba et al., 2011).

Mercury, in particular, is typically present in the emissions from cement kilns alimented with coal or pet-coke, supplemented or not with waste-derived fuels. This is due to the presence of Hg in elemental vapor form, which is less captured by the pollution control devices employed in kilns for cement production (Zemba et al., 2011).

Additional risk could derive from the presence of heavy metals (in particular the more volatile ones, as Hg) in substitution fuels (i.e., waste derived fuels), and from their transfer factors to gaseous emissions (Genon and Brizio 2008). Previous evidence showed that the substitution in cement kilns of fossil fuels with waste-derived fuels might have a negative impact on the emissions of heavy metals, and in particular Hg (Genon and Brizio 2008). This might be the case of the cement plant examined in the present study, in which an additional activity is the incineration of non-hazardous waste, which partially substituted fossil fuels to power the kiln.

A previous study exploring air pollutants generated from three commercially operating cement kilns co-burning waste, confirmed that Ni, Cd, Hg and As were among the predominant heavy metals emitted (Pudasainee et al., 2009). In the cited study, bag filters were able to remove above 98.5% of all heavy metals except Hg, which showed a removal above 60%. In the case of Hg, the removal efficiency ranged in the cited study from 77 to 28%. Thus, on average, about 40% of Hg was released into the atmosphere, as compared with 3.3% of Ni, 0.14% of Cd and 0.01% of As entering bag filters (Pudasainee et al., 2009).

Of note, these proportions (i.e., release of Hg and Ni higher than those of Cd and As) are comparable with those deriving, in the present study, from toenail concentration of the same metals in exposed children. In fact, children in the exposed area showed, on average, relatively higher concentrations of Hg (0.15 ± 0.02 µg/g) and Ni (0.97 ± 0.7 µg/g), as compared with those of Cd (0.08 ± 0.03 µg/g) and As (0.12 ± 0.07 µg/g).

The Accumulation of Metals in the Environment and in Biological Samples Surrounding Cement Plants

The presence of higher toenail concentrations of Ni, Cd, Hg and As in the exposed, than in control area is in line with previous observations confirming the accumulation of these metals in environmental matrices or in biological samples collected in geographical areas surrounding cement plants.

A recent study measuring heavy metals in the surrounding soil of a Chinese cement plant reported levels of Cd and Hg which were, respectively, two- and six times higher than background levels, thus generating a high ecological risk (Wang et al., 2018a). In France, cement plants in the Paris region have been identified as significant secondary source of soil contamination by Cd (Foti, 2017). A Turkish cement plant has been indicated as a significant contributor to depositions of trace elements, in particular Cd, in the surrounding area (Yatkin and Bayram 2010). Finally, in an Italian study, elevated Ni concentration were detected in leaves from trees close to a cement plant, as an effect of clinker production and storage (Baldantoni et al., 2014).

Similarly to studies which measured metal concentration in environmental matrices, previous biomonitoring studies showed, in biological samples from adult subjects, higher concentration of Cd in blood (Afridi et al., 2011; Isikli et al., 2006), hair(Afridi et al., 2011), and urine(Cha, 2011), higher Ni levels in blood (Afridi et al., 2011; Demir et al., 2005), and hair (Afridi et al., 2011), and higher Hg concentrations in blood (Dong et al., 2015), and urine(Cha et al., 2011) from subjects exposed to cement plant emissions, as compared with non-exposed subjects.

The Bioaccumulation of Specific Metals in Exposed Children

Our study shows, for the first time in pediatric age, higher Hg bioaccumulation in the area of maximal exposure to the emissions from the cement plant, as compared with the control area.

Cement production has been indicated as the largest Hg emission source in China, with considerable increase in Hg emissions in the last years (Chen et al., 2020). A recent study exploring positive effects of the COVID-19 lockdown on atmospheric Hg concentrations identified cement clinker production as the main responsible for Hg emission during the pre-lockdown period. In this study, the Hg emission from cement clinker production decreased markedly during the lockdown (Wu et al., 2021).

In a U.S. study, blood Hg levels measured in subjects living closer to a cement plant were associated with $PM_{2.5}$ modeling, and were significantly and positively correlated with As blood concentrations (Dong et al., 2015).

Approximately 80% of inhaled mercury is absorbed via the lungs and retained in the body (World Health Organization 1976). Although ingestion of contaminated food is a major source of Hg body levels (European Food Safety Authority (EFSA) 2012; European Food Safety Authority (EFSA) 2015), ground-level ambient air concentration of Hg is a significant predictor of body metal levels, also after controlling for covariates and other exposure variables (Hill 2020). Furthermore, in children living in industrial areas, a relatively high risk of exposure from hand-to-mouth intake is also possible (Abuduwailil et al., 2015).

These findings are in line with results from our study since, according to Tobit regression analysis, attending school in the exposed area was a significant predictor of increased Hg body levels.

Moreover, the average toenail Hg concentration recorded in the most exposed subgroup of children (0.16 ± 0.03 µg/g), was about three-times higher than that measured in a cohort of 290 children aged three years and enrolled in the New Hampshire Birth Cohort Study (0.055 ± 0.087SD) (Farzan 2021), and about 2.2-times higher than in a cohort of 222 U.S. healthy term newborns (0.07 ± 0.1SD) (Appleton et al., 2017).

A large biomonitoring survey involving, in 17 European countries, 1844 children aged 5–11 years participating in the DEMOCOPHES study, showed an average Hg concentration in hair (weighted geometric mean) of 0.145 µg/g (95% CI 0.139–0.151) (Hond 2015). Although a conversion ratio between Hg concentration in hair and in toenail has not been fully validated, according to a previous evidence this value should be equivalent to 0.05 µg/g in toenails (Choi 2009), a concentration about 3-times lower that that observed, in the present series, in the subgroup of the most exposed children.

Mercury is highly toxic to humans, in particular in terms of negative effects on the developing nervous system, and for exposures occurring in utero and during childhood (Rice et al., 2014). Thus, it has been strongly recommended to avoid Hg exposure during pregnancy and childhood as much as possible (European Food Safety Authority (EFSA) 2012; European Food Safety Authority (EFSA) 2015).

We found that the mean toenail Ni concentration measured in the whole population (0.8 ± 0.3 µg/g) was almost in the same range previously detected in other cohorts of children from Brazil (1.3 ± 1.0 µg/g, mean ± SD(da Silveira Fleck et al., 2017)), Italy (0.43 ± 0.18 µg/g, mean ± SE (Ciaula et al., 2020)), New Zealand (mean 1.08 µg/g, range 0.01–71.84 (Karatela et al., 2018)), and Pakistan (0.91 ± 0.1 µg/g mean ± SE (Bibi et al., 2016)). However, when the most exposed subgroup of children was considered (i.e., those living and attending school in the exposed area), the average Ni concentration was the highest (2.0 ± 1.7). Although a large variability existed, the maximal recorded value reached, in an exposed child, the value of 109.2 µg/g.

According to the International Agency for Research on Cancer (IARC), Ni is classified in group A1, i.e., "carcinogenic to humans". Besides the carcinogenic risk, Ni exposure can increase the risk of low birth weight (Sun 2018), preterm delivery(Chen 2018), and congenital malformations (Xu et al., 2021; Zhang, 2019b). In a cohort of adult patients with Mesoamerican nephropathy, average toenail Ni concentration (1.55 µg/g, range 0.18–42.65) was similar to that measured, in the present series, in children living and attending school in the exposed area (2.0 ± 1.7 µg/g). In the same study, control subjects showed a mean toenail Ni concentration of 0.21 µg/g (range 0.06–51.24), and the concentrations of this toxic metal were negatively correlated with the estimated glomerular filtration rate (Zhang et al., 2019b).

Cadmium has been identified as a biomarker of emissions from cement plants by biomonitoring techniques and atmospheric dispersion models (Abril et al., 2014).

In a previous Italian cohort of adult subjects, toenail Cd levels in the third (i.e., 0.0145–0.0306 µg/g) and in the fourth quartiles (i.e., ≥ 0.0306 µg/g) have been linked with an increased risk of prostate cancer, with ORs of 1.3 (95% CI 0.3–4.9) and 4.7 (95% CI 1.3–17.5), respectively (Vinceti 2007). In our study, the average toenail Cd concentration measured in children living and attending school in the exposed area was about 3-times higher than the threshold for the 4th quartile of Cd toenail concentration reported in the cited study. The average Cd toenail concentration measured in this subgroup of children (0.1 ± 0.07 µg/g) was also higher than the average value reported by the Italian National Institute of Health in another cohort of Italian subjects (0.041 ± 0.1)(Alimonti et al., 2010).

Cadmium levels have been also linked with exocrine pancreatic cancer (Kriegel 2006). A study assessing metal toenail concentrations in adult subjects with or without exocrine pancreatic cancer, demonstrated higher Cd concentrations in patients than in controls, and a significantly increased risk of pancreatic cancer in subjects with toenail Cd and As concentrations above 0.029 µg/g, and 0.1061 µg/g, respectively (Amaral 2012). Of note, in the present study, both average Cd (0.1 ± 0.07 µg/g) and As (0.25 ± 0.18 µg/g) toenail concentrations in children living and attending school in the exposed area were above the values reported in the cited study.

Besides the risk of cancer, previous studies linked increased Cd exposure in children with learning disability and cognitive delay (Ciesielski et al., 2012; Rodriguez-Barranco, 2014), altered immune response and inflammatory regulation(Zhang et al., 2020), altered renal function (Sanders et al., 2019), altered metabolic homeostasis(Pizzino et al., 2017).

Different Air Pollutants Concentration in Control and Exposed Areas

Heavy metals present in emissions generated by cement plants are vehiculated by particulate matter. Cement plants can increase atmospheric concentrations of particulate matter by both direct (Baroutian et al., 2006; Mohebbi and Baroutian 2007; Yatkin and Bayram 2010) and fugitive emissions from stocked materials (clinker and pet-coke materials) (Moreno 2009). Previous studies indicate these industrial facilities as a major source of PM_{10} in urban areas, being also responsible for the deterioration of air quality (Leone et al., 2016). This evidence is confirmed by results from the present study, which showed significantly increased air levels of PM_{10} in the exposed, as compared with the control area.

Previous authors found that the amount of particles emitted by a cement plant may be higher than levels recommended by WHO guidelines at a distance of about 600–1400 m from the plant stacks (Mohebbi and Baroutian 2007). In the present study, the distance from the cement plant and the two exposed schools is less than 1 km, and the annual average exposure to PM_{10} was above the limit set by World Health Organization (20 μg/m^3) (World Health Organization 2006) in all the examined areas. However, the highest annual mean PM_{10} level was present in the high exposure area, as compared with both control and intermediate exposure area.

In the exposed area, besides the possible health effects directly deriving by chronic bioaccumulation of heavy metals, the combined exposure to elevated PM_{10} and NO_2 air levels per se can be responsible for additional health risk. Children are particularly vulnerable to these pollutants, which can promote a number of health effects in the short term (i.e. asthma attacks and allergies Penard-Morand et al., 2010; Zhang, 2019c), and following chronic exposures (i.e., poorer performance in working memory, inhibitory control, behavioural regulation, and metacognition(Gui 2020a), reduced lung function(He et al., 2019; Oftedal et al., 2008; Xing, 2020), sleep disorders(Lawrence, 2018), altered lipid metabolism (Gui, 2020b; Kim et al., 2019)).

Limitations of the study

A limitation of the present study is the lack of evaluation of biological and epidemiological effects deriving from PM_{10} and NO_2 exposure, and from bioaccumulation of metals in enrolled children. These aspects should be investigated by future studies specifically designed to evaluate, in this geographical area, acute and chronic health effects possibly linked with a complex environmental exposure.

Inhalation of metals was the only exposure way considered in the present study. This can be identified as another limitation, since anthropogenic sources can contaminate vegetable-growing soils (Gan et al., 2018), water, and edible fish (Ramos-Miras et al., 2019), and the possible ingestion of contaminated food has not been comprehensively quantified in enrolled children. However, the consumption of locally grown vegetables has been considered as a possible confounder in the statistical analysis, and a significant role for this factor has been excluded. On the other hand, although not quantified, water composition and the average amount of fish consumption should be comparable in children living in the same city, with similar dietary habits. Furthermore, the cement plant was the only significant anthropogenic source of Hg in the explored area. Finally, it has been suggested that air concentration of metals can be considered a predictor of body metal levels, independently from other exposure variables (Hill et al., 2020). The separate role of different ways of exposure to environmental metals, however, should be better examined by further investigations.

