

# Influence of occupational cement exposure on inflammatory markers, hepatorenal function indices and oxidative stress markers among male cement handlers in Ilorin-Metropolis

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#### Abstract

**Introduction:** Cement dust is considered one of the most dangerous occupational hazards worldwide. Studies link cement dust exposure to respiratory disorders and cancer, but there is limited literature on its effect on inflammatory markers, hepato-renal function indices, and oxidative stress markers. This study examines how occupational exposure to cement dust affects different biochemical parameters in cement handlers in llorin Metropolis, an urban region in North-Central Nigeria.

**Methodology:** A total of one hundred and twenty (120) cement handlers and sixty (60) unexposed individuals aged 25 - 60 were recruited for the study after obtaining written consent. 10 ml of fasting blood was collected and dispensed into the appropriate sample bottle. Serum levels of creatinine, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, albumin, alkaline Phosphatase (ALP) and Malondialdehyde (MDA) were measured spectrophotometrically, using commercially prepared reagents. C-reactive protein and cystatin-C levels were determined using ELISA methods. The modified diet in renal disease (MDRD) formula was utilized to calculate the estimated glomerular filtration rate (eGFR).

**Results:** When compared with controls, the cement handlers' sera exhibited elevated levels of Creatinine, Urea, Cystatin C, MDA, AST, ALT and C-reactive protein. Conversely, levels of albumin, total protein, and eGFR were decreased in cement handlers compared to controls.

**Conclusion:** This study suggests that cement handlers are more susceptible to impaired kidney and liver function due to cement dust exposure. Although the exact mechanism remains unclear, increased oxidative damage and inflammation play significant roles in the observed physiological derangement.

**Keywords:** Cement dust, C-reactive protein, cystatin-C, inflammatory markers, hepato-renal indices and oxidative stress markers

### Introduction

Cement dust, a common occupational hazard, has been associated with numerous detrimental impacts on the organ system, with most of the existing research focused on the respiratory system (Zeleke *et al.*, 2010; Etim *et al.*, 2021). However, recent experimental studies have shown that exposure

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to cement dust may also impact other systems in the body (Ahmad *et al.,* 2021b; Owonikoko *et al.,* 2022; Ehi-Omosun & Olise, 2023a; 2023b).

Unfortunately, compliance with safety health preventive measures in a country like Nigeria is often suboptimal. Thus, there is also a general lack of awareness regarding the health implications of these exposures. Previous experimental research revealed that exposure to cement dust could lead to systemic alterations (Gizaw *et al.*, 2016; Mbelambela *et al.*, 2018; Sheinenzon *et al.*, 2021) especially in the kidney and liver, however, while some reported no significant changes. The mechanism of the noted significant changes remains unclear (Friday, 2016; Chen *et al.*, 2020; Pomacu *et al.*, 2021). Data from experimental studies has reported that cement dust can infiltrate several tissues, the lungs, liver and kidney, resulting in altered cellular structure and damage of membrane components by increased lipid peroxidation (Owonikoko *et al.*, 2022). The disruption of membrane integrity can result in the leakage of vital cellular components (Ammendolia *et al.*, 2021).

Glomerular Filtration Rate is an indication of the filtration rate in single nephrons and the number of functioning nephrons in both kidneys (Denic *et al.*, 2017; Cortinovis *et al.*, 2022); eGFR is the mathematical relationship between plasma creatinine and GFR (Porrini *et al.*, 2019).

Liver enzymes are crucial for assessing liver function, as liver injury leading to cytolysis or necrosis results in the release of these enzymes into the bloodstream (Singh *et al.*, 2011; Yu, 2021). ALT is the most specific liver enzyme; an elevation of its activity is common in hepatic diseases. ALT is found predominantly in the liver and widely distributed in organs like the heart, brain, red blood cells, and kidney. The enzyme GGT is found mainly in the bile ducts of the liver, pancreas, spleen, and small intestines.

Oxidative stress and inflammatory processes are believed to contribute to the development of many systemic disorders (Podkowińska & Formanowicz, 2020; Hertiš Petek *et al.*, 2022). The increased generation of free radicals could overwhelm the cellular antioxidant defence system. This could result in the integrity of the cellular membrane breaking down, allowing intracellular enzymes to seep into the plasma. Thus, an increase in the activity of these enzymes in the plasma suggests damage to the tissue producing them.

Inflammation is the body's natural immune response to harmful stimuli, including infectious agents, injured cells, toxic substances, and radiation exposure (Medzhitov, 2010). It is often a common underlying mechanism in chronic diseases such as cardiovascular disorders, bowel disorders, diabetes, arthritis, and cancer. It affirms the emergence and advancement of these various illnesses is significantly influenced by inflammation (Libby, 2007). A common thread runs through all inflammatory responses, regardless of the initial stimulus or location (Chen *et al.*, 2017).

