Toxic metals in cement induced hematological and DNA damage as well as carcinogenesis in occupationally-Exposed block-factory workers in Lagos, Nigeria

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ABSTRACT
The block-molding industry provides housing and employment globally. However, cement contains toxic metals, so molders need periodic safety monitoring. This study assessed the safety of 25 block molders and 25 control subjects in Lagos, Nigeria. After obtaining informed consent, structured questionnaires were used to obtain participants’ weight, height, age, and skin texture. Moreover, the participants’ blood samples were analyzed for heavy metals (calcium, silicon, aluminum, iron, chromium, copper, and lead) and hematological parameters (hemoglobin, packed cell volume, red blood, and white blood cells). Also evaluated were biomarkers of oxidative stress damage, namely albumin, glutamate dehydrogenase, kidney injury molecule-1, DNA-8-hydroxyguanosine, carcinoembryonic antigen, malondialdehyde, and total antioxidant capacity. The molders’ skin was dry compared to the control. The molders’ blood plasma metals were higher (p ≤ 0.05) than the control, with the exception of lead, and were over the allowed ranges. Similarly, the molders’ packed cell volume, hemoglobin, and red blood cell levels were lower than usual, while their red blood cell levels were higher. The molders’ biomarkers were outside of the acceptable ranges and were significantly different from the control. The findings show that block molders are at risk of health hazards and should take steps to reduce their cement exposure.

Introduction
The block-making industry is important in the world because shelter is a basic human need. On a daily basis, factories, offices, and residential houses are erected, which require blocks. The industry employs both skilled and unskilled workers in urban and rural areas and so contributes significantly to national economies worldwide. The global block and brick production sale was $339,597.7 million dollars in 2020 and is expected to increase to $588, 151.8 million dollars by 2020 [1]. In Nigeria, the block-making industry plays a major role in the economy, employing about 10 million people with a membership base of over 45,000 producing blocks [2]. The block industry satisfies the block needs of builders and saves builders’ time and stress of looking for materials.
and employers to mold blocks. In lieu of the above, the block industry forms the cornerstone of the building industry.

The most common materials for making blocks are cement, water, and sand. Cement, of which the most common is Portland cement, binds and hardens blocks, thus improving the processing and properties of the products [3,4]. Cement is indispensable in the building industry, which is attributable to its availability, durability, and reliability compared to other binding materials [5]. The basic constituents of cement are aluminum trioxide, calcium oxide, iron oxide, and silicon dioxide [6]. However, the production processes of cement release pollutants such as heavy metals, particulate matter, and dioxins [7]. Heavy metals are natural components of the earth’s crust and are ubiquitous, non-biodegradable, and persistent [8]. Heavy metals are toxic and very dense [9]. In minute quantities, heavy metals perform crucial biological functions, but they become toxic after a certain threshold [10]. Heavy metals’ toxicity is enhanced by their ability to maneuver the body’s defense mechanisms and lodge into cells [11]. In the cells, heavy metals displace cellular components and thus cause the cells to malfunction [12]. Heavy metals have been implicated in many diseases, some of which involve organ and DNA damage [13].

Considering the toxic metals in cement, workers in block factories can be occupationally exposed to health hazards. This necessitates periodic monitoring of the workers to safeguard their health while they carry out their work unhindered. The workers can also be exposed to toxic metals from their natural deposits in the sand used in block molding [14]. In Nigeria, literature shows there is a lack of monitoring and awareness of the danger posed by block making with regards to heavy metal exposure, particularly carcinogenic and genetic effects, which can be passed across several generations. These effects are often detected by measuring some biomarkers in the blood plasma. Toxicity biomarkers enable the detection of early effects of pollutant exposure and are therefore important tools in human bio-monitoring studies [15]. This study, therefore, measured the levels of heavy metals, hematological parameters, and biomarkers of organ damage, DNA damage, and carcinogenicity in the blood samples of block factory workers obtained in Oshodi, Lagos, Nigeria.