Conclusions

The present study demonstrates, for the first time in pediatric age, a long-term body accumulation of toxic metals (i.e., Hg, Ni, Cd, As) in children living and attending school in an urban area with the maximal estimated ground concentration of PM_{10}, as calculated by a specific pollutant dispersion model. According to previous environmental and biomonitoring evidence, the distinct panel of metals chronically bioaccumulating in children is compatible with the emission pattern of metals generated by cement plants powered with fossil fuels and waste-derived fuels. The specific bioaccumulation pattern documented in the area mainly exposed to cement plant emissions is different from that found in children in the control area, which appears to be primarily related to vehicular traffic. Evidence from the present study also confirms the role of a cement plant located in a populated urban area as a significant contributor to urban PM_{10} pollution and, thus, to related health risk, in particular during childhood. Thus, the location of cement production plants in the context of an urban area seems particularly harmful, since the negative effects produced by the plant add up to those generated by other typical sources of urban pollution. Besides the previously documented health risk in adult age, the high vulnerability of children to this toxic and chronic exposure might generate significant consequences in the short and in the long term, and suggest the need of adequate primary prevention policies. Specific strategies, in particular, should be oriented to the relocation of cement production facilities away from urban centers, and to more strict regulations for the use of fossil fuels. Combustion of

pet-coke and coal, in particular, should be discouraged, and more sustainable energy sources (i.e., natural gas, renewable energy sources, biomaterials) should be preferred. More strict regulation of fossil replacement with alternative fuels should also be useful, with limitation of waste-derived fuels containing a significant burden of heavy metals. Furthermore, in the case of cement plants located in urban areas at high population density, an implementation of health education programs at all scales (schools, mass media, political sectors) might be necessary to improve resilience in subjects at risk.

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Data Availability The data are not publicly available due to the presence of information that could compromise the privacy of research participants. Data are available after reasonable and motivated request to the corresponding author.

Declarations

Conflicts of interest The authors declare no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the local, institutional research ethics committee (inter-provincial ethics committee, ASL FG/ASL BAT authorization n. 108/CE/2019).

Consent to Participate and to Publish Data All children were enrolled after parents signed written informed consent. Children also agreed to participate as volunteers. A consent to publish individual data after anonymization was also obtained by all participants.

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Characterization and Hazard Identification of Respirable Cement and Concrete Dust from Construction Activities

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Abstract: Construction is an important segment of the economy that employs millions of people. Construction dust is an occupational health hazard to millions of construction workers worldwide. The hazards associated with respirable dust depend upon its particulate size distribution and chemical composition, as these determine the deposition pattern in the respiratory tract and reactivity, respectively. This study presents characterization of the size and composition of the dust from two key construction materials—cast cement and poured concrete. The dust was generated by cutting the cured cement and concrete blocks using an 18" hand-held circular saw as used in highway and building construction. Transmission electron microscopy, scanning electron microscopy, dynamic light scattering, and laser diffraction were performed for the size analysis of the particles. Energy dispersive spectroscopy and X-ray photoelectron spectroscopy were used for chemical analysis. X-ray diffraction was used for phase identification. Electron diffraction patterns were obtained to assess the crystallinity of individual particles. They confirm the crystallinity of particles of different size and shapes. With a particle size range between 0.5 µm and 10 µm, greater than 90% of particles fell below 2.5 µm, presenting a respirable health concern. Crystalline compounds including the metals Al, Ca, Fe, Mg, Na, and K were detected. The concrete particles were most enriched in crystalline silica with a concentration of more than 30% by weight. The presence of metals and high crystalline silica content pose a serious health concern to construction workers.

Keywords: cement dust; respiratory hazard; $PM_{2.5}$ characterization; construction; crystalline silica

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1. Introduction

Cement and concrete are essential elements of modern-day infrastructure. Cement is the most common ingredient used in the construction industry as a binding material which sets and cures over time due to chemical reaction with water. Concrete is a mixture of sand, coarse stones, and cement. Water is added to concrete to activate the cement, which binds the mixture together. By the addition of coarse stones or aggregates, concrete can serve as a building material. Construction activities involving sawing, cutting, and grinding of cast cementitious and cured concrete expose construction workers to a cloud of crystalline dust particles. Exposure to these particles can be a serious health hazard. The Bureau of Labor Statistics estimates that more than 196,000 workers are employed as cement masons and concrete finishers in the USA alone [1]. Their occupation involves smoothening and finishing concrete surfaces with a variety of hand and power tools, which exposes them to the resultant dust. Several other trades including laborers may also perform concrete grinding activities, adding significantly to the total number of exposed workers [2]. In several of these occupations, the crystalline silica exposure from respirable construction dust can exceed by several hundred times that of the NIOSH Recommended Exposure Limit (REL) of 0.05 mg/m^3 [3]. With such a large portion of the working-age population at stake, there is a necessity to characterize and analyze the dust for its potential adverse health impacts.

In cement plants, cough, sputum, and breathing difficulty is prevalent in exposed workers [4]. Several studies indicate that chronic exposure to cement dust can significantly lower pulmonary functions with duration of exposure [5–8]. Furthermore, cement dust is also known to cause cancer of the larynx and lung [9,10]. Animal studies have shown that the dust can cause emphysema and fibrosis in lung tissues [11,12].

Cement dust inhalation appears to have secondary impacts as well because of its ability to reach various organs. Pimentel et al. inferred that the inhaled cement particles can enter into the bloodstream and reach the liver because swelling, inflammation, and lesions were found around the liver in cement mill workers [13]. Meo et al. found decreased performance of intercostal muscles and suggested that when cement dust enters the bloodstream, it can also reach and deposit into skeletal muscles, affecting their structure and performance [14]. More recently, inhaled particles were seen to cause disorders in the nervous system [15,16]. Other unhealthy traits such as higher blood pressure and significant increase in weight were found to be statistically prominent in exposed workers [17]. Studies have also revealed an association between cement dust exposure and lowering of hemoglobin and red blood cells in workers [18,19]. Some research groups have also speculated about the translocation of inhaled particles from the respiratory tract to the placenta and fetus, potentially affecting the offspring [20]. Studies have shown that suspended cement particles not only affect cement workers but also residents living near a cement factory or other sources of cement dust from manufacturing operations [21–24].

Differentiated from these workplace and exposure studies are construction activities involving the action of sawing, cutting, or grinding of cementitious materials and concrete. After casting or pouring and subsequent curing, the mineralogic composition of cement and concrete has changed. Well-known mineral forms include portlandite and quartz, each with its own crystalline structure and elemental composition. As often observed at building sites, and sidewalk and highway repair, clouds of dust are generated by the often-used circular saws. The duration of these particles being suspended in air and how far they travel from the source of emission is dependent of the particle size distribution of the dust. The finer particles can remain suspended longer and reach farther distances. In addition, particle translocation and associated secondary impacts seen in various other organs such as liver, heart, spleen, muscles, and so on, are also size dependent, as found in multiple studies [14–16,25,26]. Particles finer than 2.5 µm are more hazardous, as they enter deeper into the pulmonary system and bloodstream [27] and further reach other organs. Hence, a study of dust size distribution generated during cutting activities is critical.

Apart from particle size, the chemical composition of the dust also has a direct impact on the hazards posed by the dust particles. With reference to the components of cement and concrete products, crystalline silica is a known abrasive to the lung tissues and the cause of silicosis [28]. Calcium hydroxide causes irritation of the nose and throat with a risk of permanent lung damage [29,30]. Inhalation of dust containing metal content in the dust particles can also contribute to inflammation and lung damage [31].

Although the chemical composition of cement and concrete can be easily read off the manufacturer's data sheet, the chemical phases in the cement undergo substantial changes after hydration and setting. In addition, surface composition can be more important than overall composition, as the particle surface is what will be in direct contact with cell membranes. Surface composition can differ from the overall particle composition, contingent on the way cleavage occurs at the mineral phase boundaries in cement and concrete during the cutting activities. In addition, some of the chemical phases may separate out and preferentially form finer particles, depending on hardness and other physical properties of different phases and dynamics occurring during scission. Therefore, an in-depth study regarding the chemical nature of the dust is crucial for assessing the health concerns.

To understand the risks of cement and concrete dust toxicity, it is necessary to quantify the physical and chemical properties of these particles. Prolonged exposure to even small concentrations of toxins can be a serious health concern. To our knowledge, no study to date

has collected and performed size and chemical characterization of actual dust produced by cutting and grinding cement-based construction materials. To date, studies and regulations have focused upon cement dust exposure from factories. However, as routinely observed at construction sites, pre-cast concrete panels require cutting (e.g., for making slots and holes). Similarly, the replacement and repair work observed routinely on highways exposes the road crews (and passers-by) to cement dust during cutting. Workers are commonly seen without respiratory protection; even a mask is not required for such work. Although cutting of cement and concrete is extensive, surprisingly, very little is known about the particulate emissions from such activities. The toxic effects of this inhalation hazard will fundamentally depend upon particulate properties such as size, surface area, chemical composition, and crystalline structure. This study aimed to characterize the physico-chemical properties of cementitious dust as a basis for gauging potential health hazards. Armed with this knowledge, appropriate precautions and protective actions can be implemented.

2. Methodology

The cement paste was prepared by adding water to Portland cement concrete mix (Commercial Grade Quikrete Type I/II), with 67.3% cement by weight and the remainder of water. The mixing was carried out in a clean plastic bucket using a drill connected to a spiral mixing attachment. Cement paste was mixed according to the procedure prescribed in ASTM C305, with the exception that the mixing time was tripled to ensure consistency. The mixture was then poured into the mold. After, the mold was put on a vibrating table for 3–5 min to allow gases to escape. It was then covered for 24 h to set. As shown in Figure 1, the block of set concrete paste was cut using a TS 420 STIHL Cutquik Concrete Saw equipped with a diamond blade, while a custom homemade dust shroud attached to a vacuum collected the generated particles. A block of concrete obtained from a local manufacturer was used to generate the concrete dust using the same saw and collection apparatus.

Figure 1. Image showing the dust collection method and apparatus.

2.1. Laser Diffraction

Laser diffraction is the most common technique used to determine cement particle size distribution (PSD) [32]. The analysis is based on angular variation in scattered light intensity by particles of varying sizes. The sample solution was prepared by mixing collected cement dust in distilled water (~5% mass fraction) using a magnetic stirrer for 5 min, followed by ultrasonication for another 5 min. A Malvern Mastersizer 3000 was used to carry out laser diffraction measurements. The sample dispersion was added drop-wise into the automated sample dispersion unit containing distilled water with stirring and sonication modes turned on. The solution was added into the dispersion unit until the recommended obscuration (around 7%) was reached. The optimal obscuration eliminates the sampling error and multiple scattering error.

Cutting with the circular saw blade generates particles with a lognormal particle size distribution (PSD) for both cement and concrete, as seen in Figure 2. It was observed that more than 90% of the particles are less than 2.5 μm in size. The limitation of the laser diffraction measurement is that Fraunhofer and Mie theories are applicable to spherical particles, not the fragmented, irregularly shaped particles predominant in cement dust. Thus, other characterization techniques were employed to study the morphology of the particles.

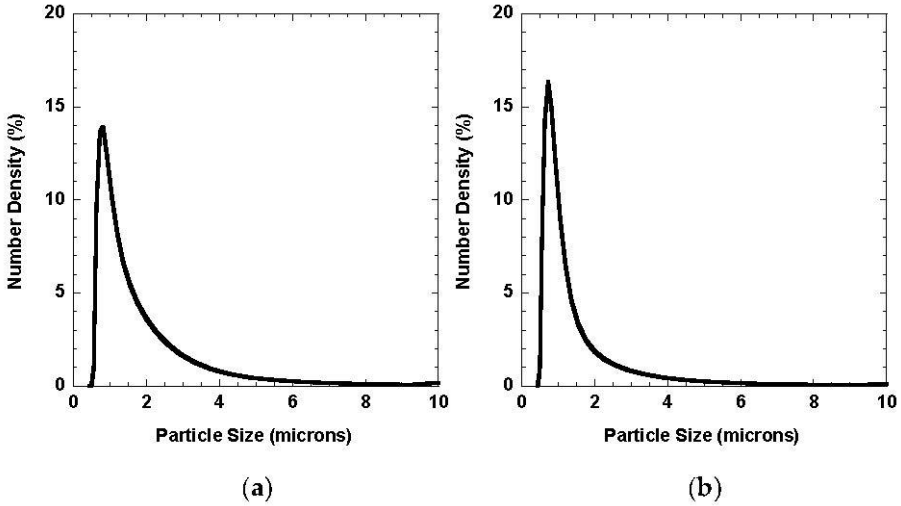


Figure 2. Fits to laser diffraction measurements of (**a**) cement and (**b**) concrete dust.