Work-related health hazards are on the increase with their attendant health implications. The use of personal protective equipment among cement handlers within the metropolis is very poor. In light of these concerns, this present study explores the effects of occupational cement exposure on inflammatory markers, hepatorenal function indices, and oxidative stress markers among cement handlers.

### Subjects and methods

The study employed a population-based and cross-sectional design. The study area was the llorin Metropolis of North Central Nigeria. The survey was conducted within four months, from September 2023 to December 2023. This study recruited only subjects exposed to cement dust through their occupation for five years.

The study included only people aged 25 to 60 who provided informed consent. The selected subjects were healthy and did not have any cardiovascular disorders, respiratory disorders or history of cancer. None of the partaking individuals were on any anti-inflammatory drugs, corticosteroids, or



hypertensive drugs. Smokers and alcoholics were also excluded from this study. A detailed questionnaire was created for the study, and the above data was collected.

The study recruited 180 participants, consisting of 120 individuals with daily exposure to cement dust and 60 unexposed individuals in accordance with similar work conducted by Dushyant et al. (2023). Each participant's demographic data was gathered and the weight (kg) divided by height (m<sup>2</sup>) gives the Body Mass Index (BMI).

## Laboratory analysis

Samples of blood were obtained from the antecubital fossa of the arm with the use of a tourniquet. Fifteen millilitres of blood were drawn by venipuncture while maintaining aseptic conditions. The blood was dispensed into a plain sample container as well as a container with lithium heparin anticoagulant. The lithium heparin anticoagulant container was inverted five times. The blood samples were centrifuged at 4000 rpm for 10 minutes, and the plasma was transferred into new, clean, dry plain containers and stored at -20°C. After two weeks, the biochemical parameters were analysed.

# **Biochemical Analysis**

# Estimation of serum creatinine and urea

Creatinine and urea estimation was done using a commercially prepared kit by Agappe Diagnostic, Switzerland. Creatinine reacts with picric acid to produce a coloured compound. Urea in an acidic medium condenses to form a red-coloured complex. The intensity of the colour formed is directly proportional to the amount of creatinine and urea.

### Determination of plasma total protein

Total protein was analyzed by direct Biuret method using a diagnostic kit of Agappe Diagnostics Ltd, Switzerland.

### Determination of albumin

Albumin was determined by the Bromocresol green (BCG) colourimetric method using a reagent kit obtained from AGAPPE Diagnostic, Switzerland. The method is based on the specific binding of bromocresol green (BCG), an anionic dye, and the protein at acid pH produce a colour change. The intensity of the coloured formation is proportional to the concentration of albumin in the sample, measured at 630 nm (Doumas *et al.*, 1971).

### Estimation of C-reactive Protein and Cystacin C

C-reactive protein and Cystacin C were determined by turbidometric immunoassay technique using a commercially prepared kit by Agappe Diagnostic Ltd, Switzerland. This is a latex-enhanced turbidimetric immunoassay. CRP samples bind to specific anti-CRP antibodies, which have been adsorbed to latex particles and agglutinates. The agglutination is proportional to the quantity of CRP in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared by the calibrators of known concentrations.

# Estimation of Malondialdehyde (MDA)

Malondialdehyde (MDA) was estimated using the thiobarbituric acid reacting substance method (TBARS) using commercially prepared reagents from Fortress Diagnostics, UK, according to the method of Varshney and Kale (1990). The principle of TBARS relies on the ability of Trichloroacetic acid (TCA) to precipitate protein, and thiobarbituric acid reacts with MDA (malondialdehyde) to give a red coloured complex that is read spectrophotometrically at 532 nm.



# Determination of serum activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Serum AST and ALT were determined spectrophotometrically using a commercially prepared reagent kit by AGAPPE Diagnostic, Switzerland as described by Reitman and Frankel 1957 (Reitman & Frankel, 1957).

# Assessment of Alkaline Phosphatase (ALP) activity

The Alkaline Phosphatase (ALP) serum activity was assessed using the Agappe reagent kit, following the procedure by Schlebusch et al. (1974).

# Determination of Gamma-glutamyl transferase

Gamma-glutamyl transpeptidase was determined by the Kinetic colourimetric method according to Szasz 1969, using a kit obtained from AGAPPE Diagnostics LTD. Gamma-glutamyl transferase in the serum catalyzes the transfer of the glutamyl group from the substrate  $\gamma$ -glutamyl-3- carboxy-4-nitroanilide to glycylglycine, forming glutamyl glycylglycine and 5-amino-2-nitrobenzoate. The rate of formation of 5-amino-2-nitrobenzoate is proportional to the activity of GGT present in the sample and can be measured at 420 nm.