**Materials and methods**

**Study population and data collection**

Twenty-five (25) workers from two block molding factories in Oshodi-Isolo local government area of Lagos state were enrolled for the study. Another 25 people from the same area who were not block factory workers were also enrolled and served as the control group. The block factories were located in residential areas, far from major roads, and the same goes for the control group. This was done to prevent the influence of vehicular and industrial emissions on the results. The participants’ age, body weight, and height were measured after they gave informed consent. After that, blood samples were taken from the participants for heavy metal, hematological, and biomarker evaluations of DNA damage and carcinogenicity.

**Criteria for selection of participants**

All participants must have agreed to participate in the study. For the test group, participants must have been molding blocks for at least two years, have no history of chronic or genetic diseases prior to working in the factory, and have not worked anywhere else. Participants in the control group must not have worked in any industry and must be free from any chronic or genetic disease. The health status of all the participants was confirmed by some health facilities in the area. Excluded participants were those that failed the above criteria. Smokers, alcoholics, obese people (those with
a body mass index of 30 or higher), and sickle cell anemia patients were also barred from participating.

**Ethics statement**

The study was approved by the National Open University of Nigeria’s Ethics and Research Committee in Lagos. The individuals also agreed to participate in the study.

**Blood sample collection**

Ten milliliters (10 ml) of whole venous blood samples were collected in the morning after an overnight fast from each participant using a 5-ml syringe and a 20-gauge needle. Exactly 4 ml of the blood was measured into an ethylene-diamine-tetra-acetic-acid (EDTA) bottle and used for heavy metal and hematological analyses in the laboratory. The remaining 7 ml was poured into a plain vial and centrifuged at 2500 rpm at 2°C for 20 minutes in the laboratory to separate the blood plasma. The plasma was collected in a fresh, clean tube and stored at −20°C before being used for measuring selected biomarkers of organ damage, namely albumin (ALB), glutamate dehydrogenase (GLDH), and kidney injury molecule-1 (KIM-1). As indicators of oxidative stress, DNA damage, and carcinogenicity, the total antioxidant capacity (TAC), malondialdehyde (MDA), DNA-8-hydroxyguanosine (8-OHdG), and carcinoembryonic antigen (CEA) were also measured.

**Heavy metal evaluation**

The levels of heavy metals in the blood samples were determined following the procedures of [16], with a slight modification. Each participant’s blood sample was homogenized, after which 1 ml was digested with 4 ml of 69% nitric acid and 2 ml of 35% H₂O₂ at 200°C for 10 minutes. The digest was allowed to cool to below 40°C, after which it was transferred into a 50-ml volumetric flask and the content made up to the meniscus with distilled water. Then, a UNICAM atomic absorption spectrometer (model 969) was used to measure the levels of silicon (Si), lead (Pb), copper (Cu), aluminum (Al), chromium (Cr), calcium (Ca), and iron (Fe) in the solution.

**Hematological examination**

The blood parameters of the participant, namely packed cell volume (PCV), hemoglobin (HB), white blood cells (WBC), and red blood cells (RBC), were determined using the Sysmex XP-300™ Automated Hematology Analyzer.

**Assessment of biomarkers of organ damage**

GLDH was measured using commercially available kits purchased from Randox Labs Ltd., Roche. Albumin was estimated using the VET 360 Veterinary Refractometer (Phoenix series). The urine level of kidney injury molecule-1 (KIM-1) was evaluated using a sandwich immunosassay technique (SunRed Biotechnology Company, Shanghai, China), as outlined by the manufacturers.

**Evaluation of biomarkers of oxidative stress, DNA damage, and carcinogenicity**

The levels of 8-OHdG were measured with the 8-OHdG check ELISA kit (StressXpress ELA Kit, StressMarq Biosciences Inc.) following the procedures of the manufacturers. Similarly, carcinoembryonic antigen (CEA) was measured using an ELISA kit by the same manufacturer mentioned above.