2.2. XRD

X-ray diffraction is one of the prominent techniques routinely used to identify and quantify crystalline phases in bulk powdered material. The measurements were carried out by a Malvern PANalytical Empyrean diffractometer equipped with a Cu source ($\lambda \cong 1.54$ A°), para-focusing optics, and a PIXcel 3D detector. The spectrum was scanned in the 2θ range of 5° to 90°. Figure 3 shows a portion of the collected spectrum for both cement and concrete dusts. Peaks corresponding to the top three crystalline components in the cement and concrete dust have been highlightedfor illustration. The background subtraction, phase identification, and quantification were performed using MDI JADE® software. Peaks at multiple diffracted angles from different lattice planes were verified for each phase using the database to ensure accuracy in phase identification. The quantification from the fit that yielded the lowest residual is reported in Tables 1 and 2.

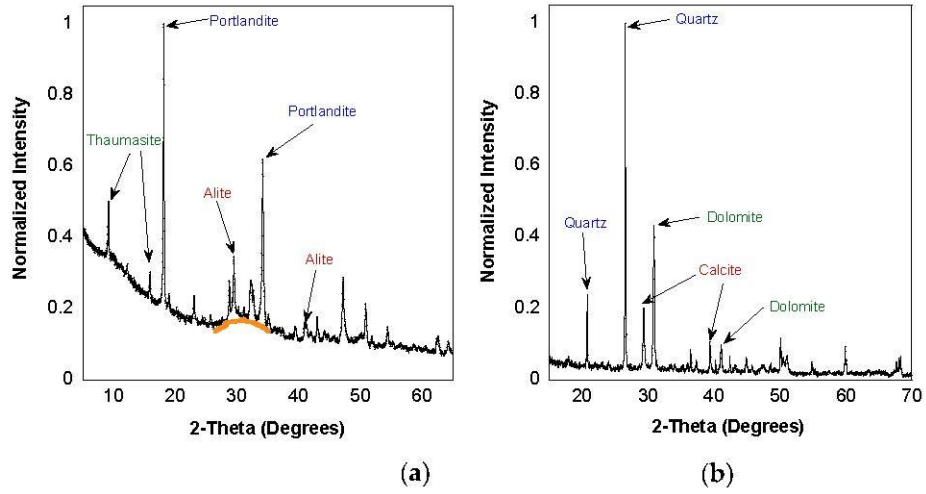


Figure 3. XRD pattern of (**a**) cement and (**b**) concrete dust.

Table 1. Quantification of crystalline phases in Cement dust from XRD.

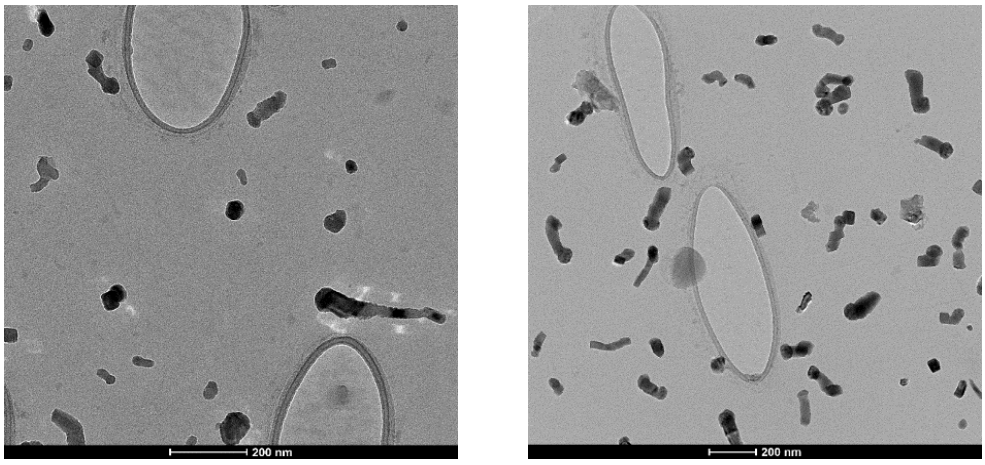
Phases	wt.%
Portlandite	38.5
Thaumasite	31.6
Lamite	7.8
Alite monoclinic	7.3
Calcite	6.9
Gypsum	4.8
Periclase	3.0

Table 2. Quantification of crystalline phases in concrete dust from XRD.

Phases	wt.%
Dolomite	45.1
Quartz	32.2
Calcite	18.3
Portlandite	2.2
Pseudo-wollastonite	2.3

2.3. TEM

Transmission electron microscopy (TEM) uses a beam of highly energetic electrons which transmits through the specimen to form an image on a fluorescent screen. The images were taken using a FEI Talos^{TM} F200X scanning/transmission electron microscope equipped with an FEG source providing 0.12 nm resolution. The TEM samples were prepared by sonicating the cement and concrete powder in ethanol for 5 min and then dropping 2–3 drops of the solution on single-layer graphene (SLG) supported on a copper TEM grid. The instrument was operated at 200 kV, and the samples were imaged at various magnifications in the range of 10 kX to 500 kX. Unlike other indirect particle size characterization techniques, direct TEM imaging can also reveal the particle morphology and compositional homogeneity. It was observed that the smaller particles (typically < 50 nm) are spherical, while the bigger particles have highly irregular shapes with sharp edges. Aggregates with varying mass thickness contrast were also observed, indicating inhomogeneous composition of primary particles. TEM images in Figure 4 show that most of the particles are below 100 nm, are non-agglomerated, and are a mix of non-spherical particles.

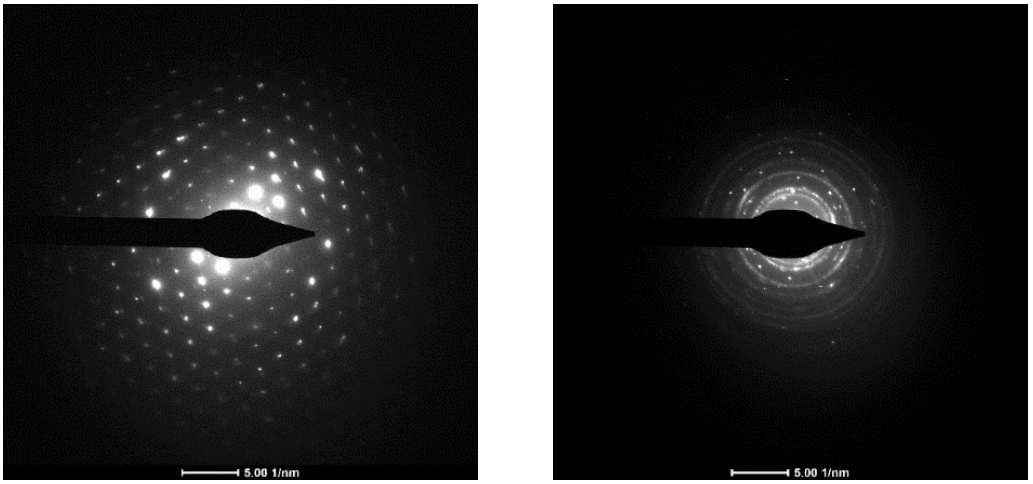


(**a**) (**b**)

Figure 4. Bright field TEM of (**a**) cement and (**b**) concrete dust on SLG grid.

2.4. Electron Diffraction

Selected area electron diffraction (SAED) patterns were obtained from samples on lacey carbon to assess the crystallinity of the particles. SAED is a unique technique in that it allows examination of a single particle. Both cement and concrete showed SAED patterns representing highly crystalline particles. A few particles showed a well-defined spot pattern as seen in Figure 5a, representing mono-crystallinity; while others, as seen in Figure 5b, exhibited a mixture of ring and spot patterns, representing both mono-crystalline and poly-crystalline phases in the same particle. This confirms that some elements like copper form separate mono-crystalline particles. The remainder of the particles consisted of a mixture of elements together wherein each element appears in its own crystalline phase.



(**a**) (**b**)

Figure 5. SAED pattern of (**a**) cement and (**b**) concrete dust.

2.5. EDS

Energy-dispersive spectroscopy (EDS) was performed for elemental composition and mapping in an FEI Talos™ F200X. The EDS mapping was performed in scanning transmission electron microscopy (STEM) mode with a low background sample holder. Using the instrument in STEM mode gives spatial resolution close to the minimum probe size, which is around 1.6 Å. The EDS maps were collected from a sample suspended on a single-layer graphene grid, while the elemental composition data were collected from a sample suspended in the vacuum region of the lacey carbon grid to avoid the background signal from the carbon in the lacy grid.

The EDS maps in Figure 6 show that particles of different size ranges are highly inhomogeneous in their chemical composition. Copper is seen to form a separate phase with relatively smaller particles (<100 nm). Magnesium and iron were found both in small and big particles (>100 nm). Calcium and aluminum were found in large but selective particles, while silicon was found in almost all large particles. Tables 3 and 4 show the chemical composition of larger size particles (~500 nm).

2.6. SEM

Scanning electron microscopy (SEM) was used to study the surface structure, morphology, and particle size of the samples. The images were taken using Thermo Scientific™ Apreo 2S SEM. The SEM images shown in Figure 7 suggest that the majority of the particles are pseudo-spherical and of size less than 100 nm. The large aggregates have a highly rough surface with many sharp edges and pointed corners. In addition, Figure 8 shows the fine-edged particles seen in SEM have potential for mechanical irritation to the tissues in contact with them.

