

ORIGINAL ARTICLE

Obaji-Ogar L.T. et al... Plasma Cadmium Concentrations among Women with Breast Cancer in Abuja, Nigeria: A Case–Control Study

**PLASMA CADMIUM CONCENTRATIONS AMONG WOMEN WITH BREAST
CANCER IN ABUJA, NIGERIA: A CASE–CONTROL STUDY**

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Citation: Obaji-Ogar LT, Nsonwu-Anyanwu AC. Plasma Cadmium Concentrations among Women with Breast Cancer in Abuja, Nigeria: A Case–Control Study. *Niger J Oncol* 2026; 2(2):69- 77

ABSTRACT

Background: Breast cancer remains the most frequently diagnosed cancer among women worldwide and a leading cause of cancer-related mortality. Environmental exposure to cadmium, a recognized human carcinogen, has been implicated in breast carcinogenesis through multiple biological mechanisms, but data from sub-Saharan Africa remain limited.

Objective: To compare plasma cadmium concentrations between women with breast cancer and age-matched apparently healthy controls attending a tertiary hospital in Abuja, Nigeria.

Methods: This hospital-based case–control study included 70 treatment-naïve women with histologically confirmed breast cancer and 70 age-matched apparently healthy controls recruited from the National Hospital Abuja between 2022 and 2024. Plasma cadmium concentrations were measured using atomic absorption spectrophotometry at an analytical wavelength of 228.8 nm. Values below the analytical limit of detection (0.009 µg/mL) were considered non-detectable and assigned a value of zero for statistical analysis. Continuous variables were summarized as medians and interquartile ranges (IQRs), and group comparisons were performed using the Mann–Whitney U test. Statistical significance was set at $p < 0.05$.

Results: Plasma cadmium concentrations were significantly higher among women with breast cancer than among apparently healthy controls (median [IQR]: 0.91 [0.61–1.06] µg/mL vs. 0.00 [0.00–0.00] µg/mL; $p < 0.001$). Cadmium was detectable in most women with breast cancer, whereas concentrations among the control participants were below the analytical limit of detection.

Conclusion: Treatment-naïve women with breast cancer in Abuja, Nigeria, had significantly higher plasma cadmium concentrations than age-matched apparently healthy controls. These findings support a possible association between environmental cadmium exposure and breast cancer and contribute to the limited evidence on environmental risk factors for breast cancer in sub-Saharan Africa. Larger multicentre prospective studies incorporating detailed environmental exposure assessment are warranted to further clarify this relationship.

Keywords: Breast cancer; cadmium; environmental exposure; atomic absorption spectrophotometry; case–control study; Nigeria.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women worldwide and remains a leading cause of cancer-related mortality. In 2020, an estimated 2.3 million new cases and approximately 685,000 deaths were reported globally, highlighting the substantial public health burden of the disease.^{1,2} In Nigeria, the incidence of breast cancer has risen steadily over recent decades, with many women presenting at advanced stages, contributing to poor treatment outcomes and high mortality.^{3,4}

Although established risk factors such as age, reproductive history, hormonal influences, and inherited genetic susceptibility contribute to breast cancer development, growing evidence suggests that environmental exposures also play an important role in breast carcinogenesis.⁵⁻⁷ Among these, cadmium has received considerable attention because of its widespread distribution in the environment and its potential carcinogenic properties.

Cadmium is a ubiquitous environmental pollutant released through industrial activities, mining, improper waste disposal, contaminated food and water, and tobacco smoke. Owing to its long biological half-life, cadmium accumulates in human tissues over time and has been classified as a Group 1 human carcinogen by the International Agency for Research on Cancer.⁸ Experimental and epidemiological studies suggest that cadmium may promote breast carcinogenesis through several mechanisms, including estrogen receptor activation, oxidative stress, DNA damage, impaired DNA repair, epigenetic

alterations, and disruption of tumor suppressor pathways.⁹⁻¹¹

Several epidemiological studies, systematic reviews, and meta-analyses have reported positive associations between cadmium exposure and breast cancer risk, although the magnitude of this association varies across populations.¹²⁻¹⁶ Recent reviews have further strengthened the evidence supporting cadmium as a potential environmental risk factor for breast cancer while emphasizing the need for additional studies in underrepresented populations.¹⁷⁻²⁰

Despite the growing body of international evidence, studies investigating cadmium exposure in relation to breast cancer remain scarce in sub-Saharan Africa. Environmental exposure patterns in Nigeria may differ substantially from those in high-income countries because of variations in industrialization, environmental regulation, waste management practices, dietary habits, and occupational exposures.^{21,22} Consequently, locally generated evidence is essential for understanding the contribution of environmental toxicants to breast cancer risk in Nigerian women.