The total antioxidant capacity (TAP) of the blood was measured following the procedures of [17]. MDA was estimated as outlined by [18].

**Quality assurance and control**

The reagents used for the analyses were formulated from chemicals of high purity. Glass and plastic wares were cleaned with a detergent solution and rinsed with distilled water. The items were sterilized with 10% concentrated HNO₃ before being rinsed with distilled water.
The accuracy of the heavy metal analyses was ensured by checking for the background contamination of the samples, in which blank samples were analyzed after every five analyses. Furthermore, each sample was analyzed three times, and values were accepted if the reproducibility was 95%.

**Data analysis**

The values were presented as mean ± standard deviation (SD). The student’s t-test was used to test the level of significance between the molders and control group, in which \( p \leq 0.05 \) was considered statistically significant.

**Results**

**Demographic characteristics of the participants**

Table 1 shows the demographic characteristics of block factory workers and the control group, which comprises people who did not work in block factories. There was no significant difference (\( p \geq 0.05 \)) between the workers and the control group with regards to age, weight, height, and body mass index (BMI). However, while the skin texture of the control group was apparently normal, the workers showed varied skin textures between normal and dry. Toxic metals in cement and sand used in block molding could be the cause of the skin problem. When cement is mixed with water, the calcium oxide in it is converted to calcium hydroxide, which raises the pH of cement to alkalis [19]. The average pH of human skin is 4.7 [20], so the alkaline pH of cement allows it to penetrate the skin and burn it [21]. Chemicals in wet cement may also react with sweat and water molecules in the skin and release free radicals that dissolve proteins and collagen fibers, break down fats, and dehydrate cells [19]. Moreover, hexavalent chromium (present in cement) can cause allergic reactions, resulting in skin conditions ranging from mild rashes to severe skin ulcers. Exposure to silica (present in cement and sand) can also cause a skin condition known as scleroderma [22]. The longer wet cement stays on the skin, the more it reacts with water molecules and the worse the burn becomes [19]. This explains the varied skin conditions of the workers in the current study. The varied skin conditions of the workers could have also been influenced by the level of compliance with the use of protective wear. In the study by [23], skin conditions were common among workers who had worked for more than a year, those who worked longer hours, and those who failed to use personal protective equipment. The results of the current study are consistent with all the retrieved documented studies on the same subject. Notably [23], reported severe skin conditions among construction workers in India [24], also noticed skin problems among construction workers in Tanzania [25], reported skin burns among construction workers exposed to wet cement in Port Harcourt, Nigeria. Pieces or particles of wet blocks can come into contact with the skin if the worker fails to wear protective gear. Wet blocks may also fall inside the boots or gloves of workers or be absorbed through protective clothing.

**Table 1.** Demographic characteristics of the block factory workers and control group selected in Oshodi, Lagos.

| Characteristic     | Control         | Worker          | P-value |
|-------------------|-----------------|-----------------|---------|
| Age (years)       | 44.5 ± 0.07     | 44.90 ± 0.03    | 0.001   |
| Weight (kg)       | 67.30 ± 1.98    | 66.91 ± 1.02    | 0.777   |
| Height (m)        | 1.59 ± 0.01     | 1.60 ± 0.02     | 0.317   |
| BMI (kg/m²)       | 24.47 ± 2.01    | 23.71 ± 0.03    | 0.547   |
| Skin texture      | Normal          | Varied between normal and dry |

Values without an asterisk (*) are not significantly different from control at \( p \geq 0.05 \) (Student’s t-test)