### Calculation of estimated gfr

Using the Modified Diet in Renal Disease (MDRD) method, the estimated Glomerular Filtration Rate was obtained using the below formula. GFR (ml per minutes per  $1.73m^2$ ) = 186 x (Serum creatinine concentration)<sup>-1.154</sup> x (age) <sup>-0.203</sup> x (0.742 if female) x (1.210)

### **Statistical analysis**

Data analysis was performed using IBM SPSS version 23 (SPSS Inc., Chicago, IL, USA). Frequency statistics were calculated to evaluate group characteristics, and the student's t-test was used to determine the significance of the means for continuous variables.

### **Ethical approval**

Permission for the research project was sought and obtained from the Kwara State Ministry of Health before its commencement, with approval number ERC/MOH/2023/04/197. The study was carried out following the ethical principles of the Declaration of Helsinki

### Results

A total of one hundred and eighty individuals were involved in the study including one hundred and twenty (120) cement handlers and sixty (60) unexposed individuals within the ages of 25-60. The study findings show that there is little variation in the average age of the cement handlers and the unexposed participants, with the average age of cement handlers (exposed) being considerably higher than those of the unexposed (control) participants (p<0.05). Table 1 shows a noticeable variation in the BMI of cement handlers and unexposed individuals (p<0.05). Table 3 illustrates the impact of occupational exposure to cement on selected inflammatory markers. The mean value of total protein and albumin levels is substantially less than that of the unexposed individuals. Conversely, C-RP levels were higher in the exposed group than in the controls. However, these variations of total



protein, albumin and C-RP levels are not statistically significant. The urea and creatinine serum levels of the exposed were higher than the controls, however, these differences were also not statistically significant. Nevertheless, e-GFR is higher in the exposed than the controls (Table 4).

#### Table 1. Study population Demographic characteristics

Age	Bivii (kg/m2)		
Exposed n=120	27.14 ± 0.33	23.75 ± 0.20	
Control n=60	26.17 ± 0.35	25.68 ± 0.35	
P value	p>0.05	p<0.05	

Values are expressed as mean ± standard error of the mean, BMI- Body Mass Index

Crea	itinine	Urea	e-GFR Cysta	itin-C
Exposed n=120	91.18 ± 1.42	5.16 ± 0.07	103.06 ± 1.61	0.92 ± 0.03
Control n=60	75.83 ± 1.81	4.97 ± 0.09	118.83 ± 1.77	0.68 ± 0.03
P value	p<0.001	p>0.05	p<0.001 p<0.001	

#### Table 2. Influence of Cement dust Exposure on Renal Function Indices

Values are expressed as mean ± standard error of the mean, e-GFR - Estimated glomerular filtration rate

Total Protein	Albumin	C-RP	
Exposed n=120	61.48 ± 0.53	32.29 ± 0.37	4.58 ± 0.99
Control n=60	71.17 ± 0.77	38.07 ± 0.57	2.83 ± 0.12
P value	p<0.001	p<0.001 p<0.001	

Table 3. Effect of Occupational exposure to cement on selected inflammatory markers.

Values are expressed as mean ± standard error of the mean, CRP- Creactive protein



parameters					
MDA		AST ALT	ALP	GGT	
Exposed n=120	1.88 ± 0.05	26.28 ± 0.6	9 28.70 ± 0.	71 65.11 ± 1.14	24.68 ± 0.60
Control n=60	1.14 ± 0.05	22.85 ± 1.12	15.48 ± 0.69	71.15 ± 1.66	21.48 ± 0.96
P value	p<0.001	p<0.05	p<0.001	p<0.05 p<0	0.05

Table 4. Effect of occupational exposure to cement dust on oxidative stress markers and Liver function parameters

Values are expressed as mean ± standard error of the mean, MDA- Malondialdehyde, AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, ALP-Alkaline Phosphatase

#### Discussions

Cement dust contains many mixed chemicals that could hurt the body's physiological processes (Ahmad et al., 2021a; 2021b). In this study, creatinine was elevated with reduced cystatin C and estimated glomerular filtration rate in participants exposed to cement dust in comparison to the control group. This implies that renal function may be adversely affected by contact with cement dust. The physiological destruction of muscle cells during physical activity, such as exercise, produces creatinine, a waste product that accumulates in the blood when the kidneys are not functioning correctly (Friday *et al.*, 2017).