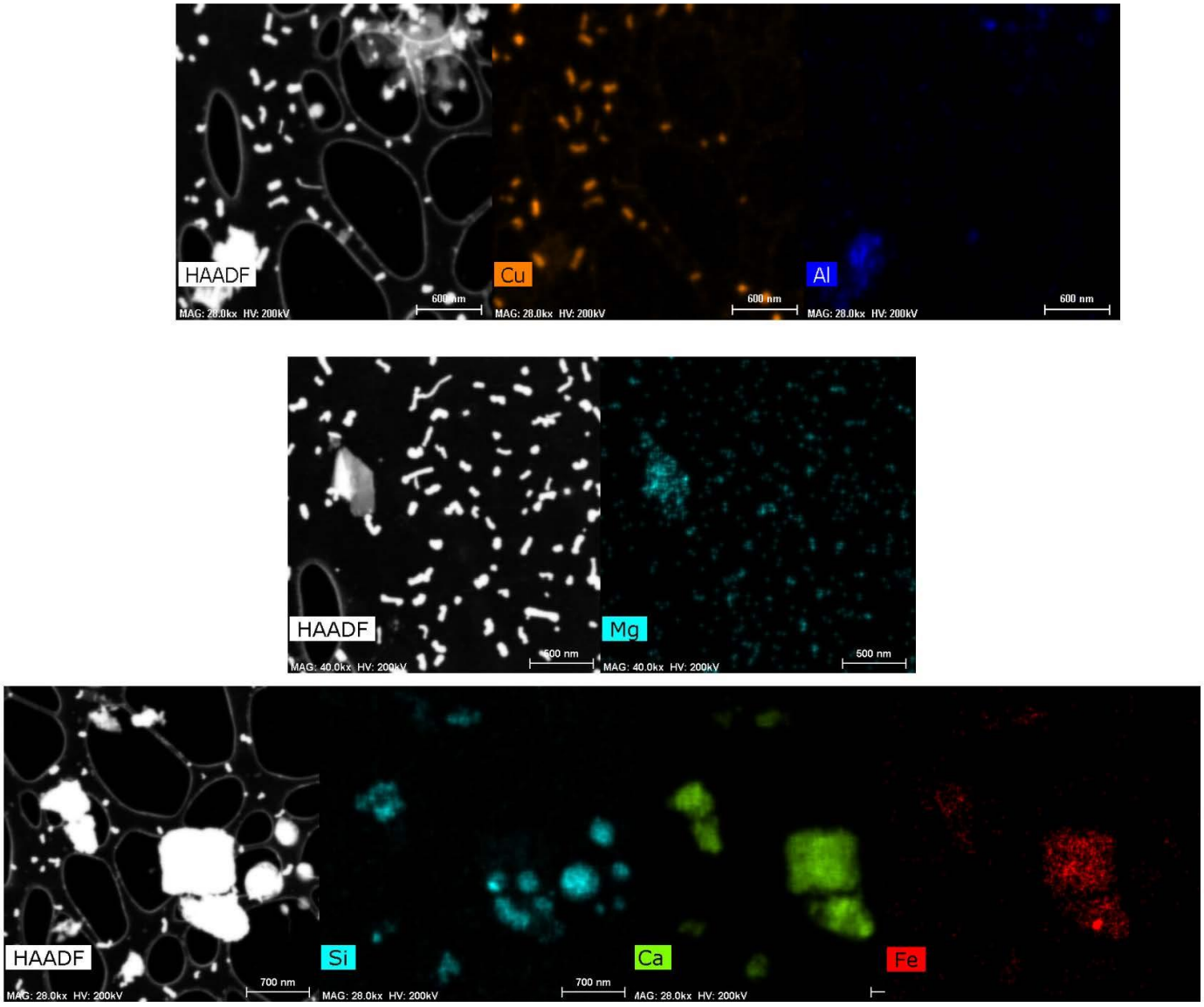


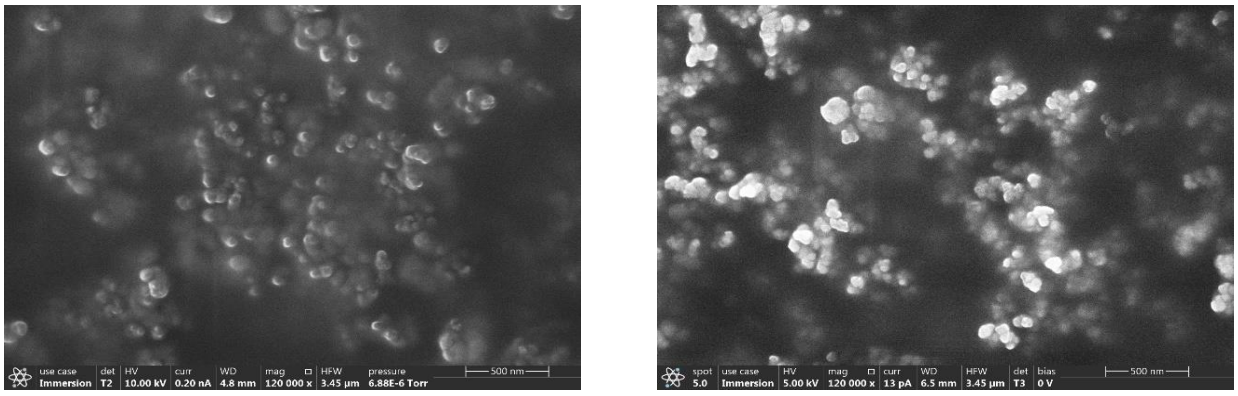
Figure 6. EDS maps showing inhomogeneous elemental distribution in particles.

Table 3. Elemental composition of cement dust from EDS.

Element	wt.%
Silicon	10.10
Calcium	38.32
Oxygen	36.14
Aluminum	1.68
Magnesium	0.30
Iron	1.09
Sulfur	1.73
Carbon	10.64
Chromium	0.008

Table 4. Elemental composition of concrete dust from EDS.

Element	wt.%
Silicon	32.56
Calcium	2.79
Oxygen	38.85
Aluminum	9.52
Magnesium	0.31
Iron	0.17
Sulfur	0.08
Carbon	3.20
Potassium	12.40
Sodium	0.132



(**a**) (**b**)

Figure 7. SEM images of (**a**) cement and (**b**) concrete.

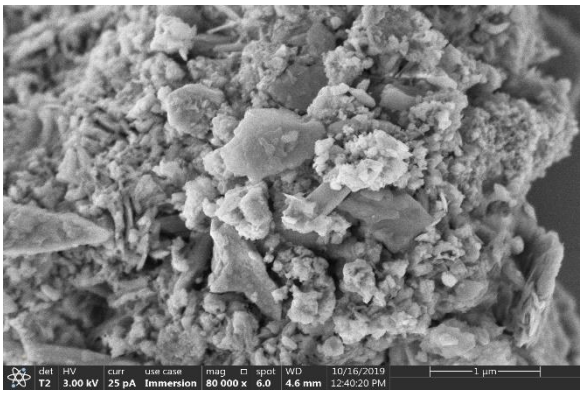


Figure 8. SEM image of representative cement aggregate.

2.7. XPS

X-ray photoelectron spectroscopy (XPS) is a widely used technique to probe surface composition, typically within the first 10 nm. XPS measurements were performed using a Physical Electronics VersaProbe II instrument equipped with a monochromatic Al kα x-ray source (hν = 1486.7 eV) and a concentric hemispherical analyzer. Charge neutralization was performed using both low-energy electrons (<5 eV) and argon ions. The binding energy axis was calibrated using sputter-cleaned Cu and Au foils. Peaks were charge referenced to the C1s band at 284.8 eV. Measurements were made at a takeoff angle of 45° with respect to the sample surface plane. Figure 9 shows XPS survey spectra from cement and concrete dust. Quantification was done using instrumental relative sensitivity factors (RSFs) that account for the incident X-ray cross section and inelastic mean free path of the emergent

electrons. Tables 5 and 6 give surface elemental composition from quantification of XPS survey spectra of cement and concrete dust.

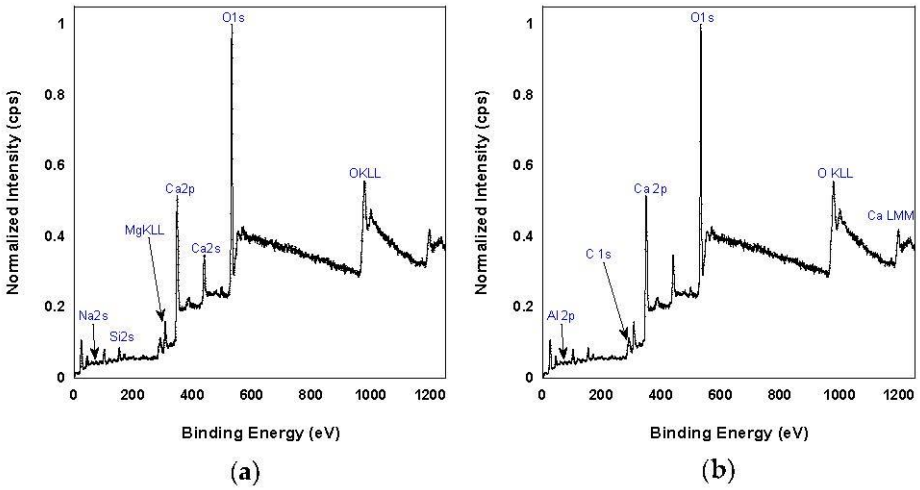


Figure 9. XPS survey spectra of (**a**) cement and (**b**) concrete.

Table 5. Surface elemental composition of cement dust from XPS.

Element	wt.%
Aluminum	1.1
Calcium	17.8
Iron	-
Potassium	0.8
Magnesium	1.2
Sodium	-
Oxygen	59.1
Silicon	4.4
Carbon	15.5

Table 6. Surface elemental composition of concrete dust from XPS.

Element	wt.%
Aluminum	3.7
Calcium	12.4
Iron	0.2
Potassium	0.6
Magnesium	4.4
Sodium	2.8
Oxygen	52.7
Silicon	8.8
Carbon	14.3

3. Discussion

3.1. Particle Size

Particle size is a key characteristic of any respirable dust, as it determines lung penetration and the ultimate fate of the particle thereafter [26]. The particle size distribution due to saw-cutting of cement and concrete was found to be very broad, ranging from ultrafine (<100 nm) to a few microns. This particle size range is similar to what is found in PM emissions from cement plants—0.05 to 10 µm [27]—and hence saw-generated dust from cement and concrete has similar potential for negative health effects as seen in cement plant workers based on particle size.

Most of the primary particles appear roughly spherical. As a measure of physical size, aerodynamic diameter is defined as the diameter of an equivalent spherical particle with unit density and having the same terminal velocity in air as the particle being analyzed. The aerodynamic diameter is thus relevant to particle transport and deposition within the airway passages. The particles between 2.5 and 10 μm are accumulated in the upper part of the respiratory system [27]. The $PM_{2.5}$ (particulate matter < 2.5 μm) can go deeper into the lungs, and some can even enter the bloodstream, and hence pose the greatest health risks [33]. Particles in the range of 7 to 15 μm are deposited in the bronchi and bronchioles [34,35]. Particles larger than 15 μm are generally deposited on the mucous membranes in the nose and pharynx [12].

3.2. Composition

Cement can contain various materials which are deemed hazardous, such as calcium oxide (lime), aluminum oxide, magnesium oxide, sulfur dioxide, hexavalent chromium, alkaline oxides, and so on [36]. Silicosis is the most well-known hazard caused by inhalation of respirable dust containing silica and is predominantly an. occupational disease. Crystalline silica is especially hazardous because it is stable, insoluble in water, and generates reactive oxygen species on exposed surfaces which are responsible for oxidative damage to lipids, proteins, and even DNA [37,38]. Silicosis is marked by inflammation and scarring of tissues [39] and is dependent upon severity of exposure. Crystalline silica exposure can also result in many other respiratory diseases such as pulmonary tuberculosis, chronic bronchitis, emphysema, cancer, and other renal and immunologic diseases [38].

Inflammation is believed to be the principal cause for pathogenesis of diseases due to PM exposure [40]. The declining ventilatory function in cement workers is attributed to inflammation [41] and is observed in animals as well as humans subjected to cement dust exposure [42,43]. Meanwhile, the hydration reaction product calcium hydroxide causes irritation of the nose and throat with potential for severe and permanent lung damage [29,30].

As shown here, cement and concrete dust also contains several metal compounds which are of particular concern, as even trace amounts of metals in particulates can generate inflammation via receptor-mediated cell activation or oxidative stress pathways [40]. Reactive oxygen species (ROS), generated by the well-known Fenton reaction (due to iron redox catalysis), are recognized as initiators and mediators of cell death [44]. Inhalation of dust containing magnesium can irritate mucous membranes and the upper respiratory tract [45], while dolomite (calcium magnesium carbonate) causes shortness of breath and reduced respiratory function [31]. Inhalation of aluminum can cause pulmonary fibrosis and lung damage and increase the risk of cardiovascular disease [46,47].

Concrete dust contained more than 30 wt.% of crystalline silica, while cement paste had very little crystalline silica. Most of the silicon in the cement paste was in the form of calcium silicates and in compounds such as thaumasite, lamite, and alite. Cement dust contained more than 35 wt.% of calcium hydroxide in the crystalline phases. Concrete dust contained much higher wt.% of silicon, aluminum, and potassium than cement paste, while the cement was rich in calcium.

4. Conclusions

This study reports a comprehensive size and chemical characterization of dust generated during saw-cutting of cement and concrete. Such data is lacking, despite thousands of workers being routinely exposed to this dust. Cutting generates particles of great health concern, as >90% of the particles are smaller than 2.5 μm. Larger aggregates have morphology with sharp edges and protrusions. Concrete dust could have more potential to cause silicosis compared to cement, as it contains >30 wt.% crystalline silica, while cement dust contains mainly calcium silicates. Metal content and other compounds in cement and concrete dust pose a risk of lung damage and other secondary impacts. Most exposure surveys were conducted for the workers exposed to particles from cement plants. No such surveys

exist for construction workers performing cement and concrete sawing actions at worksites. Follow-on health effects of these dust particles can be investigated with animal studies. Appropriate precautions and protective equipment should be recommended for the workers being exposed to cement and concrete dust generated during construction activities.

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Standardized experimental model for cement dust exposure; tissue heavy metal bioaccumulation and pulmonary pathological changes in rats

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ABSTRACT

A controlled experimental model of exposure to aerosols particularly for cement dust was recently invented in a study from the laboratory that found high serum levels of heavy metals, decrease gastrointestinal motility, and altered hematological variables in cement dust exposed rats. However, reproducibility was not considered. This work aims at standardizing the model and investigating preliminary toxicological indicators. Thirty male rats used in this study were divided into 3 groups (n = 10). Group 1; control, while groups 2 and 3 were exposed to cement dust for 14 days and 28 days respectively. We assessed clinical signs of toxicity, tissue heavy metal concentration, histopathological, and body weight (BW) changes. We observed poor movement coordination, abnormal posture, cephalic fur loss. Evidence of ischemia and fibrotic pneumoconiosis were grossly observed in the lungs of the exposed groups. There was a significant increase in tissue level of heavy metals with pulmonary and gastric heavy metal content showing a trendy relationship during the period of the exposure as the value of Lead, Chromium, Cadmium, Iron, Calcium, and Nickel increased by nearly similar percentages in both tissues. Organs weights increased; the 14-day exposed (198 ± 31; 168 ± 22) and 28-day exposed (198 ± 22; 187 ± 26) groups had significantly reduced body weight at the first and second weeks of exposure compared to the control group (265 ± 26; 357 ± 40) respectively. Exposure to cement dust induced low bone density in the exposed rats ($p < 0.05$). Histopathological alterations include necrosis, inflammatory cellular infiltration, and alveolar hyperplasia suggestive of the proliferative response of pulmonary tissue to the dust. The operation of the standardized apparatus mimics a typical occupational exposure and the findings show that cement dust induces systemic toxicity via respiratory perturbation and body/organ weight discordance mediated by heavy metal bioaccumulation.