**Levels of toxic metals in the blood plasma of the participants**

The levels of Ca, Si, Al, Cr, Pb, Fe, and Cu in the blood plasma of the participants are shown in Table 2. With the exception of Pb, the levels of the metals in the blood
plasma of the workers were above the permissible limits of the Occupational Safety and Health Administration (OSHA). This shows that the workers may experience metal toxicities. Excessive Ca exposure can cause coronary artery disease, migraines, and renal colic [26]. High body concentrations of Si can cause hypersilicaemia, characterized by fatigue, bone pain, headaches, loss of appetite, forgetfulness, lethargy, depression, memory loss, or irritability [27]. Overexposure to Al can cause neuropsychological decline and Alzheimer’s disease [28]. Hexavalent Cr is an established carcinogen, and current studies indicate that Cr (III) complexes can accumulate around the cell membrane, rupturing it and thus causing DNA damage [13]. Excess Fe can cause multi-organ damage [29]. Cu toxicity is associated with liver diseases, including Wilson’s disease and cirrhosis [30]. The results of the current study are in line with previous studies retrieved from academic databases. In particular [31], reported high levels of selected heavy metals in the tissues of some rats exposed to cement dust [32], noticed high levels of heavy metals in the serum of cement loaders in Benin City, Nigeria [33], also reported a significant increase in the levels of heavy metals in the blood plasma of some rats exposed to cement dust.

### Hematological parameters of the participants

Table 3 reveals the levels of the hematological parameters of the participants. Compared with the control, the levels of the PCV, Hb, and RBC of the workers were significantly (p ≥ 0.05) reduced and lower than the permissible limits of the Mayo Foundation for Medical Education and Research (MFMER). On the other hand, the WBC of the workers significantly increased compared with the control and was greater than the limits set by MFMER. The decreased PCV, Hb, and RBC show that the workers were anemic and that cytotoxic interactions occurred between the blood parameters and toxic metals in the blood. Cr (VI) may enter erythrocytes and lymphocytes and induce microcytic anemia [35]. Excessive blood Cu causes lipid peroxidation, which ruptures red blood cells, resulting in hemolytic anemia and even death [36]. Al overload inhibits heme synthesis, resulting in microcytic anemia, characterized by a decrease in Hb and RBC [37]. Regarding the increased WBC, it is an indication of leukocytosis and a sign of immune response to foreign bodies, including toxic metals. The results of the current study are consistent with all available previous studies. Notably [38], observed blood disorders in some rats exposed to cement dust [39], reported hematological disorders among cement loaders in Enugu, Nigeria. Moreover [33], observed...

#### Table 2. Mean levels of heavy metals in the blood plasma of block factory workers and control group selected in Oshodi, Lagos.

| Element [mg/kg] | Control | Worker | P-value [34] |
|----------------|---------|--------|-------------|
| Ca 8.50 ± 0.95 | 60.23 ± 2.72 | 0.00* | 8–10 |
| Si 0.09 ± 0.01 | 1.53 ± 0.49 | 0.007* | 0.1 |
| Al 3.0 ± 0.50 | 8.50 ± 0.02 | 0.00* | 5.0 |
| Cr 0.04 ± 0.02 | 1.21 ± 0.03 | 0.00* | 0.5 |
| Pb 0.05 ± 0.02 | 0.05 ± 0.02 | 0.830 | 0.05 |
| Fe 0.12 ± 0.01 | 0.27 ± 0.02 | 0.003* | 0.1 |
| Cu 0.09 ± 0.01 | 0.15 ± 0.02 | 0.006* | 0.1 |

OSHA stands for Occupational Safety and Health Administration; Values with an asterisk (*) are significantly different from control at p ≤ 0.05 (Student’s t-test)

#### Table 3. Mean levels of the hematological parameters of the block factory workers and control group selected in Oshodi, Lagos.

| Parameter       | Control | Worker | P-value | Normal range [41] |
|-----------------|---------|--------|---------|-------------------|
| PCV (L/L)       | 0.37 ± 0.04 | 0.28 ± 0.02 | 0.027* | 0.36–0.48 |
| Hb (g/dL)       | 12.11 ± 0.95 | 9.11 ± 0.02 | 0.005* | 11.5–15.5 |
| RBC (mc/ mm³)   | 4.89 ± 0.25 | 3.59 ± 0.03 | 0.001* | 4.35–5.653 |
| WBC (c/ mm³)    | 5634 ± 4.00 | 7503 ± 3.00 | 0.00* | 3400–9600 |

MFMER is short for Mayo Foundation for Medical Education and Research; Values with an asterisk (*) are significantly different from control at p ≤ 0.05 (Student’s t-test)
hematological anomalies in some rats exposed to cement dust [40], reported an increase in WBC and a decrease in RBC of cement factory workers in Obajana, Kogi State.