Therefore, this study compared plasma cadmium concentrations between treatment-naïve women with histologically confirmed breast cancer and age-matched apparently healthy controls attending the National Hospital, Abuja, Nigeria.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based, age-matched case–control study was conducted at the National Hospital Abuja, a tertiary referral center in North-Central Nigeria, between January 2022 and December 2024. The study compared plasma cadmium concentrations between women with histologically confirmed breast cancer and apparently healthy women without a history of breast cancer.

Study Participants

A total of 140 women participated in the study, comprising 70 women with histologically confirmed breast cancer (cases) and 70 age-matched apparently healthy women (controls). Cases were recruited consecutively from the Surgical Oncology and General Surgery Clinics of the National Hospital, Abuja, during the study period.

Controls were recruited from the hospital community and outpatient clinics. They had no previous diagnosis or clinical evidence of breast cancer and were frequency matched to cases by age to minimize confounding.

Sample Size

The minimum sample size was calculated using the formula for unmatched case–control studies described by Kothari.²³ Assuming a two-sided significance level of 5% ($Z\alpha/2 = 1.96$), 80% statistical power ($Z1-\beta = 0.84$), an anticipated odds ratio of 2.0, and an estimated population proportion of 0.78%, the minimum required sample size was 64 participants per group. To allow for an anticipated 10% non-response rate, the sample size was increased to 70 participants per group. Consequently, 70 women with histologically confirmed breast cancer and 70 age-matched apparently healthy women were enrolled.

Inclusion Criteria

Cases

Women were eligible for inclusion if they:

- had histologically confirmed breast cancer;
- were newly diagnosed and treatment-naïve;
- were aged ≥ 18 years;
- provided written informed consent.

Controls

Women were eligible as controls if they:

- had no previous history of breast cancer or any other malignancy;
- were apparently healthy at recruitment;
- were within the same age distribution as the cases;
- provided written informed consent.

Exclusion Criteria

Women were excluded if they:

- were pregnant or lactating;
- had received chemotherapy, radiotherapy, endocrine therapy, or breast cancer surgery before blood sample collection;
- had chronic systemic illnesses known to influence trace-element metabolism;
- were current smokers or had significant alcohol dependence;
- declined participation.

Data Collection

Data were collected using a structured interviewer-administered questionnaire. Information obtained included socio-demographic characteristics, reproductive history, family history of breast cancer, selected lifestyle factors (including alcohol consumption and dietary habits), and clinical symptoms.

Anthropometric measurements, including height, weight, body mass index (BMI), waist circumference, and blood pressure, were obtained using standardized procedures. Hormone receptor status (estrogen receptor, progesterone receptor), HER2 receptor status and other relevant clinical information were extracted from participants' medical records where available.

Blood Sample Collection

Following an overnight fast, approximately 5 mL of venous blood was collected aseptically from each participant into trace element-free lithium-heparin tubes.

All women with breast cancer were treatment-naïve at recruitment, and blood samples were obtained before the initiation of surgery, chemotherapy, radiotherapy, or endocrine therapy to minimize the potential influence of treatment on plasma cadmium concentrations.

Samples were centrifuged at 3,000 rpm for 10 minutes. Plasma was separated into trace element-free cryovials and stored at -80°C until analysis.

Determination of Plasma Cadmium Concentrations

Plasma cadmium concentrations were determined using atomic absorption spectrophotometry (AAS) with a GBC Scientific Equipment Explore AA spectrophotometer (GBC Scientific Equipment Pty Ltd., Melbourne, Australia). Cadmium was analysed at an analytical wavelength of 228.8 nm in accordance with the manufacturer's operating procedures.

Calibration was performed using certified cadmium standard solutions, and internal quality-control samples were analysed with each analytical batch to ensure analytical accuracy and instrument precision.

The analytical limit of detection (LOD) for cadmium was $0.009\text{ }\mu\text{g/mL}$. Instrument-generated negative values, representing analytical signals below the detection limit following background correction, were regarded as non-detectable concentrations and assigned a value of zero for statistical analysis.

Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Committee of the National Hospital Abuja (Approval No. NHA/EC/066/2021). Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test. As plasma cadmium concentrations were not normally distributed, continuous variables are presented as medians and interquartile ranges (IQRs). Comparisons between breast cancer cases and age-matched controls were performed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. All statistical tests were two-

tailed, and $p < 0.05$ was considered statistically significant.

Missing data were assessed before analysis. Complete-case analysis was performed because no missing laboratory measurements were identified.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.²⁴

RESULTS

A total of 140 women participated in this study, comprising 70 women with histologically confirmed breast cancer (cases) and 70 age-matched apparently healthy women (controls).

Plasma cadmium concentrations were significantly higher among women with breast cancer than among apparently healthy controls (median [IQR]: 0.91 [0.61–1.06] $\mu\text{g/mL}$ vs 0.00 [0.00–0.00] $\mu\text{g/mL}$; $p < 0.001$) (Table 1; Figure 1).

Cadmium was detectable in the majority of women with breast cancer, whereas concentrations among apparently healthy controls were below the analytical limit of detection. This finding demonstrates a marked difference in plasma cadmium concentrations between women with breast cancer and apparently healthy controls.

Table 1: Plasma Cadmium Concentrations among Women with Breast Cancer and Apparently Healthy Controls

Group	n	Plasma cadmium ($\mu\text{g/mL}$), Median (IQR)
Breast cancer	70	0.91 (0.61–1.06)
Apparently healthy controls	70	0.00 (0.00–0.00)
<i>p</i> -value		<0.001

Values below the analytical limit of detection (0.009 $\mu\text{g/mL}$) were considered non-detectable concentrations and assigned a value of zero for statistical analysis. Cadmium was detectable in most women with breast cancer, whereas concentrations among apparently healthy controls were below the analytical limit of detection.

DISCUSSION

This hospital-based case-control study demonstrated significantly higher plasma cadmium concentrations among treatment-naïve women with histologically confirmed breast cancer than among age-matched apparently healthy controls in Abuja, Nigeria. The findings support the growing body of evidence that environmental cadmium exposure may be associated with breast cancer development and add to the limited body of literature from sub-Saharan Africa examining this relationship.⁸⁻¹⁶

Cadmium has been implicated in breast carcinogenesis through several biological mechanisms. Experimental studies have

shown that cadmium can function as a metalloestrogen by activating estrogen receptor- α signaling, thereby promoting the proliferation of hormone-responsive breast epithelial cells.⁹ In addition, cadmium induces oxidative stress, DNA damage, epigenetic alterations, mitochondrial dysfunction, and

impaired DNA repair, all of which may contribute to malignant transformation.^{10,11} These mechanisms provide biological plausibility for the elevated plasma cadmium concentrations observed among women with breast cancer in the present study.

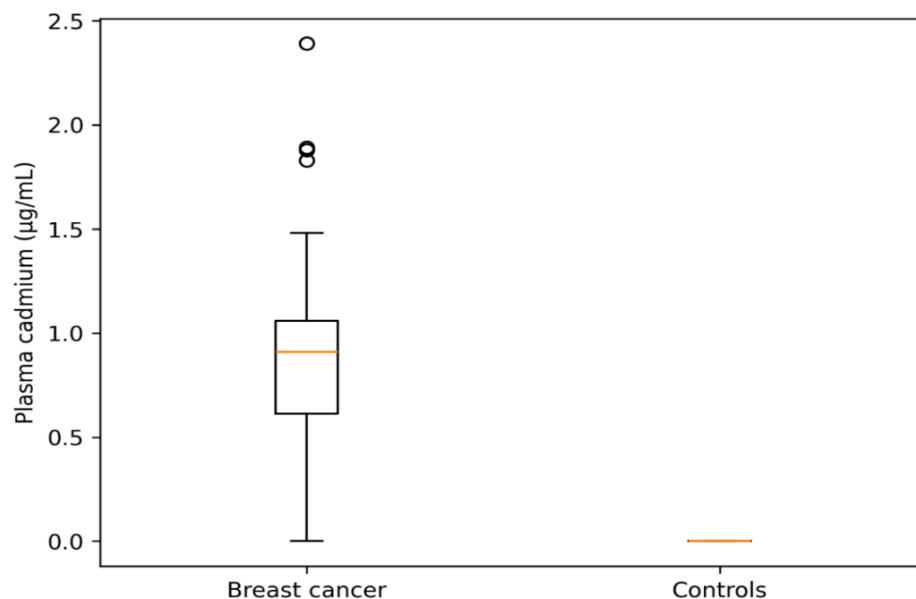


Figure 1: Plasma Cadmium Concentrations among Women with Breast Cancer and Apparently Healthy Controls. Box-and-whisker plot showing plasma cadmium concentrations among women with breast cancer ($n = 70$) and age-matched apparently healthy controls ($n = 70$). The central line represents the median, the boxes represent the interquartile range (IQR), and the whiskers extend to $1.5 \times$ IQR. Plasma cadmium concentrations were significantly higher among women with breast cancer than among apparently healthy controls ($p < 0.001$). Values below the analytical limit of detection ($0.009 \mu\text{g/mL}$) were regarded as non-detectable concentrations and assigned a value of zero for statistical analysis.