1. Introduction

Cement industries constitute a notable source of environmental toxicants [1,2] encountered during the manufacturing, distribution, and utilization of cement product. Occupational and environmental exposure to cement dust has been known to precede a number of systemic injuries with particular reference to the respiratory, gastrointestinal, and integumentary systems characterized by fibrosis, emphysema, cough, cancer, inflammation, and liver diseases among workers and host community residents of cement factories [3,4]. Cement product which has wide application in the construction industry is a homogenous mixture of hazardous heavy metals such as Cobalt (Co), Iron (Fe), lead (Pb), cadmium (Cd), Chromium (Cr), Nickel (Ni), Manganese (Mn), and arsenic (As) at different relative proportions [5–7] which have been considered to be toxic to the body system. Deleterious health effects of cement production at host communities such as Kashmir valley and Krew in India [8,9]; Ewekoro in Nigeria [10] and Oromia, Addis Ababa in Ethiopia [11] have been severally reported. These reports have attracted the attention of researchers to cement dust studies.

Increased level of consciousness on the adverse health effects of cement dust culminates in scientific research since over two decades ago; an intervention which has been overtly impeded by the dearth of a known model of experimental exposure. Data hitherto analyzed stemmed basically from questionnaires [12–17,9], examination of health/-medical records [18,19], interviews [16,20,21] and case report [22].

Toxicosis of cement dust is still poorly understood because, hitherto, empirical investigations have been achieved only by the deployment of crude experimental procedures of merely placing experimental animals

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in proxy distance to cement factories [10,23]. Meanwhile, this method of exposure gives wide room for controversies as a number of other confounding environmental factors could be responsible for the reported pathologies considering the appreciable physical distance between the location of the experimental animals and the actual cement factory. The need for experimental research on the pathophysiological mechanisms involved in the reported effects of cement dust is required for validation and further investigation of its toxicosis. Therefore, an experimental/laboratory method of exposure characterized by simplicity and reproducibility is required. Recently, our laboratory developed a model for regulated exposure which has been deployed in a preliminary study to access the effect of cement dust on some hematological variables and indices with interesting outcomes. Emanating data suggest that an increase in serum concentration of some heavy metals including the alteration of hematological variables accompany the exposure to cement dust [24]. Although the results from this study mimic earlier reports in the literature on human subjects, however, the efficacy and reproducibility of the model cannot be guaranteed. The initial generation and distribution of dust by the chamber is characterized by significant entropy, a condition that may be substantially different from the instantaneous distribution. These provisions make the effusion rate of the chamber dust generation unquantifiable. Also, some important parameters of the chamber such as the diameter were not taken into cognizance which further precipitates the challenge of reproducibility. Hence, the rationale for this study is to standardize the chamber and since inhalation is one of the three major routes of exposure to respirable particulate matters from the external environment, we set to investigate the attendant effect of cement dust exposure on the pulmonary cytoarchitecture and the probable accompanying heavy metal accumulation tendency particularly in the visceral tissues.

2. Materials and methodology

2.1. Animals

Thirty (30), 3-month-old male Wistar rats weighing between 150−180 g were purchased from the animal house of the college of Medicine, University of Ibadan, and were kept in plastic cages with wood shavings. They were housed under standard conditions of temperature (23 ± 2 °C), humidity (55 ± 15 %), and natural 12 h light and dark cycle in the Animal house of Department of Physiology, University of Ibadan, Ibadan. They were allowed access to water and standard laboratory chow *ad libitum*.

Following two weeks of acclimatization, they were exposed to cement dust with the aid of an exposure chamber fabricated according to the specifications below (Fig. 1A and B). This study was conducted in accordance with the current Animal Care Regulations and standards approved by the Institute for Laboratory Animal Research [25] and the experimental protocol was approved by the Animal Care and Use Research Ethics Committee, University of Ibadan, Ibadan, Nigeria having been assigned the approval number UI-ACUREC/18/0129.

2.2. Standardized design and operation of the Exposure Apparatus

The dust exposure was carried out with the use of a fabricated non-mobile apparatus designed to simulate a cement factory environment for the exposure of experimental animals to particulate matters. Unlike the previous report [24], the method was standardized by modifying it into a perfect square of 60 cm in height, breadth, and width, made of transparent plexiglass. An internal subchamber of height 20 cm, breadth 26 cm, and diameter of 32.8 cm is specifically designed to house the dust. Made of plexiglass, the subchamber is designed to contain cement dust with its walls adequately perforated to ensure constant effusion of cement dust-laden air into the portion of the chamber housing the rats. There is no available entrance to the subchamber from the internal portion of the apparatus. This is with the intention to prevent the explorative animals from mechanical injury, to prevent the interruption of the dispensing circuitry of the chamber to ensure sustained; maintaining constant effusion rate, and to prevent direct ingestion of the dust. The apparatus which is particularly designed to avail the experimental animals a wide range of movement consists of a manipulative chimney of 30 cm by 10 cm dimension located on the apparatus lid (dorsally) and diagonally to the internal subchamber, perpendicularly to the internal subchamber and opened during operational periods but closed thereafter.

The subchamber houses two miniature metallic quadri-bladded aerators situated at an anterodorsal right angle to each other. The aerators are heavy duty type of model CNS-3−20/620 (serial number S40141392) running in main alternating current of 220 V, power of 27 W, current of 0.25A, and frequency of 50/60 Hz. They are capable of moving with a speed of 2400/3400 rpm. When connected to a power source, sufficient torque equips the aerators as they synergistically generate, propel and deliver the dust in inhalable form from the subchamber to the internal portion of the apparatus housing the

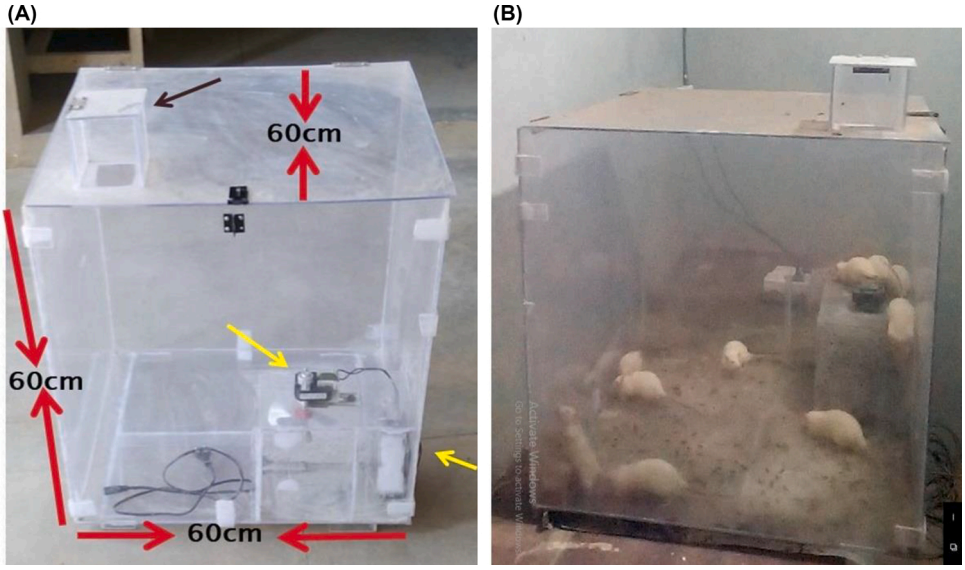

Fig. 1. A: The Description of the apparatus. B: The apparatus in operation (Advancement and modifications stated in Table 2).

experimental animals. The specificity of the aerators enables the generation and dispensation of about 0.2 g/h of the dust.

2.3. Cement material and exposure

A full intact and freshly supplied bag of Nigeria Portland cement was purchased from an accredited depot in Ibadan, Oyo state, Nigeria. The exposure began daily by introducing 100 g of cement dust into the subchamber. Old and remnant dust were evacuated prior to exposure every other day. This routine practice was maintained on daily basis. Exposure was 5 h daily for periods of 14 days and 28 days using the exposure chamber. The control rats received sham exposure to normal atmospheric oxygen. They were all sacrificed thereafter.

2.4. Experimental rats grouping

There were three (3) groups in this study each with 10 animals. The first group (Group 1) of rats were the control group. The second group (Group 2) received cement dust exposure for 14 days (14-day group) while the last group (Group 3) were exposed to cement dust for 28 days (28-day group). Exposure was carried out 5 h daily. The control Group animals were allowed to thrive in completely dust-free environment. The experimental animals were all allowed free access to standard laboratory chow and water.

2.5. Body and organ weights

The weekly weight changes of the animals in the groups each were determined using Acculab® USA, Model-vic-303 electronic analytical weighing balance and recorded while weekly percentage change in weight throughout the study was calculated as:

$$[(B - A)/A \times 100] \quad (1)$$

Where "A" represents the "initial weight", "B" is the "final weight".

During sacrifice, visceral organs including the stomach, lungs, heart, spleen and brain were collected. The relative organ weight was calculated by using the formula;

$$(X/ Y) \times 100\ g \quad (2)$$

Where "x" represents the "Absolute Organ Weight"; the raw weight of the organ as obtained from the weighing balance while "y" is the "Terminal Body Weight (TBW)"; the instantaneous weight of the animal at the point of sacrifice.

Mean Femoral Weight (MFW) is the sum of the weight of the femur divided by "n" per group while Relative Femoral Weight (RFW) was calculated from the equation below

$$(FW/TBW)\ g \quad (3)$$

Mean Relative Femoral Weight (MRFW) is the sum of the RFW divided by "n" per group

The same as above was applicable to the femur after collecting and the attached muscles carefully trimmed off.

2.6. Clinical observations

Each animal in the different groups were carefully examined on daily basis before and after experimental exposure for possible clinical signs of cement dust-induced toxicity in the respiratory and behavioural patterns, skin, fur, eyes and other mucous areas while morbidity/mortality case was equally noted. At the end of the experiment, the animals were fasted overnight but were allowed access to water. All visceral organs including the stomach, spleen, lungs and brain were excised, carefully examined before weighing and thereafter digested for heavy metal analysis except the lungs tissue that was divided into two and part of it was fixed in 10 % formalin for histopathology.

2.7. Digestion of tissue and heavy metal analysis

Heavy metal level in the lungs, brain, stomach and spleen of the exposed animals were investigated according to [26]. Nitric acid (1 mL) followed by perchloric acid (1 mL) was added to 100 mg of the tissues each in a clean sample bottle. The mixtures were then digested over a sand bath until the solution becomes clear and yellow in colour. In the instance of the outcome of brown-coloured digest, the above process was repeated. The digests were aliquoted after being made up to known volume of ionized water and read using Atomic Absorption spectrophotometer model (Buck Scientific AAS Model 210/211 VGP, Connecticut, USA) at various wavelengths according to the standard working parameters stated in Table 1 below. Results of accumulated heavy metals were recorded in mg/L and presented as mean ± SEM. Radiation source were the hollow cathode lamp of Lead (Pb), Chromium (Cr), Cadmium (Cd), Nickel (Ni), Iron (Fe), Manganese (Mn), Cobalt (Co) and Calcium (Ca) while the fuel was air acetylene.

2.8. Macroscopy and histomorphological investigation

Following the sacrifice of the animals, the lungs were excised and carefully examined for any macroscopic pathology before fixing in 10 % formalin for histological examinations. They were thereafter embedded in paraffin wax; sectioned at 5 μm and were stained with haematoxylin and eosin before viewing under light microscope (PEC MEDICAL USA; X400 Mag) for any pneumopathological alterations according to [27]. The histological and pathological evaluations were carried out by a blinded pathologist.

2.9. Statistical analysis

Statistical analyses were done using Graphpad prism 5.0® and data presented as mean ± SEM for $n = 5$ per group while One-way ANOVA and Dunnette post-hoc test were used for mean comparison between the different groups with $p < 0.05$ considered significant as stated at each case.

3. Results

The chamber as modified and standardized is pictorially represented above in Fig. 1A and B. The major discrepancies and the standardizing factors are analysed in Table 2 below.

The width of the chamber and the subchamber had been slightly adjusted to suit that of a perfect square. Although the height of the chamber remains the same but that of the subchamber was slightly reduced. The diameter and the dust effusion rate were determined. This is expected not only to increase the internal space of the major part of the chamber but also to modify the aerosolized dust. Overall, the modifications ensured effective and calculable dust effusion rate.