**Levels of biomarkers of organ damage in the blood plasma of the participants**

The levels of selected biomarkers of organ damage (albumin, GLDH, and KIM-1) in the blood plasma of the participants are presented in Table 4. The biomarkers were significantly (p ≤ 0.05) higher compared with control and were above the normal range, except for albumin. Albumin is an antioxidant and an important plasma protein manufactured solely by the liver. When the liver is injured, albumin is oxidized, affecting its molecular conformation and structure and resulting in decreased serum levels of the protein [42]. So, a drop in serum albumin is a sign of liver or kidney disease. GLDH is a liver-specific enzyme, but it is released into the blood serum upon liver injury, so an increase in serum GLDH is indicative of liver injury [43]. KIM-1 is a glycoprotein produced in the kidney and parts of its cellular components are released into urine following kidney injury, so its increased levels in urine are suggestive of kidney damage [44]. Liver and kidney injuries are often caused by infections and toxic metals like those detected in the blood samples of the workers in the current study. Heavy metals cause these injuries by following nearly the same pathway, which involves the generation of free radicals, impairing the antioxidant defense and enzyme activities, and oxidative stress [45]. The results of the current study are consistent with those of [46], who reported elevated levels of ALT and AST (a liver enzyme like GLDH) in people occupationally exposed to cement dust in Cross River, Nigeria. Similarly, in a study by [47], the serum ALT, AST, and ALP levels were significantly higher, while creatinine levels [a kidney biomarker like KIM-1] were significantly lower in construction workers compared with those in the control group. However, the results of the current study contradict those of [48], who observed an increase in the level of serum albumin among cement factory workers in Ogun State, Nigeria. There is a dearth of documented studies to sufficiently compare with the current study.

**Levels of biomarkers of DNA damage and carcinogenicity in the blood plasma of the participants**

Table 5 shows the levels of selected biomarkers of DNA damage and carcinogenicity in the blood plasma of the participants. Compared with control, the levels of 8.0HDGI, CEA, and MDA of the workers were significantly (p ≤ 0.05) increased beyond the normal ranges, while TAC was significantly reduced. 8.0HDGI is a component of DNA that seeps into the blood and urine after oxidative stress-induced DNA damage and repair. DNA is constantly being repaired and its oxidized product (8.0HDGI) is released into the blood and urine, so an increased level of 8.0HDGI is suggestive of DNA damage [52]. Heavy metals detected in the blood plasma of the workers in the current study could be the cause of the elevated 8.0HDGI. In a study by [53], high plasma Cr levels were associated with high plasma 8-OHdG levels [54], also implicated high urinary

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**Table 4. Mean levels of biomarkers of organ damage in the blood plasma of the block factory workers and control group selected in Oshodi, Lagos.**

| Biomarker | Control | Worker | P-value | Normal range |
|-----------|---------|--------|---------|--------------|
| Albumen (g/dL) | 3.95 ± 0.04 | 2.65 ± 0.03 | 0.00* | 3.4–5.4 [49] |
| GLDH (U/L) | 3.01 ± 0.01 | 12.00 ± 0.01 | 0.00* | ≤ 7.0 [50] |
| KIM-1 (ng/ml) | 0.91 ± 0.00 | 2.30 ± 0.02 | 0.00* | <1.0 [51] |

UCSF is short for University of California San Francisco, DDSG stands for DaisyDiagnostic Systems GmbH, and All means Advanced ImmunoChemical Incorporation, Values with an asterisk (*) are significantly different from control at p ≤ 0.05 (Student’s t-test)
levels of Cr, Ni, Cd, and Pb in the elevated levels of 8-OHdG among welders occupationally exposed.