Our findings are consistent with previous epidemiological investigations reporting positive associations between cadmium exposure and breast cancer risk. Case–control studies conducted in Europe demonstrated

significantly higher cadmium concentrations among women with breast cancer than among healthy controls.^{12,13} Similarly, systematic reviews and meta-analyses have concluded that higher cadmium exposure is associated with an increased risk of breast cancer,

although variations exist across study populations, exposure assessment methods, and biological specimens analysed.^{14–16} Cadmium-induced oxidative stress and interaction with metallothionein may contribute to its biological accumulation and carcinogenic potential.^{11,25} More recent systematic reviews and comprehensive reviews continue to support cadmium as an important environmental toxicant with potential relevance to breast carcinogenesis while emphasizing the need for high-quality studies from low- and middle-income countries.^{17–20} The complete absence of detectable plasma cadmium concentrations among the control group should be interpreted in the context of the analytical characteristics of atomic absorption spectrophotometry. Instrument-generated signals below the analytical limit of detection are expected to fluctuate around zero because of background correction and analytical noise and do not represent true negative concentrations. In accordance with accepted analytical practice, all values below the analytical limit of detection (0.009 µg/mL) were regarded as non-detectable concentrations and assigned a value of zero for statistical analysis. This approach provides a conservative estimate of cadmium exposure and minimizes the influence of analytical noise on statistical comparisons.

Environmental cadmium exposure in Nigeria may arise from multiple sources, including contaminated food, drinking water, improper waste disposal, industrial emissions, and other environmental pollutants.^{21,22} Although the present study did not quantify individual environmental exposure sources, the observed differences between cases and controls underscore the importance of further

investigations into environmental contributors to breast cancer in Nigeria.

Strengths and Limitations

A major strength of this study is the inclusion of treatment-naïve women with histologically confirmed breast cancer, thereby minimizing the potential influence of surgery, chemotherapy, radiotherapy, or endocrine therapy on plasma cadmium concentrations. The age-matched case-control design reduced confounding by age, while the use of standardized atomic absorption spectrophotometry with internal quality-control procedures enhanced analytical reliability.

Several limitations should also be acknowledged. First, the case-control design precludes causal inference between cadmium exposure and breast cancer. Second, plasma cadmium primarily reflects recent exposure and may not fully represent cumulative body burden compared with biomarkers such as urinary cadmium. Third, environmental exposure sources were not directly quantified, preventing assessment of specific exposure pathways. Finally, although values below the analytical limit of detection were appropriately treated as non-detectable, assigning these values to zero may have reduced variability among participants with very low cadmium concentrations.

Overall, the present findings provide additional evidence supporting a possible association between environmental cadmium exposure and breast cancer among Nigerian women and highlight the need for larger multicenter prospective studies incorporating

detailed environmental exposure assessment together with complementary biomarkers of long-term cadmium accumulation.

CONCLUSION

This hospital-based case-control study demonstrated significantly higher plasma cadmium concentrations among treatment-naïve Nigerian women with histologically confirmed breast cancer than among age-matched apparently healthy controls. The findings support a possible association between environmental cadmium exposure and breast cancer in this population and add to the limited body of evidence from sub-Saharan Africa.

Although the observational design precludes causal inference, the results highlight the need for larger multicenter prospective studies incorporating detailed environmental exposure assessment, molecular biomarkers, and genetic susceptibility to better elucidate the role of cadmium in breast carcinogenesis. Strengthening environmental health surveillance and reducing exposure to potentially carcinogenic heavy metals may contribute to future breast cancer prevention strategies in Nigeria and other low- and middle-income countries.

Declarations

Conflict of Interest

The authors declare that they have no competing interests.

Funding

This research received no external funding.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgements

The authors thank the staff and participants of the National Hospital, Abuja, who contributed to this study.

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