An increase in creatinine and urea levels indicates that the kidneys may not be functioning optimally, which may be a result of toxic exposure to cement chemicals.

The reduced eGFR and increased level of creatinine further strengthen the fact that cement exposure may impair renal function. All nucleated cells make and release cystatin C, an inhibitor of cysteine protease, at a consistent rate. Due to its low molecular weight, it is also readily filtered by the glomerulus. Because it is not greatly affected by race or muscle mass, some researchers have hypothesized that it may be a more reliable predictor of glomerular filtration rate than serum creatinine (Thomas *et al.*, 2011). Cystatin C is an alternative blood marker that rises as the glomerular filtration rate (GFR) declines. This further reinforces the idea that cement exposure negatively affects renal function. The elevated cystatin C with a reduced glomerular filtration rate suggests a decline in the number of functioning nephrons even though it has not been clinically obvious.

Results from this study indicate an increase in plasma levels of AST, GGT, and ALT in cement handlers. This is consistent with (1.19) and in contrast with results from studies which indicate that there is an increase in ALT activity in non-cement handlers while the AST and ALP activities of both groups were similar (Festus *et al.*, 2021). As reported in this study, ALT increased significantly while AST and GGT also increased in the cement handlers, however, not significantly. Thus, ALT being more specific to the liver indicates that cement handlers are more predisposed to hepatic diseases

This study suggests that the toxic substances like silica and aluminium in cement dust cause the peroxidation of the hepatocyte membrane as indicated by the increase in the MDA levels, an oxidative stress marker which in turn results in inflammation of the liver leading to the overproduction of CRP, an inflammatory marker resulting into liver injury causing the leakage of liver enzymes like ALT, AST and GGT into the plasma.

The data generated from this study indicates that there is an increase in the level of C-Reactive protein in cement handlers and there is a decrease in total protein and albumin. Albumin, the primary protein in plasma, helps regulate the distribution of body fluids and is synthesized in the liver. On the



other hand, hepatocytes generate C-reactive protein (CRP), which is frequently used to measure inflammation. It has been observed that during inflammatory conditions, the acute-phase concentration of proteins like CRP increases, while albumin levels tend to decrease (Sheinenzon *et al.*, 2021). This simply explains that inflammation enhances the production of CRP by the hepatocyte, conversely reducing the synthesis of Albumin as a result of the production of free radicals (Adunmo *et al.*, 2024). Albumin being the most abundant serum protein (constituting around 60% of total plasma protein will affect the levels of serum total protein (Barnett *et al.*, 2013).

Based on this study, there is a noticeable variation in inflammatory markers among cement handlers compared to the control group. While the differences are not statistically significant, they may have potential implications for health in the long term. Cement dust contains toxic substances which are reported to be pro-inflammatory and can promote inflammation in vital organs (Ahmad *et al.*, 2021b).

An increase in oxidative stress markers like MDA is caused by extended contact with aluminium, which is present in cement dust (Ahmad *et al.*, 2021a; 2021b). Prolonged exposure to cement dust results in an elevation in free radicals' generation, which in turn causes overproduction of MDA in cancerous patients (Ahmad *et al.*, 2021b). This is in agreement with this study, which shows an elevation in MDA levels in the exposed individuals compared to the controls, however, this increase was not significant enough to cause cancer.

#### Conclusion

This study indicates elevated levels of Creatinine, Urea, Cystatin C, MDA, AST, ALT, GGT and C-reactive protein. Conversely, levels of Albumin, Total protein and eGFR were decreased in cement handlers compared to unexposed individuals. In conclusion, this study suggests that cement dust handlers are prone to impaired kidney and liver functions. The mechanism shows that an increased inflammatory and oxidative marker may be the reason behind the observed pathology.

#### Limitations

The limitations of this study were the inability to properly quantify the level of exposure of each cement handler to the cement dust, the strategy for sampling which is prone to bias in selection and other compounding factors like smoking, alcohol consumption, preexisting health conditions and dietary habits.

#### Recommendations

Laws that require employers to educate their workers on the negative effects of direct exposure to cement dust and the provision of Personal Protective Equipment (PPE) should be put in place.

### Author contributions

AGO: Conceptualization, Project administration and supervision, writing original draft, Methodology, Visualization and Validation, ATD: Writing-Review and Editing, Methodology and Validation, OMG: Writing-Review and Editing, Methodology, Validation, AGT: Writing-Review and Editing, Methodology, data acquisition and data analysis, AEO: Writing-Review, Methodology and data analysis, OT: Writing-Review, Methodology and data analysis. All authors have read and agreed to the final version of the manuscript

#### **Conflict of interest**

None declared.



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