CEA is a glycoprotein that is abundant in the fetus but drastically drops after birth [55]. However, certain cancers can raise the levels of CEA again, making the protein a good biomarker of such cancers. Heavy metals present in the blood of the workers could be responsible for the increased serum CEA observed in this study. In a study by [56], a correlation was established between heavy metal exposure and increased urine and plasma CEA levels. 57, also reported a correlation between increased serum CEA and overexposure to Cd, Ni, and Pb in patients suffering from colorectal cancer.

TAC is the antioxidant capacity of the body whose levels are influenced by oxidative stress and so can be used as a biomarker of oxidative stress-induced DNA damage and carcinogenesis. In a study by [58], there was a significant reduction in TAC in women with cervical cancer compared with healthy controls. Moreover [59], reported a link between reduced plasma TAC and DNA damage. Some studies, including [60], have demonstrated that decreased serum TAC is correlated with overexposure to heavy metals.

MDA is a biomarker of lipid peroxidation, which causes cellular and DNA damage, and a high level of MDA has been detected in some cancers [61]. In a study by [62], the serum levels of TAC were reduced while MDA were increased, and both were correlated with high levels of some heavy metals [63]. also noticed a link between increased serum MDA levels and high heavy metal exposure among smelters.

The results of the current study are consistent with those of [64], who reported increased levels of MDA in people occupationally exposed to cement dust. The results are also in line with those of [65], who reported high serum DNA damage indicated by high serum 8-OHdG and MDA in people exposed to asbestos cement compared to control.

**Conclusion**

The results show that the blood samples of the workers contained non-permissible levels of Ca, Si, Al, Cr, Fe, and Cu, indicating that they may be at risk of metal toxicities. This is evident in the skin defects and hematological disorders (PCV, Hb, RBC, and WBC) observed in the workers. Disorders were also observed in the workers’ plasma levels of albumin, GLDH, KIM-1, 8.OHDGI, CEA, MDA, and TAC, which are biomarkers of organ injury, DNA damage, and carcinogenesis. Overall, the results suggest that toxic metals in cement may be predisposing block molders in Lagos to health hazards.

**Recommendations**

Based on the results, the following steps are recommended:

- Block molders should practice personal hygiene and always wear protective gadgets such as coverall clothing, alkali-resistant gloves, water-proof boots, and goggles.
- Molders should not allow wet cement to stay on the skin for a long time.

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**Table 5.** Mean levels of biomarkers of DNA damage and carcinogenicity in the blood plasma of the block factory workers and control group selected in Oshodi, Lagos.

| Biomarker | Control | Worker | P-value | Normal range |
|-----------|---------|--------|---------|--------------|
| 8.0HDGI (ng/ml) | 16.31 ± 0.01 | 21.41 ± 0.02 | 0.00* | <27.72 [66] |
| CEA (ng/ml) | 1.30 ± 0.03 | 4.62 ± 0.02 | 0.00* | 0–2.5 [67] |
| TAC (µg/ml) | 50.31 ± 0.01 | 32.00 ± 0.03 | 0.00* | >40 [68] |
| MDA (nmol/ml) | 3.15 ± 0.05 | 5.46 ± 0.06 | 0.00* | 2.0–4.6 [69] |

CTCA is short for Cancer Treatment Center of America; Values with an asterisk (*) are significantly different from control at p ≤ 0.05 (Student’s t-test)
- Molders should not work for prolonged hours at a time, so as to minimize their levels of exposure.
- Molders should not wash their hands with water from buckets used for cleaning tools.

Molders should seek periodic medical examinations, so as to detect early signs of exposure.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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