3.1. Clinical signs

One rat died after two weeks of exposure out of the 28-day exposed animals (Group 3) while the period of exposure lasted. A number of clinical signs of toxicities such as mortality, laboured breathing,

Table 1
Operational parameters of atomic absorption spectrophotometer.

S/NO	METAL	WAVELENGTH (nm)	SLIT WIDTH
1	Lead	283.3	0.7
2	Chromium	357.9	0.7
3	Cadmium	228.9	0.7
4	Cobalt	352.7	0.7
5	Manganese	279.5	0.7
6	Iron	248.3	0.7

Table 2
Modifications entrenched to standardize the earlier model of cement dust exposure.

PARTS	SPECIFICATIONS	MODIFICATIONS	FUNCTIONAL ALLOWANCES
DUST GENERATOR	1Plastic and 1 iron bladed industrial fan	2 iron bladed aerators	Enhanced effective and sustained delivery of dust from the subchamber to the larger compartment housing the experimental animals
CHAMBER WIDTH	59.9cm	60 cm	
CHAMBER HEIGHT	60 cm	60 cm	
CHAMBER DIAMETER	Unknown	84.9cm	
SUBCHAMBER WIDTH	26.1cm	26 cm	
SUBCHAMBER HEIGHT	19.6 cm	20 cm	
SUBCHAMBER DIAMETER	Not stated	32.8 cm	
CHIMNEY AREA	10.6cm × 9.9cm	30cm × 10cm	
FAN SPEED	2400–3000rpm	2400–3000rpm	
DUST EFFUSION RATE	Unknown	0.2 g/hr	Reproducible

increased fur lability and cephalic fur loss. Other signs were frequent sneezing, abnormal posture and hypoactivity. There was evidence of poor nervous coordination resembling that of hemiballism and tremor. It was equally observed that the vigor and boisterous tendencies exhibited by the exposed animals at the beginning of the experiment gave way for docility, weakness and anorexia occasioned by restricted movement before the end of the experiment Fig. 2B. The exposed animals also show sign of drastic weight loss than the control. During sacrifice, there were grossly observable conditions of fibrotic pneumoconiosis at the caudal lobe alongside with being pus-gorged portions (black arrows in Fig. 2D, E and F) near the deep respiratory zone. There was also evidence of pulmonary ischemia with grossly observable pale red patches at the serosal surface of the anterior lobes (yellow arrow in Fig. 2F) in the 14- and 28-days exposed animals.

3.2. Body and organ weight changes

Table 4 shows that the 14-day exposed group and 28-day exposed group had significantly reduced body weight at the first and second weeks of exposure (Week 1 – week 4 in the table) compared to the control group. The rate of body weight gain in the test groups (14-day and 28-day exposed) was significantly reduced in the weeks of exposure when compared with the control. Also, the TBW and weight changes of the femur present an interesting statistic with the 14-day group showing marginal difference and 28-day showing a significant difference when compared with the control group. For instance, TBW of the 14-day exposed groups decreased by 10.67 % while the 28-day group decreased by 16.42 % when compared with the control. The MFW of the 14-day exposed group present 9.34 % while the 28-day exposed group present 31.78 %. MRFW shows the same trend with the 28- and 14-days exposed group showing 27.14 % and 8.57 % respectively. The foregoing

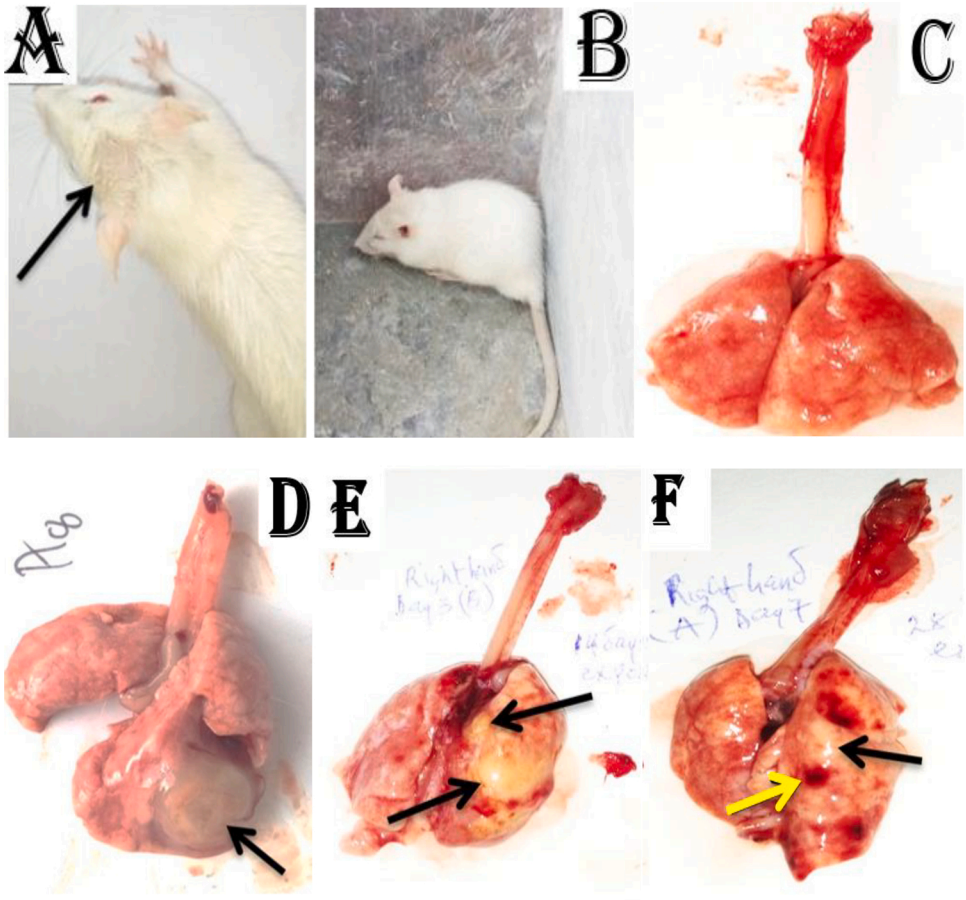

Fig. 2. A-F: Observed clinical signs of toxicity among cement dust exposed animals; **A:** Cephalic fur loss (black arrow) and abnormal posture following 28-day cement dust exposure. **B:** Docility and hypoactivity of exposed animals showing maintenance of stationary position. **D, E** and **F:** pulmonary emphysema and haemorrhages of caudal lobe of the lungs in the 14- and 28-days exposed animals. E and F: pus-gorged and pulmonary ischemia of the caudal lobes respectively (black arrows) and pale red patches on the anterior lobe of the lungs (yellow arrow); all compared with **C:** A normal lungs (from the control group) showing normal appearance and intact gross morphology. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

shows that the body weight of the 28-day exposed group is more affected than the 14-day group.

3.3. Histoarchitectural alterations

Fig. 3A-F, represent the photomicrographs of experimental animals from the control, 14-day and 28-day exposed groups respectively. The control animals (Fig. 3A and B) show normal lungs cytoarchitecture while the treated groups (3C-F) had an array of pathological manifestations including fibrinoid necrosis, evidence of emphysema and inflammatory response of the tissue marked by mononuclear cell infiltration. Alveolar type II pneumocyte hyperplasia was observed in addition to those alterations at the 28-day exposed group. Table 6 shows the distribution and severity of the pulmonary histopathological changes observed in this study with hyperplasia of histiocytes, mononuclear cell infiltration in alveoli, medial hypertrophy of muscular arteries and fibrinoid necrosis being the most predominant pathologies while presence of eosinophilic substance, fibroblast proliferation, oedema and alveolar septal thickening were the least observed which were all completely absent in the control animals.

Fig. 4A-F represent the relative weights of the stomach, spleen, lungs, heart, brain and femur respectively while Table 3 shows femoral bone weight changes. The relative weight of the lungs (F-value = 16.25, p-Value = 0.0010), stomach (F-value = 5.307, p-Value = 0.0223), and spleen (F-value = 27.64, p-Value = 0.009) were significantly higher in 14-day and 28-day groups when compared to the control. However, the

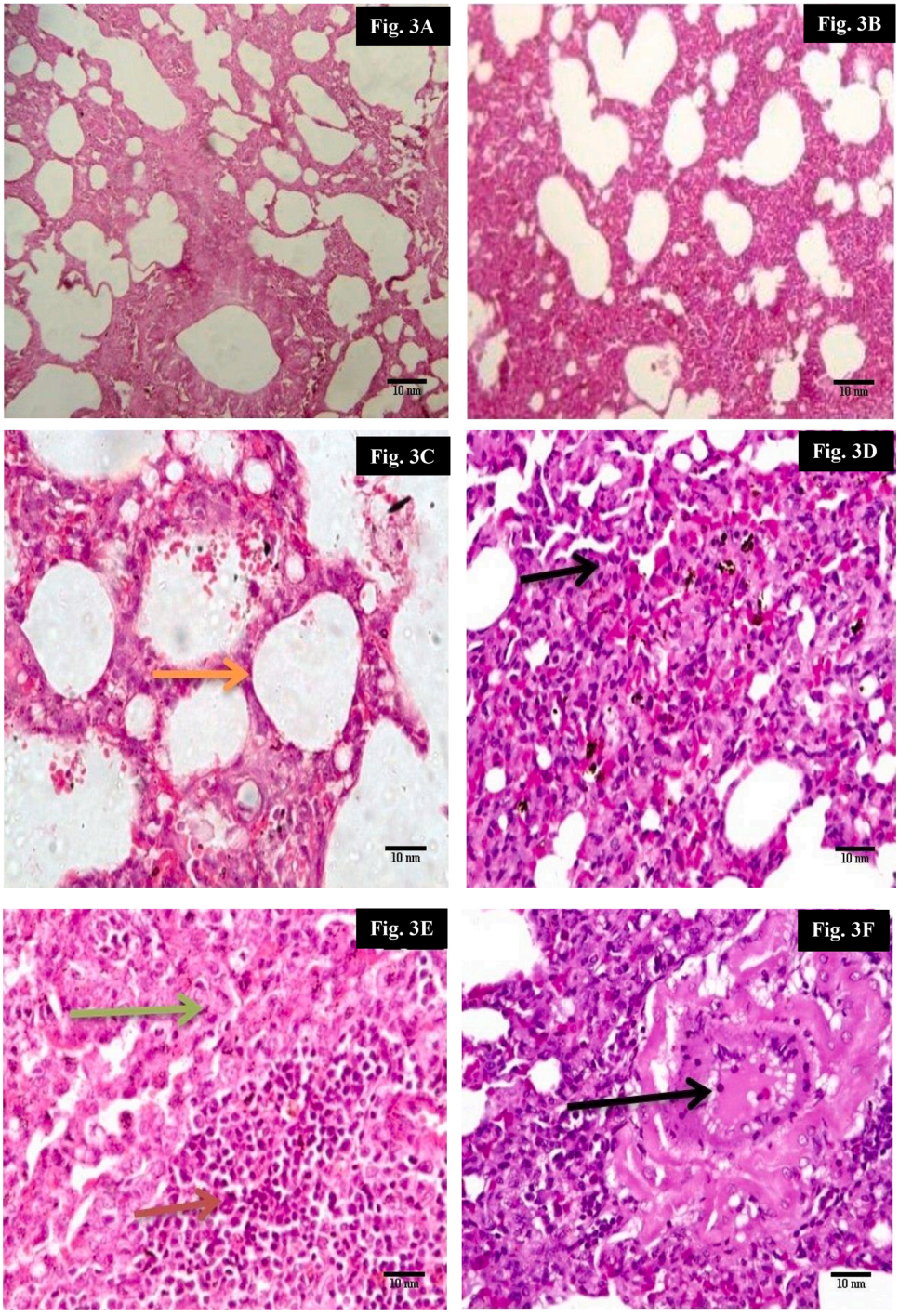

Fig. 3. A and **B**: Lung tissue showing normal architecture of control animals. **C and D**: Lung tissue showing alveolar congestion and hemorrhage (Fig. 3**C** brown arrow), Alveolar septal thickening with congestion, hemorrhages, diffuse mild type II pneumocyte proliferation and infiltration of mononuclear cell infiltration (Fig. 3**D**; black arrow) of 14-day Exposed animal. **E and F**: Lungs showing effect of cement dust on pulmonary tissue with evidence of severe alveolar type II pneumocyte cell hyperplasia (Fig. 3**E green arrow**) and mononuclear cell infiltration (Fig. 3F black arrow) and medial hypertrophy of muscular arteries and fibrinoid necrosis of 28-day exposed animals. Mag: X400. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

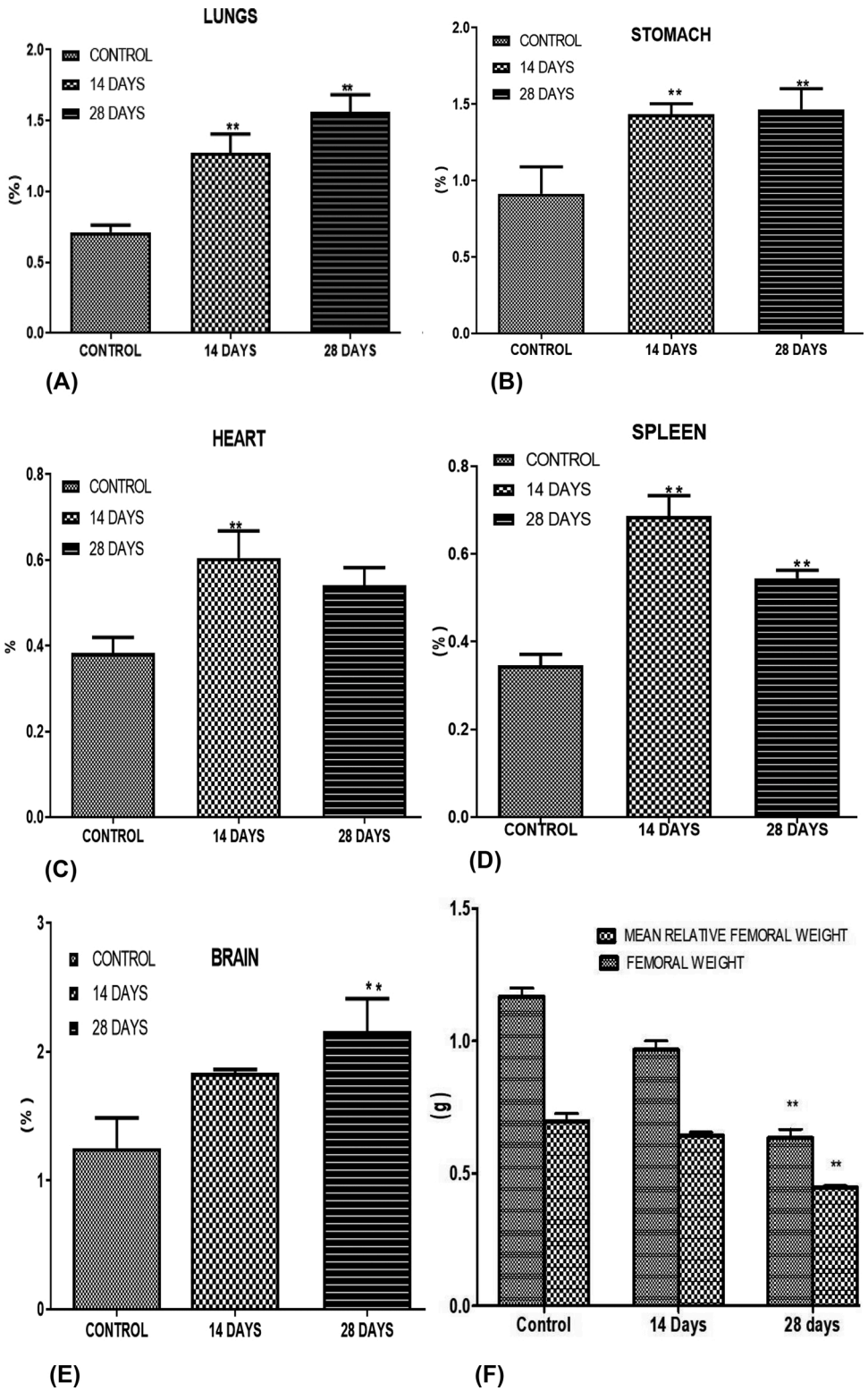

Fig. 4. A Effect of cement dust on relative **lungs** weight. ** Significant when compared with the control. **B**: Effect of cement dust on relative **stomach** weight. ** Significant when compared with the control. **C**: Effect of cement dust on relative **heart** weight. ** Significant when compared with the control. **D**: Effect of cement dust on relative **spleen** weight. ** Significant when compared with the control. **E**: Effect of cement dust on relative **brain** weight. ** Significant when compared with the control. **F**: Effect of cement dust on **femoral weight and mean femoral weight**. ** Significant when compared with the control.

relative weights of the brain (F-value = 5.323, p-Value = 0.0298) and femur (F-value = 50.33, p-Value = 0.0002) was significantly higher only in the 28-day group while that of the heart increased significantly only in the 14-day exposed group when compared with the control at $p < 0.05$. Lung, stomach and brain tissues shows somewhat similar pattern of response to cement dust exposure. While other organs (Heart and Spleen) show a mithridatic reduction in the 28-day group when compared with the 14-day group, stomach, lungs and brain tissues in Fig. 4A, B and E respectively depicted a persistent increase in weight from the 14-day to the 28-day.

3.4. Heavy metals analysis

Heavy metals analysis as found in Table 5 above represents a considerable output. Analysis of the heavy metal content of the various visceral organs shows that the lung tissue has a significantly high level of

Table 3
Mean relative femoral weight of experimental animal following exposure to cement dust.

GROUPS	TBW(g)	MFW(g)	MRFW
CONTROL	168.7 ± 4.1	1.07 ± 0.03	0.7 ± 0.03
14-DAY	150.7 ± 2.4*	0.97 ± 0.03*	0.64 ± 0.01
28-DAY	141.0 ± 5.51*	0.73 ± 0.13*	0.51 ± 0.07*

Only values of the MRFW are presented in mean ± SEM.
TBW- Terminal body weight; MFW; mean Femoral Weight; MRFW; mean Relative Femoral Weight.
* $p < 0.05$ are significant when compared with control.

Table 4
Weekly percentage mean body weight change induced by 4 weeks exposure to cement dust.

GROUPS	WEEK 1	WEEK 2	WEEK3	WEEK 4
CONTROL	165 ± 26	257 ± 40	373 ± 50	463 ± 58
14-DAY	98 ± 31*	68 ± 22*		
28-DAY	96 ± 22*	87 ± 26*	152 ± 45*	166 ± 52*

Values are presented in percentages.
* $p < 0.05$ is significant when compared to the control.

Ni at 14-day and 28-day groups, Cr and Co showed significantly high level only at 28-day while Cd was significant only at the 14-day exposed group when compared with the control. The stomach tissue has significantly high Pb, Fe at both exposed groups (14-day and 28-day exposure), while Cr and Ni were significantly high only at the 28-day exposed group when compared with the control. The brain tissue as shown by the 14-day and 28-day groups had significantly high levels of Pb, Cd, Mn, and Ni while Cr and Fe were only significantly higher in the 28-day group compared to the control. The spleen at both 14-day and 28-day groups depicted a significantly high level of Pb, Cr, Co, Ni while Cd and Mn were only significantly high at the 28-day group when compared with the control.

The values of Fe in the respective organs (brain, spleen, lungs, and stomach) are significantly higher in the test groups when compared with the control. Moreover, values of this metal in the 14-day exposed group approximately twice as found in the 28-day exposed group. This is consistent with all the assessed organs. Values of Ca in the test groups (14- and 28-day) in the respective organs are significantly higher than in the control. However, the 28-day group produced multiple folds of value as found in the 14-day except for the stomach sample where the 14-day is approximately half. Values of Pb and Cr are also significantly higher in the test group when compared with the control. Similarly, almost none of the values presents a double or multiple fold of the other. The 28-day group only show a marginal increase when compared with the 14-day group. With respect to the data from the lungs, Pb and Cr show a marginal increase over time as found in the comparison between the 14-day and the 28-day groups, Cd decreased, Co and Mn increased in multiple (5 and 7 times respectively). Only, Fe and Ni doubly increased in line with what might be expected considering the double length of exposure. In the brain tissue, only Fe increased doubly while other metals appear about the same level at both the 14- and 28-day groups. In the spleen, however, Pb and Cr increase are similar to the findings in the lungs, whereas Cd, Co, Mn, Fe, and Ni all increased 5, 3, 4, 2, and 3 times respectively, showing substantial accumulation from 14 to 28 day of exposure. Available data at the 14- and 28-day exposed groups particularly for the lungs and stomach are interesting when compared with the

Table 6
Observed pulmonary histomorphometry of rats exposed to cement dust.

ALTERATIONS/GROUPS	CONTROL	14 DAY	28 DAY
Alveolar type II Pneumocyte Hyperplasia	–	++	+++
Alveolar mononuclear cell infiltration	–	++	+++
Focal Hemorrhage	–	++	++
Alveolar Septal thickening	–	+–	++
Emphysema	–	++	++
Periarteitis	–	++	++
Medial hypertrophy of muscular arteries	–	+–	+++
Eosinophilic Substance	–	+–	++
Fibroblast tissue proliferation	–	+–	++
Fibrinoid Necrosis of blood vessels	–	++	+++
Oedema	–	+–	++

The observed morphological alteration of the erythrocyte was assessed using the grade below:
–: morphological change absent in animals in a group.
+–: morphological change rarely found in animals in a group.
+: morphological change found in some animals in a group.
++: morphological change common to all animals of a particular group.
+++: morphological change common to most animals in the exposed groups.

Table 5
Heavy metal analysis of the various tissues (mg/L) of experimental animals exposed to cement dust.

PARAMETERS		ORGANS			
HEAVY METAL	GROUPS	LUNGS	BRAIN	SPLEEN	STOMACH
	CONTROL	0.03 ± 0.00	0.05 ± 0.01	0.04 ± 0.00	0.03 ± 0.01
Pb	**14-DAY**	0.95 ± 0.07*	1.05 ± 0.06*	1.29 ± 0.14*	1.02 ± 0.04*
	28-DAY	1.02 ± 0.07*	1.08 ± 0.33*	1.43 ± 0.24*	1.10 ± 0.03*
	CONTROL	0.02 ± 0.00	0.06 ± 0.03	0.07 ± 0.01	0.03 ± 0.01
Cr	**14-DAY**	0.17 ± 0.04*	0.11 ± 0.00	0.12 ± 0.01*	0.12 ± 0.00*
	28-DAY	0.26 ± 0.08*	0.15 ± 0.00*	0.17 ± 0.01*	0.35 ± 0.12*
	CONTROL	0.04 ± 0.01	0.01 ± 0.00	0.01 ± 0.00	0.02 ± 0.01
Cd	**14-DAY**	0.35 ± 0.05*	0.05 ± 0.02*	0.05 ± 0.01*	0.06 ± 0.01
	28-DAY	0.12 ± 0.07*	0.05 ± 0.01*	0.27 ± 0.03*	0.05 ± 0.01
	CONTROL	0.02 ± 0.00	0.05 ± 0.00	0.01 ± 0.00	0.11 ± 0.01
Co	**14-DAY**	0.16 ± 0.05*	0.44 ± 0.17*	0.20 ± 0.07*	0.39 ± 0.02*
	28-DAY	0.84 ± 0.15*	0.45 ± 0.13*	0.74 ± 0.13*	0.30 ± 0.03*
	CONTROL	0.05 ± 0.01	0.00 ± 0.00	0.02 ± 0.01	0.07 ± 0.01
Mn	**14-DAY**	0.13 ± 0.01*	0.06 ± 0.00	0.04 ± 0.01	0.06 ± 0.01
	28-DAY	0.98 ± 0.00*	0.08 ± 0.0*	0.18 ± 0.08*	0.06 ± 0.01
	CONTROL	0.02 ± 0.00	0.16 ± 0.02	0.04 ± 0.00	0.06 ± 0.01
Fe	**14-DAY**	0.59 ± 0.07*	1.18 ± 0.13*	0.14 ± 0.01*	1.81 ± 0.27*
	28-DAY	1.15 ± 0.00*	2.52 ± 0.22*	0.25 ± 0.02*	3.76 ± 0.33*
	CONTROL	0.05 ± 0.01	0.02 ± 0.00	0.00 ± 0.00	0.02 ± 0.00
Ni	**14-DAY**	0.14 ± 0.01*	0.14 ± 0.01*	0.05 ± 0.02*	0.06 ± 0.01
	28-DAY	0.24 ± 0.01*	0.18 ± 0.01*	0.15 ± 0.02*	0.40 ± 0.08*

Values are presented as mean ± SEM; *$p < 0.05$ are significant when compared with control.

control. There was a substantially significant difference between the treated and control groups. A more interesting difference is observable between the 14-day and 28-day groups. Asides from Co and Mn, all other heavy metals assessed in this study follow a similar pattern of bioaccumulation in the two tissues.

4. Discussion

This study presents a standardized form of the earlier presented and deployed exposure model [24]. The morphology, operation, and modification of the model were presented in Fig. 1A, B, and Table 2. It meets the need to simplify, substantiate and normalize the suitability of the model in the assessment of the systemic effect of inhalable/particulate matters. It was deployed in this study to assess the effect of cement dust on the respiratory tract; the foremost points of call for investigation in aerosol-mediated toxicity. The primitive exposure chamber was fabricated and immediately deployed for use. Initially, it was not clear if the chamber would fill the gap of the experimental toxicological evaluation model particularly with respect to occupational/residential scale of exposure or not. However, subsequent results emanating from the study featured a number of pathological manifestations that closely mimic those earlier reported in the literature on human subjects in many conditions of case reports, questionnaires, interviews, etc. hence, the need to standardize the exposure chamber became overtly expedient. The "modification" column of Table 2 outlines the advancement of the chamber with a view to standardizing it. For the present study, the dust generation rate was stabilized at 0.2 g/hr.

Cement particles have been reported to consist of toxic metals in varied proportions [28,29] depending particularly on the raw materials used. Nigeria cement dust particles contain very high concentrations of heavy metals known to be lethal even at small doses such as Cd, Pb, and mercury (Hg) [30]. The significantly high levels of Pb, Cd, Cr, Co, Ni, Mn, and Fe observed in the stomach, lungs, heart, and brain tissues of the exposed animals confirm intoxication with heavy metallic components of the dust. There is a considerable siamese relationship between the pattern of heavy metals deposition at the lungs and stomach tissues as shown by Table 5. Almost all the heavy metals show a similar trend of bioaccumulation, particularly when the test groups are compared. This similarity is probably borne out of the anatomical relationship between the lungs and the gastrointestinal tract (GIT) as established by the mucociliary escalator. The GIT is susceptible to the toxicosis of any toxicant found within the upper respiratory tract. Germs, particles, dust, and other pollutants in the inspired air are trapped by mucus before the mucociliary escalator moves them up and out of the lungs. These materials can then be removed from the body via coughing or swallowing. The latter makes the GIT become vulnerable to the debris moved out of the lungs. In the case of this study, the heavy metal-loaded dust removed from the lungs may have found its way to the GIT where they stimulate similar pathophysiological mechanisms. Similar evidence was recently reported by [31] who found significantly high levels of heavy metal in visceral organs of rats co-exposed to cadmium and lead, and [32] who similarly found significantly high levels of heavy metals in various tissues of snails picked around cement factory. Also, in plant physiology, similar evidence has been reported where heavy metallic constituents of cement dust have been demonstrated to leach into the soil around cement factory site causing a significantly higher proportion of toxic metal within the factory neighborhood [2,33,34]. Recently, our laboratory reported an increase in plasma concentration of heavy metals following exposure to cement particles [24]. The present study provides the first evidence using experimental animals that cement dust could trigger heavy metal bioaccumulation in living tissues. After heavy metal intoxication; sequestration and bioaccumulation precede a number of pathological manifestations [35] as they are not easily metabolized or excreted [36]. Apart from Cd, Pb, and Hg that are known to elicit systemic toxicities even at low concentrations [37,38], most divalent cations have been implicated in effective cytophysiology as they participate in most intracellular activities such as oxidative phosphorylation, enzymatic activities, nucleic acid, and protein synthesis, membrane stabilization, and transport. However, regulation of their relative biological abundance and bioavailability is a requirement for the effective functioning of the cell. Asides from the sole toxicities of heavy metals, their influx into the cell as typified by cement dust exposure is deleterious as they compete for transporters with essential trace elements especially when they exceed the homeostatically tolerable limit [39,40]; thereby leading to loss of function as a result of deficiencies of essential minerals [41].

Clinical presentations are often indicators of systemic toxicity. The observed clinical signs following exposure in this study confirm the systemic toxicity of cement dust. The animals exhibited vigour at the initial stage of the study exploring every accessible point within the apparatus including the top of the subchamber. The fabricated chamber differs significantly in internal morphology and space from the plastic cages they were housed. This answers for the rambunctious behavior initially exhibited by the animals. However, towards the end of the experiment, they appeared docile, hypoactive, and anorexic constantly maintaining a stationary position. This could be due to the stress accumulation occasioned by the exposure to the dust or perhaps due to anorexia. The mortality of one animal which occurred while the exposure was ongoing may be due to multi-organ failure caused by the acute effect of the heavy metal in the dust. The observed laboured breathing and frequent sneezing are suggestive of respiratory distress induced by cement dust.

The source of bodily functions, regulation, and integration is the central nervous system (CNS) being principally composed of the brain and the spinal cord. It gathers information from far and near extremities for coordination and control. Maintenance of gait, posture, and coordination of movement right from thought to execution are all the functions of the CNS. Dyskinesia and other poor movement coordination resembling hemiballism, abnormal posture, and hypoactivity as observed in this study following the exposure to cement dust indicate a central nervous disorder. The dermal route is one of the major routes of exposure to cement aerosol; others being inhalation and gastrointestinal routes. Since cement dust is an airborne toxicant, the skin, by virtue of its large surface area remains the most affected. It quickly settles on the skin and exerts topical effects with toxicoses yet to be studied in detail. In this study, exposure to cement dust may be responsible for the integumentary degradation as marked by increased fur lability. It was evident that more than one animal showed signs of loss of fur at the cephalic region at different times during the study.

Abnormal body weight change is considered a veritable toxicity index [42–44]. Similarly, organ weight is an indicator of the physiological or pathological condition of experimental animals [45,46]. There was a significant reduction in weekly body weight gain which is in contrast with an increase in the relative visceral organs (stomach, spleen, lungs, and brain) weights of the exposed groups when compared with the control (Fig. 4A-F). Although daily food intake was not assessed, the exposed and the control were equally allowed free access to food and water. The weight discrepancies observed in this study may either be due to anorexia or the direct systemic toxicity induced by the dust. The foregoing is expected since visceral organs are directly exposed to the deleterious effect of toxicants [47]. Most organs have the ability to sequester heavy metals following entry into the body [35]. This finding is in concert with several other findings [48–50]. Also, [51] in their study involving exposure of experimental animals to silica found significantly higher lung weight of the exposed animals when compared with the control. The condition of organomegaly observed in this study is an indication that the exposed rats bioaccumulated the heavy metals. The latter which is a condition typical of heavy metal toxicity remains an inevitable precursor to pathological manifestations especially during carcinogenesis [52].

Bone density changes have been shown to inversely correlate with heavy metal toxicity (Hee-Sook et al., 2016). Bone has been regarded as

one of the major target sites for heavy metal toxicosis [53–55]. Heavy metals such as Pb and (Cd) which accumulate in the bone matrix can store up significantly and displaced calcium, leading to bone demineralization, and in the process makes the bone susceptible to osteoporosis. Even though the comprehensive and holistic explanation is not yet available in the literature, exposure to a higher concentration of Cd alone has been strongly linked to lower bone densities, decrease trabecular number and decrease thickness [53,55,56]. Co-exposure to Pd and Cd stimulates bone histopathological damage [57]. As the largest bone in the body, the decrease in femoral density observed in this study suggests the possibility of chelation of essential minerals like calcium from the bone matrix causing mineral imbalance which may eventually predispose the bone to osteoporosis. Low bone density observed in this study does not only corroborate but is also suspected to be responsible for the low body weight gain observed in the exposed groups.

Pulmonary tissue reaction to dust particles is known to be dependent on a number of factors such as the composition of the dust, the length of exposure, and the immunological status of the exposed [58]. Of more significance is the composition of cement dust owing to its multi-heavy metallic composition. Pneumoconiosis was grossly observed in the lung tissue of the exposed groups (Fig. 2D-F) when compared to the control (Fig. 2C). The topical pulmonary effect of the dust culminates the observed pneumoconiosis; the fibrogenic tendency of the dust is thereby suspected. The onset of the pneumopathology may be the stimulus for the respiratory distress observed in some of the exposed animals as they show irregular and laboured breathing. The clinical signs of toxicity observed in this study show a wide range of semblance with the pathological manifestations that accompany occupational exposure to cement dust [12,16,59,60]. In addition, the serosal surface of the lungs shows signs of infarction (Fig. 2F). This is suggestive that exposure to cement dust may significantly affect blood supply at the organ level. Cytoarchitectural investigations play a significant role in establishing pathological alterations at the tissue level following exposure to toxicants. It gives reliable information about the extent of degradation in exposed tissues difficult to be observed macroscopically, cellularly, or even with the aid of subcellular biomarkers [61]. Pulmonary histopathological disruptions after exposure to cement dust had been earlier reported by a study of in-situ exposure [10] where inflammation, disrupted bronchiole and bronchus, and degenerated the epithelial lining were observed. Fig. 3A–F shows an array of histopathological alterations while Table 6 shows the frequency and severity of the observed alterations secondary to cement dust exposure. The black arrow in Fig. 3D shows infiltration of inflammatory cells. Inflammatory cells play significant roles in the development and healing of either chemical or topical injuries. Analogous to any condition of heavy metal intoxication, infiltration of inflammatory cells is considered a reliable yardstick for the assessment of the pathogenesis of heavy metal-induced toxicosis as they are known to produce and release pro-inflammatory cytokines, proteolytic enzymes, reactive oxygen, and nitrogen species [62]. Neutrophilic infiltration is known to precede the cascade of mechanisms that herald injuries on tissues. Hence, the histopathological changes observed in this study which feature inflammatory cell and mononuclear cell infiltration are indicators of the pro-inflammatory tendency of the dust. Meanwhile, according to Balduzzi and colleagues, crystalline silica elicits inflammatory cell production which ultimately leads to free radical generation [63]. The respiratory distress observed in the exposed animals may be due to the free radicals generated via the topical pulmonary effect of crystalline silica, a major compound constituent of cement dust, or by the inflammatory cell infiltration observed in the histoarchitectural alteration above. The “black arrow” in Fig. 4B depicts alveolar hyperplasia in the lung tissues. This condition is suggestive of the proliferative reaction of pulmonary tissue to the dust; a notable characteristic of the onset of carcinogenesis. Howbeit, [64] and [65] had established the positive correlations between cancer of the respiratory system and the length of cement dust exposure period, the literature has been devoid of laboratory-based support for the claim. Air space enlargement is an early sign of emphysema.

5. Conclusion

This study provides a standardized laboratory-based experimental model of exposure for investigation on cement dust toxicity. It generally revealed heavy metal bioaccumulation and histoarchitectural alteration as organ damaging mechanisms with respect to the respiratory system. The exposure apparatus has been modified and standardized to mimic the cement factory environment and host communities of cement factories alike who are equally vulnerable to cement dust toxicities as occupationally exposed individuals. The results from this study add to the relatively few experimental-based data available on cement dust and therefore advance the existing claims of its toxicity. The pathogenesis of cement dust-induced toxicities is not limited to bioaccumulation of the heavy metal content of cement dust but also includes organomegaly and pneumopathological alterations. Further studies on the toxicosis of cement dust are hereby encouraged in order to validate the epidemiological reports in the literature on cement dust-induced pathologies and to incite policies geared towards the protection of occupationally and geographically exposed individuals.

Authors’ agreement

We the authors of this manuscript write to clearly state that there is no conflict of interest whatsoever in in the conception, design and writing of this work.

Declaration of Competing Interest

The authors report no declarations of interest.

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Cement plant emissions and health effects in the general population: a systematic review

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Abstract

Adverse health effects of cement plant exposure have been found in occupational contexts but are less defined for the general population living near plants. We aimed to summarize the evidence on the health effects of people exposed to ambient air pollution by cement plants. A systematic review using Embase, PubMed and Web of Science was performed. We included only non-occupational studies with a comparison group that focused on adverse health outcomes and biomarkers of internal dose or subclinical effect associated with cement plant exposure. Selection of articles was performed by two authors independently. Of 1491 articles identified by the initial search, 24 were included: 17 of them were included in the analysis of adverse health outcomes and 9 in the analysis of biomarkers of internal dose or subclinical effects. The studies were very heterogeneous in study design, measure of cement plant exposure, outcome detection, measure of association and adjustment for confounding. Almost all the studies found positive associations between cement plant exposure and respiratory diseases and symptoms. An excess risk of cancer incidence and mortality in both children and adults mainly concerning respiratory tract cancers was also reported in some studies. Higher values of heavy metals and of a biomarker of renal toxicity were found in the exposed compared to unexposed populations. In conclusion, there is some evidence for a possible role of cement plant exposure on health adverse effects, although many studies had serious or critical risk of bias and overall level of certainty was low.

Keywords: Biomarkers of internal dose; Cement; Health effects; Plant.